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Trochleadysplasi hos barn – en klinisk studie av ultralydundersøkelse av patellofemoralleddet fra nyfødt til 6 års alder.

Symptomer fra kneskåla er relativt vanlig hos barn og ungdom. Plagene kan variere fra fremre knesmerter til en ustabil kneskål som glir ut av ledd, den vanligste akutte kneskaden hos denne aldersgruppen. Tilstanden er smertefull og medfører betydelig risiko for skade av leddbrusken. Når kneskåla glir ut av ledd for første gang kan denne hendelsen representere starten på et langvarig forløp med smerter og gjentatte utglidninger av kneskåla. Gjentatte utglidninger vil skje hos opptil 50%. Vedvarende smerter, svikttendens i kneet og følelse av en ustabil kneskål medfører nedsatt knefunksjon på sikt hos 30% - 50% av alle de som for første gang opplever en utglidning av kneskåla.

Det er mange faktorer som disponerer til en ustabil kneskål. Kneskåla skal vanligvis spore mot en leddflate som har en langsgående fordypning som skal sikre kneskåla mot utglidninger. Den viktigste enkeltårsaken til en ustabil kneskål er en liten og grunn leddflate mellom kneskåla og lårbeinsknoken, en tilstand som betegnes trochleadysplasi. Hos mange med gjentatte utglidninger av kneskåla vil operative prosedyrer for å bedre stabiliteten være indisert, hos enkelte vil en korreksjon av dysplasien være en løsning, gjerne kombinert med andre prosedyrer. Dette medfører relativt store, åpne kneoperasjoner med risiko for komplikasjoner.

Den tilgrunnleggende årsaken og forekomsten til trochleadysplasi er ukjent. Denne formen for dysplasi har tidligere aldri vært påvist ved fødselen. Vi ønsket å se nærmere på hvorvidt trochleadysplasi er en medfødt tilstand eller om det kan være et resultat av gradvis utvikling gjennom veksten. For å kunne gjøre en slik studie var det først nødvendig å undersøke en gruppe av nyfødte barn for å kartlegge normalanatomien til leddflata mellom lårbeinsknoken og kneskåla, da denne tidligere ikke var tilstrekkelig kjent. Ultralyd er en etisk akseptabel undersøkelsesmetode til bruk på barn, den medfører ingen kjent risiko, ubehag eller behov for medisinering. Det var imidlertid nødvendig å evaluere ultralyd som metode til bruk for kartlegging av kneskålleddet hos nyfødte, da ultralyd til dette formålet ikke tidligere har vært evaluert.

Metodeevalueringen ble utført som en separat studie hvor begge knær hos 40 nyfødte ble undersøkt med ultralyd. Måleresultatene til to forskjellige undersøkere ble sammenliknet, både med hensyn til nøyaktigheten for gjentatte målinger for den enkelte undersøker og de to undersøkere imellom. Det var godt samsvar for måleresultatene fra denne testen og måleverdiene var sammenlignbare med de registrert hos eldre barn. Ultralyd kunne dermed aksepteres som metode til bruk i hovedstudien.

I alt 348 knær ble undersøkt med ultralyd innen 3 dager etter fødselen. Flere forskjellige målinger ble utført og vurdert opp mot hverandre for å se hvilken som var best egnet til å beskrive anatomien. Vitale fødselsparametere som kjønn, gestasjonsalder, lengde og vekt ble registrert samtidig med demografiske data som fosterleie, hoftestatus med hensyn til dysplasi og familiær forekomst av smerter eller instabilitet av kneskåla.

Det ble gjort ultralydmålinger blant de nyfødte som var sammenliknbare med funn hos voksne med trochleadysplasi. Samtidig ble det påvist en sammenheng mellom det å ha en dysplastisk utseende trochlea og seteleie under siste del av svangerskapet. Især seteleie med oppslåtte bein og strake knær ga en høy risiko for dette, hvor sjansen ble økt 45 ganger i forhold til barn i vanlig hodeleie.

For å se om dysplasien registrert ved fødselen vedvarte gjennom veksten og dermed potensielt senere å kunne forårsake en ustabil kneskål, ble barn med markert dysplastisk form og en kontrollgruppe med normal form fulgt med gjentatte ultralydmålinger av kneet fram til 6 års alder. Det viste seg at en dysplastisk utseende trochlea hos en nyfødt forblir slik og at et barn født med en normalformet leddflate ikke utvikler dysplasi i løpet av de første 6 leveår.

Studien gir ny kunnskap i det dysplasi av kneskålleddet ble påvist blant nyfødte. Seteleie i siste del av svangerskapet gir en betydelig økt risiko for dysplasi og denne dysplasien ser ut til å vedvare gjennom de første 6 leveår. Studien bør betraktes som en innledende studie og bør følges opp av studier av større populasjoner, helst fordelt på flere sentre og undersøkere.

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Ovennevnte avhandling er funnet verdig til å forsvares offentlig for graden Philosophiae Doctor i klinisk medisin.

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Contents

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List of papers

This thesis is based on the following papers, referred to in the text by their roman numerals.

I: Øye CR, Holen KJ, Foss OA. Mapping of the femoral trochlea in a newborn population: an ultrasonographic study. *Acta Radiol 2015; 56(2): 234-43.*

II: Øye CR, Foss OA, Holen KJ. Breech presentation is a risk factor for dysplasia of the femoral trochlea. *Acta Orthop 2016; 87(1): 17-21.*

III: Øye CR, Foss OA, Holen KJ. Minor change in the sulcus angle during the first six years of life: a prospective study of the femoral trochlea development in dysplastic and normal knees*. A revised version of the manuscript has been accepted for publication in the Journal of Children's Orthopaedics.*

List of acronyms and abbreviations

CI	confidence interval
CT	computed tomography
IS	Insall Salvati index
LCH	lateral condyle height
MCH	medial condyle height
MPFL	medial patellofemoral ligament
MRI	magnetic resonance imaging
OR	odds ratio
PL	patellar length
PTL	patellar tendon length
SA	sulcus angle
SD	standard deviation
SH	sulcus height
TA	trochlear area
TD	trochlear depth
TI	trochlear index
3D	3 dimensional

Summary

The knee-cap is causing a variety of symptoms among children and adolescents. The ailments vary from anterior knee-pain to an unstable knee-cap with recurrent dislocations. A dislocation of the knee-cap is the most common knee-injury at this age. Substantial pain accompanied with risk of damage of the cartilaginous joint-surface are characteristics of a dislocation. A first-time dislocation may be the triggering event of a prolonged history of pain and recurrent instability, which may lead to functional disability for 30% - 50% of all patients who have sustained a primary dislocation of the knee-cap.

There are different causes to an unstable knee-cap. The knee-cap share a common joint-surface with the anterior part of the femoral condyles which, by having the shape of a U, contributes to stability. A shallow or flat joint-surface, namely trochlear dysplasia, is the single most crucial factor of instability of the knee-cap joint. For patients with recurrent instability, surgery may be indicated to restore stability. When the trochlear dysplasia is prominent, surgery may be a challenge and involves major open knee-surgery.

The etiology behind and the incidence of trochlear dysplasia is unknown. This dysplasia has never before been detected at birth. Our intention was to study whether trochlear dysplasia is congenital or not. Since the normal anatomy of the femoral trochlea at birth is vaguely described, a study to describe the anatomy of a new-born population was indicated. Ultrasound examination is ethically accepted to use on children, involving no known risks, discomfort or need of sedatives or anesthetics. An evaluation of ultrasound as a method for visualizing the trochlear joint-surface of a new-born population was necessary, since ultrasound for this purpose not had been evaluated before.

The evaluation of ultrasound as an examination method of the patellofemoral joint was conducted as a separate study. Both knees of 40 new-born children were examined. The results of two examiners were compared, both regarding the repeatability of the measurements of each examiner and the accuracy of the measurements in between the two examiners. The measurements were consistent and the results comparable with those registered in older children by other observers. Ultrasound was thus accepted as the method for further use.

Altogether 348 knees were examined by ultrasound within 3 days after birth. Different measurements were registered and evaluated, to decide which one to be best suited to describe the trochlear anatomy. With acceptable repeatability, being easy to record and to interpret, the trochlear sulcus angle (SA) proved to be a suitable parameter and the one best correlated with trochlear dysplasia. Other vital birth-parameters were noted, such as sex, gestational age, length and weight. Demographical data were registered, as the presentation at birth, status of the hip joints according to dysplasia and familial occurrence of pain or instability of the knee-cap.

Among the new-born population, measurements indicative of trochlear dysplasia were made. These were comparable with known markers of dysplasia among adults. A correlation between an ultrasonographic dysplastic trochlea and breech presentation was detected. In particular, frank breech with the knees extended, gave a 45-fold increased risk for trochlear dysplasia.

To assess whether the dysplasia found at birth persisted through growth and consequentially causing instability of the knee-cap later in life, children with a dysplastic trochlea, as measured by the SA, were followed with repeated ultrasound examinations until

6 years of age. Children with a normal shape of the trochlea were chosen as a control group. This study showed that a dysplastic shape of the trochlea at birth persists, and that a child born with a normal shaped trochlea does not develop dysplasia during the first 6 years of life.

The studies provide novel knowledge of the etiology of trochlear dysplasia. Breech presentation during the last phase of pregnancy is a risk factor for dysplasia, which seems to persist during early growth. Our research should be considered as initial and furthermore studies on larger populations, preferentially multicenter studies done by multiple observers, are recommended.

Introduction

Focus / topic

This dissertation examines the anatomy, the natural variances and the development of the femoral trochlea from new-born to six years of age in children born during a period of two months in 2010 at the University Hospital of Trondheim.

Perspective / rationale

The patella, or knee-cap, articulates with the femoral condyle through the joint surface called the femoral trochlea. The patella and the femoral trochlea form the patellofemoral joint. Disorders of the patellofemoral joint are common, especially among children and adolescents where complaints from this joint constitutes the most common knee disorder (Fithian et al. 2004; Nietosvaara, Aalto, and Kallio 1994). Symptoms varies from pain to recurrent patellar dislocation. Typical signs are refusing to take part in sports or acute episodes of "give way" of the knee during activity. The dislocation may be triggered during minor activities, most often by rotation of the body while the knee goes into flexion. A stable

patella is crucial for a well-functioning joint and the anatomy of the femoral trochlea is vital to ensure stability. Among the causes afflicting the stability, a shallow femoral trochlea, or trochlear dysplasia, is the single most important factor causing instability (Dejour et al. 1994). Trochlear dysplasia represents a challenging condition to manage. Surgical correction implies open knee procedures that shouldn't be performed during growth due to the possibility of damaging the growth zones of the knee.

The etiology of trochlear dysplasia remains unclear. There is no consensus as to whether dysplasia has a genetic origin (Glard et al. 2005), is caused by maltracking and remodeling during infancy and growth (Nietosvaara 1994; Wright et al. 2014), or due to other unexplored factors.

A thoroughly reading of the literature reveals that the anatomy of the femoral trochlea in newborns is vaguely described (Nietosvaara 1994; Mizobuchi et al. 2007). To our knowledge, trochlear dysplasia has not been studied or detected among newborns. A study of the anatomy of the femoral trochlea in newborns seems decisive in the efforts to increase our knowledge of the etiology of femoral dysplasia, by both describing the normal anatomy and to see if dysplasia is present at birth. The aim of our research was to examine and follow a population of newborns using ultrasound to;

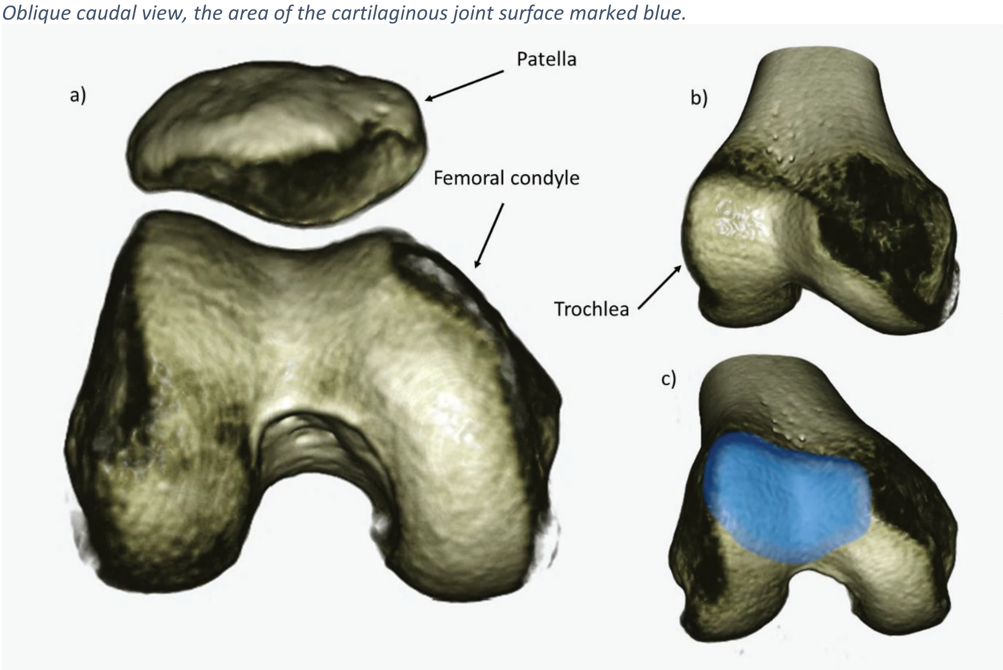
a) Describe the anatomy of the femoral trochlea and its natural variances.
b) To see if trochlear dysplasia could be found, and if so, to detect specific risk factors.
c) Furthermore, to describe the natural development of the trochlea of an immature, growing skeleton influenced by the forces generated by standing and ambulation during the first 6 years of childhood.

General background

Anatomy of the patellofemoral joint and the extensor mechanism of the lower limb

The patellofemoral joint consists of two osseous structures, the patella and the femoral trochlea. The patella is a sesamoid bone enclosed within the tendon of the quadriceps muscle, which is the extensor musculature of the lower limb. The femoral trochlea constitutes the anterior part of the femoral condyles of the knee, and share an articulating surface with the patella (Figure 1). The patellofemoral joint is a highly complex structure. The femoral trochlea has two joint facets, that by their orientation to each other form a sulcus. In the upper part of the trochlea, the joint surface is narrow and the sulcus is at its

Figure 1: 3D CT scan of the patellofemoral joint. The cartilage joint surface is not visible. a) Skyline view seen form below showing a congruent joint. b) Oblique medial view of the femoral trochlea, patella removed. c) Oblique caudal view, the area of the cartilaginous joint surface marked blue.



shallowest. The joint surface widens and the sulcus gets deeper towards the distal part of the trochlea. The articular surface of the patella consists of seven patellar facets, three lateral and four medial. Throughout the range of knee-motion, the contact surfaces between the patella and the trochlea change continually. In full extension, the patella is usually out of contact with the trochlea. It gains contact with the trochlea between 10° to 20° of flexion. The contact area of the trochlea moves from proximal to distal, whereas the patellar contact area moves from inferior to superior when the knee flexes from 0° to 90° (Scuderi 1995).

The function of the patellofemoral joint is intimately associated with dynamic lower limb muscle activity. The patella acts as a biomechanical lever enhancing the pulley effect from the extensor musculature by increasing the moment arm distance from the center of motion of the knee, thus improving the efficiency of extension by as much as 50% (Schindler and Scott 2011). Normal daily activities exposes the patellofemoral joint to forces between 0.5 to 9.7 times body weight, rising up to 20 times the body weight during sport activities (Schindler and Scott 2011). These considerable forces in relation to the relative small contact areas of the patellofemoral joint, make the joint vulnerable to disturbances in the mechanical equilibrium of the lower limb that is required for optimal function.

The factors of stability

The stability of the patellofemoral joint relies on the integrity of three principal factors; the articular geometry or static stabilizer, the muscles or dynamic stabilizers and the surrounding ligaments or passive stabilizers (Feller et al. 2007). A normal articular geometry implies a congruent joint surface between the patella and the trochlea as the patella moves down the trochlea during flexion of the knee. As the trochlear facets forms a sulcus, the shape of the joint surface of the patella forms a ridge to fit in this sulcus. The lateral trochlear facet is larger and higher than the medial to counteract for the tendency to laterally displacement of the patella created by the muscles (Ahmed and Duncan 2000; Feller et al. 2007). The quadricep muscle is in fact a group of four muscles; the rectus femoris that originates from the pelvis, and the vastus lateralis, the vastus medialis and the vastus intermedius that all originates from the femur. Contraction of the recuts femoris provides flexion in the hip and extension of the knee, thus the quadriceps is classified as a biarticular muscle. The patella unifies the divergent forces of the quadriceps muscle through the quadriceps tendon inserting broadly at the proximal part of the patella, transferring the forces to the patellar ligament (Schindler and Scott 2011). Along with extension of the knee, the quadriceps muscle also provides stabilization and shock absorption of the limb. In humans, the shaft of the femur is angled so the knee is closer to the midline of the body than the hips. This creates a valgus angulation over the knee joints. As the quadriceps muscle follows the axis of the femur, it creates a line of pull with a lateral directed vector. Together with the lateral trochlear facet, patella is supported by soft tissue constraints that are vital to create counterbalance (Desio, Burks, and Bachus 1998). Ligaments between patella and femur and between patella and tibia exists on both sides of the patella, with the medial patellofemoral ligament (MPFL) as the primary soft tissue restraint (Feller, Feagin, and Garrett 1993; Amis 2007). The ligaments are important for the stability of the patellofemoral joint, especially when the knee is between 0° to 20° of flexion, guiding the patella to enter the sulcus of the trochlea correctly and provide vital support when the contact between the patella and trochlea is low.

The forces acting upon the patellofemoral joint are dependent on the body posture. In the sagittal plane, the distance of the body's center of gravity relative to the patellofemoral joint shifts while leaning forward or backward and during knee flexion and extension. A longer distance means a greater moment arm. To maintain an upright position, muscle activity and consequently joint load increases.

Patellofemoral instability

The concept “patellofemoral instability” is used to describe the recurrence of patellar luxation or subluxation after a first-time luxation. It usually presents during childhood or adolescence, and is a distinct entity from congenital patellar luxation which is beyond the scope of this theses.

Incidence of patellofemoral instability

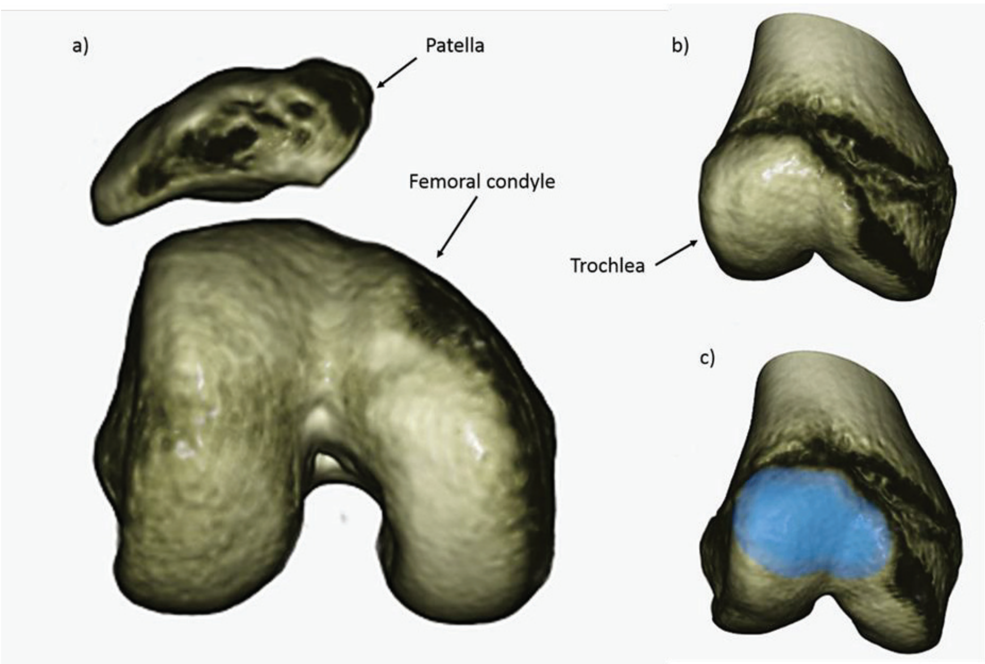
Acute patellar dislocation is the most common knee injury in children and adolescents. 69% of persons with a first-time dislocation of the patella are between ten and nineteen years (Atkin et al. 2000). The annual incidence is reported between 29 and 43 per 100,000 (Fithian et al. 2004; Nietosvaara, Aalto, and Kallio 1994). A first-time patellar dislocation may be the triggering event of a lifelong condition. Recurrence after a first-time dislocation is reported between 15 – 44% (Lewallen, McIntosh, and Dahm 2013; Hawkins, Bell, and Anisette 1986; Sanders et al. 2017), based on these results the incidence of recurrent instability should be between 4 and 19 per 100,000. After a subsequent dislocation, the chance of recurrence is 50% (Fithian et al. 2004). Of all patients who have sustained a primary patellar dislocation, 30 – 50% report functional disability (Hawkins, Bell, and Anisette 1986).

The factors of instability

The stability of the patellofemoral joint is all about balance. As a small joint with relatively restricted contact areas between the osseous parts, being located near the middle of the lower extremity and exposed to high load values, the patellofemoral joint is vulnerable to disturbances in the mechanical equilibrium of the extremity. Every change to the three principal factors of stability, namely the joint geometry, the action of the muscles and the integrity of the ligaments, is a possible threat. For simplicity, factors of instability can be regarded as locally to the patellofemoral joint or more distant due to the alignment of the limb.

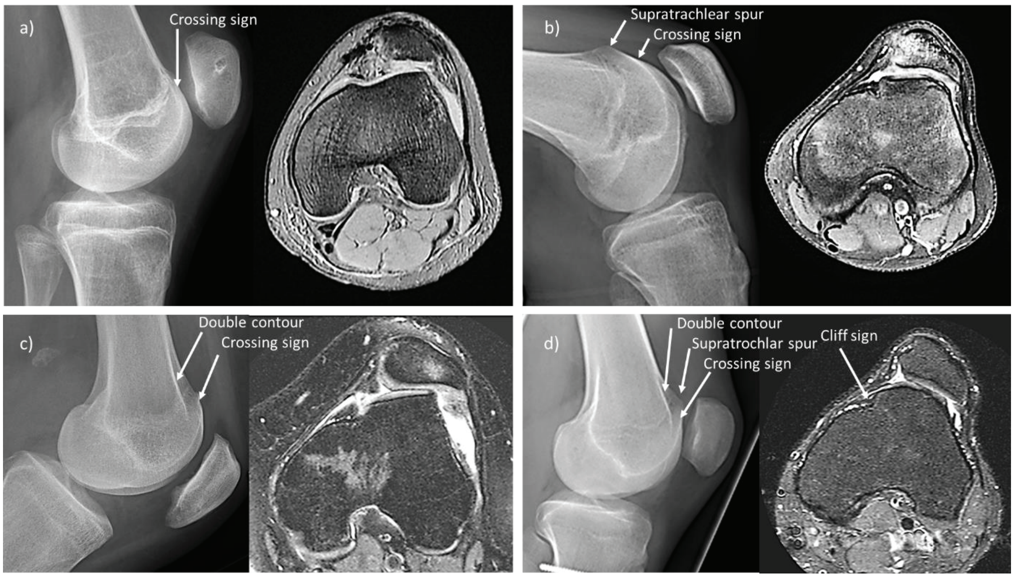
The local instability factors are anatomical changes of the articular surface or disruption of the ligaments of the joint. Of all known causes of instability, dysplasia of the femoral trochlea seems to be the most prominent (Jaquith and Parikh 2015). Trochlear dysplasia is defined as an anatomical abnormality of the shape and depth of the trochlear sulcus. A flat, short and ventrally displaced trochlea is the key feature of dysplasia (Figure 2). Severe dysplasia may present a convexity of the proximal part of the joint, and both facets might be hypoplastic.

Figure 2: 3D CT of a patellofemoral joint with trochlear dysplasia. a) Skyline view seen from below shows a trochlea with a convex surface in the proximal part of the joint, the patella is subluxated laterally. b) Oblique medial view showing a short trochlea with a hypoplastic medial facet. c) Oblique caudal view, the area of the cartilaginous joint surface marked blue. The trochlea is shallow and short.



A dysplastic trochlea provides less support for the patella. As the dysplasia is most prominent in the proximal and ventral part of the trochlea, the lack of support appears when patella is at its most vulnerable position between 10° – 30° of flexion. The most prominent dysplasia, with a ventrally displaced and convex shaped joint surface, literally pushes the patella laterally out of track in the end of knee extension or at the start of flexion. Trochlear dysplasia is traditionally classified according to Dejour into four grades, based on three distinct radiographic signs on a true lateral radiograph (Dejour et al. 1994) (Figure 3).

Figure 3: Dejour classification of trochlear dysplasia based on radiographic signs on a true lateral radiograph. Transverse plane MR of the knees are shown to illustrate the differences of the trochlear anatomy. A) Type A dysplasia, where the line representing the sulcus crosses the contours of the facets resulting in a "crossing sign". The trochlea is shallow. B) Type B dysplasia, where in addition to the crossing sign there is a supratrochlear spur indicating a flat and ventrally displaced trochlea. C) Type C dysplasia, where in addition to the crossing sign there is a double contour representing a hypoplastic medial facet. The trochlea is convex. D) Type D dysplasia, with crossing sign, supratrochlear spur and double contour. The trochlea is convex, ventrally displaced with a marked "cliff" due to the hypoplastic medial facet.



The association between instability of the patellofemoral joint and trochlear dysplasia has been known for more than a century, Richer reported in 1802 a connection between an anomaly of the lateral condyle in patients with recurrent patellar dislocations. Wiberg studied the congruity of the patellofemoral joint surfaces and classified different patellar shapes in 1941 (Wiberg 1941). Brattstrøm undertook in 1964 a study to describe the anatomy of the femoral trochlea (Brattstroem 1964). In a well-known study in 1987, Dejour and Walch discovered specific radiographic signs for dysplasia, described the first classification of dysplasia and defined four principal risk factors for patellofemoral instability (Dejour et al. 1994). The four factors were trochlear dysplasia, a high riding patella, excessive lateral quadriceps vector defined by a lateral displacement of the insertion of the patellar ligament in relation to the trochlea, and excessive lateral patellar tilt. They reported presence of trochlear dysplasia in 96% of patients who underwent surgery for patellar instability compared to 3 % in the control group. In a study of anatomic factors associated with recurrent patellar dislocation, Steensen et al found a prevalence of trochlear dysplasia of 68% (Steensen et al. 2015). Another study of predictors of recurrent patellar instability in children and adolescents found an odds ratio of 3.56 for dysplasia and risk of recurrence, ahead of other predictors as contralateral dislocation (OR 3.05), skeletal immaturity (OR 2.23) and a high riding patella (OR 2.06) (Jaquith and Parikh 2015).

Disruption of the patellofemoral and patellotibial ligaments are other local instability factors. As a consequence of unbalanced forces over time, the surrounding ligaments are sustained to overload and become stretched and damaged. During a first-time patellar dislocation, the medial patellofemoral ligament ruptures or its bony attachments are teared off and may be permanently damaged (Vainionpaa et al. 1986). Laxity of the ligaments renders the patella vulnerable to instability, especially during the first 30° of flexion.

The distant factors of patellofemoral instability can be assigned as limb alignment problems. The skeleton defines the direction of the forces and thereby where the load will cross the patellofemoral joint. Any variation from optimal skeletal alignment may result in inappropriate forces acting on the joint. Consequently, ligament failure with subsequent instability may follow (Feller et al. 2007). Rotational and angular deformities of both femur and tibia, or often a combination of different deformities may be the origin of instability problems(Dejour and Le Coultre 2007). Such deformities may change the position of the muscular attachment of the quadriceps muscle relative to the insertion of the patellar ligament, disturbing the equilibrium between the stabilizing factors.

Review of research

An overview of research and papers about the etiology of trochlear dysplasia includes the research regarding the anatomy and development of the femoral trochlea both intrauterine and after birth until the age of skeletal maturity. Different authors use different phrases to categorize their work. Studies describing anatomy are commonly named anatomic, morphologic or biometric studies. The term anthropologic is used in studies describing human evolution through time. Current theories can principally be divided into three. One theory suspects genetics to be the main determinant to the shaping of the femoral trochlea(Gardner and O'Rahilly 1968; Glard et al. 2005). A second theory predicts that the femoral trochlea is flat at birth. As the embryonal and infantile femoral condyles consist mainly of cartilage, they are soft and vulnerable to the influence of mechanical forces. The final anatomy after ossification is dependent upon the ability to move the knees(Tardieu 1998). If the forces over the patellofemoral joint are well-balanced, normal tracking of the patella and thereby adequate shaping of the trochlea is achieved. If, on the other hand, the movement of the knees is restricted, the deepening of the femoral sulcus may not develop normally. Correspondingly, if the forces acting over the patellofemoral joint become imbalanced due to development of skeletal deformities, maltracking of the patella might flatten the contact area between the patella and trochlea causing dysplasia to develop during growth. A third theory postulates that the shape of the embryonal femoral trochlea is genetically determined and mirrors the anatomy of adults. As the femoral condyles are susceptible to remodulation due to patellar tracking and forces acting on the joint and its growth centers, the final shape is dependent upon a combination of both genetics and mechanical molding(Doskocil 1985).

In 1940, Walmsley studied a series of formalin fixed specimens of embryonal and fetal knee joints. Transverse sections of the knee in a fetus of 23 - 40 mm, equivalent to 9-10 weeks, showed a trochlear sulcus with an elevated lateral facet compared to the medial one (Walmsley 1940). The trochlear joint surface seemed to develop independently of the patella and was not found to be completed until after birth.

Gardner and O`Rahilly studied in 1968 the early development of the knee in 34 embryos ranged from 5 to 8 weeks since ovulation (Gardner and O'Rahilly 1968). The embryos had been sectioned and stained before examination through microscope. During the sixth week, the chondrofication of the femur was detected. At 7 weeks, the femoral condyles were formed as well as the patella with its ligament. At 7.5 to 8 postovulatory weeks, the femur, tibia and fibula had clear-cut cartilaginous shapes and the knee joint resembled an adult. One embryo had “incipient cavitation” between the patella and femur in one of the knees, in the other knee a “definite femoropatellar cavity” was found. This finding is not subject to further discussion in the paper. Possibly, this might be the first description of prenatal trochlear dysplasia.

Doskocil published in 1985 a series of 14 formalin fixed knee-joints from embryos in the stage between 4 to 10 weeks (Doskocil 1985). He found the joint space of the patellofemoral joint to be the first joint space of the knee to develop. In the youngest embryos, the contact surface between the patella and femur was straight, it then took the shape of a V until the concave-walled shape of a U formed at the end of the period. He postulated that the initial shape of the patellofemoral joint was genetically determined but that the joint surface was susceptible to remodeling due to variations in the orientation of the patellar tendon and the rectus femoris muscle, altering the position of the patella relative to the trochlear sulcus.

More recently, Glard et al. performed a biometric study of the femoral patellar grove in fetus (Glard et al. 2005). Digital images were used to measure the femoral trochlea in forty-four formalin-preserved fetuses between 13 to 38 weeks. Measurements included the sulcus angle (SA) and the inclination angles of the facets. The distance from the posterior condylar line to the highest point of the lateral facet, the highest point of the medial facet and the lowest point of the sulcus were measured. The results were compared with corresponding measurements in an adult population. The geometry of the trochlea showed no significant difference in the SA and inclination angles in fetus and adults. The authors support the conclusions made earlier by Gardner, O`Rahilly and Doskocil. These studies of prenatal development of the knee supports the theory of a genetically determinant of patellofemoral joint shape since the morphology of the joint surfaces seems determined early in utero life.

Nietosvaara examined the femoral trochlea of 50 children with ultrasonography (Nietosvaara 1994). Measurements of the SA angle of the cartilaginous surface were compared to the osseous SA angle, that is the bony outline underneath the cartilage. The immature femoral condyles are mainly made of cartilage. During growth, ossification starts centrally and as the ossification take place the osseous outline gradually changes and takes a shape relative to the cartilage. The children were up to 18 years of age, the age distribution is not exactly accounted for, but from the plots it seems to be only 2 individuals under the age of one year. The measurements were taken at the level of the most ventral point of the lateral facet. The mean cartilaginous SA angle was 146° (135°-155°). The osseous angle changed gradually during growth from near flat to become the same as the cartilaginous SA at adolescence. There was a trend towards a slight narrowing of the cartilaginous SA during growth. No differences between left or right knee or between gender were found. The author concluded that the shape of the femoral sulcus was well developed at birth and that the cartilaginous SA stayed virtually constant during childhood. No conclusion of the cause of trochlear dysplasia is made, developmental causes or as a consequence of abnormal tracking of the patella during growth are suggested.

Mundy et al performed a retrospective study of the patellofemoral morphology in 144 near normal knee MRIs in children with open distal femoral physis (Mundy et al. 2016). In the 1-4-year-old, small findings that would have negligible effect on patellofemoral anatomy were accepted, as Baker`s cysts, discoid menisci or small effusions. Among other parameters, the SA was recorded. With 10 knees in each age group, the age distribution was equal. The mean SA was 146° and showed an age dependent morphology where the younger children had a wider SA. Until the age of 8, the SA seemed to be reasonably consistent around 150°, decreasing to under 145° from 9 years of age. Children with patellofemoral abnormalities, as trochlear dysplasia, were excluded from the study. The authors concluded that the morphology of the patellofemoral joint is age dependent and showing a gradual trend toward adult values with increasing age.

Anthropologic studies of human development point out that the femur undergoes morphological modifications during infantile and adolescent growth. In normal standing posture and during bipedal gait, the femur is obliquely oriented to the knee joint-line. The hip is adducted, relocating the knee medially, resulting in a knee and ankle that is placed almost directly under the center of gravity during single stance phases of gait. In newborn infants, the femur is vertical to the knee joint-line (Tardieu and Damsin 1997). In a study published in 1994 by Tardieu (Tardieu 1998), a sample of 46 adult and 38 juvenile human femora were examined. She found a remodeling of the distal femoral diaphysis to take place during infantile and early growth, mainly between 1.5 and 4 years of age, resulting in an oblique femur. Intuitively, this remodeling develops consequently to upright standing and walking as the load to the epiphysis is unevenly applied, causing greater growth on the compressed medial side. Later, during adolescent growth, a reshape of the distal femur epiphysis takes place including a deepening of the trochlear sulcus and increased protuberance of the lateral facet. This reshaping is acquired in response to the oblique femur, containing the patella in the trochlear groove. The author postulates that these morphological changes to the femur and knee is acquired and not genetically determined.

An earlier study by Wanner in 1977 found no correlation between the angle of obliquity of femur and the depth of the trochlea femoris (Wanner 1977), a finding that does not support the theory of Tardieu of an functional connection between these components.

Different animal research studies throw light on the etiology of trochlear dysplasia. Two of them are especially interesting, both performed on rabbits. In 2013 Kaymaz et al studied 16 rabbits by performing a lengthening of the patellar tendon of the right knees before 1 month of age, the left knees were used as controls (Kaymaz et al. 2013). CT scan of the knees were obtained before the intervention and 6 months after. They found a higher SA and a shallower trochlea in the middle and distal part of the joint among the intervened knees compared to the controls. In the proximal part of the trochlea they did not detect any differences, a possible explanation may be that the rabbits keep their knees in hyperflexion and that the proximal part of the trochlea was not deprived of the molding effect of the patella. The authors concluded that misposition of the patella may result in a flat or dysplastic femoral trochlea in rabbits.

The other study on growing rabbits investigated whether early reduction of patellar subluxation would reduce trochlear dysplasia (Wang et al. 2016). Sixty one-month-old rabbits were divided into four groups, three intervention groups and one control. Both knees of the rabbits were used, all the knees in the three intervention groups underwent surgical patellar subluxation. One group had the patella reduced surgically after 1 month, the next after 2 months and the third did not have reduction surgery. Measurements including SA and trochlear depth were performed by monthly CT scans. Significant differences were detected regarding SA and trochlear depth in the late-reduced group and the non-reduced group 6 months after the subluxations were performed. The trochlea was more flat and shallow compared to the control group and the early-reduced group, were no obvious differences in the measurements were detected. They concluded that dislocation of the patella in early development may lead to dysplasia of the femoral trochlea. Early reduction of the patella, when there is still sufficient time to remodel, may prevent dysplasia due to molding of the trochlea by a normal tracking patella.

Hereditary predisposition of trochlear dysplasia or tendency of patellar instability is scarcely reported in the literature. Crosby and Insall found an inherited association in 28% of cases in a study from 1976 where 107 patients with recurrent patellar instability were compared regarding the results of non-operative or operative treatment (Crosby and Insall 1976). Only 53 of the patients were specially questioned about any tendency of instability among family members. No explanation is given why only half of the patients were inquired and the topic is not subject for further discussion in the paper.

In a descriptive epidemiological study of patellar dislocation in the USA, Waterman et al calculated the incidence of patellar dislocation with respect to gender, age and race. They found a fourth fold risk among black and white race compared with the Hispanic race (Waterman, Belmont, and Owens 2012), but no difference between females and males. As biologic anthropology seems to have influence, genetics play a role in patellofemoral instability. Since no further analyses regarding the underlying reasons for the dislocations were made, any deductions regarding inheritance of dysplasia cannot be drawn. A weakness of this study is that race was documented in only 67% of the datasets of the study.

Only one case report is found regarding familial disposition of trochlear dysplasia. Rebolledo et al reported trochlear dysplasia in a family with recurrent bilateral patellar dislocation(Rebolledo et al. 2012). A 54-year old woman with a former history of recurrent bilateral dislocations and progressively worsening knee pain had bilateral trochlear dysplasia. In addition, she had windswept angular deformities of her lower-extremities, gonarthrosis and maximum knee-flexion of 120°. The patella was hypoplastic and the femoral trochlea was dysplastic. Her two children, a 9-year old girl and 6-year old boy, had recurrent patellofemoral instability. The girl had been treated for growth hormone deficiency for three years and had obligatory lateral patellar dislocation during extreme knee flexion. The boy had mild bilateral varus deformity of the lower-extremities, the patella dislocated obligatory under flexion and he kept his knees locked in extension to stabilize his knees during walking. Both children had trochlear dysplasia. The authors suggest the existence of an autosomal dominant inheritance.

Obligatory dislocation in knee flexion, as was true at least for the two children, is rare and represents another entity of patellofemoral instability and luxation. Therefore it is not addressed in this thesis (Batra and Arora 2014). Although trochlear dysplasia is present, both growth-disturbance and angular deformities were found in the family. As to the question of inheritance, trochlear dysplasia cannot be assessed alone as a cause to the instability of this family.

Reports of familial recurrent dislocation of patella do exist, as the study of Miller who found a pattern of autosomal dominance inheritance among a family (Miller 1978). It was not possible to identify any common predisposing factors to instability that might be inherited.

Summary of literature

The different studies mentioned above represents existing theories behind the determinants of the femoral trochlear anatomy. Emphasis is placed on genetics as a probable determinant among several authors, pointing out that the anatomy seems to be set during intrauterine or early postnatal life and resembles the shape of adults. Other authors believe that a molding process of the trochlea takes place during early growth due to patellar tracking and joint load during ambulation. This molding might affect trochlea with a sulcus genetically predetermined by birth, thus both genetics and mechanical molding is held responsible for the final anatomy. A theory where the shaping of the distal femur including the trochlea is solely acquired through growth and changes of joint loads due to transition to upright posture, is proposed by one author. Animal studies conclude that a normal tracking patella is a presumption for joint congruence and if patellar tracking can be ensured within a few months after birth, a dysplastic trochlea may recover and develop a sufficient sulcus.

A prospective study of the anatomy of the femoral trochlea among a newborn population and its development during early childhood has not been done earlier. It is being increasingly recognized by clinicians that trochlear dysplasia is a main factor causing instability. Greater knowledge of the etiology to dysplasia seems important in the efforts to develop methods to treat dysplasia and thereby patellar instability. A study with the possibilities to detect trochlear dysplasia among newborns or see it develops during growth should provide novel knowledge to this field.

Aims of the study

The general aim of the study was to describe the anatomy of the femoral trochlea with its natural variances in a population of new-born children. Furthermore;

-To see if dysplasia of the femoral trochlea could be found, make estimations of the thresholds defining trochlear dysplasia, and to identify possible risk factors.

-To see if the congenital trochlear anatomy persisted, by follow-up examinations until 6 years of age, through growth and the child's transition to upright posture.

The specific aims of the papers were:

1: To evaluate ultrasound as a method for imaging the femoral trochlea in newborn, as ultrasound not has been reviewed regarding examination of the immature knee and its joint surfaces (paper 1).

2: To define the normal anatomy of the femoral trochlea with its natural variances, and to describe specific measurement data for the femoral trochlea in a newborn population (paper 1).

3: To see if trochlear dysplasia could be detected at birth (paper 1) .

4: To explore whether any predisposing factors to trochlear dysplasia could be found (paper 2).

5: To follow the natural development of the trochlear anatomy during early childhood growth by follow-up examinations until six years of age, to get a better understanding of possible remolding of the immature trochlea as a response to increased joint load and ambulation (paper 3).

Methods

Designs of the studies

Study 1, paper 1; A cross-section survey of a population of new-born children, the point in time defined relative to each child within 3 days after birth.

Study 2 / paper 2; Identical design to study 1.

Study 3 / paper 3; A prospective cohort study of a subpopulation emanated from the original population.

The rationality behind ultrasonography

The femoral condyles in newborn is mainly made up of cartilage. During growth, the cartilage is gradually replaced by bone, which originates from the ossification center located centrally in the condyles distally to the epiphysis.

Standard radiographs do not depict cartilaginous structures and cannot be used to obtain images displaying the joint surfaces and outline of the infantile knee. Used together with contrast liquid injected into the joint, it is possible to get an impression of the contours of the joint surface. Such methods are invasive and ethically not acceptable as the method of choice when performing research, particularly not on children.

CT scan, an imaging technique which make use of computer-processed combination of x-rays from different angles, has the same limitation as radiographs regarding picturing cartilaginous structures. In addition, the radiation it inflicts and the probable need of sedation or anesthesia, makes CT scans not suitable to use during research involving children.

MRI, which make use of magnetic fields and radio waves, is today the method of choice in medical imaging of joints of children. It is not in itself invasive and pictures the structures of the joint, both osseous and soft-tissue structures. Due to a relatively long and noisy procedure, anesthesia or sedation is obligated when used on infants and young children. Therefore, it is not ethically justifiable for research in newborns.

Ultrasound is sound waves with frequencies which are higher than those audible to humans (>20,000 Hz). Medical ultrasound, also known as ultrasonography, applies ultrasound to provide images of internal body structures. Pulses of ultrasound are sent into tissues and are reflected as an echo. The different tissues return sound waves with frequencies specific to the tissues. These are recorded and images displaying structures, such as tendons, muscles, vessels, internal organs and cartilage of joint surfaces, are made. Bony structures will be displayed as a relief of the surface of the bone, structures behind will be difficult to visualize. It is a non-invasive procedure, providing images in real-time. It is substantially lower in cost compared to CT and MRI, it does not expose patients to harmful radiation, is portable and the procedure can be carried out bedside. Ultrasound imaging is without any known adverse effect or pain, it is therefore accepted and widely used in fetal medicine and in children(Salvesen 2007). An examination of the patellofemoral joint in a child is done without any sedation and takes up to 10 minutes. Descriptions of the method and recommendations of its use picturing the knees of children are published (Nietosvaara and Aalto 1993; Nietosvaara 1994; Mizobuchi et al. 2007), the method hason the other hand never been evaluated scientifically for use on a knee of a newborn.

In view of these considerations, ultrasonography was our desired imaging technique. However, its value regarding the intended use for examination of the immature knee of a new-born child had to be proved.

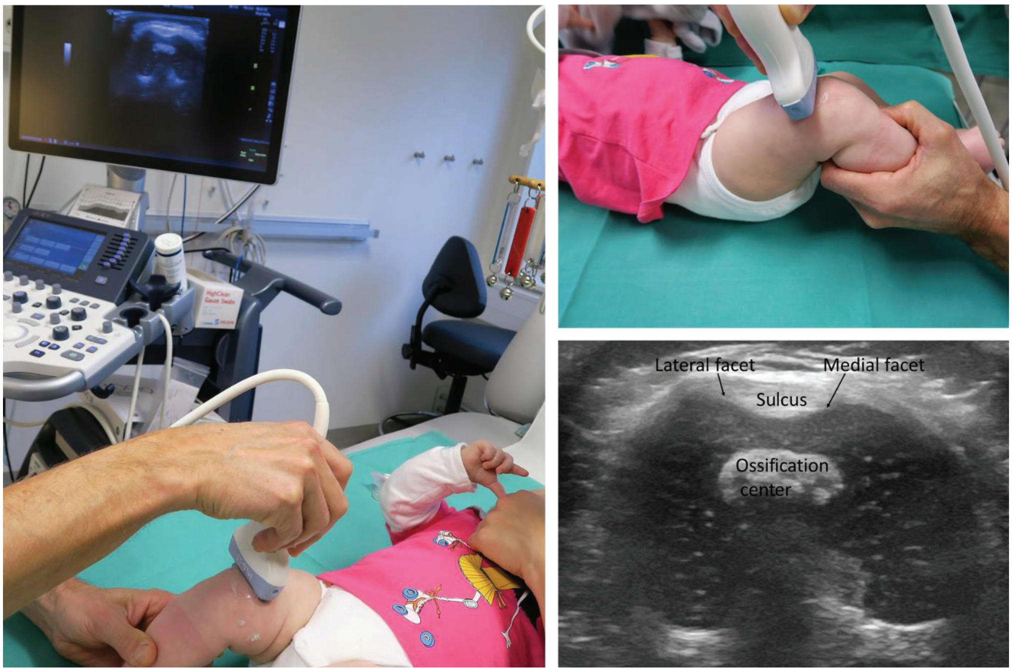
Evaluation of ultrasonography

A separate study was performed to evaluate the reliability of ultrasonography for imaging the patellofemoral joint in new-born children. The population comprised of 40 newborns assessed due to increased risk for congenital hip dysplasia because of hereditarily predisposition. The intra-observer and inter-observer repeatability was studied. Each of the knees were examined by ultrasound by two examiners. Only one examiner was present in the room during the separate examinations. Examiner 1 performed the first examination, then a second examination by Examiner 2, followed in the end by a third examination by Examiner 1. The same set of parameters obtained in the main study was validated by intra-observer repeatability, inter-observer repeatability and coefficient of variation, an indication of the natural variation of the parameters. Possible relations of magnitude and differences for the measurements were evaluated by visual inspection of Bland-Altman plots.

Ultrasound procedure

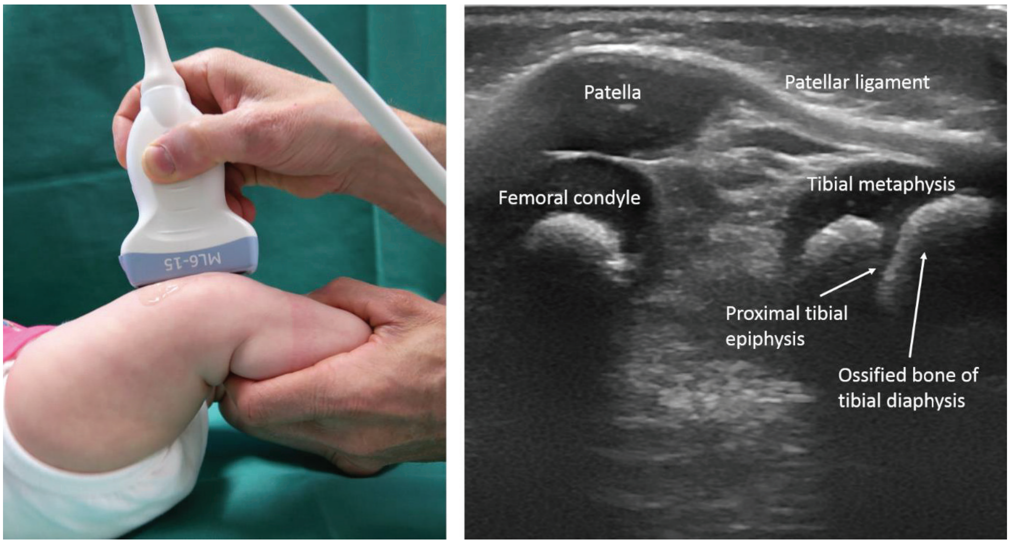
In our study, ultrasound was used to provide images of the patellofemoral joint of children. When examining a new-born, the procedure was performed bedside with a portable ultrasound scanner, GE Logiq Book XP (GE Healthcare CO., Jiangsu, China), with a linear GE 8L probe. The infants were in their beds or in comfort beside their mother, many of the children slept through the examination. None expressed pain or substantial discomfort. The knee was flexed above 45° to position the patella distal to the part of the joint surface of the trochlea where the measurements were taken. The probe was placed transversely and perpendicular to the axis of the femoral diaphysis. By slightly moving the transducer caudally beyond the epiphysis (which was clearly displayed), the trochlea with its most ventral part was defined. At this position, the trochlea was at its widest. Holding the transducer perpendicular with respect to the femoral axis, images were taken with the posterior relief of the two femoral condyles well visualized. The ossification center of the distal femur should be visualized, indicating correct perpendicular angulation of the probe (Figure 4).

Figure 4. Ultrasonographic examination while recording transversal image of the femoral trochlea. The images are produced for illustration of the technique, the child is 4 months old and not a participant of the study.



Then, with the knee slightly less flexed, the transducer was placed in the sagittal plane and longitudinally centered over the patella. Then, images of the patella, the distal femur with the epiphysis, the patellar ligament and the tibial tuberosity were obtained (Figure 5).

Figure 5: Sagittal image of the knee joint. Patella with the patellar ligament are displayed. The ossification center of both the femoral condyle and the tibial metaphysis are visible as well as the proximal tibial epiphysis and ossified bone of the tibial diaphysis.



In the evaluation of the repeatability of the ultrasound method, an intra- and interobserver study of a separate population of new-borns was performed. For practical reasons, the same ultrasound scanner was used for both the hips and the knees; A Siemens Acuson Antares Premium Edition (Siemens Healthcare, Mountain View, CA, USA) ultrasound scanner with Siemens VFX 9-4 Multi-D linear probe.

At the follow-up examinations, two ultrasound scanners were used due to the need of parallel examinations by two examiners. Together with the GE Logiq Book XP used for examinations of new-born, a second scanner was used; GE Logiq 7; (GE Medical Systems Co., Jiangsu, China), with linear GE 10L probe.

The pictures were stored on a computer with software for editing and measuring provided by GE; LOGIQworks Rev. 5.

To describe the anatomy of the femoral trochlea by the application of ultrasound, different parameters were measured, all listed below. The sulcus angle (SA) is a parameter commonly used to assess adolescent and adult trochlear dysplasia by X-ray, MRI and ultrasonography. In addition, other parameters were measured and evaluated to see if they were appropriate for the purpose to map the anatomy, detect trochlear dysplasia among infants and to follow the natural development during early childhood growth (Figure 6).

Ultrasonographic parameters

Sulcus angle (SA): the closed angle defined by the intersection of the lines parallel to the articular cartilage of the medial and lateral femoral facet.

Medial condyle height (MCH): the height of the medial condyle measured from the tangential line between the dorsal borders of the femoral condyles and the most ventral point of the medial facet.

Lateral condyle height (LCH): the height of the lateral condyle measured from the tangential line between the dorsal borders of the femoral condyles and the most ventral point of the lateral facet.

Sulcus height (SH): the shortest perpendicular distance from the tangential line between the dorsal borders of the femoral condyles and the point representing the deepest part of the femoral sulcus.

Trochlear depth (TD): the perpendicular line through the deepest part of the femoral sulcus is elongated. The distance from the point where this line intersects a line between the ventral border of the medial and lateral facet to the deepest point of the femoral sulcus represents the trochlear or sulcus depth.

Trochlear area (TA): the area restricted by the points of maximum height of the medial condyle and the lateral condyle and the deepest part of the sulcus measured in mm^2. This was obtained by counting the pixels within this area. The number of pixels in 1 mm^2 was a known value, the TA was calculated by dividing the number of pixels by the number of pixels per mm^2.

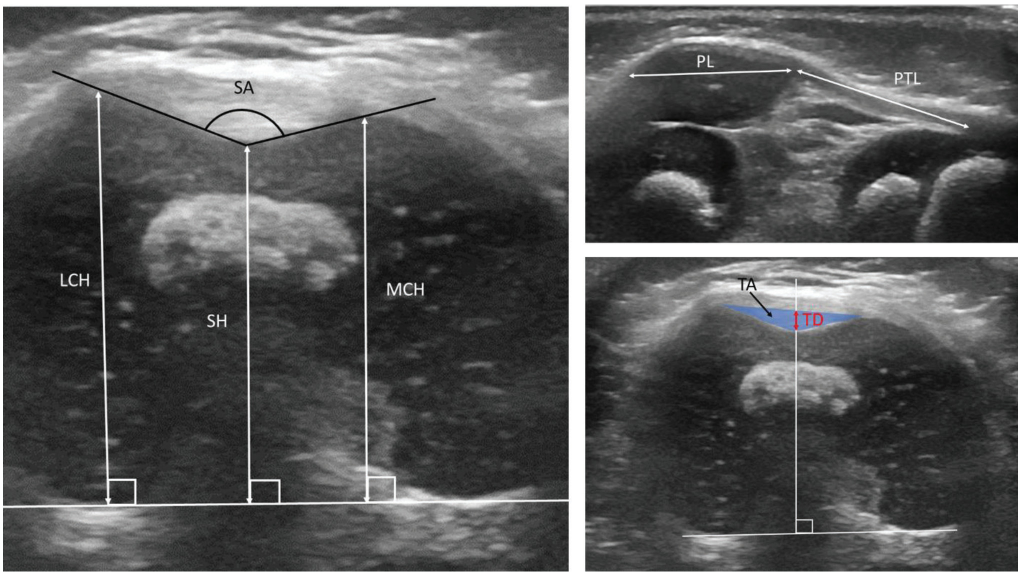
In the sagittal plane, we registered the following *parameters:*

Patellar length (PL): the length of the patella measured on an image viewing the largest sagittal image of the patella together with the patellar ligament and its insertion on the tibial tubercle.

Patellar tendon length (PTL): the length of the patellar tendon measured from the apex of the patella to the tibial tubercle.

Figure 6 displays the different UL parameters.

Figure 6: UL images with the different parameters displayed.



Naturally, measurements of length, height and depth are parameters that will be influenced by the general dimensions of the skeleton and not only the geometry of the joint. Intuitively, angular data and indexes should be independent of the size of the skeleton. To adjust for size variations among the children, a new index calculated from ultrasonographic measurements and evaluated for its usefulness as a parameter of dysplasia was made;

Trochlear index (TI): Defined as the sum of the height of the condyles divided by the height of the sulcus: $TI = \frac{MCH+LCH}{SH}$.

A measurement commonly used to describe the position of the patella relative to the tibia, a measurement of patellar height, is the Insall Salvati (IS) index (Phillips et al. 2010). It is an index originally calculated from lateral radiographs. Since both the length of the patella and its ligament were easy to obtain by ultrasound, the IS index was calculated and evaluated;

Insall Salvati index (IS): Defined as the patellar tendon length divided by the length of the patella: $IS = PTL/P\mathrm{L}$.

Demographic parameters

In addition to the ultrasound parameters, demographic parameters were collected. Sex, length, weight and gestational age were obtained from the birth journal. The birth presentation was categorized into cephalic, breech, or transverse / unknown. Breech presentation was further divided into complete, incomplete or frank according to the flexion of the knees (Figure 7). The presentation at birth is indicative of the intrauterine positioning of the fetus during the last stage of pregnancy. As all newborn are screened for hip dysplasia, our population was categorized into one of the following subgroups according to their hip status; normal, dysplastic, subluxated, luxated, unstable, doubtful or irregular caput femoris.

Figure 7: The various categories of breech presentation.

Statistics

Several statistical methods have been employed in this thesis.

Descriptive statistics were used to present numeric data. Visual inspection of various kinds of plots has been used in evaluation of data distribution, correlation and agreement.

Q-Q (quantile-quantile) plot is a probability plot. In this kind of plot, two probability distributions are plotted against each other. It was used to compare the actual distribution of measurements against theoretical normally distributed data, where the percentiles are distributed along the classic bell-curved standard normal distribution. If the plot follows the 45° line, the measurements are normally distributed and visual inspection are used to verify if this is the case ore not ("the fat pencil method").

There are good reasons to explore if data are normal distributed or not. Normal distributed results make interpretation of SD simple, since 95% of the data can be expected to lie within mean ± 2 (1.96) SD. In addition, parametric statistical test such as the Student t-test have the assumption of normal data distribution. Pared t-test was used in an overall comparison of the SA between left and right knees. Two-sample t-test was used in an overall comparison of the SA between the sexes. Here, Q-Q plots verified the assumption of normality before the tests was made.

The "standard statistical tests" assumes independent observations. This is not the fact in many of the analyses in this thesis. We have measurements made from both knees of the children and we have repeated measurement of each knee. Measurement from the left and right knee within a child is expected to be closer to each other compared to measurements between children. Also, measurements of a specific knee made at follow-ups are expected to be closer within a knee compared with measurement from knees in other children.

We have a situation in which knees are nested within children with repeated measurements over time- multilevel and longitudinal measurements. Using standard statistical tests in this situation could lead to estimation of to low p-values, stating statistical significance wrongly. This is caused by an underestimation of the variance since data not are independent. Mixed Linear Models was used modeling data with continuous outcome data and Generalized Mixed Linear Model modeling categorical outcomes. Both can handle data dependency caused by knees nested within children and repeated measurements nested within children.

Some statistical significant differences can be expected to be found just by chance when many statistical comparisons are made. Several multiple-comparison procedures may be used to ensure that too many false statistical significant differences are reported. The simplest and often used is the Bonferroni adjustment. The method can be a bit too conservative, however reporting false statistical significant differences should be best avoided by this procedure.

Visual inspection of scatterplots was used to evaluate correlations. For those scatterplots showing a graphically tendencies of correlation between the two parameters plotted, the Pearson`s correlation coefficient was calculated.

The Bland and Altman method was used to calculate the inter- and intra-observer repeatability. First, we calculated the differences between two sets of pared measurements, measurements made twice by one observer or by comparing the corresponding measurements made by two observers. The repeatability coefficients were calculated as twice of the SD of the differences.

Results

The results of the study are displayed by separate presentations of the papers.

Summary of the papers

Paper 1: Mapping of the femoral trochlea in a newborn population: an ultrasonographic study

Instability of the patellofemoral joint is the most common knee pathology during childhood and adolescence. A first-time dislocation may be the start of recurrent instability and functional disability for up to 30-50% of the patients. The anatomy of the femoral trochlea is of vital importance to the stability of the patellofemoral joint. Trochlear dysplasia characterized by a shallow and flat joint surface is, among others, an important risk factor for instability. The anatomy of the infantile femoral trochlea is barely known. There is no consensus regarding determinants to the final adult trochlear anatomy, being genetic or molded by patellar tracking and forces acting on the immature joint. Knowledge of the characteristics of the femoral trochlea in newborns might prove useful in the search for the etiology behind predisposing factors to patellar instability. Ultrasonography has been used and recommended for imaging the immature knees of children. The method has, on the other hand, not been evaluated scientifically for use in newborns.

The paper accounts for two separate studies. The main purpose of the study was to describe specific measurement data to define the normal anatomy and the natural variances of the femoral trochlea in a newborn population. Another aim of the study was, to accomplish the main purpose, evaluation of ultrasonography as a method of imaging the joint surface of the femoral trochlea. Both knees of 174 newborns (82 girls and 92 boys) were examined using ultrasonography within 3 days after birth. For evaluation of ultrasonsgraphy as a method, an intra-observer and inter-observer repeatability study of a separate population of 40 newborns by two examiners was performed. The parameters registered were; sulcus angle (SA), medial condyle height (MCH), lateral condyle height (LCH), sulcus height (SH), trochlear depth (TD), trochlear area (TA), patellar length (PL) and patellar tendon length (PTL). Calculations were made for the trochlear index (TI) = $\frac{MCH+LCH}{SH}$ and the Insall Salvati index $(\mathrm{IS}) = \frac{PTL}{P\mathrm{L}}$.

Ultrasonography proved to obtain measurements with acceptable intra-observer and inter-observer repeatability. The Sulcus Angle (SA) and Trochlear Index (TI) were found to be the most reliable and reproducible parameters by displaying a consistent intra- and inter-observer repeatability combined with a low coefficient of variation. The overall mean SA was 148° (SD 5.6). An angle of more than 159° was defined as dysplastic, and 17 of the knees were categorized in this group. The overall mean TI was 2.21 (SD 0.05). A value of less than 2.11 was defined as dysplastic and 11 of the newborns fell into this category. The SA was chosen as the parameter to obtain to assess trochlear dysplasia, being easy to record and showing a good correlation with dysplasia.

Ultrasonography is a reliable method of visualizing the newborn femoral trochlea and the position of the patella. Among the population of newborn, measurements of the SA indicative of dysplasia among adults were found. Our results indicate that dysplasia of the femoral trochlea may be congenital. In a further perspective, knowledge of the anatomy of a normal versus a dysplastic newborn trochlea renders it possible to follow the development of the trochlear anatomy during growth. To be capable of diagnosing trochlear dysplasia at an early stage may open alternative methods of treatment other than open surgery in the future.

Paper 2: Breech presentation is a risk factor for dysplasia of the femoral trochlea

Trochlear dysplasia, characterized by a shallow and short femoral trochlea, is the single most crucial factor for instability of the patella. The etiology of trochlear dysplasia is unknown. Our findings presented in paper 1 indicate that dysplasia can be present at birth. The dysplasia might have a genetic determinant or it might be a result of morphological modifications during prenatal, infantile and adolescent growth. The aim of the study was to evaluate possible risk factors for trochlear dysplasia and to assess whether birth presentation, as an indicator of the intrauterine positioning of the fetus at the last stage of pregnancy, could be a possible risk factor for trochlear dysplasia in the newborn.

The population of the study is presented in paper 1. 348 knees in 174 newborns were examined by the use of ultrasonography, concentrating especially on the trochlea femoris. Different parameters to describe the anatomy of the patellofemoral joint were obtained. In paper 1, the sulcus angle (SA) was the parameter found to be the most reliable for distinguishing a normal trochlea from a dysplastic. Thus, the SA was chosen to be the measurement to use in the statistical analyses together with different demographic parameters. The way of fetal presentation at birth and standard parameters such as sex, gestational age, and length and weight at birth were registered. As breech presentation is a known risk factor for dysplasia of the hip, we also looked for an association between dysplasia of the femoral trochlea and dysplasia of the hips.

No significant difference between the left and right knees was found. There was a significant difference between the sexes (p = 0.05), girls had a mean SA of 149° compared with 147° for boys. Weight was statistically significant and length was not, their influences on the SA were marginal and appear not to be of clinical importance. Only 4 children presented with hip dysplasia, the study sample was too small for statistical interpretation.

In contrast to the other possible risk factors assessed, breech presentation gained distinction with a strong correlation to trochlear dysplasia. The incidence of breech presentation among children with knees defined as dysplastic with a SA ≥ 159° was 15-fold higher. Breech presentation was divided into 3 groups; complete, incomplete or frank according to the position of the knees. A child in frank breech with the knees extended had a 45-fold increased risk of having trochlear dysplasia. Of totally 17 extended knees (16 frank breech and 1 incomplete breech), 9 were dysplastic. None of the 11 flexed knees were dysplastic. The only child with incomplete breech, with one knee extended and the other flexed, had correspondingly one dysplastic and one non-dysplastic knee. Knee position appeared to be the most important determinant for trochlear dysplasia. Thus, we conclude that breech presentation with knees extended appears to be a major risk factor for development of trochlear dysplasia.

Paper 3: Minor change in the sulcus angle during the first six years of life: a prospective study of the femoral trochlea development in dysplastic and normal knees

The aim of this prospective cohort study was to describe the development of the femoral trochlea in a newborn population during the first 6 years of life, to see if dysplasia found at birth is persistent or changes during early childhood. The population of our former cross-sectional survey of new-born children (paper 1), in which both knees of 174 newborns were examined within 3 days after birth by the application of ultrasonography, was the basis for this study. Trochlear dysplasia was described at birth in paper 1. On the other hand, the etiology of dysplasia is not known. Different theories to the determinants of the trochlear anatomy exist, both genetics, mechanical molding of the joint, or a combination of both are pointed out as probable causes to dysplasia. A population was followed from newborn to 6 years of age, as we studied the trochlear development in order to increase our understanding of the underlying causes for trochlear dysplasia.

In our former cross-sectional study, 348 knees of newborns were examined by ultrasound of the femoral trochlea within three days after birth. The anatomy was described by different measurements, of whom the sulcus angle (SA) gained distinction as a reliable parameter. Based on these results, a SA of 159° was set to be a dysplastic threshold value by adding 2 SDs to the population mean SA of 148°. 17 knees were defined dysplastic.

This last paper presents a follow-up study of the dysplastic knees together with a control-group of 101 non-dysplastic knees. The control-group comprised patients with knees holding a SA closest to the population mean of 148°. The contralateral knees of the dysplastic knees were included as controls if their SA was under 159°, thus classified as non-dysplastic. Altogether 59 of the original 174 children were assessed for eligibility, one child with bilateral dysplasia was lost to all follow-up examinations. Three follow-up evaluations were performed- at 6, 18 and 72 months, with ultrasound examination of the trochlea. The definition and diagnosis of a dysplastic knee at birth was retained throughout the sequential follow-ups. At 72 months, approximately 20% of the knees in both groups were lost to follow-up.

The overall SA through all follow-ups was 158.6° for the dysplastic knees and 151.1 for the non-dysplastic knees. The difference of 7.5° is statistical significant ($p < 0.001$). For every follow-up, the difference between the dysplastic and the non-dysplastic group kept the same level of significance ($p < 0.001$). A small but statistical significant change in the SA between 0 to 72 months was found for the dysplastic group ($p = 0.03$) as well as the non-dysplastic group ($p \leq 0.001$).

A general agreement to the definition of trochlear dysplasia by ultrasonographic measurements does not exist. In the literature, others have suggested 155°as the dysplastic threshold value (Dejour et al. 1994; Nietosvaara 1994; Askenberger et al. 2017). To explore whether a threshold of 155° would change the results, a sub-analysis was performed. Knees were dichotomized into dysplastic (SA ≥ 155°) and non-dysplastic (SA < 155°). With an overall SA of 156.6° in the dysplastic group and 148.5° in the non-dysplastic group, the difference of 8,1° was statistical significant ($p < 0.001$), as for the differences at the individual follow-ups ($p < 0.001$). Correspondingly, a minor change in the SA between 0 to 72 months was found, this was statistical significant for both groups ($p < 0.001$).

Only minor changes in the SA of the femoral trochlea were registered during the first 6 years of life. Whether the dysplastic threshold level was 155° or 159° seemed not to have impact on the changes in the SA between the groups. A dysplastic trochlea remained shallow, thus congenital dysplasia of the femoral trochlea persists during the first 6 years of age. Infants having a trochlea with normal SA angle seems not to develop dysplasia during the same time span.

These results are novel and important and will likely aid in the further efforts to find the etiology behind and methods to treat trochlear dysplasia.

Discussion

In this thesis, the anatomy of the femoral trochlea in a new-born population has been studied. Without any known adverse effect or pain, ultrasonography was considered an ethically accepted method for imaging infants. The reliability of the method to produce images of the patellofemoral joint in newborns has not been evaluated earlier, consequently evaluation of ultrasonography was accomplished. A special emphasis was laid on the possibilities of proving trochlear dysplasia among infants and to see if any predisposing factors could be detected.

Measurements of the sulcus angle and trochlear index indicated that trochlear dysplasia may be congenital. Follow-up examinations up to 6 years of age were performed to follow the development of the anatomy of the femoral trochlea.

Comments regarding the concept of studying a population of new-born children

Why did we find it necessary to examine the knees of infants when descriptions of the anatomy of children and adults already exists? What would justify asking parents about permission to do ultrasound examinations of their child and to call on them to follow-up examinations? The answer to these fundamental questions is the knowledge of the potential of an immature joint to respond to the surrounding environment and to make adaptions of the anatomy according to joint load and movement. The potential of remodeling through this molding process increases the younger the child is, due to rapid growth and a longer period of remaining growth.

Today, much efforts are made to diagnose and treat developmental dysplasia of the hips. There is a mutual understanding among clinicians of the necessity of joint containment and normal joint load during early growth to ensure a normal development of the hip joint (Barlow 1964; Bialik et al. 1999; von Rosen 1962). A dysplastic hip joint can be treated nonoperatively if diagnosed early and efforts are made to ensure containment of the joint during the first months of life. Even a luxated hip with a very shallow acetabulum might develop a congruent joint if the femoral head is contained in the normal position in relation to the growth zones of the acetabulum.

Subconsciously, the idea of transferring this knowledge to the knee joint grew stronger during my work as a surgeon treating patellofemoral instability, sometimes with major open surgery to correct trochlear dysplasia. What if we could diagnose and treat dysplasia of the femoral trochlea in the same way as for dysplasia of the hip? A throughout reading of existing literature showed that the etiology of trochlear dysplasia is unknown, it has never been described at birth and has never been found to develop during growth.

This was our fundamental question. To find an answer, a study of the anatomy of the femoral trochlea from birth and during early growth seemed inevitable.

Main findings

The main findings of our studies were:

1. Ultrasonography proved to give reliable and reproducible measurements and was accepted as our method in the further studies for depicting the femoral trochlea of infants. The different parameters together with the mean values and SD to describe the anatomy of the trochlea of a new-born child, are accounted for. Of all the parameters, the sulcus angle (SA) was found to be the one best suited to describe the

trochlea and detect dysplasia. The parameter is easy to obtain, understand and interpret.

2. The SA measurements among the new-born population showed comparable values and variations to those reported among adolescents. The measurements indicated that trochlear dysplasia might be present at birth, thus providing novel knowledge of the etiology of dysplasia. Girls had a statistically higher mean SA compared to boys. On the contrary, in the dysplastic group of 14 children, the distribution between girls and boys was equal with 7 individuals in each group.
3. Breech position showed, among the risk factors assessed, a clear association to trochlear dysplasia. Frank breech in particular, gave a 45-fold increased risk of being born with trochlear dysplasia.
4. A dysplastic trochlea in a newborn child remains shallow during the first 6 years of life. Children being born with a normally shaped trochlea seems not to develop a shallow trochlea during the same time span.

Comments regarding basal research

Basal research aims at the acquirement of novel knowledge. The incidence of trochlear dysplasia among children was not known, no other existing research provided us with the information needed for statistical sample size calculations. As a cross-sectional survey, the population size was based on practical considerations regarding the feasibility of the study. We had no knowledge as to trochlear dysplasia being congenital, or on the contrary, caused by remodeling of the immature trochlea due to imbalanced forces and maltracking of the patella during childhood. Our studies should be regarded as initial, generating hypothesis that should be tested at other centers and in larger populations.

Discussion of main findings in relation to the papers

Paper 1: A main topic of this paper is the evaluation of ultrasound as a method of imagingthe joint-surfaces of the immature knee. Ultrasound used to visualize the knees of children,to measure the SA, the cartilage thickness and the position and tracking of the patellarelatively to the trochlea has been described by Nietosvaara in 1993 and 1994 (Nietosvaaraand Aalto 1993; Nietosvaara 1994) and by Mizobuchi in 2007 (Mizobuchi et al. 2007). An evaluation of its value regarding which parameters to measureand the repeatability of the method usedon neonates does not exists and seemed necessaryto execute. By repeated examinations bytwo examiners performed within a 15-min period,statistical testing of the intra-observer and inter-observer repeatability of theultrasonographic method was possible.   Ultrasonography proved applicable to obtainmeasurements with acceptable repeatability. The Sulcus Angle (SA) and Trochlear Index (TI)were found to be the most reliable and reproducible parameters by displaying a consistentintra- and inter-observer repeatability combined with a low coefficient of variation.

The femoral trochlea of neonates is tiny and the difference of a normal SA compared to a dysplastic is just 10°, a challenge to the method of imaging. The SA is a known parameter used to evaluate the femoral trochlea by radiographs, CT and MRI. The parameter is regularly used to describe the extent of trochlear dysplasia in adolescents and adults. In a dysplastic knee, on the other hand, the contour of the joint line flattens and the measuring-points defying the SA will be more difficult to find. This is the reason why we found it expedient to assess other parameters, to find those best suitable to describe the anatomy and to distinguish between a normal and dysplastic femoral trochlea. Some of the parameters are commonly used in medical imaging and research of the patellofemoral joint, such as the medial condylar height (MCH), lateral condylar height (LCH), the trochlear depth (TD) and calculation of the IS index by patellar tendon length (PTL) and patellar length (PL). Other measurements were designed for this study, as the trochlear area (TA) and trochlear index (TI). Since measurements to describe the infantile trochlea does not exist, direct comparison of our results to others was not possible. Nevertheless, the parameters that intuitively should be independent of size of the skeleton, were comparable with those measured among older children and adults. Angular data, as the SA, and indexes, as TI and IS, are such measurements and should thus be comparable with the results of Mizobuchi et al in2007 (Mizobuchi et al. 2007). In a study of 40 children up to two years of age (averaging 9,65months) they measured a mean SA of 148,9° (148,7° - 149,3°) by the application of ultrasound. Mizobuchi defined the IS index as PL/PTL and found the mean IS to be 1.09 (1.04 – 1.13). As a rule, the definition of the IS index is PTL/PL, which were used in our study. Another much citated work describing the use of ultrasound to examine the femoral sulcus in children is Nietosvaaras from 1994, who published an ultrasonographic study of both knees in 50 children from 0 to 18 years of age, all without knee-problems (Nietosvaara 1994). The age-distribution or mean age is not accounted for. By visual evaluation of the scatterplots, most of the children are over the age of 5 and very few under one year of age. The mean SA was 146° (134° - 155°), staying virtually constant from birth to adolescence. Among our new-born population, we found a mean SA of 148° (133° - 169°) and a mean IS index of 0.9 (0.63 – 1.53). The almost identical values of the mean SA between these related studies strengthen the quality of our measurements among the new-born population. A narrower range of SA among the population of Nietosvaara might be due to the exclusion of children with knee-symptoms. It might also give an indication of some modeling of the trochlea during early growth. By defining the IS index as PTL/PL, our result is the same as Mizobuchi found in his population. None of the children in the study of Mizobuchi had SA values indicating dysplasia, this might be explained by a small population size. The population of Nietosvaara showed a variation more comparable to ours even if none of them would have been classified as dysplastic.

With the confirmation that the comparable parameters showed comparable readings, and our intra-observer and inter-observer repeatability study showed acceptable repeatability, we could draw the conclusion that ultrasound was applicable as the method of imaging of the femoral trochlea.

One of the purposes of the study was to describe novel measurement data of the new-born trochlea, making it possible to distinguish a normal anatomy from a pathological and to lay the foundation of further research. The different parameters were tested to look for differences between sexes and between right or left knee. Girls had a statistically higher mean SA of 149° compared to boys at 147°. The TI was correspondingly lower (p=0,04). On the contrary, there were 7 girls and 7 boys in the group with pathological high SA. The differences between the sexes are small and cannot be given great clinical importance. It might be a topic in the discussion of what makes the girls more vulnerable to develop chronic instability of the patellofemoral joint, even if the distribution among the sexes for first-time patellar dislocation are the same (Fithian et al. 2004).

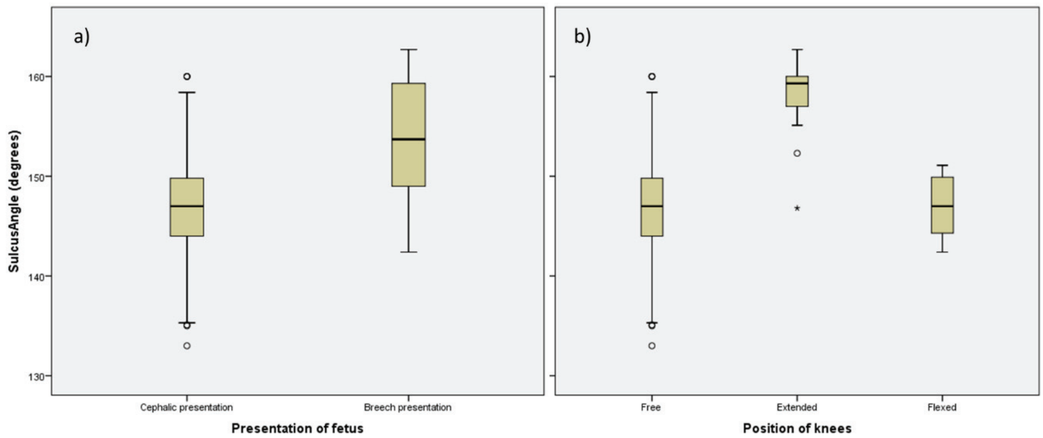
Our measurements of the SA among newborn are comparable with those found among adolescents by Nietosvaara in 1997 (Nietosvaara and Aalto 1997). In this study, the SA at the level of the most ventral point of the lateral facet was measured by ultrasonography in 33 persons with patellar dislocations (mean age 15,6 years) and in 25 normal children (mean age 14,8). The mean SA was 164° (154° - 195°) and 145° (134° - 153°) respectively. Compared with the values of our population with a total mean SA of 148° (133° - 169°), the variations are very much the same. This may indicate that the anatomy of the femoral trochlea is defined at birth and stays approximately unaltered during growth.

Currently, diagnostic criteria of trochlear dysplasia is obtained by plain lateral radiographs of the knee (Dejour et al. 1994). SA measurements are done on standard radiographs by flexing the knee 45°, angulating the x-rays 30° from the horizontal position which produces a sky-line or Merchant view. The osseous SA is measured, and a value greater than 145° -149° indicates dysplasia (Dejour et al. 1994; Davies et al. 2000). In this way, the SA is measured at a point distal to where the patella is most vulnerable regarding instability, and the sensitivity for dysplasia will be low. There is no collective agreement of the definition of trochlear dysplasia when assessed at CT of MRI. Different studies report a SA greater than 154° as a typical finding among patients with patellar instability (Askenberger et al. 2017; Duppe, Gustavsson, and Edmonds 2016). Most of these studies uses a measuring point of 3 cm proximal to the joint line of the knee as the point to measure the SA. We found no descriptions of measuring the SA on CT or MRI that could be compared with ultrasound measurements. In our case, the most intuitive way to set the limit between a normal trochlea and a dysplastic was using statistics, by adding 2×SD to the population mean. Regarding SA, the threshold of dysplasia was an angle ≥ 159°. As Nietosvaara found the SA among the group of patellar dislocation to be between 154° - 195° (Nietosvaara and Aalto 1997) and Dejour found evidence of trochlear dysplasia in 96% of patients treated for instability (Dejour et al. 1994), our threshold might be reasonable but should be regarded as an estimate. Intuitively, readings indicative of trochlear dysplasia were proved, providing novel knowledge of dysplasia being congenital.

Paper 2: Breech presentation showed an exceptional position among the risk factors for trochlear dysplasia, assessed with an approximately 15-fold higher risk of having trochlear dysplasia as opposed to children born with cephalic presentation. This was unexpected, and such a connection have never been found earlier. It should be regarded as novel knowledge. We do emphasize that the 95% confidence interval was wide (6,4 – 34), giving some uncertainty of the magnitude of the risk estimate. From 28-30 weeks` gestation, the intrauterine position of the fetus is categorized into cephalic, breech or transverse position. A child in breech position have restricted possibilities to move the knees the last weeks of pregnancy. The knees are kept either extended or flexed. When breech presentations were grouped according to the position of the knees, extension of the knees gained distinction with a 45-fold higher risk of dysplasia compared to the knees free to flexion (the 95% confidence interval was wide here too). Thus, knee position seems to be an important factor for congenital trochlear dysplasia. The fact that the only child with incomplete breech presentation had one dysplastic knee that had been kept in extension, and one normal knee that had been kept in flexion, supports this theory. The differences of the SA according to cephalic and breech presentation and position of the knees are presented (Figure 8).

Breech presentation is a well-known risk factor for hip dysplasia, this is also the case at our hospital (Holen et al. 1996), knowledge which has resulted in screening of children born with breech presentation with ultrasound of the hip joints soon after birth. Even if a connection between trochlear dysplasia and dysplasia of the hips among the infants in the breech group not could be detected, the postulate is raised of the underlying cause of these dysplasias. Intuitively, restricted motion of the joints of the lower-extremities during the last phase of pregnancy might have influence on the development of the joint anatomy. The knowledge of the importance of ability to move, containment of the joint and balance of joint forces during early growth supports this postulate.

Figure 8: Boxplot displaying the differences of the SA according to a) the presentation of the fetus and b) position of the knees during the last phase of pregnancy. "Free" represents cephalic presentation, "Extended" represents frank breech and "Flexed" represents complete breech. Transverse and unknown presentation are not displayed.



Paper 3: In paper 3 we present the development of the SA, as an indication of the development of the trochlear anatomy, during the first 6 years of growth. It is discussible whether the SA is a parameter good enough to use as a single representative for the anatomy. As pointed out in paper 1, there exists no mutual acceptance of the use of ultrasonography for the evaluation of trochlear dysplasia. Radiographs of the knee with support of CT or MRI are the accepted methods of imaging to describe the trochlea in adults.

As cartilage is the main tissue in the distal femoral condyles in children under the age of skeletal maturity, x-rays will not capture the shape of the joint surface, excluding radiographs and CT. MRI will demand the use of sedatives combined with excessive costs, and is therefore not applicable for research purposes. In a context of growing children, parameters of length, width and area will intuitively increase and make comparison challenging. Angular data (SA) and an index made of measurements of length (TI) should make allowance for the growth. The measuring points of the joint surface to set the SA and the TI is virtually the same. The SA showed the best correlation with dysplasia and it is a parameter that is commonly known by clinicians. Therefore, the SA was chosen to be the parameter to follow.

Special interest was paid to those born with a high SA, to see if the signs of dysplasia persisted during this period. Our follow-up analyzes show that a high SA at birth remains high during the first 6 years of childhood growth, indicating a persistence of dysplasia. Small but statistical significant changes in the SA were found during the first 72 months of life, most of the changes happened within 18 months. This might indicate that the anatomy of the femoral trochlea is susceptible to molding, presumably the potential will be at its highest soon after birth.

Assumptions can be made that the dysplasia found at birth might give instability of the patellofemoral joint later in life. As breech presentation is a risk factor for being born with dysplasia of the femoral trochlea, a connection between breech presentation and patellofemoral instability might be proved. A trochlea with a normal SA at birth do not seem to develop dysplasia during these first 6 years.

Strengths and limitations of study

The strength of our study is its originality by addressing a topic where knowledge is limited. The need of new knowledge and better understanding of the development of the femoral trochlea through the early years of growth is based on years of clinical experience treating patients with patellofemoral instability. Basal research in this field is necessary if progress in therapy should be made.

Ultrasonography is a method widely used for medical imagining in fetal medicine, without any known adverse effect or pain. A throughout evaluation proved it applicable for our purpose, giving us no ethical hesitations for choosing ultrasonography as the method of imaging.

The data regarding birth presentation were collected from birth-journals displaying detailed information where the different breech-presentations are given.

The study, involving data collection and measurements, were performed by experienced clinicians.

The limitations of the study are those often encountered in basal science; information needed to calculate sample size and to calculate the strength of the study are difficult to obtain. The anatomy of the femoral trochlea from birth to 6 years, especially the shape and development during the first 2 years, has scarcely been described. The incidence of trochlear dysplasia is still unknown. We had to base the size of the study-population on what was practically feasible. As a basal research study, the population is relatively small.

Methods of imaging the trochlea of children at this age have not been evaluated earlier. Our definition of trochlear dysplasia is set by us and has not been evaluated by others. The limits between normal and pathologic anatomy must be regarded as estimates. Comparisons of ultrasound, CT and MRI in the evaluation of the femoral trochlea among adults have been done. Studies where the accuracy of ultrasound is proved and recommendation of ultrasound as a method of SA measuring on a level with CT do exist (Martino et al. 1998). On the other hand, studies where ultrasound is criticized can also be found (Toms et al. 2009).

The ultrasound examinations are executed at a single hospital by 2 observers. To strengthen the study, a multi-center study on larger populations and by more observers should be executed to develop the ultrasound method and to define the threshold of trochlear dysplasia.

Our study provides novel knowledge and should be regarded as an introductory study.

Suggestions for future research

Further studies to explore the possible connection between breech presentation and patellofemoral complaints would be welcome. Under our supervision, two medical students conducted a master degree study where they by clinical and ultrasonographic examinations in addition to KOOS questionnaire (Knee injury and Osteoarthritis Outcome Score), assessed the patellofemoral joint of two groups adolescents. All participants were between 16 – 18 years old. 20 persons that had been born in frank breech presentation confirmed by birth-journals, were compared with 16 persons delivered in cephalic presentation as controls. The SA angle showed a significant difference between of the two groups (p=0.04), being highest among the breech group (153°) compared to the controls (149°). 5 knees had an SA angle ≥ 159° in the breech group compared to 1 in the control group, this was not a significant difference. By clinical examination, findings indicating patellofemoral pathology were found in 4 of the participants, all among the breech group. The KOOS score showed no statistical difference, although the breech group reported lower score for all subcategories. A lower score indicates more pain and symptoms, less participation in sport activities and lower quality of life. As not every person with trochlear dysplasia develop symptoms from the knee, we believe that the populations of this study was too small to prove a possible connection. Further research on other and larger populations are suggested.

Today, considerable research has provided substantial knowledge in the field of development of the hip joint. Due to vast capacity of the joint to remodel and adapt to the load created by increasing movement and transition to upright posture during early living, significant efforts are done to recognize and correct dysplasia or incorrect containment of the joint at an early stage. By ensuring correct positioning of the proximal femur in the acetabular joint surface, gradually correction of the anatomy towards a congruent and stable joint is likely to occur. Intuitively, the distal femur should have the same potential for remodeling. Research on animals do support this theory. The next step should be a study to explore the possibility to correct a congenital dysplastic femoral trochlea by ensuring correct tracking of the patella relatively to the trochlea in the first months of living. This might be achieved by passive flexion of the knees and possible retaining the patella with soft braces. Talking to the midwifes and nurses of the neonatal wards at our hospital, they expressed concerns regarding the knees of children born in frank presentation. For days after birth they keep their knees extended and do resist efforts to movement of both hips and knees. If our suspicion is proved, that breech presentation gives risk for later complaints due to instability of the patella, an experimental study of correcting trochlear dysplasia by non-surgical procedures after birth is justified.

Conclusions

The paramount aims of the study were to examine the anatomy of the femoral trochlea in a population of new-born children to define the normal anatomy and its natural variances. Furthermore, to follow the development of the trochlea through early childhood growth, to see if the shape of the trochlea was persistent or changed. Specific emphasize was paid to see if trochlear dysplasia could be detected after birth and to compare the development of a dysplastic looking trochlea to a normal. Before the study of the anatomy of the femoral trochlea was done, a separate study in which ultrasonography was evaluated and accepted as an applicable method, was performed.

By ultrasonographic examinations of both knees to 174 new-born children, the anatomy was described by different measurement parameters. Limits defying the natural variance and estimations of the threshold of trochlear dysplasia has been proposed.

Measurements indicating trochlear dysplasia has been detected among new-born children. Breech presentation proved to be a risk factor for dysplasia. By follow-up examinations until 6 years of age, ultrasonographic measurements showed minor changes in the shape of the femoral trochlea. A dysplastic trochlea at birth is persistent and a trochlea with normal anatomy does not seem to develop dysplasia.

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Appendices

Questionnaire new-born examination

ULTRALYDUNDERSØKELSE AV PATELLOFEMORALLEDDET HOS NYFØDTE

Mor Etternavn, fornavn ______________________________ Adresse ____________________________

Barn Etternavn, fornavn ______________________________ Født ____.____.____

Kjønn *1=jente, 2=gutt* ☐

Barn nr ☐ Tvilling *0=nei, 1=ja* ☐ Vekt_______ Lengde _______

Fødsel *1=hode, 2=sete, 3=ext sete* ☐ Gestasjonsalder _______
4=sectio/hode, 5=sectio/sete
6=sectio

Patellasymptomer i nærmeste familie *0=nei, 1=smerter, 2=luksasjon* ☐
3=dysplasi

Dersom ja(1-3), hvem? *1=mor, 2=far, 3=søsken, 4=andre* ☐

Medfødte misdannelser *0=nei, 1=fotdeformitet, 2=nevromuskulær, 3=annen* ☐

Konklusjon hoftescreening *0=normal, 1=dyspl, 2=sublux, 3=lux, 4=instab,* ☐
5=tvil, 6=uregelm caput

		Høyre	Venstre
UL	**Sulcusvinkel**	______	______
	Mediale fasettvinkel	______	______
	Laterale fasettvinkel	______	______
	Høyde mediale condyl	______	______
	Høyde laterale condyl	______	______
	Høyde sulcus	______	______
	Dybde sulcus	______	______
	Areal	______	______
	LP	______	______
	LT	______	______
	LP/LT	______	______

Kontroll *0=nei, 1=ja* ☐ Evt. tidspkt_______ *Sign* ______________________________

Original papers

Paper I

Original Article

Acta Radiologica
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Mapping of the femoral trochlea in a newborn population: an ultrasonographic study

Christian R Øye, Ketil J Holen and Olav A Foss

Abstract

Background: The anatomy of the femoral trochlea is of vital importance to the stability of the patellofemoral joint. Knowing the characteristics of the femoral trochlea in newborns might prove useful when considering the predisposing factors to patellar instability.

Purpose: To define the normal anatomy and the natural variances of the femoral trochlea in a newborn population as well as evaluation of ultrasonography as a method of imaging.

Material and Methods: The femoral trochlea of both knees of 174 newborns (82 girls and 92 boys) was examined using ultrasonography within 3 days after birth. For evaluation of the repeatability of the method, a separate population of 40 newborns was examined by two examiners.

Results: The sulcus angle (SA) and Trochlear Index (TI) proved to be the most reliable and reproducible parameters. The overall mean SA was 148° (SD 5.6). An angle of more than 159° was defined as dysplastic, and 17 of the knees were categorized in this group. The overall mean TI was 2.21 (SD 0.05). A value of less than 2.11 was defined as dysplastic and 11 of the newborns fell into this category.

Conclusion: As a method of visualizing the newborn femoral trochlea and the position of the patella, ultrasonography is a reliable tool and might be of vital importance. In a further perspective, knowledge of the anatomy of a normal *versus* a dysplastic newborn trochlea renders it possible to study the predisposing factors to patellar instability and methods of treatment. Our results indicate that dysplasia of the femoral trochlea may be congenital.

Keywords

Knee, ultrasound, anatomy, pediatrics, congenital, dysplasias

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Introduction

Acute patellar dislocation is the most common acute knee disorder in children and adolescents with an annual incidence reported between 29 (1) and 43 (2) per 100,000. A first-time dislocation may be the triggering event for subsequent patellofemoral complaints. Recurrence rates in the range of 15–44% have been reported, and with a subsequent dislocation, the chance of recurrent episodes is 50% (3). This may lead to functional disability for 30–50% of all patients who have sustained a primary patellar dislocation (4). Several authors have found trochlear dysplasia to be one of the most important factors predisposing to patellar instability (5,6). To the best of our knowledge, the incidence of children with trochlear dysplasia is unknown. Recent literature reviews reveal that the anatomy of the femoral trochlea in newborns is poorly described (7,8).

Early diagnosis of hip dysplasia in newborns is the key to successful treatment. Knowledge of the natural anatomical variances in the hip joint together with methods to visualize the joint is needed to identify these patients. A parallel could possibly be drawn in

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understanding the femoral trochlea in newborns. If so, knowledge of the natural anatomical variances in the knee joint and visualization methods are also needed here.

Biomechanically, the patellofemoral articulation in humans is complex. Stability and patellar tracking are both affected by the articular geometry, muscle actions and soft-tissue restraints (9). Lateral dislocation of the patella occurs in early flexion. During flexion, the patella is at its most lateral position at 20°, just as it enters the femoral sulcus (10). A dysplastic trochlea has a ventrally displaced joint surface which is flat or even convex. In early flexion, this results in premature contact between the patella and the trochlea causing the patella to tilt laterally. Medial structures including the medial patellofemoral ligament might then suffer from overloading (11). Lateral mispositioning of the patella in respect to entering the femoral sulcus might be the result. With further flexion, the tracking and stability of the patella are largely dependent on the femoral trochlear geometry (12). Consequently, we decided to examine the trochlea in the area where the patella is at its most vulnerable position for lateral dislocation, where it engages the trochlea at its most ventral part.

The aim of the study was to describe specific measurement data for the knee in a group of newborns using ultrasonography and to use these novel data to estimate the limits defining trochlear dysplasia.

Material and Methods

Patient selection and demographic data

The examinations were performed at the University Hospital of Trondheim, Norway, a hospital managing around 3800 births annually. Over a period of 2 months in 2010, we examined all newborns, 348 knees of 174 children (82 girls and 92 boys) admitted to one out of three wards. All of the newborns were examined within 3 days after birth. The children were examined regardless of other conditions. Only those with conditions demanding treatment in the intensive care unit and children with major deformities or syndromes were excluded. The mean gestational age of the population was 39.1 weeks (SD 3.5), the mean birth weight was 3476 g (SD 562) and the mean birth length was 49.4 cm (SD 2.7). According to the Medical Birth Registry of Norway, these results are very similar to the national mean values (3475 g and 50.2 cm), thus representative of a Norwegian newborn population.

Ultrasonographic method

Ultrasonography of the patellofemoral joint provides dynamic and static images, the latter comparable with magnetic resonance imaging (MRI), where the articular cartilage, the femoral ossification center, and the posterior edge of the condyles are visualized.

Ultrasonographic examinations were performed by a single examiner (Examiner 1) with the child in the supine position. A portable ultrasound scanner, GE Logiq Book XP (GE Healthcare CO., Jiangsu, China), with a linear GE 8 L probe was used, enabling examination of the newborns in their beds or in comfort beside their mothers. Many of the children slept through the examination, and none expressed pain or substantial discomfort. The knee was flexed above 45° to position the patella distal to the ventral point of the lateral facet. The transducer was placed in a transverse plane perpendicular to the axis of the femur diaphysis (Fig. 1a). By slightly moving the transducer caudally beyond the epiphysis, the trochlea and its most ventral

(a)

(b)

Fig. 1. Images showing an ultrasonographic examination of the knee with (a) positioning of the transducer to obtain a transverse view of the trochlea femoris and femoral condyles holding the knee flexed above 45°; and (b) the transducer held in the sagittal plane with the knee slightly less flexed to obtain a view of the patella, the patellar ligament and the tibial tuberosity. The images were taken during an ultrasonographic examination of the knee in a 3-month-old girl; the method used is identical to an examination of a newborn.

point were defined. At this position, the width of the trochlea has reached its maximum. Holding the transducer perpendicular with respect to the femoral axis, images were taken with the dorsal border of the two femoral condyles well visualized (Fig. 2a and b). Correct perpendicular angulation of the probe was verified with the ossification center visualized, serving as a checkpoint. Then, with the knee slightly less flexed, the transducer was placed in the sagittal plane (Fig. 1b). By doing so, we obtained images of the patella, the patellar ligament, and the tibial tuberosity (Fig. 3a and b).

Selection of parameters

The geometry of the trochlea is vital to patellofemoral stability. The lateral facet of the trochlea counteracts the resultant lateral force created by the pull of the muscles and the alignment of the limb (Fig. 4). At present, there is a consensus on how to evaluate the patellofemoral joint radiographically in adults using X-rays with true lateral and Merchant views combined with either computed tomography (CT) or MRI (3,6,13). A Merchant view is obtained while flexing the knee by 45°. Angulating the X-ray beam 30° from the horizontal plane pointing towards the feet, a sky-line view of the patella and trochlea femoris is produced. The femoral sulcus angle (SA) is used to describe this geometry together with the crossing sign and trochlear depth (TD). A high SA, a low TD, and a positive crossing sign are indicative of dysplasia. Typically, the trochlea is both shallow and short (14).

Preliminary examination of data to define potential useful parameters and evaluation of possible

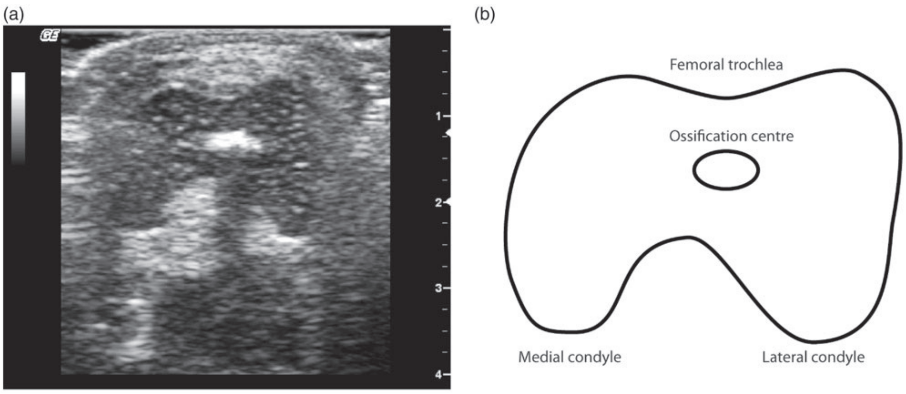

Fig. 2. (a) Transverse view of the trochlea femoris and femoral condyles; and (b) line diagram to illustrate the image.

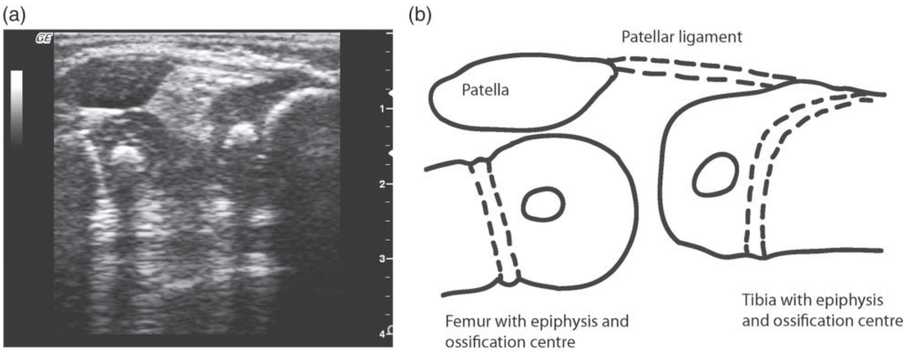

Fig. 3. (a) Sagittal view of the knee visualizing the patella, the patellar ligament, and the tibial tuberosity; and (b) a line diagram to illustrate the image. The epiphysis and the ossification center of the distal femur and proximal tibia are visible.

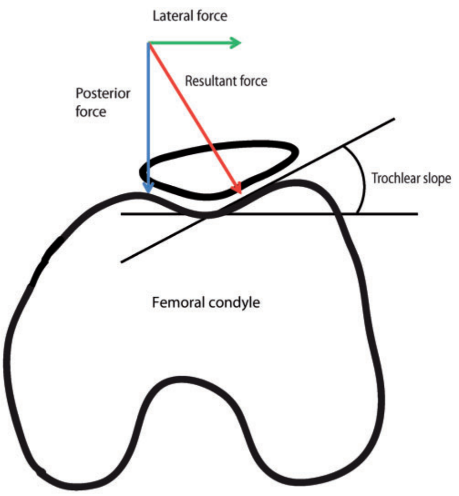

Fig. 4. The trochlear slope is the principal opponent neutralizing the resultant force created by the pull of the muscles. The inclination of the slope is affected by dysplasia of the trochlea. Any variation from normal when considering muscular strength and lower limb alignment may alter the direction and magnitude of the resultant force.

meaningful correlations were performed by visual evaluation of scatterplots (Fig. 5).

We registered the following parameters (Fig. 6a–c):

SA: the closed angle defined by the intersection of the lines parallel to the articular cartilage of the medial and lateral femoral facet.

Medial condyle height (MCH): the height of the medial condyle measured from the tangential line between the dorsal borders of the femoral condyles and the most ventral point of the medial facet.

Lateral condyle height (LCH): the height of the lateral condyle measured from the tangential line between the dorsal borders of the femoral condyles and the most ventral point of the lateral facet.

Sulcus height (SH): the shortest perpendicular distance from the tangential line between the dorsal borders of the femoral condyles and the point representing the deepest part of the femoral sulcus.

TD: the perpendicular line through the deepest part of the femoral sulcus is elongated. The distance from the point where this line intersects a line between the ventral border of the medial and lateral facet to the deepest point of the femoral sulcus represents the sulcus depth.

Trochlear area (TA): the area restricted by the points of maximum height of the medial condyle and the lateral condyle and the deepest part of the sulcus measured in mm^2. This was obtained by counting the pixels within this area. Knowing the number of pixels in 1 mm^2, we calculated the TA.

Trochlear index (TI): Defined as the sum of the height of the condyles divided by the height of the sulcus: $TI = (MCH + LCH)/SH$.

In the sagittal plane, we registered the following parameters:

Patellar length (PL): the length of the patella measured on an image viewing the largest sagittal image of the patella together with the patellar ligament and its insertion on the tibial tubercle.

Patellar tendon length (PTL): the length of the patellar tendon measured from the apex of the patella to the tibial tubercle.

Intra-observer and inter-observer repeatability study

To evaluate the repeatability of the ultrasonographic method, we performed a separate study with a new population of 40 newborns. The mean gestational age of this population was 39.4 weeks (SD 1.6), the mean birth weight was 3462 g (SD 527) and the mean birth length was 48.9 cm (SD 3.7). For each knee, Examiner 1 performed two examinations while Examiner 2 performed one. The two corresponding examinations were made within a 15-min period with the examiner leaving the room between the two sessions. A Siemens Acuson Antares Premium Edition (Siemens Healthcare, Mountain View, CA, USA) ultrasound scanner with Siemens VFX 9-4 Multi-D linear probe was used.

Statistical analysis

All statistical calculations were performed using IBM SPSS Statistics version 20, (SPSS Inc., Chicago, IL, USA). Visual inspection of Q-Q plots showed all parameters to be normally distributed. Consequently, data were presented as mean and standard deviation (SD). Mixed linear models were used to account for data dependency caused by repeated measures within each child when investigating possible differences between left and right knee and gender. A diagonal covariance structure was finally selected based on the Akaike Information Criterion. The coefficient of variation was calculated by dividing the parameter's standard deviation by its corresponding mean value and multiplying the result by 100. Pearson's correlation was used to describe the association between SA and gestational age. The inter-observer and intra-observer repeatability were calculated according to the method of Bland and Altman where the repeatability coefficients are twice the standard deviation of the differences between the two sets of measurements (15). The limits defining dysplasia were set to mean + 2 SD for some parameters, and mean –2 SD for others.

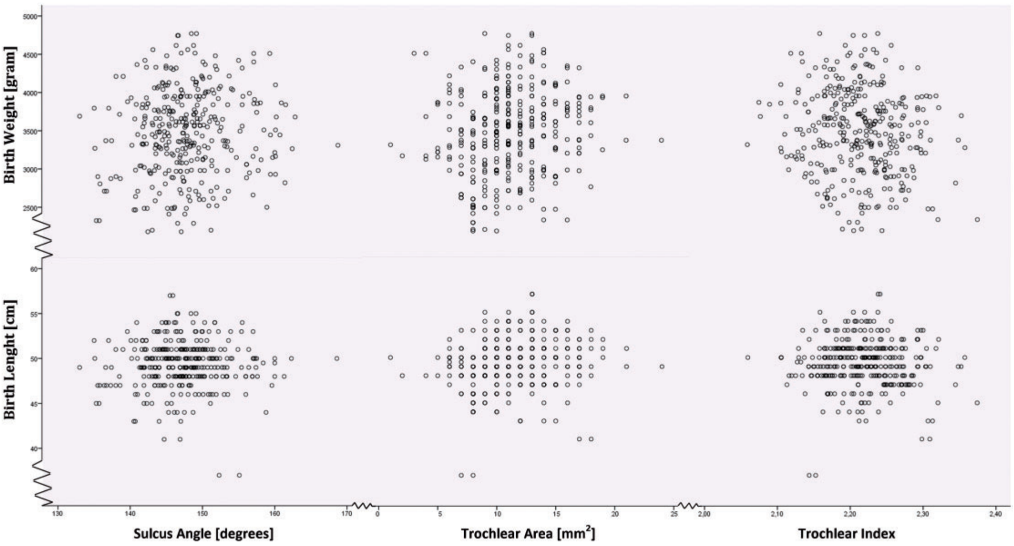

Fig. 5. Scatterplots displaying the correlation between birth weight, birth length, and the parameters SA, TA, and TI.

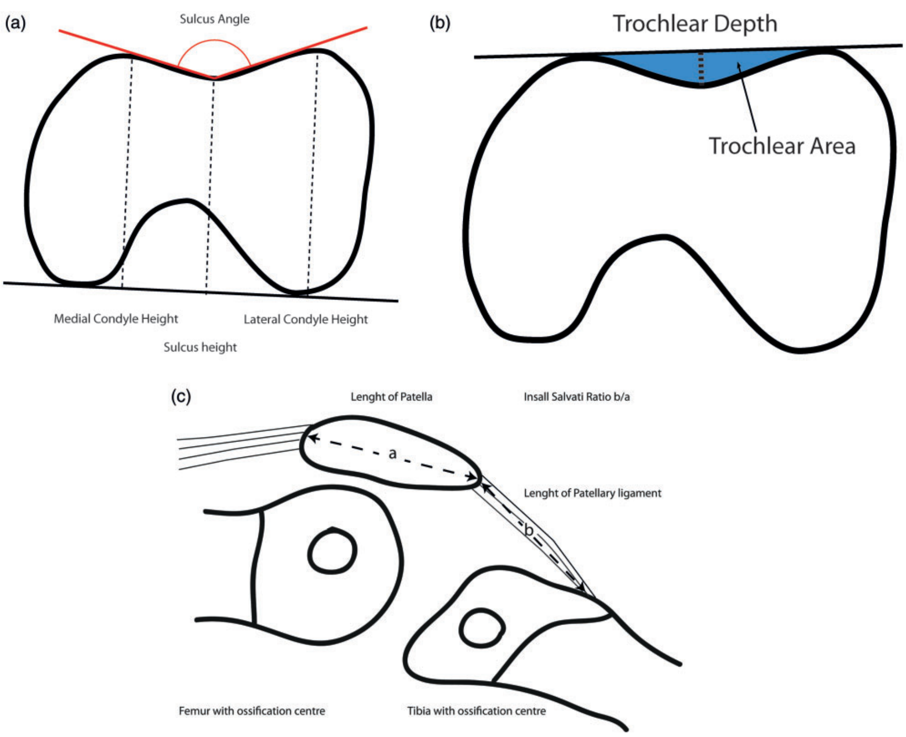

Fig. 6. Schematic illustrations of the parameters in both transverse (a and b) and sagittal (c) planes.

Table 1. Data of different parameters in a population of 174 newborns.

		n	Mean	SD	Diff.	*P* value	Dysplasia borderline
Sulcus angle (°)	Right	174	148	5.3	0.2	0.67	≥159
	Left	174	148	5.9			
	Girl	164	149	5.4	1.5	0.04	
	Boy	184	147	5.6			
Medial condyl height (mm)	Right	174	18.1	1.2	−0.13	0.03	≤15.7
	Left	174	18.2	1.1			
	Girl	164	18.0	1.1	−0.29	0.13	
	Boy	184	18.3	1.2			
Lateral condyl height (mm)	Right	174	19.5	1.4	−0.15	0.07	≤16.9
	Left	174	19.6	1.2			
	Girl	164	19.4	1.3	−0.29	0.21	
	Boy	184	19.7	1.4			
Sulcus height (mm)	Right	174	17.0	1.2	−0.14	0.02	≥19.4
	Left	174	17.1	1.1			
	Girl	164	17.0	1.1	−0.16	0.48	
	Boy	184	17.1	1.4			
Trochlear depth (mm)	Right	174	1.8	0.4	−0.01	0.75	≤1.0
	Left	174	1.8	0.4			
	Girl	164	1.7	0.4	−0.15	<0.01	
	Boy	184	1.8	0.4			
Trochlear area (mm^2)	Right	174	11.1	3.3	−0.14	0.47	≤4.4
	Left	174	11.3	3.5			
	Girl	164	10.5	3.3	−1.32	<0.01	
	Boy	184	11.8	3.4			
Patellar length (mm)	Right	174	15.1	1.2	−0.31	<0.01	≤12.9
	Left	174	15.4	1.1			
	Girl	164	15.2	1.1	−0.23	0.15	
	Boy	184	15.4	1.2			
Patellar tendon length (mm)	Right	174	14.1	1.6	–0.39	<0.01	≥17.5
	Left	174	14.5	1.6			
	Girl	164	14.3	1.6	–0.13	0.54	
	Boy	184	14.4	1.6			
Insall Salvati	Right	174	0.9	0.1	−0.01	0.51	≥1.1
	Left	174	0.9	0.1			
	Girl	164	0.9	0.1	0.01	0.67	
	Boy	184	0.9	0.1			
Trochlear Index	Right	174	2.21	0.05	0.00	0.42	≤2.11
	Left	174	2.21	0.05			
	Girl	164	2.21	0.05	0.02	0.04	
	Boy	184	2.22	0.05			

Results

The results are presented in Table 1. The overall mean SA was 148° (SD 5.6). Girls had a statistically higher value at 149° (SD 5.4) compared to boys at 147° (SD 5.6), $P = 0.04$. The mean SA showed no significant difference with respect to the right and left knee. The left knees showed statistically significantly higher values than the right knees with respect to the following parameters: MCH, SH, PL, and PTL and near significantly higher values regarding LCH. The trochlea of girls showed statistically significantly lower values with

Table 2. Intra-observer and inter-observer differential values (Diff. val.) of Examiner 1 (Ex1) and Examiner 2 (Ex2) together with the repeatability and coefficient of variation (Coeff. of variation).

	Diff. val. Ex1 Mean (SD)	Diff. val. Ex1 − Ex2 Mean (SD)	Intra-observer repeatability	Inter-observer repeatability	Coeff. of variation	
					Ex1	Ex2
Sulcus angle (°)	−1 (2.5)	0 (2.1)	4.3	4.3	3.09	2.92
Medial condyl height (mm)	−0.1 (0.4)	−0.3 (0.6)	0.84	1.24	6.26	5.76
Lateral condyl height (mm)	−0.1 (0.6)	−0.1 (0.6)	1.16	1.19	5.89	6.12
Sulcus height (mm)	−0.2 (0.4)	−0.3 (0.5)	0.78	1.02	6.37	5.76
Trochlear depth (mm)	0.0 (0.2)	0 (0.3)	0.46	0.54	24.46	19.56
Trochlear area (mm^2)	0.3 (2.8)	−0.4 (2.5)	5.56	4.92	27.62	27.94
Patellar length (mm)	−0.3 (1.1)	0.7 (1.1)	2.29	2.16	6.80	6.88
Patellar tendon length (mm)	−0.2 (1.4)	0.3 (1.3)	2.77	2.70	8.90	7.23

regard to TD, TA, and TI. The correlation between SA and gestational age was 0.06, $P = 0.58$. The femoral SA, TI, and TA showed no correlation to the weight and length of the newborn (Fig. 5).

Intra-observer and inter-observer repeatability study

The same set of parameters as obtained in the main study was validated herein. The intra- and inter-observer differences together with the repeatability and coefficient of variation are presented in Table 2. Regarding the interpretation of the intra- and inter-observer repeatability, a low value represents a high repeatability. The "coefficient of variation" gives an indication of the natural variation of the parameters. Possible relationships between magnitude and differences for both intra- and inter-observer measurements were investigated by Bland-Altman plot. No relationship was found based on visual inspection of the plots.

Discussion

Knowledge of the natural anatomical variances in the knee joint is needed to identify trochlear dysplasia in newborns. The applicability of ultrasonography when examining knee joints in newborns should also be examined. Both of these questions were addressed in the present study.

A thorough review of recent literature did not reveal trochlear limits defining trochlear dysplasia in newborns. Based on our findings we present suggestions of the limits defining dysplasia. We must emphasize that these limits are regarded as estimates. Further studies on other populations and also on larger populations are needed to define the limits more robustly.

We found small but statistically significant differences between the sexes for several of the selected parameters but we do not believe the differences are of clinical importance. Consequently, the same limits defining dysplasia were set for both sexes.

Naturally, the dimensions of the newborn skeleton vary. Intuitively, angular data should be independent of the size of the skeleton. In a non-dysplastic knee, the femoral SA is easy to measure because the measurement points, which are placed at the most ventral locations on the medial and lateral joint surface, are easy definable. In a dysplastic knee, the contour of the joint line smoothens. The femoral SA will become more difficult to measure when the dysplasia becomes significant. The reciprocal placement of the measurement points will influence the value of the femoral SA (Fig. 7a, c). On the other hand, the medial and lateral condyle height together with the SH will not be influenced to the same extent. We wanted to see whether an index made from these measurements, named the Trochlear Index (TI), might be a more appropriate parameter of dysplasia. As the SA, the TI should be independent of the weight and the length of the newborn, which was confirmed by our results.

Hypoplasia of the medial facet is commonly seen in dysplasia of the femoral trochlea. This hypoplasia results in a shallow trochlea with inadequate support for the patella. Occasionally the SA is almost unaffected by this hypoplasia because the slope of the facet is normal. In this situation, the stability of the patella is reduced. Trying to produce a more consistent parameter that mirrors this dysplasia, we introduced the TA (Fig. 7a and b). In the process of choosing the most reliable parameters for validating the femoral sulcus, we searched for those having a low "coefficient of variation" combined with low intra- and inter-observer repeatability. The parameters should also be easy to record and to interpret intuitively. Of all the different parameters, the SA was the one with the best correlation with dysplasia. The MCH, LCH, and SH all have a low "coefficient of variation" and good repeatability

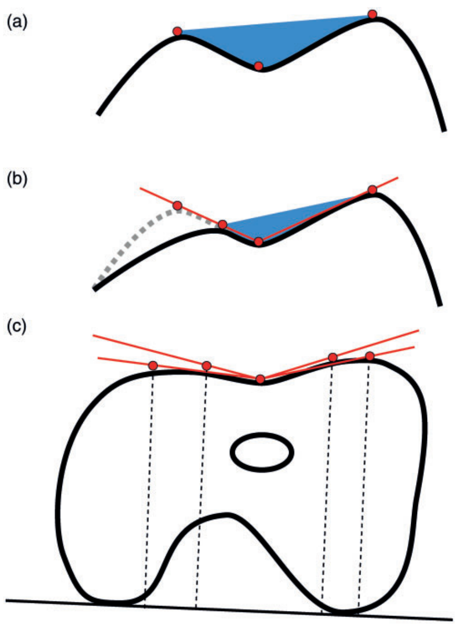

Fig. 7. (a) A normal femoral trochlea with easily definable measurement points representing the most ventral locations on the medial and lateral joint surface and the bottom of the sulcus. Both the SA and the TA are simple to define. Hypoplasia of the medial facet, as in (b), might give a shallow trochlea femoris without altering the SA. Theoretically, the TA as a parameter would be better suited to differentiate a dysplastic trochlea from a normal one. (c) illustrates that, in a severely dysplastic trochlea, it might be difficult to define the measurement points. This might give a SA that is difficult to reproduce whereas the TI, defined as the sum of the height of the condyles divided by the height of the sulcus, would not be influenced in the same way.

but all lack an intuitive interpretation. They are not suitable to describe the anatomy of the trochlea on their own but together, they may be used to calculate the TI, providing an index that has acceptable variation, repeatability and ease of interpretation. Both the TD and TA showed high variation making them less useful to describe the trochlea.

The measurements regarding the position of the patella, the PL and PTL, showed good results regarding "coefficient of variation" and repeatability. The Insall-Salvati Ratio (16) is the ratio of the length of the patellar tendon to the length of the patella and calculation of this ratio seems reliable using ultrasonography measurements.

Traditionally, the patellofemoral joint in the skeletally mature has been visualized using the Merchant view. As the dysplasia is mainly in the ventral and proximal part of the femoral trochlea, only 65% of the trochlear dysplasia is diagnosed by this method (Fig. 8) (6). Ultrasonography as a method for examining articular cartilage in the hip joint has been described previously (17). It has also been used to examine patellar tracking and the femoral sulcus in children (7,18).

In the present study, the ventral area of the femoral trochlea that was examined corresponds to the area examined by Nietosvaara in 1994 in his ultrasonographic study of the femoral sulcus in children (7) giving us comparable reference values. Nietosvaara examined 100 knees of patients from 0 to 18 years of age, and found the SA to vary between 134° and 155° with a mean of 146° (SD 3.7). Mizobuchi et al. reported a mean SA of 148.9° (SD 6.2) ranging from 148.7° to 149.3° in an ultrasonographic study of 40 infants up to 2 years of age (8).

We found the mean SA to be higher among girls compared to boys. Seventeen of the knees in 14 of our newborns had a SA >159°. Three of the children had bilateral high SA. High scores were equally distributed between girls and boys: seven of the girls (two with bilateral high SA) and seven of the boys (one with bilateral high SA).

When a child experiences a patellar dislocation for the first time, the chance of the child being a girl is 52% (1). Girls are more vulnerable to chronic instability constituting 70% of the group with one or more dislocations. Trochlear dysplasia is one of the main predisposing factors of patellofemoral instability. Girls are also more vulnerable to other instability factors such as genu valgum and hypermobility of the knee. Patella alta, a high tibial tuberosity-trochlear groove distance (TTTG), and rotational deformities are factors that might be influenced by gender. Our results indicate that the increased risk for girls with respect to chronic instability of the patellofemoral joint might be influenced by instability factors other than trochlear dysplasias.

The knees of the boys were larger than those of the girls. The boys in our population were in general 100 g heavier and 5 mm longer than the girls. However, these differences were not statistically significant. We found the left knee to have somewhat greater dimensions compared to the right knee. Anthropometric measurements of the pelvis and the foot have shown the left side to be larger than the right (19), as with our findings for the knee.

The mean TI of the newborns was 2.21, and 11 newborns had a TI ≤2.11. A lower value for the index indicates a more shallow trochlea. Nine of these were included in the group of 17 newborns with a SA ≥159.0°. The remaining two were in the upper part of the normality range with SAs of 157.9° and 157.0°. Thus, a low TI is indicative of trochlear dysplasia and can be used to define trochlear dysplasia in cases were

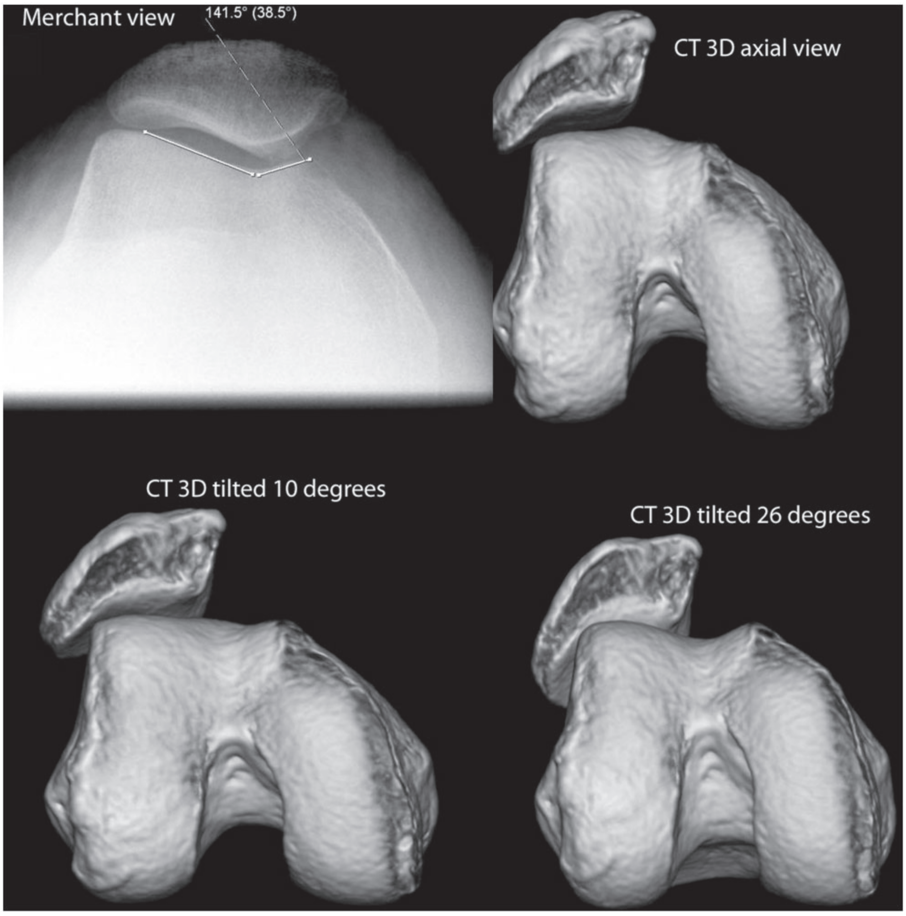

Fig. 8. X-ray (Merchant view) and CT scan of the knee of a 17-year-old girl with chronic patellofemoral instability caused by dysplasia of the femoral trochlea. A Merchant view is obtained from axial radiographs taken with the knee in 45° flexion and with the X-ray beam angled at 30° from the horizontal position. A sky-line view of the patella and trochlea femoris is obtained. A sulcus angle greater than 145° indicates dysplasia. As illustrated, the Merchant view misses the dysplasia of the proximal part of the trochlea. The axial 3D views show the full magnitude of the dysplasia. This illustrates the importance of examining the trochlea in the ventral area where the patella is at its most vulnerable position for lateral dislocation, when it engages the trochlea at its most ventral part. This supports our decision of where to make our measurements.

the SA is difficult to define. The validation study described the TI to have both a low "coefficient of variation" combined with good intra- and inter-observer repeatability.

A high-riding patella (Patella alta) has been shown to be strongly associated with patellofemoral instability (6). The mean Insall-Salvati Ratio was 0.9 regardless of gender or side. By defining the Insall-Salvati Ratio as PL/PTL, Mizobuchi et al. found the mean Insall-Salvati Ratio to be 1.09 in a population of 40 normal infants aged under 2 years (8). We believe our results to be comparable.

Our SA threshold at 159° is well outside the limits defined by other authors. Nietosvaara measured the cartilaginous SA in the most ventral part of the trochlea in 33 children with patellar dislocation and found it to lie between 154° and 195° compared to between 134° and 153° in the normal control group (20).

When comparing results from different studies of children and adults, other authors assume that the femoral trochlea maintains its shape during growth. These assumptions are based on studies where few if any newborns were included. In dysplasia of the hip, we know that substantial re-modulation of the joint may occur during infancy. When the forces acting upon the cartilage are directed against and balanced around the center of the acetabulum, a normal stable joint may develop from a dysplastic situation. Therefore, it could be important to investigate a possible similarity between the patellofemoral joint and the hip joint in respect to modulation and re-modulation.

A limitation of our study is that our examination of the femoral trochlea in a newborn population employing ultrasonography is executed at a single hospital by few examiners in a relatively small population and should therefore be regarded as an initial study. Our thesis should therefore be tested at other centers and in other and larger populations to define the reference intervals more robustly.

In conclusion, knowing the characteristics of a normal *versus* a dysplastic newborn trochlea and being able to differentiate between them gives us the opportunity to study the predisposing factors and possible treatment modalities. Of all the different parameters investigated, the SA had the best correlation with dysplasia.

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Paper II

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Paper III

Minor change in the sulcus angle during the first six years of life: a prospective study of the femoral trochlea development in dysplastic and normal knees.

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Abstract

Aims: The aim of this prospective cohort study was to describe the femoral trochlear development in a newborn population during the first 6 years of life.

Patients and Methods: In an earlier study, the femoral trochlea was examined by ultrasound in 174 newborns. A dysplastic trochlea was defined with a sulcus angle (SA) above 159°. Two groups were defined, one group of 15 knees with SA > 159° (dysplastic group), and one group of 101 knees with SA < 159° (non-dysplastic group). In the present follow-up study, the children were further examined at 6, 18, and 72 months.

Results: There was a statistically significant difference in the SA between the dysplastic and the non-dysplastic group at all follow-ups ($p < 0.001$). A small but statistical significant change in the SA between 0 to 72 months was detected for the dysplastic knees ($p = 0.03$) and for the controls ($p \leq 0.001$).

Conclusion: A dysplastic trochlea at birth remains shallow and a trochlea with normal SA angle does not seem to develop dysplasia.

Take home message:

- Congenital dysplasia of the femoral trochlea seems to persist until at least 6 years of life.

- The anatomy of the femoral trochlea doesn`t change from normal to dysplastic during the same time span.

Introduction

Instability of the patellofemoral joint usually presents with discomfort or anterior knee pain most frequently in the second decade of life. A patellar dislocation may be the initiating event, followed by recurrent patellar instability in up to 48% of patients (1). Ailments from patellar instability among children and adolescents are common (2). Although the predisposing anatomical factors that may cause patellar instability are defined (3), the etiology remains unclear. It is being increasingly recognized by orthopedic surgeons that trochlear dysplasia is one of the main factors causing patellar instability (4, 5); Dejour et al. found such dysplasia in 96% of 143 patients operated for patellar instability (6).

The geometry of the neonatal trochlea has been described (7), and ultrasonography has proven to be a reliable and safe method for examination of the patellofemoral joint (7, 8). The shape seems to be comparable with the anatomy later in life (9). A high sulcus angle (SA) indicating a flat or dysplastic trochlea has been found in newborns (10). Breech presentation with extended knees appears to be a major risk factor of trochlear dysplasia, particularly frank breech with the knees locked in extension.

Significant efforts are made to diagnose and treat developmental dysplasia of the hip (DDH). Correct positioning of the femoral head in the acetabulum is crucial for normal development of the joint. Our knowledge of the potential for re-modulation of this joint during infancy may also be applied to the newborn patellofemoral joint (11), and hopefully, as is true for the hip joint, there exists an opportunity for early non-surgical treatment of trochlear dysplasia.

The formation of the patellofemoral joint in early embryonal life between 4 and 10 weeks has been described by Doskocil (12). The later embryonal development has been published by Glard et al (9, 13). All studies have found the trochlear sulcus to be defined at an early stage and postulated a theory of a genetic determinant to the initial shape of the trochlea.

Although Nietosvaara performed ultrasonographic examinations of the femoral trochlea in 50 children (14), data of its development during the first years of life is very sparse.

Knowledge of the natural history of trochlear development during early childhood seems important in order to understand the underlying causes for trochlear dysplasia. There is uncertainty whether this dysplasia will be permanent with the potential to cause patellar instability later in life or if it modulates to a normal trochlea during infancy. The aim of this study was, therefore, to determine whether SA measurements changed during the first 6 years of life.

Materials and Methods

The basis for the present prospective cohort study was the population of our former explorative cohort study in which both knees of 174 newborns had been examined by ultrasonography within 3 days after birth (7). As we had no previous information needed for sample size calculations, the size of our population was intuitively decided to be comprised of newborns admitted to one out of three neonatal wards at the University Hospital of Trondheim over a period of 2 months. Different parameters to describe the trochlear anatomy and to detect trochlear dysplasia were investigated (7). The sulcus angle (SA) seemed to be the best parameter, owing to its ease of recording and interpretation. Limits defining trochlear dysplasia in newborns do not exist. Based on the findings in the explorative cohort study, the most intuitive way to define the threshold of a pathologic high SA, was by adding 2 SDs to our population mean SA of 148°, resulting in a dysplastic threshold value of 159°. This defined 17 as dysplastic- and 331 as non-dysplastic knees.

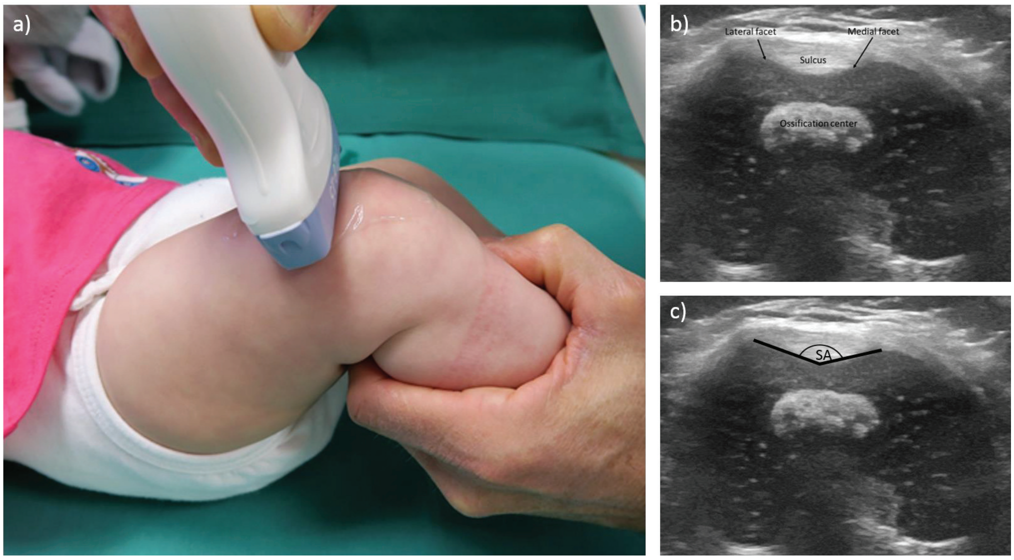
The present study is about follow-up of 58 of the 174 children. The 17 dysplastic knees were scheduled for follow-up examinations together with a control group of 101 non-dysplastic knees comprised of patients with knees holding a SA closest to the population mean of 148°. If the contralateral knees to the dysplastic knees were classified as non-dysplastic, these were included as controls as the statistical methods adjusted for bilateral coherence. Three follow-up examinations were scheduled: The first after 6 months before the possible influence of weight bearing; the second at 18 months, after the start of weight bearing; and the last examination, just before 6 years of age to evaluate whether the shape of the femoral trochlea changes during childhood.

Both knees of all newborns had been examined within 3 days of birth by one examiner (7). The follow-up examinations were performed in collaboration with a second examiner using the same procedure. The examiners were blinded with respect to the name, birth presentation, and previous clinical findings of the children.

Ultrasonography

The ultrasonographic examination of the knees was conducted with the children in bed or on the examination table in the supine position, as described in detail in a previous study (7). Two ultrasound scanners were used due to the need of parallel examinations by two examiners. A GE Logiq Book XP with linear GE 8L probe and a GE Logiq 7 with linear GE 10L probe, both GE Medical Systems Co., Jiangsu, China. The patella was positioned in the distal part of the trochlea by flexing the knee over 45°. By holding the transducer in a transverse plane perpendicular to the axis of the femoral axis levelled at the most ventral point of the lateral facet, images of the femoral trochlea were obtained. The ossification center of the distal femur should be visualized, ensuring correct perpendicular angulation of the probe (Figure 1).

Figure 1 Ultrasonographic examination of the femoral trochlea. a) The UL probe is held perpendicular to the femoral axis levelled at the most ventral point of the lateral facet, obtaining a transverse image of the femoral trochlea (b). c) The sulcus angle (SA) is shown. The images are produced for illustration of the technique, the child is 4 months old and not a participant of the study.



The cartilaginous SA, which is the closed angle defined by the intersection of the lines parallel to the articular cartilage of the medial and lateral femoral facet, was measured.

Participants lost to follow-up

Details of the number of participants during follow-up are given in Table 1. One participant with dysplasia of both knees was lost for all follow-ups and was not eligible. At 72 months, approximately 20% of the knees were lost to follow-up in both groups. Being settled far away was the prime reason to decline follow-up. All the participants that originally were chosen to follow were invited at all the follow-up examinations.

Statistics:

All statistical calculations were made using IBM SPSS Statistics for Windows version 23. Visual inspection of Q-Q plots was used to describe whether data were normally distributed. The SA measurements were normally distributed.

Knees were dichotomized into a dysplastic group (SA ≥ 159°) and a non-dysplastic dysplastic group (SA < 159°) based on the SA measurements at birth. In a sub-analysis, a new dichotomization was performed—a dysplastic group (SA ≥ 155°) or a non-dysplastic dysplastic group (SA <155°). Generalized mixed linear models were used when analyzing the SA angle to account for data dependency caused by knees nested within children together with repeated measures (four-time points, AR (1) covariance structure). Fixed effects were "group," "time," and “group*time.” The residuals in the models were normally distributed. A figure presents plots of the model estimates. Bonferroni-adjusted significant levels are reported. The significance level was set at $p < 0.05$.

Ethics, registration, funding, and potential conflicts of interest:

The study was approved by the Regional Committees for Medical and Health Research Ethics (REC) 2010/160-1 and 2010/160-4 (doc-id: 689468). Written information of the study was provided to all parents who gave written consent to participate in the study. The study received grants from The Norwegian Orthopaedic Association in 2010 and from The Research Foundation of Unimed (#97191) in 2011. No competing interests declared.

Results:

The number of knees at the follow-ups together with descriptive statistics are presented in Table 1.

Table 1. The mean SA displayed with SD and range for both the dysplastic and non-dysplastic group. The number of the knees at 0, 6, 18 and 72 months follow-up are presented. n represents the number of knees examined at the different follow-ups.

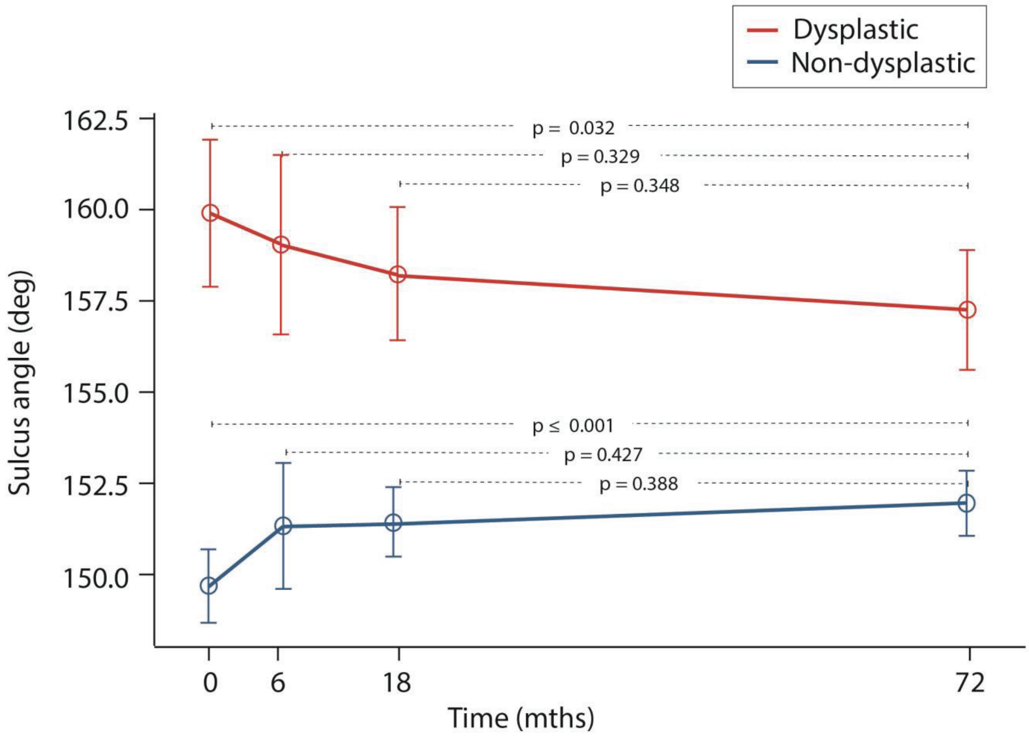
Follow-up (months)	SA							
	Dysplastic group				Non-dysplastic group			
	n	mean	sd	range	n	mean	sd	range
0	15	161.0	2.4	159.2-168.6	101	149.5	4.6	140.2-158.8
6	14	160.0	3.9	154.0-168.1	56	150.0	5.5	131.0-165.1
18	10	158.5	2.4	154.2-161.2	86	151.2	3.8	145.6-159.9
72	12	158.3	3.3	153.0-164.0	80	151.6	3.8	144.0-161.0

The overall SA across all follow-ups was 158.6 degrees in the dysplastic- and 151.1 degrees in the non-dysplastic group holding a statistical significant difference of 7.5 degrees ($p < 0.001$).

The difference between the two groups was statistical significant at all follow-ups ($p = 0.03$ for the dysplastic group, $p \leq 0.001$ for the non-dysplastic group).

The SA differences within the groups, between follow-ups, are presented in Figure 3.

Figure 2. Graphical presentation of the SA. The threshold for dysplasia ≥159°.



For both the dysplastic and the non-dysplastic group, a small but statistical significant change in the SA between 0 to 72 months was detected.

Discussion

The main finding of this study shows that there is minor change in the trochlear sulcus angle from newborn to age 6 years. A shallow trochlea at birth with SA measurements consistent with adult dysplasia, remained shallow during the first 6 years of growth. Ultrasonography as a method for examining the femoral trochlea in infants has been evaluated in an intra-observer and inter-observer repeatability study (7). Ultrasonographic imaging is reliable and is the only method that is ethically accepted for use in infants and children. Our measurements are comparable with other studies using the same examination technique (8, 14).

The anatomy of the femoral trochlea is a vital determinant of patellofemoral joint stability. Even so, there is no agreement regarding factors that influence the shaping of the joint surface. The development of the joint in utero has been described by Doskocil in 1985 (12) and Glard et al. in 2005 (9, 13). Doskocil studied the femoral trochlea in 14 joints of embryos aged 4–10 weeks and described an asymmetric trochlea where the lateral facet was larger than the medial. He postulated that the shape of the joint was genetically determined early *in utero*, but influences of mechanical forces later in the intrauterine environment could cause remodeling. Glard performed a biometric study of the femoral trochlea in 44 fetuses aged 13–38 weeks and compared their findings with similar studies on adults. No significant differences were determined, which implied a genetically determined anatomy of the femoral trochlea.

Nietosvaara (14) conducted ultrasonographic examinations of 50 normal children from birth to 18 years and measured the SA between 134° and 155° at all ages. He found the femoral sulcus to be well developed early in life, and the SA stayed virtually constant during the growth phase. By assessment of the plots, only a few individuals seem to be under 1 year of age, consequently congenital dysplasia is probably missed and the trochlear development through infancy still unknown.

On the contrary, anthropologic studies of human development show that the femur undergoes morphological changes during infantile and adolescent growth (15, 16). A shift from a vertical to an oblique femur relative to the knee joint line takes place during infantile and early growth. Later, with adolescent growth, a remodeling of the distal femur epiphysis takes place with deepening of the trochlea and increased protuberance of the lateral facet. The authors predict these morphological changes to the femur and knee to be acquired owing to transition to an upright posture, rather than being genetically determined.

In the literature, others have defined 155° as the dysplastic threshold value (6, 14, 17). As our threshold of 159° was higher, we performed a sub-analysis using 155° as the threshold value. The overall SA across all follow-ups was then 156.6 degrees in the dysplastic- and 148.5 degrees in the non-dysplastic group holding a statistical significant difference of 8.1 degrees ($p < 0.001$) with a small statistical significant change in the SA of 1.4° in the dysplastic- ($p < 0.001$) and 2.2° in the non-dysplastic group ($p < 0.001$) between 0 to 72 months. The difference between the groups was statistical significant at all follow-ups ($p < 0.001$). The changes in SA were similar to those found using 159° as threshold.

The effects of the patella on shaping the femoral trochlea has been investigated in rabbits showing flattening of the groove during growth with an inadequate position of the patella (18). Early reduction seems to prevent dysplasia development (19). These studies indicate that the immature skeleton is influenced and molded by the forces acting upon it. Expectantly, the possible molding effects that growth and increasing activity might afflict on the trochlear anatomy should result in gradual equalization of the SA. However, our findings indicate that after 6 years, there is still a significant difference in the SAs between those being born with a high SA and the normal controls. A small shift towards equalization of the SA between the groups do seem to occur, which take place during the first 18 months of life.

Today, we have knowledge of the hip joint and its potential for re-modulation during infancy (11). Correct positioning of the femoral head in the acetabulum is crucial for normal development of the joint, and treatment when hip instability has been detected is based on achieving and maintaining this correct position. Intuitively, a correct position and tracking of the patella might be essential for developing a normal trochlear groove. If no initiative is taken to correct a maltracking patella, a child born with a tendency towards trochlear dysplasia may have the condition persisting at least for the first 6 years of life and possibly result in instability of the patellofemoral joint later in life.

A child born in the frank breech position have a significantly higher risk of a shallow or flat trochlea (10). Breech positions seem to be a common risk factor for trochlear and hip dysplasia, and both conditions can be detected by ultrasonography. Since the dysplastic appearance does not change during the first 6 years of childhood, the dysplasia found at birth might cause instability of the patellofemoral joint. Consequently, one should consider efforts to detect and treat trochlear dysplasia early in life, comparable with existing procedures to treat developmental dysplasia of the hip. This topic should be further studied. Intuitively, as breech presentation appears to be a risk factor for congenital dysplasia, a connection between breech presentation and patellofemoral instability should be explored.

Strengths and limitations:

The strength of the study is the prospective cohort design. This study seems to be the first prospective study published covering the development of the femoral trochlea. The limitations include our definition of trochlear dysplasia in newborns which has not been evaluated by others. The limits defining dysplasia should be regarded as estimates. Also, the number of knees included in the follow-ups are small. To make the dysplasia definition and description of changes in SA more robust, further studies including larger population are needed.

Future perspectives:

We do believe that at least a type of trochlear dysplasia is congenital. Intuitively, the dysplasia found at birth might cause instability of the patellofemoral joint later in life. As breech presentation appears to be a risk factor for congenital dysplasia, a connection between breech presentation and patellofemoral instability should be explored.

Summary:

In this prospective study of femoral trochlea development in dysplastic and normal knees, only minor changes in the sulcus angle from newborn to age 6 years are found. Indication of developmental trochlear dysplasia was found among newborn children A shallow trochlea in a newborn child remains dysplastic during the first 6 years of life. Children born with a normally shaped trochlea seem to not develop a shallow trochlea during the same time span.

Contribution of authors

All the authors contributed to the design of the study. CRØ and KJH collected data. OAF performed the statistical analyses. CRØ drafted the manuscript, and KJH and OAF contributed with editing and design of figures and tables.

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