Cruciate ligament rupture and the role of radiological knee shape

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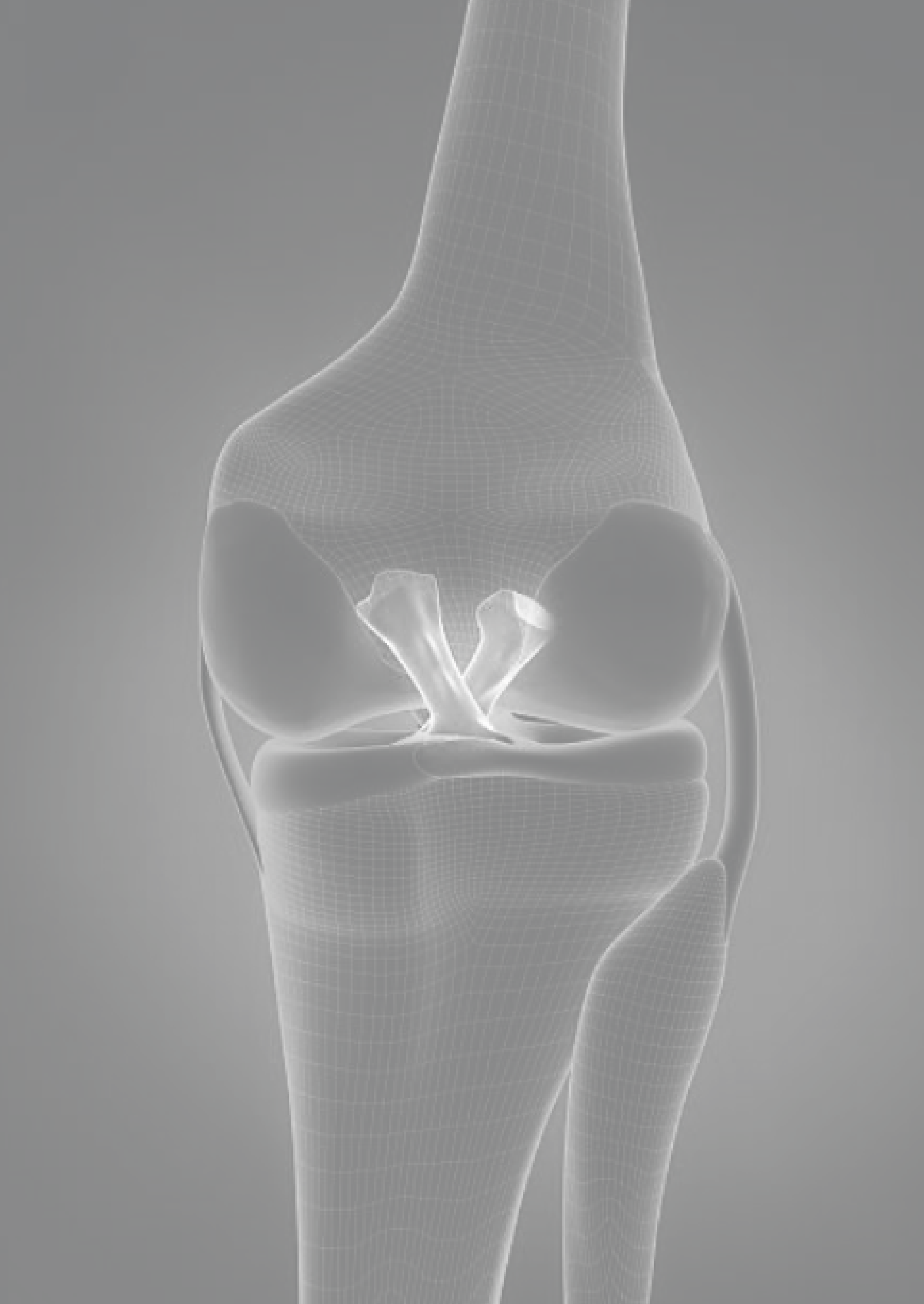
TABLE OF CONTENTS



Chapter 1

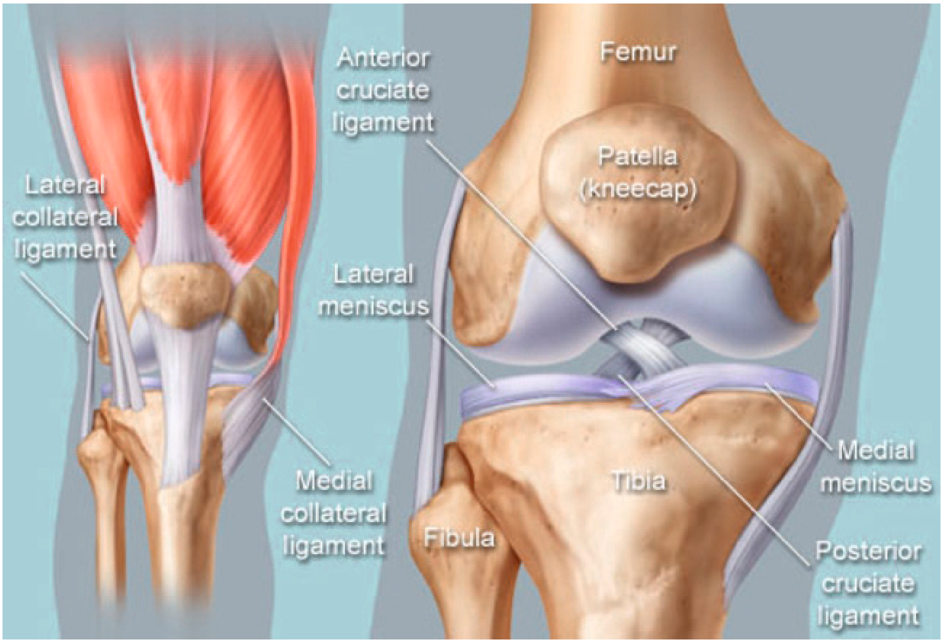
General introduction

When looking at a human being, one of the first things noticeable is that we all look the same as a species, but we all have our unique characteristics. We all have two eyes, a nose, and a mouth; however, we can immediately distinguish one from another. We are all different in size, different in shape, and thus different in how we look. This is used daily to recognize familiar faces, but this is also used in for example facial recognition programs. These differences continue when looking at the inside. Our bones make up the most characteristic shapes of our bodies. This must mean that our bones are also very different from each other on the inside. When our bones are different from one another, this means that the soft tissues surrounding them are also very different. With this in mind, I started the studies in this thesis with the use of software originally developed for facial recognition. Focusing on the shape of the knee, both the bones and the soft tissues within the knee, known as the cruciate ligaments. Before you start reading the chapters, it is good to know the basic anatomy of the knee joint, and the function of the cruciate ligaments.

I THE KNEE: BASIC ANATOMY AND IMAGING

Gross anatomy

The knee joint is a synovial joint, which connects the femur, the longest bone in the body, to the tibia. There are two main joints in the knee: 1) the tibiofemoral joint, where the tibia meets the femur 2) the patellofemoral joint, where the patella meets the femur.



These two joints work together to form a modified hinge joint that allows the knee to flex and extend, but also to rotate slightly from side to side (1). To maintain a stable joint, the knee is a complex joint not only consisting of bones but also ligaments, cartilage, menisci, muscles, tendons, bursae, and plicae. There are four bones around the knee: the femur, the tibia, the patella, and the fibula. The round prominence on the inner part of the knee is known as the medial condyle, and the round prominence on the outer part of the knee is called the lateral condyle. The space between those two condyles is the intercondylar notch. The intercondylar notch helps to stabilize the knee joint. The reason why this groove at the bottom rear of the femur helps to stabilize the knee joint is that it is home to several ligaments of the knee, which will be discussed later.

Imaging

Imaging the knee is essential in diagnosing knee pathology. Different types of imaging modalities are used for different clinical indications. For this thesis, I will describe the modalities that we used in our research, the conventional radiograph and magnetic resonance imaging (MRI).

Radiograph

Indication and technique.

X-rays (Rontgen radiographs) of the knee joint are requested frequently, particularly at the Emergency department. They are used primarily to confirm/exclude a fracture or to assess the level of osteoarthritis in the knee joints (= gonarthrosis). To establish the presence of a fracture, the knee should be imaged in at least two directions. A standard examination includes an anterior-posterior image and a lateral image. Additional directions may be added when indicated, for example, the Rosenberg view (2). The most commonly used examinations are explained below.

AP and Rosenberg view image

The front-to-back or anterior-posterior knee image can be made in both supine and standing positions (fig. 1 & 2). In the supine position, the X-rays pass through the knee from anterior to posterior (= AP image). An alternative to the supine position is the standing AP image. The knee is fully extended and imaged in the craniocaudal direction under a 10° angle. Additionally, a standing posterior-anterior image (= PA image) may be opted for, also known as the Rosenberg method. In the Rosenberg method, knees should be flexed at 45° (fig. 2).

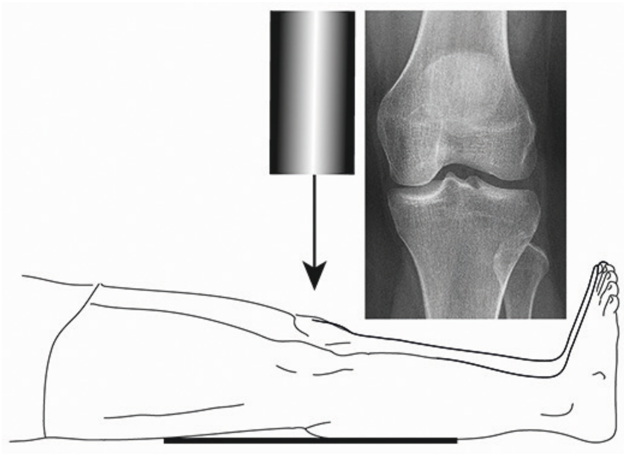


Figure 1. Technique for supine anterior-posterior (AP) image.

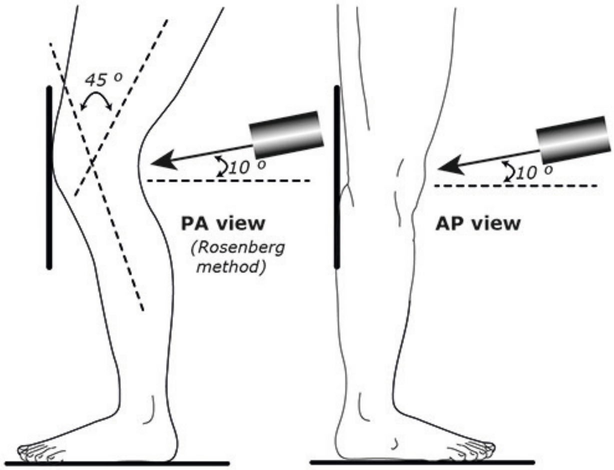


Figure 2. Technique for standing Rosenberg view image and standing anterior-posterior (AP) image.

Lateral image

Lateral images are made in the supine position with the knee flexed to 30°. The X-rays pass through the knee joint from medial to lateral (fig. 3). In a good lateral image, the medial and lateral femoral condyles project over each other, and the patellofemoral joint is projected free.

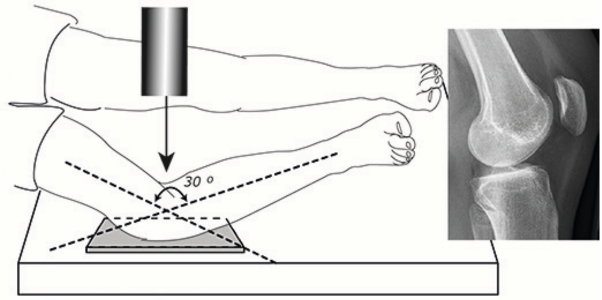


Figure 3. Technique for lateral image of the right knee (mediolateral projection).

MRI

MRI has been widely used to image internal derangements of the knee (3). Especially soft tissues can be assessed excellent with this modality. Ligament ruptures, meniscus tears, and bone bruises are some of the most diagnosed on MRI. To obtain images of good quality, a dedicated extremity coil should be used (as can be seen in figure 4). A field of view of appropriate size should be used to maximize the resolution, typically 16 cm. Slice thickness can be 1-4 mm, with a small interslice gap, not exceeding 0.4 mm, to reduce partial volume artifacts. The knee should ideally be imaged in 3 orthogonal planes: sagittal, coronal, and axial (figure 5). The patient lies supine in the scanner, with the knee relaxed and in slight external rotation (5-10 degrees). This enables the ACL to be orthogonal to the sagittal plane of imaging.

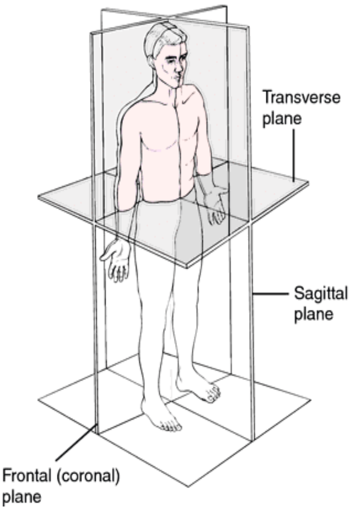


Figure 4. MRI of the knee with the knee in an extremity coil. **Figure 5** the orthogonal planes

MRI sequences.

To differentiate between normal anatomy and pathology, contrast differences are required. Contrast is best when two areas next to each other have a low and high signal intensity. There are many (>100) MRI sequences, and all these sequences try to give a large contrast between structures. The exact mechanism of MRI goes beyond the content of this thesis.

II THE NORMAL CRUCIATE LIGAMENTS

The first mention of the cruciate ligaments originates from an Egyptian papyrus roll dated around 3000 BC. Hippocrates described the typical subluxation of the knee joint caused by cruciate ligament deficiency around 460–370 BC. It is believed that Claudius Galen von Pergamon (129–199 BC) is responsible for the naming of the cruciate ligaments, calling them “ligament genu cruciata.” The first English detailed description of cruciate ligament anatomy, biomechanics, and injury pattern was presented by I. Palmer in 1938 (4).

Macroscopic anatomy

The anterior cruciate ligament (ACL) and the posterior cruciate ligament (PCL) are located centrally in the knee joint. These ligaments connect the femur to the tibia and play a crucial stabilizing role. The ACL restrains the anterior translation (forward movement) of the tibia relative to the femur. The PCL restrains posterior translation (backward movement) of the tibia relative to the femur. Both are also important for varus/valgus (sideward) and rotational stability of the knee joint during movement (5). The ACL extends from the anteromedial aspect of the tibia toward the posterolateral area of the lateral femoral condyle. The PCL arises from the posterior tibia and moves anteromedial behind the ACL to the lateral surface of the medial femoral condyle (6). The bony stability of the knee is not enough for maintaining a stable joint (7). The ACL and the PCL facilitate an elaborate interaction with the medial and lateral structures, the menisci and bony anatomy of the patella, and the tibiofemoral joint. This enables the knee joint to move in six degrees of freedom (three translational motions: anteroposterior, mediolateral, proximodistal; three rotational motions: flexion-extension, internal-external, abduction-adduction)(8).

ACL functional anatomy

The ACL is composed of 2 functional bundles, the anteromedial (AM) and the posterolateral (PL) bundle (9). Although Amis (10) and Hollis et al. (1) found three different functional structures (AM, intermediate band, PL). The simplified two-bundle model has become the most accepted model and a blueprint for anatomic ACL reconstruction. Both the AM and PL bundles are non-isometric during flexion-extension. They are parallel to each other in the intercondylar notch during extension. During flexion, the AM wraps around the PL bundle (1). The ACL is the primary constraint for anterior tibial translation (49). It limits internal rotation as a secondary stabilizer, mainly in conjunction with the medial collateral ligament and posteromedial structures of the knee joint (11).

PCL functional anatomy

The PCL consists, similarly to the ACL, of two main bundles, the anterolateral and posteromedial bundles (12). Some authors have suggested that the fiber anatomy and behavior may be more complex, consisting of up to four geographical fiber regions. These regions have different functional roles depending on the joint angle and the type of load to which the knee is subjected (13). The PCL is the primary constraint to posterior tibial translation in flexion (11, 12, 14). At 90° the PCL carries 95% of a posteriorly directed load (15), which is reduced to 83% or below with increasing extension (16). A secondary function of the PCL is to constrain external rotation as well as adduction and abduction of the knee joint.

III INJURIES TO THE CRUCIATE LIGAMENTS

ACL injury

Injuries to the ACL are common sports-related injuries, causing both short and long-term complaints of the knee joint. The incidence rate in the general population reaches up to 5-8 per 10.000 persons per year (17-19). These numbers are even higher in professional athletes: 15 to 367 per 10.000 persons (17). The incidence rate in the Netherlands is suspected to be around 1 in 3000 persons per year, resulting in an ACL reconstruction rate of 8500 per year in the Netherlands alone (20). Because of the relatively young patients with an ACL rupture, the mean age is 32 (18), consequences are severe and long-lasting. It results in the short term in pain, instability of the knee, and loss of function of the knee. In long term, 40% of the patients cannot return to their pre-injury sports level (21). In addition, there is almost a tenfold risk of developing osteoarthritis (22-24). These consequences of ACL rupture are resulting in lower quality of life, lower activity level for the patients, and high health care costs (25)

PCL injury

Injuries to the posterior cruciate ligament (PCL) occur in approximately 1% to 4% of all sport-related traumatic knee injuries, depending on the type of sport (26, 27). Non-sport-related incidence of a PCL rupture varies between 1% and 44% of all traumatic knees(28). With the growing number of athletes and a growing number of competitive athletes (29), the absolute number of PCL injuries is growing and will keep on growing in the next couple of years. In the short term, a PCL rupture causes pain and posterior laxity and reduces an individual's ability to take part in sports. In the long term, deficiency of the PCL results in abnormal kinematics and increased contact pressures in the medial and patellofemoral compartments of the knee and may increase strain on the posterolateral knee structures, placing them at risk of subsequent injury (30-32). Long-term studies have found that degenerative changes after PCL injury occur primarily in the medial and patellofemoral compartments (33-37). PCL injuries are still often overlooked during primary check-ups (38), resulting in delayed diagnosis and delayed treatment.

Treatment of cruciate ligament injury

ACL rupture current treatment options.

Whilst surgical interventions have become commonplace for athletic individuals, initial non-operative (conservative) treatments, based on physiotherapy, are used more commonly in the general population (39). ACL reconstruction is primarily performed as an arthroscopic procedure. Of those who undergo surgical reconstruction, 94% are performed within one year of the initial injury (40). Anterior cruciate ligament reconstruction is the predominant method of surgery in current practice and hundreds of thousands of these operations are carried out each year worldwide (41).

Conservative (non-operative) treatment for people with an ACL rupture can include the use of cryotherapy (ice), continuous passive motion (movement of the joint by a machine), restrictive bracing, electrotherapy (muscle stimulation), and exercises aimed at strengthening and balance (41). The use of plaster casts for initial immobilization of the knee is rare nowadays (42).

Rehabilitation regimens used for both treatment options commonly use a three-stage progressive program: acute, recovery, and functional phases (43). The acute stage following injury, or immediately after surgery, aims to restore range of motion and resolve inflammation. The recovery phase is from approximately three to six weeks, to improve lower limb muscle strength and functional stability. Finally, the functional stage of rehabilitation (from six weeks onwards) concentrates on returning the individual to previous levels of activity and decreasing the risk of re-injury (44).

PCL rupture current treatment options.

The appropriate treatment plan for PCL ruptures remains a topic of debate among orthopedic surgeons. Although there is limited evidence regarding the topic, PCL reconstruction is becoming a more common choice for treatment. Many of the studies performed are limited as most are small case series with short-term follow-ups with significant heterogeneity in patients' population and surgical technique. It is still unknown whether reducing PCL laxity with PCL reconstruction, which improves subjective outcomes, will also reduce the risk of secondary osteoarthritis (OA). Although favorable non-operative results have been observed, the long-term consequences of isolated PCL deficiency remain unknown. Boynton and Tietjens (34) have observed deterioration at extended follow-up of non-operative treatment despite good early results.

Shape of the knee as a risk factor for cruciate ligament injury

Cruciate ligament injuries are of great impact on a person's life, and have a significant burden on both the economy and the healthcare system, as you have read above. Preventing cruciate ligament injuries is a topic that had the interest of many researchers. A review done by Eggerding et al. (45) suggested that the shape of the femur, and the intercondylar notch, was related to the need for ACL reconstruction after an ACL rupture. This inspired me to start this thesis, wondering if the shape of the knee was related to the risk of sustaining a cruciate ligament injury. Many studies focused on fixed shape variants(46-52), determined before the start of the study, possibly excluding many other, equally important shape variants. Ideally, a study into finding risk factors is done without a predetermined hypothesis, so all possible shape variants are included in the search. With this in mind, I started using a software, statistical shape modeling, primarily used as facial recognition software, to find shape variants of the knee, possibly related to cruciate ligament injury. This software is a hypothesis-free program that can find shape differences in the knee. Ideally, anatomical risk factors can be used to prevent cruciate ligament injuries. Recently, a number of studies showed that ACL prevention programs work in athletes (53, 54). Finding risk factors can possibly help make these programs more effective.

IV AIMS OF THIS THESIS

The general aim of this thesis is to identify differences in the anatomical shape of the knee and the cruciate ligaments between patients with and patients without a cruciate ligament rupture. These differences can be used in future research for preventing cruciate ligament ruptures. Identifying risk factors for cruciate ligament rupture is the first step if we want to be able to prevent them from happening.

In **chapter 2,** we analyzed the bony morphology of the knee using Statistical shape modeling software. This unique software makes it able to objectively assess (bony) knee shape, hypothesis-free, and search for shape variants between a large group of patients with an ACL rupture, and a large group of control patients. With this method, we can assess the entire shape of the knee and not just predefined measurements.

We repeated the method used in chapter 2 in **chapter 3,** with a different set of patients. We selected a group of patients who had torn their PCL, in comparison to control patients. This is the first research to look into the anatomical risk factors as a predictor for a PCL rupture.

We found several shape variants to be different between patients with an ACL rupture and patients without. To further analyze these differences, we used MRI to assess not only the shape but also the volumes of the ACL, PCL, intercondylar notch, and correlations between the volumes of the cruciate ligaments. In **chapter 4**, we measured the volumes of the ACL, the PCL, the intercondylar notch, the bicondylar width, the notch width, and the notch width index. In a large retrospectively selected group of patients, we compared these measurements between patients with an ACL rupture and a matched group of control patients.

In **Chapter 5** we selected 30 patients with a PCL rupture and matched them to 30 control patients. We compared the volumes of the ACL, the PCL, the intercondylar notch, the bicondylar width, the notch width and, the notch width index. To our knowledge, this has not been investigated before.

Additionally, we were curious to find out, if shape variants found in the knee could not only predict the occurrence also but predict the outcome after ACL reconstruction. We used SSM to assess the shape of the knee and compare these to the functional outcome, after ACL reconstruction. The results of this study can be found in **chapter 6.**

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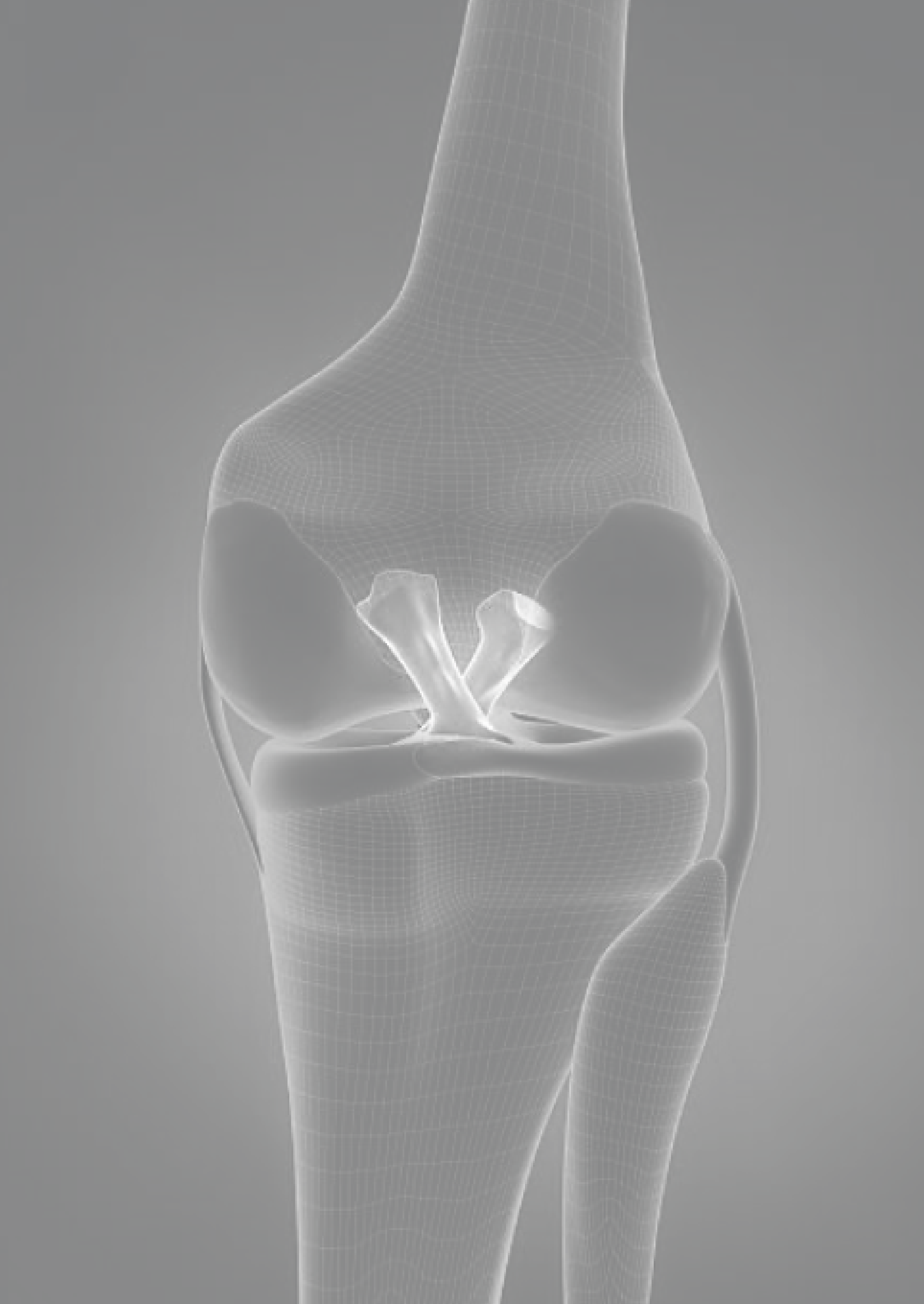

Chapter 2

Differences in Knee Shape between ACL Injured and Non-Injured:
A Matched Case-Control Study of 168 Patients

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ABSTRACT

Objective

Anterior cruciate ligament (ACL) injury prevention programs could be more effective if we could select patients at risk for sustaining an ACL rupture. The purpose of this study is to identify radiographic shape variants of the knee between patients with and patients without an ACL rupture.

Methods

We compared the lateral and Rosenberg view X-rays of 168 prospectively followed patients with a ruptured ACL to a control group with intact ACLs, matched for gender, after knee trauma. We used statistical shape modeling software to examine knee shape and find differences in shape variants between both groups.

Results

In the Rosenberg view X-rays, we found five shape variants to be significantly different between patients with an ACL rupture and patients with an intact ACL but with knee trauma. Overall, patients who had ruptured their ACL had smaller, flatter intercondylar notches, a lower lateral tibia plateau, a lower medial spike of the eminence, and a smaller tibial eminence compared to control patients.

Conclusion

Patients with an ACL rupture have smaller intercondylar notches and smaller tibial eminences in comparison to patients with an intact ACL after knee trauma.

INTRODUCTION

A rupture of the anterior cruciate ligament (ACL) is a common, usually sports-related injury. The annual incidence varies between 5 to 8 per 10,000 persons in the Western population (1-4). Rupture of the ACL has immediate consequences resulting in swelling of the knee and pain, but also long-term consequences, as there is an almost fourfold risk to progress to moderate or severe radiological osteoarthritis after ten years (5). Furthermore, in the young population ACL rupture has a direct impact on sport participation. It has been found, for instance, that after ACL reconstruction 82% of the patients returned to sport participation, however only 63% returned to their preinjury sport level (6, 7). Amongst young patients who return to their pre-trauma sports activity, the prevalence of a re-rupture of their ACL may be as high as 30%.(8, 9). Also, reports show that around 7% of patients need revision ACL surgery and around 3.4% of patients have ACL reconstructions on the contralateral side(10).

This has led to a rise of interest in the mechanism of ACL rupture, risk factors, prevention of ACL rupture, and secondary ACL injury. Neuromuscular and proprioceptive prevention programs have been demonstrated to significantly reduce the prevalence of ACL ruptures in young athletes by approximately 50 % (11-14). However, these prevention programs can be more efficient if they focus on athletes who are at increased risk of sustaining an ACL rupture. Therefore, it is essential to understand the mechanisms that lead to ACL rupture and to identify individuals with an increased risk of ACL rupture.

There is a relationship between shape variants of the knee and the need for reconstruction of the ACL after rupture (15). This has encouraged us to investigate the relationship between the shape and rupture of the ACL more profoundly. Risk factors for ACL rupture can be categorized into anatomical, hormonal, neuro-mechanical, and environmental. In the present study, we focused on osseous anatomical risk factors; Anatomical risk factors have previously been studied with a focus on selected aspects of the anatomical properties of the knee. Anatomical factors that previously have been reported to be related to the risk of ACL rupture are increased tibial slope, decreased femoral notch size, and smaller ACL size (16, 17). With the use of Statistical Shape Modeling (SSM), a hypothesis- generating methodology that identifies independent shape variants, we can quantitatively describe the complete morphology of a bone or joint. SSM reproduces all variation in shape that is present in the studied population. With the use of SSM, we can identify new shape variants of the knee that are clinically relevant in relation to an ACL rupture. Furthermore, it enables us to objectively review shape variants that have been investigated before. Although not all clinicians will have a program like SSM in use, the results of this study can be used in daily practice and can help doctors in selecting patients at greater risk for sustaining an ACL rupture.

SSM has been used earlier by our group to determine whether certain shape aspects are correlated to clinical outcomes after ACL rupture (18). We found that operatively treated patients with good subjective outcomes had a smaller intercondylar notch and a less width intercondylar eminence, as evaluated by The International Knee Documentation Committee (IKDC) questionnaire, compared to patients with worse outcomes. Non-operatively treated patients with good subjective outcomes had a more pyramidal-shaped intercondylar notch.

The purpose of this study is to find radiographic shape variants of the knee between patients with and patients without an ACL rupture, which can be used in daily practice to help select patients with a greater risk of sustaining an ACL rupture.

EXPERIMENTAL SECTION

Cases

We included patients with a ruptured ACL from two previous series: the KNALL (19)and the CAS-ACL study(20).

The KNALL (KNee osteoArthritis anterior cruciate Ligament Lesion) study is a prospective observational follow-up study of 154 patients with a recent ACL rupture, who were treated operatively or non-operatively. Patients were selected from January 2009 to November 2010 and there was a two-year follow-up period. Physical examination and MRI confirmed ACL rupture. Patients were included from three collaborating hospitals.

The CAS-ACL study is a double-blinded randomized controlled trial of 100 patients who underwent ACL reconstruction. In this study, computer-assisted ACL reconstruction was compared to conventional ACL reconstruction (20,21). The inclusion period was from January 2007 to November 2009 with a two-year follow-up period. Of the 254 patients included in the two studies, 183 had both Rosenberg view and lateral view radiographs and were enrolled in the present study.

All patients (both ACL injured as healthy controls) included had a Kellgren & Lawrence grade 0-1 at presentation (no radiological signs of osteoarthritis). Our medical ethics committee (MEC-2006-223 and MEC-2008-068) approved both studies. For the use of the data of control patients, the medical ethics committee ruled that no specific approval was required (MEC-2017-422).

Controls

The control group consisted of patients identified retrospectively from the hospital records. They had consulted a trauma or orthopedic surgeon because of a knee trauma (median of 3 months and a range of 1-60 months between trauma and x-ray) with proven intact ACL on MRI and/or by arthroscopy. Hospital records from January 2003 until July 2013 were searched. Patients were selected for the control group if they had both standard lateral view and Rosenberg view radiographs at the time of the first consult; were practicing sports before the injury and had a Kellgren & Lawrence grade 0-1 at presentation (no radiological signs of osteoarthritis).

Control patients and cases were matched for gender. For age, our patients were matched with a control patient older of age. We chose older control subjects to make sure that the older controls were exposed to pivoting sports for a longer period. This way they were more sufficiently at risk for sustaining an ACL rupture. Of all patients found in the database, 168 control patients were matched to 168 patients with a ruptured ACL. See figure 1. We were unable to match all patients due to younger age since we wanted to only include older control patients. Fifteen control patients were younger than the matches from the ACL ruptured group.

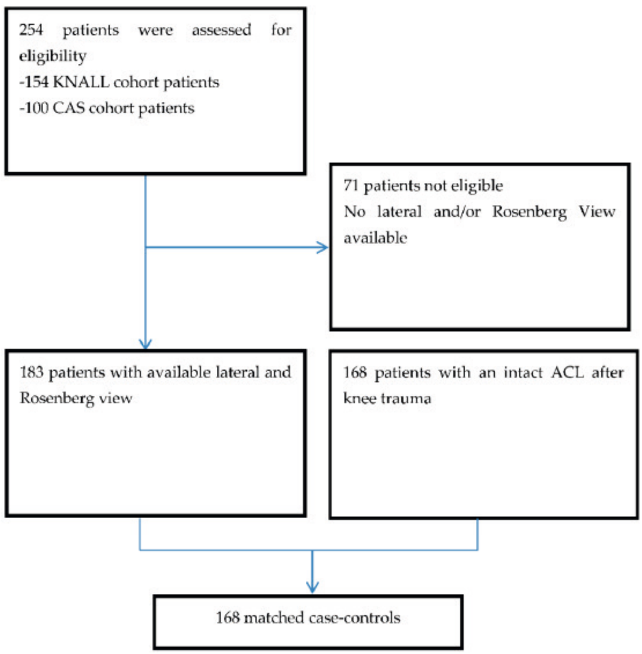

Figure 1. Flowchart of the selected patients included in the study. KNee osteoArthritis anterior cruciate Ligament Lesion (KNALL); Computer Assisted Surgery (CAS).

X-rays and Statistical Shape Modeling

We performed the radiological measurements on standard lateral view x-rays and Rosenberg view x-rays. The Rosenberg view is a weight-bearing postero-anterior radiograph taken at 45 ° flexion of the knee (22). We have chosen to include the Rosenberg view x-rays because it gives a better view of the intercondylar notch and gives better insights into the shape of the femur.

With statistical shape modeling (SSM) (23) it is possible to quantify all shape aspects of the knee joint on the radiographs. This method is unique because it dissects nearly all possible shape variations into a limited number of objectively quantitative measures that each describe a certain shape variant. SSM has been used in studies of a possible association between knee shape variants and osteoarthritis (24). On the radiographs, we outlined the distal femur, the proximal tibia, and the fibula (ASM tool kit, Manchester University, Manchester, UK).

For the lateral view x-rays, the femur and tibia were outlined by 60 landmark points on the bones. For the Rosenberg view, 25 landmark points were necessary to completely outline the bones. Each point was placed in the same location in each image, as exactly as possible, to allow comparison between shapes. For the exact placement of each landmark point, see the addendum. Statistical shape modeling transforms the set of points into a statistical shape model, which comprises several shape variants that together explain 95 % of the variation in the shape of the individual knee of the study population. SSM represents relative variation in shape, independent of differences in the size of the joint. In this way, the method corrects errors caused by variations in magnification or the size of the patient's knee.

Intra-observer reliability was established by randomly selecting 25 Rosenberg view x-rays of patients with a ruptured ACL and 25 Rosenberg view x-rays of patients with an intact ACL which were outlined a second time after 2 weeks.

The description of which shape aspects a variant represents was determined at a consensus meeting. At this consensus meeting an orthopedic surgeon, an expert on SSM, the first authors, and the principal investigator determined the different shape variants.

Statistical analysis

We used logistic regression analysis to study the association between each shape variant and whether or not patients had a ruptured ACL. As the dependent variable, we used whether or not a patient had an ACL rupture (yes or no) and as independent variables, we selected the different variants. We applied Bonferroni correction for multiple testing.

We investigated if there was a significant effect of the x-ray protocol on knee shape, by comparing the shape models of the x-rays taken in the three participating hospitals. Furthermore, we analyzed if correction for age changed the outcomes. All Statistical analyses were performed with IBM SPSS Statistics for Windows (Version 20.0. Armonk, NY: IBM Corp).

RESULTS

Patients

The study population consisted of two groups of 168 patients; each group consisted of 119 males and 49 females. The mean age of the 168 patients after ACL rupture was 31 (± standard deviation (SD) 7,4) years and of the control group 38 (± SD 12) years(Table 1). The diagnoses of the included control patients can be found in table 1, including additional injuries of the ACL ruptured patients. The mean time between trauma and radiograph was 1.0 months for the ACL injured and 6.9 months for the control group.

Table 1. Baseline Demographic Variables.

	ACL injured (n=168)		*Control group (n=168)*	
Age, year	31 ± 7.4		38 ± 12.0	
BMI, kg/m^2	24.5 ± 3.4		24.7 ± 3.2	
Female n (%)	49 (29.1)		49 (29.1)	
Mean time in months between trauma and radiograph	1.0		6.9	
Alternative/additional diagnosis, n (%)				
Medial Meniscus tear	10	(6)	57	(33.9)
Lateral meniscus tear	12	(7)	32	(19)
Cartilage lesion	60	(35)	15	(8.9)
Bone contusion	50	(30)	11	(6.5)
Collateral ligament lesion	0	0	7	(4.2)
No intra-articular lesions	0	0	46	(27.4)

Data are expressed as mean ± standard deviation or as n (%). BMI, body mass index.

SSM

SSM produced 30 variants for the Rosenberg view and 24 variants for the lateral view x-rays. After we applied Bonferroni correction for multiple testing, we considered a p-value of 0.0017 for the Rosenberg view (0.05/30=0.00167) and a p-value of 0.0021 for the lateral view (0.05/24=0.0021) as statistically significant.

2

On the Rosenberg view, five variants were significantly associated with rupture of the ACL (see Table 3). For the lateral view x-rays, none of the variants were statistically significantly associated with rupture of the ACL. For every increase in 1 SD, the OR is given, meaning that if a patient scores 1 SD on a specific variant, the given OR is the odds ratio for sustaining an ACL rupture compared to a patient who scores the mean (0 SD).

Table 3. Shape variants associated with ACL rupture.

	Odds ratio	95% C.I.	Sig.
Variant 1	2.2	(1.7 – 2.8)	.001
Variant 3	1.8	(1.4 - 2.3)	.001
Variant 6	2.1	(1.6 - 2.7)	.001
Variant 10	1.5	(1.2 - 1.8)	.001
Variant 17	1.4	(1.1 – 1.8)	.0015

We analyzed whether the protocols of the x-rays differed in the period in which the x-rays were taken. We did not find a significant difference between the three hospitals, nor did we find a significant difference in time. Correction for age did not alter the outcomes, therefore we did not correct for age.

The intraobserver (ICC) was considered good to excellent with a range of 0.48-0.97 and 89% above 0.7.

Description of the variants

Here we present the description, defined at the consensus meeting, of the variants significantly associated with an ACL rupture. In figure 2, we present the graphics of each variant. On the outside, the +2SD and -2SD variants are shown, in the middle, we present an overlay. Higher variants describe more subtle shape aspects, e.g. the variation in shape represented in shape variant 17 is much more subtle than the variation represented by shape variant 1.

Variant 1

Variant 1 describes a variation in height of the intercondylar notch. Positive values represent a more flattened intercondylar notch. Patients with an ACL rupture had flatter intercondylar notches than control patients.

Variant 3

Variant 3 shows a variation in the width and height of the intercondylar notch. Positive values represent a smaller intercondylar notch. Patients with an ACL rupture had smaller intercondylar notches than control patients.

Variant 6

Variant 6 represents the size of the footprint of the ACL on the tibial eminence. Positive values represent a smaller, flattener tibial eminence. Patients with an ACL rupture had a smaller tibial eminence than control patients.

Variant 10

Variant 10 outlines the footprint of the ACL on the tibia, the width of the tibial eminence, and the width of the intercondylar notch. Positive values represent a smaller tibial eminence and a smaller intercondylar notch. Patients with ACL rupture had a smaller tibial eminence and a smaller intercondylar notch.

Variant 17

Variant 17 depicts a very subtle difference. Positive values represent a lower height of the lateral tibial plateau and a lower medial spike of the tibial eminence. Patients with an ACL rupture had a lower lateral tibia plateau and a lower medial spike of the intercondylar eminence.

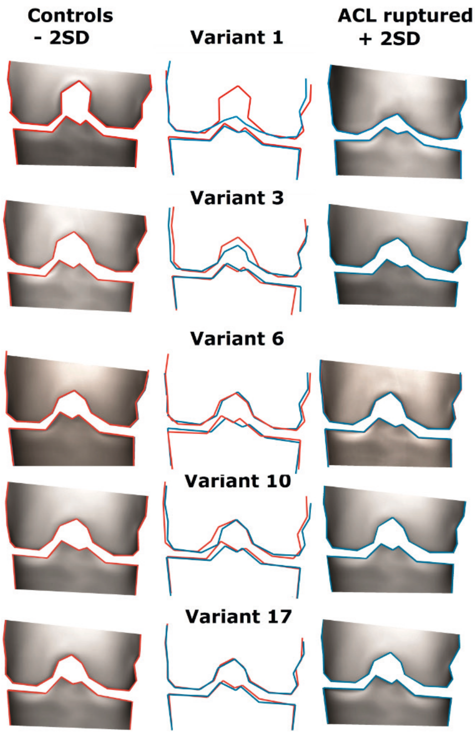

Figure 2. Graphic outcomes of statistic shape modeling: five variants that are significantly different for patients with intact and ruptured ACL. On the left and right sides are the two extremes (+/- 2.5 SD); in the middle is the overlay of both sides. SD = Standard.

DISCUSSION

The most important finding of the present study is that aspects of bony morphology on the Rosenberg view X-ray of the knee joint were different between patients with a ruptured ACL and a matched control group. Our findings indicate that a smaller, flatter intercondylar notch, lower lateral tibia plateau, a lower medial spike of the eminence, and a smaller tibial eminence are more common in patients who ruptured their ACL compared to control patients. Lower body strength exercises (for example Nordic hamstring, lunges, and heel-calf raise) are not performed by all (professional) athletes but have proven to reduce the risk of ACL rupture (25). If we can identify patients at higher risk for ACL injury, injury prevention programs might be even more effective, although this should be confirmed in a different study. Our results could, for example, be used during sports medical screening: Most professional athletes already undergo x-rays of the knee in the medical screening process.

The results of our study are consistent with studies in the past, which also found the notch width index and femoral notch size, related to ACL rupture (26). However, these previously conducted studies were primarily focused on anterior-posterior x-rays, while we used the Rosenberg view x-rays. The study of van Diek et al.(27) found no differences in morphology between patients with an ACL rupture and a control group in measurements with MRI. Though, another MRI study performed by Whitney et al (28) found a decreased femoral notch width to be related to ACL rupture. This was also a case-control study. A smaller femoral notch and smaller tibial eminence are related to a smaller ACL size (29, 30). It is plausible that a smaller ACL could be less strong compared to a larger-sized ACL. The ACL is the main structure to prevent the bony relatively unstable lateral compartment from rotatory dislocation, i.e. rotation anterior of the tibia relative to the femur. The finding of a lower lateral tibia plateau in ACL patients could inspire the theory that these patients have even worse bony stability regarding the lateral compartment, which could be a risk factor for ACL injury.

In the Lateral view x-rays, we did not find an association between shape variants and ACL rupture. Earlier, it has been demonstrated that the femoral condyle configuration (31) and the posterior tibial slope (PTS) (32-34) are related to increased stress on the ACL, but it is not known if this is connected to a higher risk of ACL rupture.

With the results of this study, we can identify individuals with certain shape variants of the knee, who are at greater risk for sustaining an ACL rupture. Because we did not use a predefined hypothesis, the found risk factors are truly objective, whereas other researchers used a predefined hypothesis, potentially excluding numerous risk factors.

These results can be used in daily practice, without the use of our program. Almost all clinicians can view the x-rays of their patients, and thus view the shape of the tibial eminence and the shape of the intercondylar notch.

Screening programs for professional athletes could focus on the intercondylar notch and tibial eminence as risk factors. With our results, screening programs could focus on the found shape variants and include patients with a higher risk of sustaining an ACL in their training programs, potentially making them more effective. In the past, research stated that the tibial slope could also be a determinant for sustaining an ACL rupture. With our hypothesis-free method, we did not find similar results. Excluding potential risk factors is also important because research should focus on risk factors that are more likely to be associated with sustaining ACL rupture

Although the odds ratios are relatively small, all the provided variants show a significant relationship to an ACL rupture, with odds ratios comparable to that of other studies investigating anatomical variants of the knee(16, 27). Further research could focus primarily on the shape variants found in this study and see if these results can be reproduced. Furthermore, prospective studies should be performed to see if, with these risk factors, the prevalence of ACL ruptures could be reduced.

We understand that in the current literature there are already studies using 3D reconstructions of MRIs of the knee. However, our goal was not to confirm previously conducted research but to objectively describe the shape variants of the knee that contribute to the risk of sustaining an ACL rupture. If we would have used MRI, we had already made a hypothesis. Furthermore, 3D reconstructions of the knee are not used in daily practice by every clinician. With the use of x-rays, we are confident that more clinicians can use these results in their practice, without the use of complicated extra software.

A drawback of SSM is that the shape represented by each variant needs to be reviewed personally (which we did in the consensus meeting). SSM does not provide a measurable cut-off point, this should be determined in follow-up studies.

When we examined the different variants in our consensus meeting, we viewed 3D, moving animations of the shape variants, on this animation, the differences are more clearly visible than in 2D images.

We did not perform a power analysis before conducting the study, because we did not know how many shape variants would be found beforehand. Therefore, we used the

Bonferroni correction for multiple testing. Although we understand these are not the same thing, we are confident the method provided is valid and reproducible.

The strength of our study is the use of a large study population of 336 patients, who all practiced sports. One of the advantages of SSM is that the programs scale all differences in the size of the joints, thus reducing variation in magnification and reducing measurement errors. A limitation of our study is the use of older control patients. We used older control patients, to make sure they were sufficiently exposed to rotational trauma. Older patients potentially have more degenerative changes. To make sure this did not affect our outcomes, we chose patients with a K&L score of <1 (no signs of osteoarthritis) for both the patients with an ACL rupture and the control patients. Another limitation could be the use of a hypothesis-free program, which makes it, for some clinicians, harder to use in daily practice. However, we are confident that the shape variants found, are usable in daily practice. You do not need a program to assess the wideness of the intercondylar notch on a Rosenberg view x-ray. Clinicians and radiologists with some experience in knee x-rays can easily give an impression of the findings in our study.

We used Rosenberg and standard lateral view X-rays for our analyses. In 1997 Shelbourne et al(35) already advocated the use of Rosenberg view X-rays, because of the standardized protocol. The advantage of the use of x-rays is that they are easily obtained, relatively cheap, have a low patient radiation dose, and thus are ideal for identifying risk factors for sustaining an ACL rupture in large groups of asymptomatic patients.

An interesting sequel of this research would be to compare the differences in bony morphology between patients with and without a re-rupture after ACL reconstruction. This could help the clinician in giving the patient individualized information on the risk of re-rupture.

CONCLUSIONS

This study indicates that a smaller, flatter intercondylar notch, a lower lateral tibia plateau, a lower medial spike of the eminence, and a smaller tibial eminence are more common in patients who ruptured their ACL compared to control patients.

Further research should focus on ways to implement these differences in bony morphology in prevention programs to prevent ACL rupture in an individual who is at greater risk for sustaining ACL rupture.

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ADDENDUM

Remarks:

- The description of the placements are made in the anatomical position
- All points are placed on the contours of bones.

Points on the Lateral view x-ray: Femur

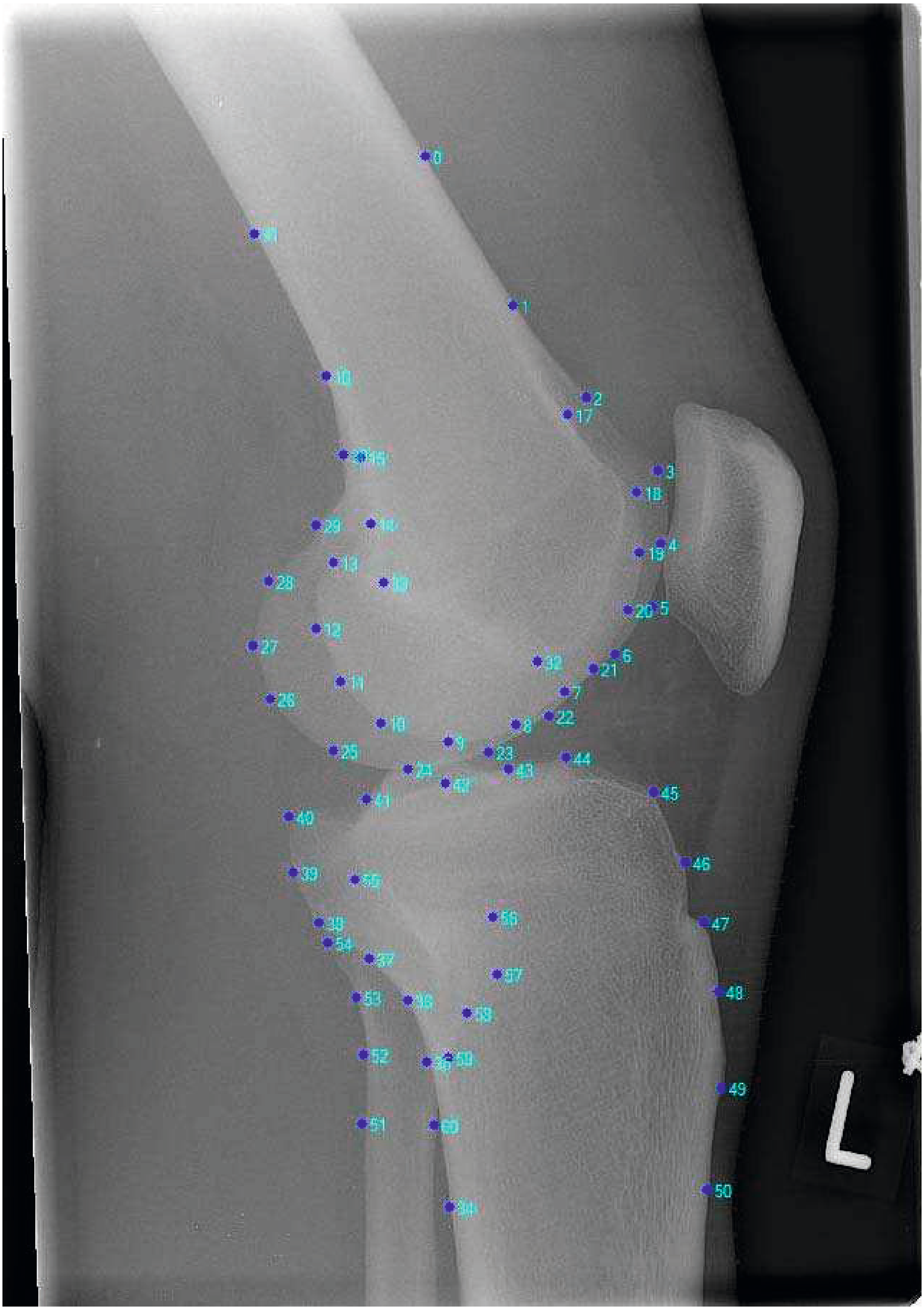
0. the width of the femur, above point 1.
1. the anterior part of the femoral diaphysis at the most proximal point of the femoral condyles.
2. ½ between point 1 and 3, on the contour of the condyle.
3. most anterior of the lateral condyle.
4. ¼ of the distance between point 3 and 7.
5. ½ of the distance between point 3 and 7.
6. ¾ of the distance between point 3 and 7.
7. The most distal point of the lateral condyle.
8. ¼ of the distance between point 7 and 11.
9. ½ of the distance between point 7 and 11.
10. on ¾ of the distance between point 7 and 11.
11. The most posterior point of the lateral condyle.
12. 1/5 of the distance between point 11 and 16.
13. 2/5 of the distance between point 11 and 16.
14. 3/5 of the distance between point 11 and 16.
15. 4/5 of the distance between point 11 and 16.
16. The dorsal end of the femoral diaphysis, opposite to point 1
17. ½ between point 1 and point 18.
18. Point most anterior of the medial condyle.
19. ¼ of the distance between point 18 and 22.
20. ½ of the distance between point 18 and 22.
21. ¾ of the distance between point 18 and 22.
22. The most distal point of the lateral condyle.
23. ¼ of the distance between point 22 and 26.
24. ½ of the distance between point 22 and 26..
25. ¾ of the distance between point 22 and 26.
26. The most posterior point of the medial condyle.
27. 1/5 of the distance between point 26 and 16.
28. 2/5 of the distance between point 26 and 16.
29. 3/5 of the distance between point 26 and 16.
30. 4/5 of the distance between point 26 and 16..
31. Point opposite to point 0, above point 16
32. Most distal point of the Blumensaats line
33. Most proximal point of the Blumensaats line

Points on the Lateral view x-ray: Tibia

34. on the posterior side of the tibia, 2 centimetres under point 35.
35. Posterior side of the tibia, where it starts to curve.
36. 1/3 of the distance between point 35 and 38
37. 2/3 of the distance between point 35 and 38
38. Lower point of the tibia plateau, posterior side.
39. ½ of the distance between point 38 en 40.
40. Upper point on the tibia plateau, posterior side
41. ¼ of the distance between point 40 and 44.
42. ¼ of the distance between point 40 and 44.
43. ¼ of the distance between point 40 and 44.
44. Upper point of the tibia plateau, anterior side
45. From this point the tibia declines to the tibia shaft/
46. ¼ of the distance between point 45 and 49.
47. ½ of the distance between point 45 and 49.
48. ¾ of the distance between point 45 and 49.
49. Point opposite to point 35 on the tibia shaft.
50. Point opposite to point 34 on the tibia shaft

Points on the Lateral view x-ray: Fibula

51. the posterior side of the fibula shaft, the width of the fibula below point 52
52. End of fibula shaft, posterior side, above this point the fibula head starts.
53. ½ the distance between point 52 and 54
54. Start of the lower fibula head, right under point 55
55. The most posterior, proximal point of the fibula head
56. The most anterior proximal point of the fibula head
57. End of the fibula head, on the anterior side
58. ½ of the distance between point 57 and 59
59. opposite to point 52, start of the fibula shaft
60. opposite to point 51, on the anterior side of the fibula.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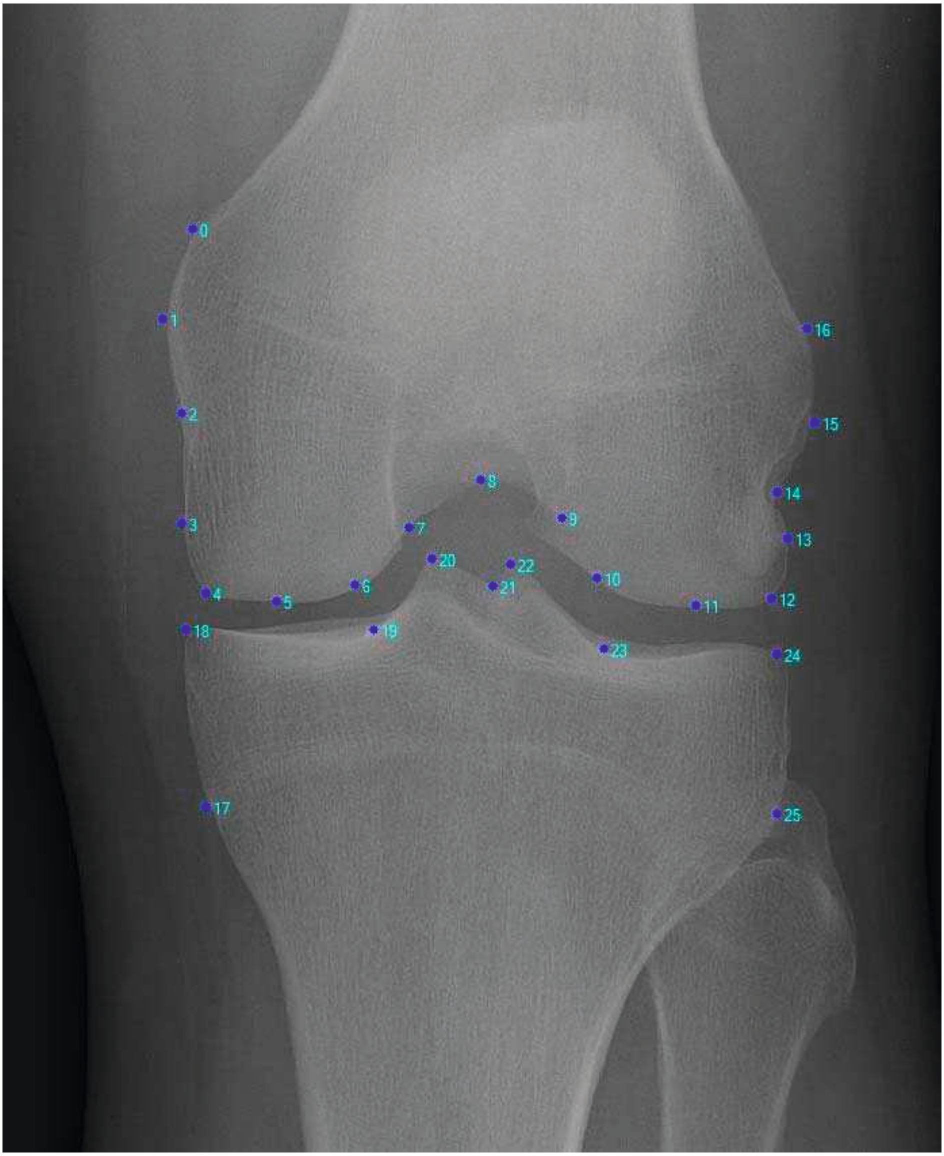
Points on the Rosenberg view x-ray:

0. End of the femur shaft, start of the medial condyle
1. Most medial point, right under point 0. (the medial condyle has to bulbs, on the first one, we placed point 0, on the second one we placed point 3)
2. ½ of the distance between point 1 and 3, medial condyle
3. Most medial point on the condyle (see information point 1)
4. Start of the inner joint, end of the outer medial condyle
5. ½ of the distance between point 4 and 6
6. Start of the intercondylar notch.
7. ½ of the distance between point 7 and 8
8. 8 highest point of the intercondylar notch
9. ½ of the distance between point 8 and 10
10. End of the intercondylar notch
11. ½ of the distance between point 11 and 12
12. End of the inner joint, start of the outer lateral condyle
13. Most lateral point on the first bulb of the lateral condyle
14. Point in the NWI
15. Most lateral point on the lateral condyles second bulb
16. End of the lateral condyle.
17. The end of the tibia shaft, start of the tibia plateau on the lateral side of the tibia
18. Above point 17, on the most medial point op the tibia plateau
19. Start of the medial point of the intercondylar eminence.
20. The highest point of the medial part of the intercondylar eminence.
21. Lowest point between point 20 and point 22
22. Highest point of the lateral intercondylar eminence
23. End of the intercondylar eminence, lateral side.
24. End of the tibia plateau, lateral side.
25. Point below point 24, start of lateral side of the tibial shaft.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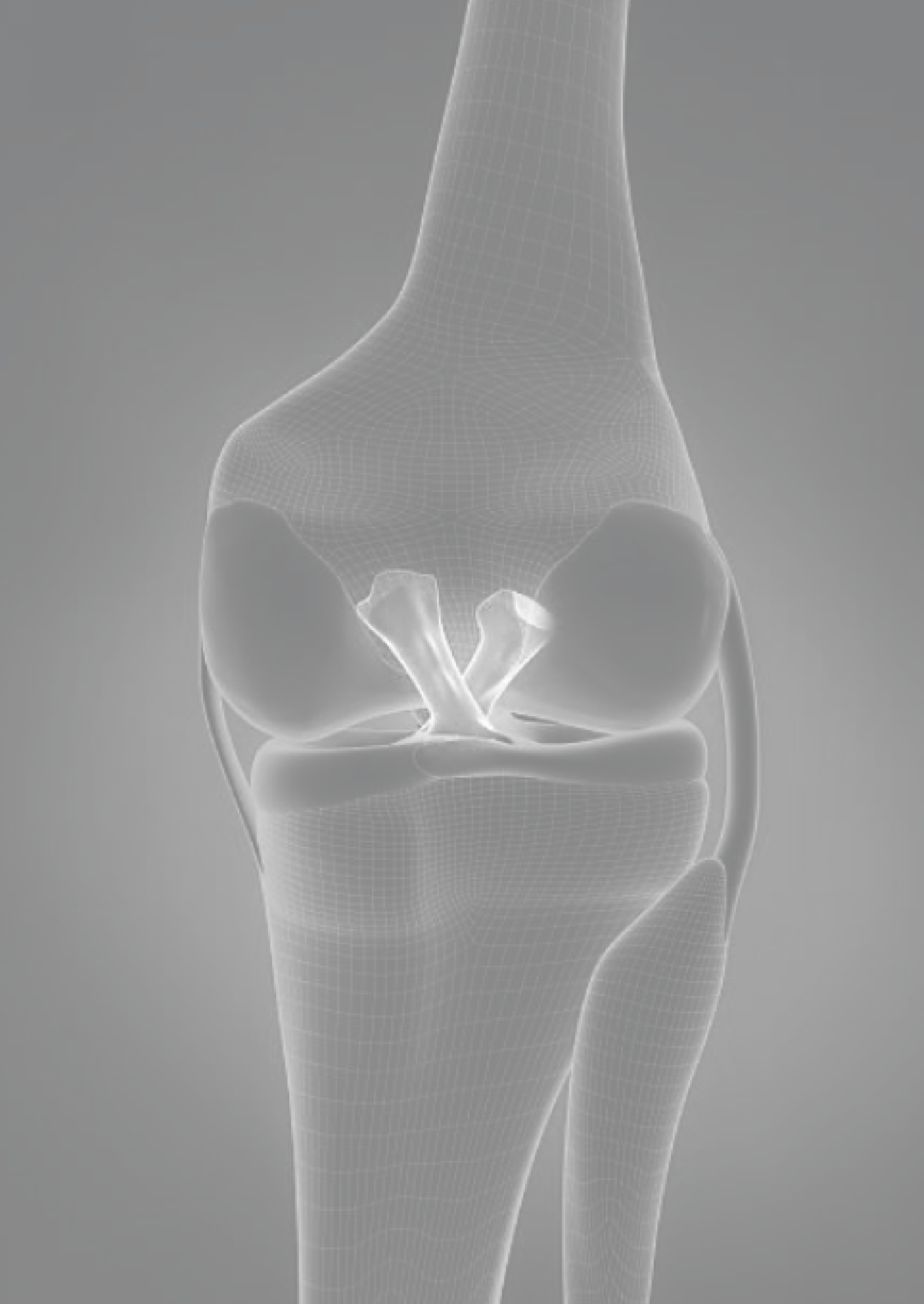

Chapter 3

Anterior Cruciate ligament rupture is related to the shape and volume of the intercondylar notch and the size of the cruciate ligaments assessed on MRI

Van Kuijk KSR, Reijman M, Bierma-Zeinstra SMA, Meuffels DE

ABSTRACT

Purpose

Anatomical variations of the knee have often been a subject of interest in finding predictors for an anterior Cruciate Ligament (ALC) rupture. Due to differences in methodology, results vary between studies and therefore consensus is lacking. A recent study suggested that smaller intercondylar notches are related to an ACL rupture on 2D x-rays. Our objective is to verify that intercondylar notch dimensions, as well as 3-D volumes of the intercondylar notch and the 3-D volumes of both the ACL and the posterior cruciate ligament (PCL), are correlated to the risk of sustaining an ACL rupture.

Methods

We retrospectively compared Magnetic resonance imaging (MRI) scans of 121 patients with a proven ACL rupture to 92 control patients with proven intact ACLs and PCLs. Patients were selected for age, weight, height, and sex (by manual selection). We measured the volumes of the intercondylar notch and ACL and PCL, the bicondylar width (BW), the notch width (NW), and the notch width index (NWI). Secondly, we compared the result between males and females.

Results

Patients with an ACL rupture had, on average, a smaller NW ($P<.001$), a smaller NWI ($P<.001$), smaller intercondylar volumes ($P<.001$), and smaller volumes of the PCL ($P<.001$). Secondary results showed that females have on average a smaller NW ($P<.001$), smaller volumes of the intercondylar notch ($P<.001$), ACL ($P=.004$), and PCL ($P<.001$). However, the NWI was not significantly different between the sexes ($P=0.508$).

Conclusion

A smaller notch dimension, smaller volumes of the intercondylar notch, and smaller volumes of the PCLs are related to the presence of an ACL rupture. Secondly, females have smaller volumes of the intercondylar notch, ACLs, and PCLs, but do not have a smaller NWI, when compared to males.

INTRODUCTION

Does size matter? Recent studies suggested that the width of the intercondylar notch and the width of the tibia eminence are related to the risk of sustaining anterior cruciate ligament (ACL) rupture [2, 6, 8, 9, 12, 14, 16, 17, 25, 38] and a study showed that they have a worse outcome after suffering an ACL injury [10]. A hypothesis-generating program, to objectively analyze the shape of the knee showed that the size and the width of the intercondylar notch are related to a higher risk of sustaining an ACL rupture[34]. However, some of these studies were performed on 2D radiographs, while the knee is a complex 3-dimensional structure. MRI imaging has the advantage over x-rays in that not only the osseous structures but also the ligaments and other soft tissues can be assessed. Also, MRI has become a general practice after a knee trauma, with an increasing number of MRIs made each year [1], providing a more widespread availability of MRI both in control patients, and in patients with an ACL rupture. These MRIs of subjects can be used for research into anatomical risk factors for ACL rupture.

Previously published research into the 3-Dimensional volumes of the intercondylar notch and the volumes of the cruciate ligaments looked at gender differences [7]; other studies had smaller sample groups [22, 26, 32]. Sturnick et al published a study in 2015 investigating the anatomical risk factors but produced very small odds ratios [30]. Uncontradictable evidence that a smaller intercondylar notch volume relates to a greater risk of sustaining an ACL rupture is still lacking.

To prevent ACL ruptures in athletes, we have to be able to identify a person who is at greater risk for sustaining an ACL rupture. Studies investigating predictors for an ACL rupture have, to date, failed to produce a usable predictor for an ACL rupture[23]. Some predictors that are found in these studies are not modifiable, such as sex and genetic factors [3, 13, 18, 20, 21, 28]. When risk factors are determined, individuals can be counseled for example, to avoid pivoting sports, join neuromuscular prevention programs or maybe have intercondylar notch surgery after an ACL ligament rupture, to prevent future re-rupture.

Therefore, the study aimed to provide evidence on 3-D MRI reconstructions that the volume and dimensions of the intercondylar notch and the cruciate ligaments are determinants for sustaining an ACL rupture.

PATIENTS AND METHODS

Patients

Patients included in this study were identified from a previously conducted prospective study at our Department of Orthopaedics; the KNee osteoArthritis anterior cruciate Ligament Lesion (KNALL)[10]. The KNALL is a prospective observational study of 154 patients with an ACL rupture, who were treated either operatively or non-operatively. MRIs were performed within 3 months after knee trauma. Patients were included in the KNALL study from January 2009 to November 2010, with a follow-up period of two years. All patients had suffered complete ACL rupture. For convenience, the term rupture is used in this paper for all patients with a complete ACL rupture.

Control patients

The control group consisted of 92 patients who had had a knee injury, either comprising of 1) meniscus injuries or 2) collateral ligament and meniscus injury. We performed the search in the database of our university medical center with a time interval from January 2003 until February 2014. Inclusion criteria were: intact ACL and PCL, diagnosis proven by MRI or by arthroscopic surgery of the knee; MRI scans and knee X-rays of the knee were available; patients had to be practicing (pivoting) sports, regularly, before the trauma. Table 1 shows the type of sports of the control patients. Exclusion criteria were: radiographic evidence of knee osteoarthritis defined as Kellgren and Lawrence score 2 or higher.

Our study and the KNALL study were both approved by our hospital's ethical review commission.

Table 1: Types of sports in which the knee injury occurred

	N	Percentage
Fighting sports/ self defence	6	7%
Dance	7	8%
Cycling	8	9%
Running	9	10%
Other (hockey, volleyball etc)	13	14%
Soccer	49	53%
Total	92	100%

MRI protocol and Segmentation

At baseline, MR images were obtained using MRI scanners with a magnetic field strength of 1.0, 1.5, or 3.0 Tesla. The patients' legs were positioned neutrally. All MRI examinations included a set of routine clinical MRI pulse sequences. To assess ACL features, we used sagittal and coronal proton density-weighted turbo spin echo (TSE) sequences (slice thickness 1 mm, repetition time (TR)/echo time (TE), 2700/27 ms) and the coronal T2-weighted TSE sequence with fat saturation (slice thickness 1 mm, TR/TE 5030/71 ms). Differences in field strength are proven to be irrelevant in diagnosing an ACL rupture [5, 19].

ACL and PCL volume measurements

The volumes of the PCL in both groups, and the ACL in the controls, were obtained from sagittal T1-weighted series. Osirix software (open-source medical imaging software for MacOS X [Apple, Cupertino, CA]; OsiriX, Geneva, Switzerland) was used to manually segment the ACL and PCL. This method was tested and found to be precise and accurate[37]. The volume was calculated as the sum of the outlined areas multiplied by the slice thickness. (See figure 1). We tested the correlation between the intercondylar notch volume and the volume of the PCL.

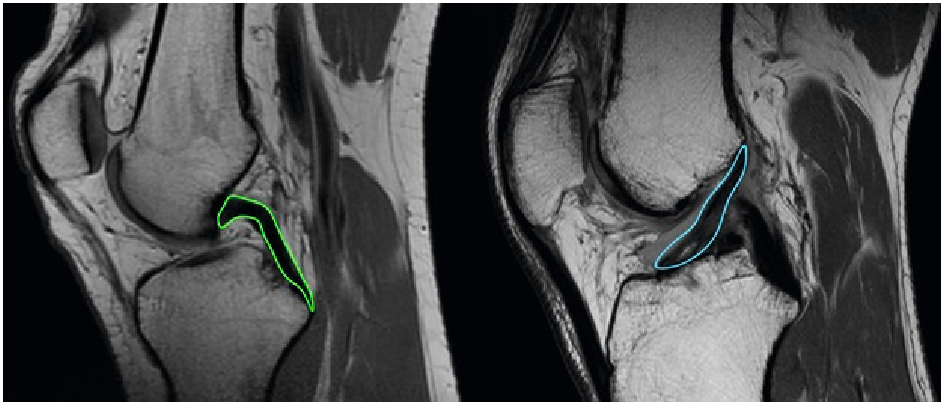

Figure 1 Sagital view MRI of the knee, in which the PCL (left, green) and the ACL (right, blue) are outlined

Femoral notch measurements

The volumes of the intercondylar notch were measured using Osirix software. Charlton et al[7] and Van Eck et al[33] previously described the boundaries of the intercondylar notch. The proximal border of the notch is defined as the image in which both femoral condyles were first clearly visible (Figure 2A). The distal border of the notch is defined as the last image in which the condyles were continuous (Figure 2B). We also measured the notch width index (NWI) according to a method first described by Staubli et al [27] and later modified by Whitney et al [35]. A reference line (RL) is defined as a tangent to the

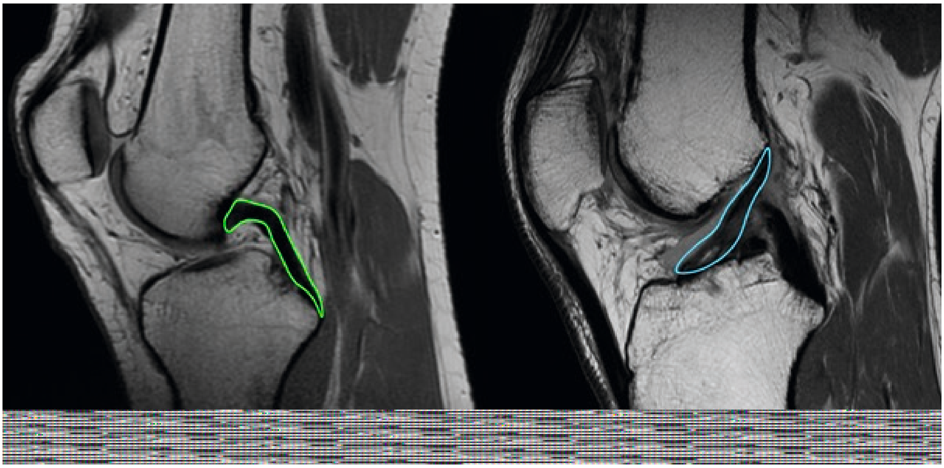

Figure 2 Axial MRI image of the knee, A most proximal, B most distal of the intercondylar notch.

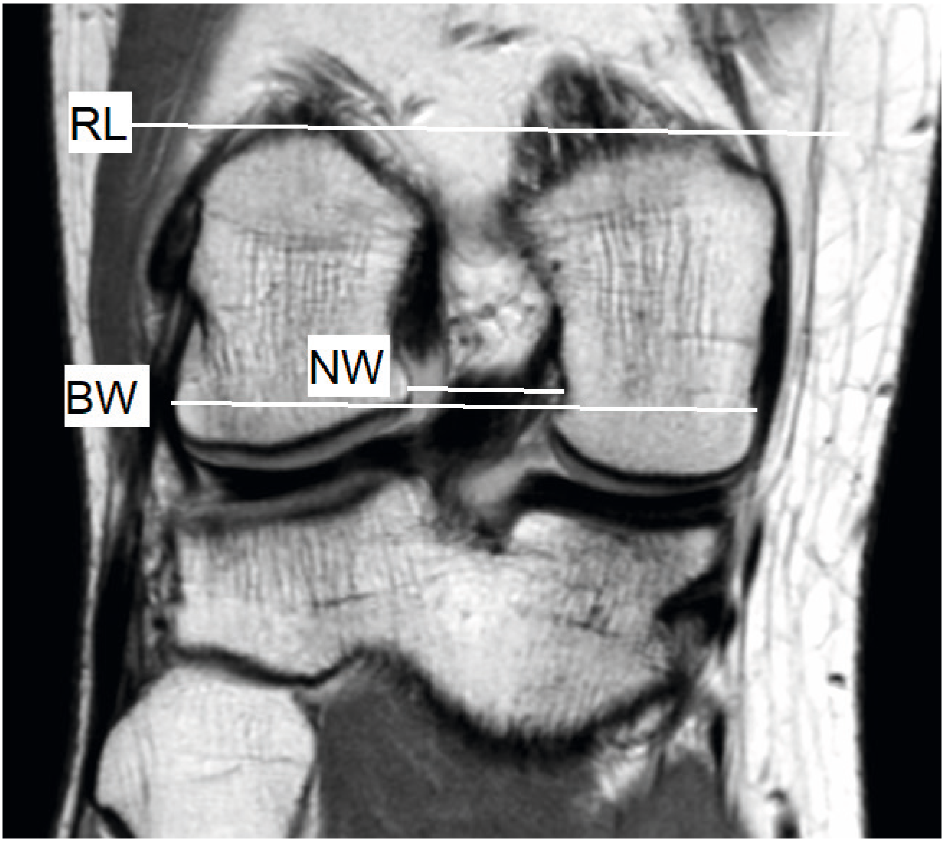

Figure 3: coronal MRI of the knee, with the described measurements. RL= Reference Line; NW = Notch Width; BW= Bicondylar width.

posterior subchondral aspect of both femoral condyles. All femoral widths are measured parallel to this reference line. In the coronal plane, the following measurements were applied: Bicondylar width (BW) and notch width outlet (NW). The Notch Width Index was calculated by dividing the NW by the BW. (figure 3).

A T2 coronal plane was used in each patient to measure BW and NW. The slice chosen in every knee was the plane in which the ACL and PCL cross one another as close as possible to the midsubstance of the ACL in the control cases. This point was typically found in the ACL injured group on the first slice anterior to the appearance of the roof of the intercondylar notch.

Statistical analysis

We used an independent t-test to assess whether or not the volume of the intercondylar notch and the NWI were significantly related to the presence of an ACL rupture. We used the presence or absence of an ACL rupture as a dependent factor and the volume of the intercondylar notch and the NWI as independent variables. We adjusted the analysis for BW, NW, and NWI. We did not correct for weight, height, age, and sex, since we selected our cases with our patients on those factors. We chose our controls slightly older age than our patients with an ACL rupture to make sure the control group had been longer at risk for sustaining an ACL during their longer period of practicing sports. A value of $P < .05$ was chosen as the level of significance.

The reliability of the measurements performed in this study was established using variance component analysis to estimate the variability within examiners. Intraclass correlation coefficients (ICCs) were then calculated for assessing intra-observer reliability. We randomly selected 28 MRI scans (14 of ACL ruptured patients and 14 of control patients) to be assessed a second time, two weeks after initial measurements. The observer did not know the values of previous measurements. The ICCs were considered excellent with values of 0.9 for BW, 0.99 for NW and 0.95 for NWI, and 0,92 for the PCL volume.

RESULTS

The study population consisted of 121 patients who met our inclusion criteria with a complete ACL rupture and 92 controls (see flow chart). The mean age for the ACL injured was 31 (± 7.4) years versus 38 (±12.0) for the controls ($p<0.05$). The groups had comparable BMI, with a mean BMI of 24.5 (± 3.9) for the ACL injured versus 25.6 (± 3.9) for the controls (p=0.1). The groups consisted of 37 females in the ACL-injured group (30%) and 22 females in the control group (24%) (p=0.3). Both groups consisted of comparable numbers of males and females. As stated before, the control group was on average seven years older than our ACL ruptured group.

The correlation between the intercondylar notch volume and the volume of the PCL was a Pearson correlation of 0,44; ($p < 0.001$). There was a positive correlation between the volumes of the ACLs and PCLs of our control patients (Pearson correlation of 0,40; $p < 0.001$). All patients had an MRI of the affected knee within 2 months of the knee trauma.

Measurements

Table 2 shows the mean for the BW, NW, NWI, and the intercondylar volumes. The NW, NWI, and intercondylar volumes were significantly different between patients with an ACL rupture and the control group, all p<.001. There was no significant difference between both groups in BW. We analyzed notch and ligament volumes by sex overall and then stratified according to case-control groups. (table 3 and table 4). Females had smaller intercondylar volumes than men (5.78 cm^3 ± 1.74 compared to 7.03 cm^3 ± 1.97; p<.001), and smaller volumes of the ACL and PCL. When divided into ACL injured and ACL intact groups, we found that for males the NW, NWI, intercondylar volumes, and the volumes of the PCL were all significantly different. For the females, only the notch width and the intercondylar volumes were significantly different between the two groups.

Table 2 Overview of measurements of the Bicondylar Width (BW), the Notch Width (NW), the Notch Width Index (NWI), the intercondylar volumes and the cruciate ligament volumes. Measurements presented in mean with ± SD.

	ACL injured (n=121)	**ACL intact (n=92)**	**p-value**
BW (mm)	77.1 ± 6.5	78.2 ± 6.1	.175
NW (mm)	19.5 ± 2.8	21 ± 3.3	<.001
NWI	0.25 ± 0.03	0.27 ± 0.04	<.001
Intercondylar volumes (cm^3)	6.29 ± 1.89	7.33 ± 2.02	<.001
PCL volumes (cm^3)	1.92 ± 0.44	2.17 ± 0.5	<.001
ACL volumes (cm^3)	-	1.26 ± 0.35	

Table 3 Descriptives of measurements divided between males and females. Measurements presented in mean with ± SD

	Males (n=154)	Females (n=59)	p-value
BW (mm)	80.2 ± 4.8	71.1 ± 4.6	<.001
NW (mm)	20.9 ± 3.1	18.8 ± 2.8	<.001
NWI	26.1 ± 4	26.6 ± 4	0.508
Intercondylar volumes (cm^3)	7.0 ± 1.9	5.8 ± 1.7	<.001
PCL volumes (cm^3)	2.16 ± 0.45	1.65 ± 0.32	<.001
ACL volumes, controls only (cm^3)	1.32 ± 0.32	1.08 ± 0.31	0.004

Table 4 Descriptives of measurements divided between males and females and between controls and injured patients. Measurements presented in mean with ± SD

	Males			Females		
	ACL injured (n=84)	ACL intact (n=70)	P-value	ACL injured (n=37)	ACL intact (n=22)	P-value
BW (mm)	80.1 ± 5.0	80.3 ± 4.6	.789	70.3 ± 4.1	72.4 ± 5.3	.113
NW (mm)	20.2 ± 2.9	22.0 ± 3.3	.001	18.2 ± 2.5	20.0 ± 3.0	.022
NWI	25.3 ± 3.6	27.3 ± 3.8	.001	26.0 ± 3.7	27.6 ± 3.4	.105
Intercondylar volumes (cm^3)	6.6 ±2.0	7.5 ± 1.9	.007	5.3 ± 1.3	6.6 ± 2.2	.003
PCL volumes (cm^3)	2.06 ± 0.4	2.30 ±0.4	.001	1.60 ± 0.3	1.74 ± 0.4	.105
ACL volumes, controls only (cm^3)	-	1.31 ± 0.3	-	-	1.10 ± 0.3	-

DISCUSSION

Our results showed that the volume of the intercondylar notch, the volume of the PCL, the Notch Width, and the Notch Width Index are significantly related to the presence of an ACL rupture. These findings provide evidence that a smaller volume of the intercondylar notch is related to the risk of sustaining an ACL rupture, as are the notch width and the notch width index. This study provides further evidence that the intercondylar notch width and the intercondylar notch volume play an important role in ACL injuries.

A smaller volume of the PCL is also significantly related to the presence of an ACL rupture. The most accepted explanation for this is that a smaller intercondylar notch holds a smaller PCL. Our study found a positive correlation between the intercondylar notch volume and the volume of the PCL (Pearson correlation of 0,44; $p > 0.001$). Although we were unable to measure the volumes of the ruptured ACLs, there was a positive correlation between the volumes of the ACL and PCLs of our control patients (Pearson correlation of 0,40; $p > 0.001$), suggesting that patients with an ACL rupture had smaller ACLs.

Previous studies focussing on the morphology of the knee had conflicting results [7, 37]. This could be due to differences in methods and smaller group sizes where we used a larger group of patients and controls. Few studies are focussing on the volume of the intercondylar notch, while previous studies showed the importance of the shape of the intercondylar notch in relation to the ACL[9, 27].

The findings of our current studies confirm the hypothesis from our previously conducted study[34]; in this study, we used a hypothesis-free program to analyze shape variants between patients with and patients without an ACL rupture. The hypothesis generated with this 2D study was that a narrower intercondylar notch was related to an ACL rupture, as shown in this current study with 3D measurements.

The influence of intercondylar notch width as a risk factor for ACL tears is believed to be related to the size of the ACL[24]. In a cadaver study by Stijak et al.[29] in a large sample of 50 cadaver adult knees, notch width correlated significantly with ACL size in males.

Secondary results show that there is a statistically significant difference in intercondylar volume, PCL and ACL volume, notch width, and bicondylar width between males and females, but that there is no significant difference in the notch width index between males and females. This means that the relative sizes of the intercondylar notch are comparable between males and females. The differences in BW, NW, and volume of the intercondylar notch between males and females could be related to the fact that males are, in general, of greater size than females and thus the intercondylar notch of males holds larger ligaments. This could also account for the known fact that women have a threefold higher risk of sustaining an ACL rupture [15, 25, 31]. A smaller notch holds a smaller ACL volume[12, 26], which in turn can withhold less force[36].

One of the strengths of our study is the use of a large group of patients with an ACL rupture and a large control group. They were selected from a database but had a similar exposure environment for suffering an ACL rupture, and even longer exposure time for obtaining an ACL rupture. We specifically included only controls practicing sports and with knee trauma. This makes the two selected groups of patients more comparable than when we would have selected controls without a traumatic event.

A limitation of this study is that although the results of this study are very promising, it is still difficult to implement this in daily practice for selecting patients at risk for an ACL rupture. Although there is an increasing rate of knee MRIs for all kinds of patients, it is still not routinely done. More and more professional sport clubs (such as football clubs) are having MRIs of the knee taken as a routine sports checkup or pre-contract workup, which in the future could be used for pre-selecting patients at risk for an ACL rupture.

We understand that not every clinician will have time or the inclination to analyze the measurements we provide for all patients visiting the clinics. Therefore we would suggest that clinician could focus on the notch width index for selecting patients who are at greater risk for an ACL rupture because this is a reproducible, simple measurement, every clinician can perform on an MRI of the knee. We found that when selecting a cut-off point for the NWI of 26, 70 percent of the patients were patients with an ACL rupture, and only 30 percent of the patients had an intact ACL.

In addition, a growing number of patients with an ACL rupture will have an MRI after the occurrence. The results of our study could therefore have important implications for the treatment and prevention of re-ruptures, which cause major health and economic issues [4].

The role of the intercondylar notch in ACL injury was recently studied in children, concluding that a narrow notch with low NWI may be a risk factor for ACL tears in children suggesting that anterior impingement could indicate the need for notch-plasty to decrease the risk of recurrence following primary ACL reconstruction[11]. Further research could focus on investigating if notch-plasty could decrease the re-rupture risk in adults.

In summary, this study showed that patients with a smaller intercondylar notch volume, smaller PCL volumes, a smaller bicondylar width, and a smaller notch width index are more prone to sustaining an ACL rupture when compared to a large group of control patients, who had a knee injury during sports but did not tear their ACL. Further research should investigate how to use these results for selecting patients at risk for an ACL rupture and if these results have any implication for lowering the re-rupture risk.

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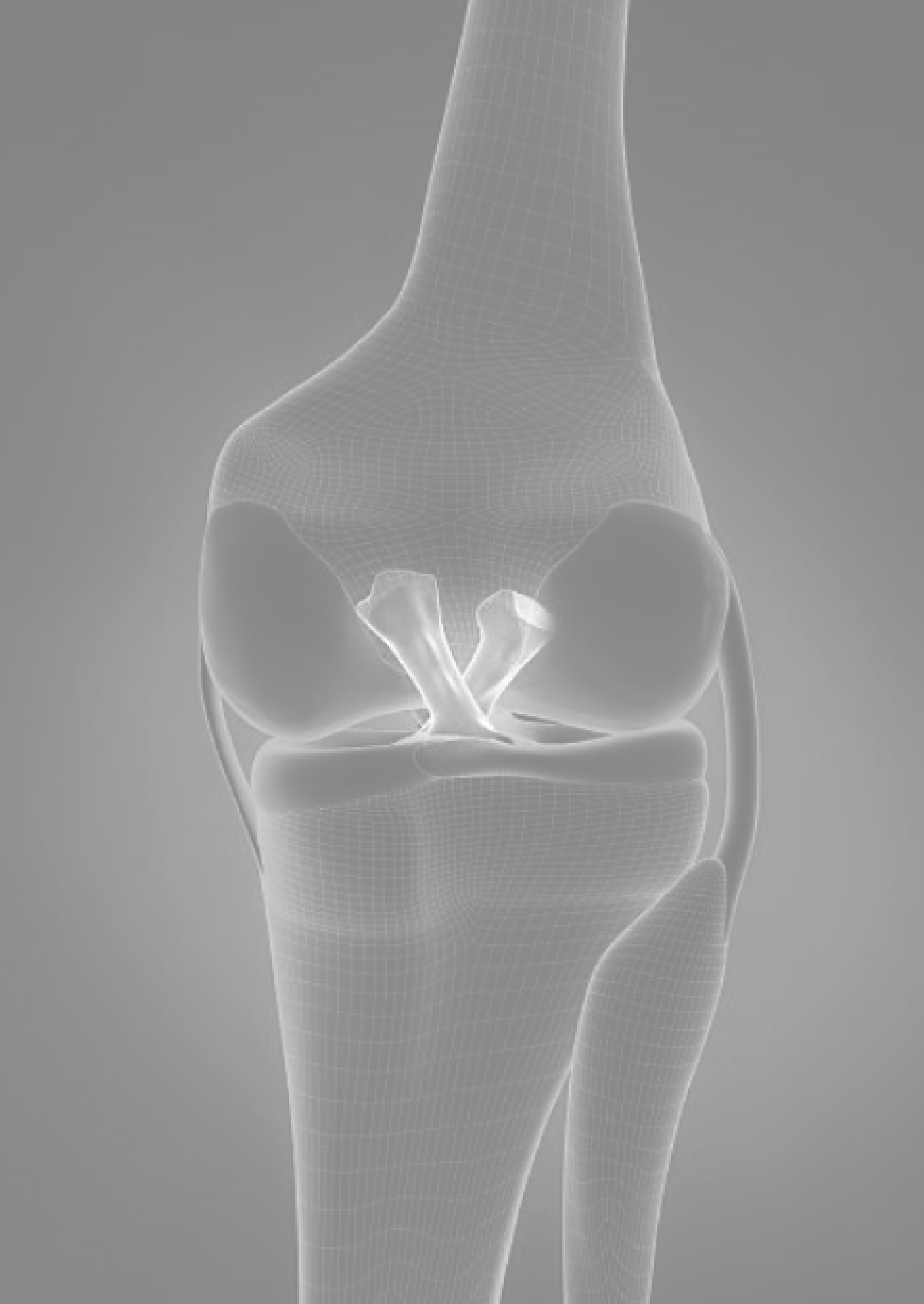

Chapter 4

Posterior cruciate ligament injury is influenced by intercondylar shape and size of tibial eminence

Van Kuijk KSR, Reijman M, Bierma-Zeinstra SMA, Waarsing JH, Meuffels DE

ABSTRACT

Aims

Little is known about the risk factors that predispose to a rupture of the posterior cruciate ligament (PCL). Identifying risk factors is the first step in trying to prevent a rupture of the PCL from occurring. The morphology of the knee in patients who rupture their PCL may differ from that of control patients. The purpose of this study was to identify any variations in bone morphology that are related to a PCL.

Patients and Methods

We compared the anteroposterior (AP), lateral, and Rosenberg view radiographs of 94 patients with a ruptured PCL to a control group of 168 patients matched by age, sex, and body mass index (BMI), but with an intact PCL after a knee injury. Statistical shape modeling software was used to assess the shape of the knee and determine any difference in anatomical landmarks.

Results

We found shape variants on the AP and Rosenberg view radiographs to be significantly different between patients who tore their PCL and those with an intact PCL after a knee injury. Overall, patients who ruptured their PCL have smaller intercondylar notches and smaller tibial eminences than control patients.

Conclusion

This study shows that differences in the shape of the knee are associated with the presence of a PCL rupture after injury. A smaller and more sharply angled intercondylar notch and a more flattened tibial eminence are related to PCL rupture. This suggests that the morphology of the knee is a risk factor for sustaining a PCL rupture.

INTRODUCTION

The posterior cruciate ligament (PCL) is the strongest ligament in the knee [1,2]. Injuries to the PCL have been studied far less than those of the anterior cruciate ligament (ACL), perhaps because they occur less commonly. The exact incidence of a PCL injury remains uncertain but reported rates vary between 4% [3] and 38% [4] of all knee injuries seen in accident and emergency departments. As more people take part in sports, these injuries are likely to increase in number.

In the short term, a PCL rupture causes pain and posterior laxity and reduces an individual's ability to take part in sports. In the long term, it is a risk factor for developing osteoarthritis. [5-8] A recent study by Agolley et al [9] showed that patients who are managed non-operatively have a better chance of returning to sports and less risk of developing osteoarthritis in the medium-term to long term. However, it would be preferable to prevent the PCL rupture in the first place.

To date, no risk factors for PCL rupture have been identified. If such factors could be identified, ways to prevent them could be developed, in the same way, that specific training programs for athletes have been used successfully for those at risk of an ACL rupture. [10-12]

The shape of the knee can be assessed using standard radiographs. In general, a radiograph will be obtained after a knee injury or at medical screening for athletes. The role of variation in bony anatomy in the injured knee has been investigated in ACL-deficient knees using statistical shape modeling. [13] Statistical shape modeling is a hypothesis-generating model that can be used to predict which patients have an increased risk of a rupture, and which have a better or worse clinical outcome, depending on the shape of the knee. [14]

When variations in the shape of the knee are identified, it is helpful to screen patients who are prone to PCL rupture, such as athletes. Patients at greater risk could be counseled and offered additional training. These training programs are only cost-efficient when patients with a high risk of sustaining a PCL rupture are selected. [15]

The purpose of this study was to identify any variations in the bony shape of the knee that are related to PCL rupture.

PATIENTS AND METHODS

We performed a case-control study. All patients with an injured knee who visited the outpatient clinic of our hospital (Erasmus Medical Centre, Rotterdam, The Netherlands) between January 2003 and May 2014 were eligible for inclusion. We included only patients with a PCL rupture confirmed by MRI or arthroscopy.

Controls were selected from patients who had sustained a meniscal tear or a combined medial collateral ligament and meniscus injury and had an intact PCL and ACL confirmed by MRI or arthroscopy.

Anteroposterior (AP) and lateral radiographs had to be available both for patients and their controls. We also selected the Rosenberg view radiograph when available (45% of patients with a PCL rupture). Controls also had to have sustained a sports injury to ensure that the mechanism of injury was similar to those of the patients studied. There were no significant differences between the two groups in terms of sex, age, and body mass index (BMI). Both groups were of Kellgren and Lawrence [16] grade of 0 to 1 at presentation.

Radiographs and statistical shape modelling.

Radiological measurements were carried out on standard non-weight bearing AP, lateral, and Rosenberg view radiographs. We outlined the distal femur and the proximal tibia and fibula (ASM tool kit; Manchester University, Manchester, United Kingdom). The shape of the distal femur and proximal tibia was defined by 25 landmark points on the AP and Rosenberg views and 60 landmark points on the lateral view placed along the surface of the bone. Each point was located in the same place on each image to allow comparison between shapes.

Statistical shape modelling transforms the set of points into a statistical shape model, which comprises several shape variants. These together describe 95% of the variation in the shape of the knee. Intraobserver reliability was observed by two authors (KSRvK and DEM) and was assessed by outlining 25 radiographs for a second time two weeks later. These 25 radiographs were blinded for the observer. The description of what shape aspects a variant represents was determined at a consensus meeting.

Statistical analysis.

The association between the shape of the knee and a ruptured PCL was analyzed by logistic regression analyses. The presence or absence of a PCL rupture was used as the dependent variable and the different shape variants as independent variables.

In total, 30 shape variations were found per radiograph view. To correct for multiple testing, we applied Bonferroni correction for multiple comparisons (0.05/30 = 0.002). All statistical analyses were performed with SPSS Statistics for Windows (version 20.0; IBM Corp., Armonk, New York). A p-value < 0.05 was considered statistically significant.

RESULTS

Of the patients seen in the period 2003 to 2014 with a knee injury (1824 patients in total), 94 with a PCL rupture were eligible and included in the study. Of the control patients, 168 patients without a PCL rupture (all with AP, lateral, and Rosenberg view radiographs) met the inclusion criteria. Rosenberg views were available for 42 patients with a PCL rupture. Patient demographics are shown in Table I and the diagnoses of the individual control patients are shown in Table II.

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Table 1: Patient dempgraphics.

	PCL injured (n = 94)	Control group (n = 168)	p-value*
Mean age, yrs (sd)	40 (13.6)	38 (12.0)	0.148
Mean body mass index, kg/m2 (sd)	25 (3.0)	25 (3.2)	0.873
Female sex, n (%)	24 (*26*)	49 (*29*)	0.940
Mean time between trauma and radiograph, mths (sd)	12.6 (16)	12.6 (16)	0.002

*Independent-samples Student's *t*-test. PCL, posterior cruciate ligament

Table 2: Diagnoses of control patients

Diagnosis	n (%)
Medial meniscus tear	57 (*33.9*)
Lateral meniscus tear	32 (*19*)
Cartilage lesion	15 (*8.9*)
Bone contusion	11 (*6.5*)
Collateral ligament lesion	7 (*4.2*)
No intra-articular lesions	46 (*27.4*)

Shape variants and PCL rupture.

Statistical shape modelling provided 30 shape variants for each of the lateral, Rosenberg, and AP view radiographs (variants 0 to 29). Statistical shape modelling consists of variants that together describe the total variation in shape in the study population. Shape aspects that are correlated are captured in one variant, such that each single variant represents an independent shape variant. The mean shape of each variant is quantitatively described as 0, and the positive or negative deviation from the mean is expressed as the standard deviation. One variant consists of the entire study population. This means all patients with a PCL rupture receive a score on variant 1, all patients receive a score on variant 2, and so on.

The intraobserver intraclass correlation coefficient (ICC) of the placement of the points thereafter found different variants were considered good, with a mean of 0.81 (0.48 to 0.97), with 89% of the variants having an ICC above 0.7.

For the lateral view radiographs, we found two shape variants that were significantly different between cases and controls (Table III). However, while analyzing these shape variants, it became clear they were due to the positioning of the knee when the radiograph was taken. For the completeness of the article, we decided to publish these results, although they are not caused by variation in the shape of the knee itself. For the AP view radiographs, we found two variants that differed significantly between patients with a PCL rupture and the control group. For the Rosenberg view, we found three variants that differed significantly between patients with a PCL rupture and the control group.

Table 3: Relation between shape variants and posterior cruciate Ligament rupture at different views. CI, confidence interval.

View	Odds ratio (95% CI)	p-value
Anteroposterior		
Variant 13	1.6 (1.2 to 2.2)	0.001
Variant 22	1.6 (1.2 to 2.1)	0.001
Rosenberg		
Variant 1	0.4 (0.3 to 0.6)	< 0.001
Variant 6	0.5 (0.3 to 0.7)	0.001
Variant 9	1.9 (1.3 to 2.7)	< 0.001
Lateral		
Variant 0	1.6 (1.2 to 2.1)	0.002
Variant 1	0.001 (0.001 to 0.008)	< 0.001

Description of the significant shape variants.

Below we present a description of the variants significantly associated with PCL rupture. The software produced graphics, of which standard deviation scores of -2.5 to 2.5 for each variant are depicted on the left and right sides, respectively, of Figures 1, 2, and 3. In the middle, an overlay is presented. Higher variants describe more subtle shape aspects (e.g. the variation in shape represented in variant 17 is much subtler than that represented in variant 1).

AP view.

The intercondylar notch differed significantly between patients with a PCL rupture and those without. This was found in both variant 13 and variant 22 on the AP view radiographs, as shown in Figure 1. Patients with a PCL rupture had, on average, a relatively smaller width of the intercondylar notch, a smaller tibial eminence, and a smaller medial condyle than patients who had an intact PCL. Variant 22 showed a difference in the shape of the tibial eminence. Patients with a PCL rupture had, on average, higher tibial eminences than those without.

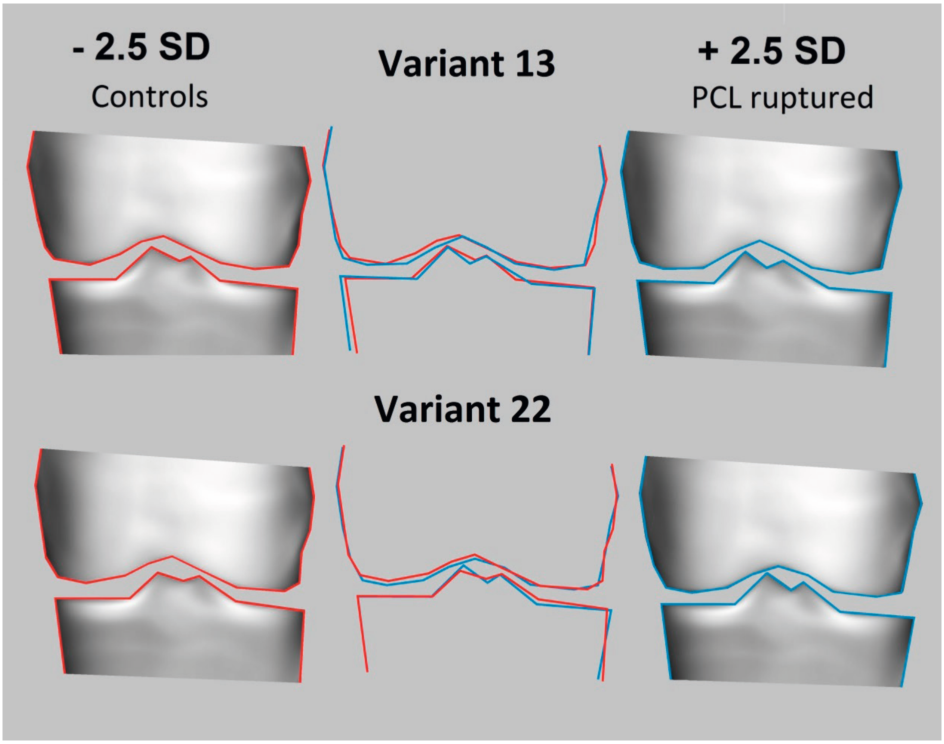

Figure 1: Graphic outcomes of statistic shape modelling, showing two variants that are significantly different in patients with intact and ruptured posterior cruciate ligament (PCL). On the left and right side are standard deviation scores of -2.5 and 2.5, respectively, and in the middle is the variant.

Rosenberg view.

The intercondylar notch differed significantly between patients with a PCL rupture and those without. This was found in variant 1, variant 6, and variant 9 on the Rosenberg view radiographs, as shown in Figure 2. Patients with a PCL rupture had, on average, a narrower intercondylar notch than patients with an intact PCL. Variant 6 showed a difference in the shape of the tibial eminence. Patients with a PCL rupture had, on average, higher tibial eminences than those without.

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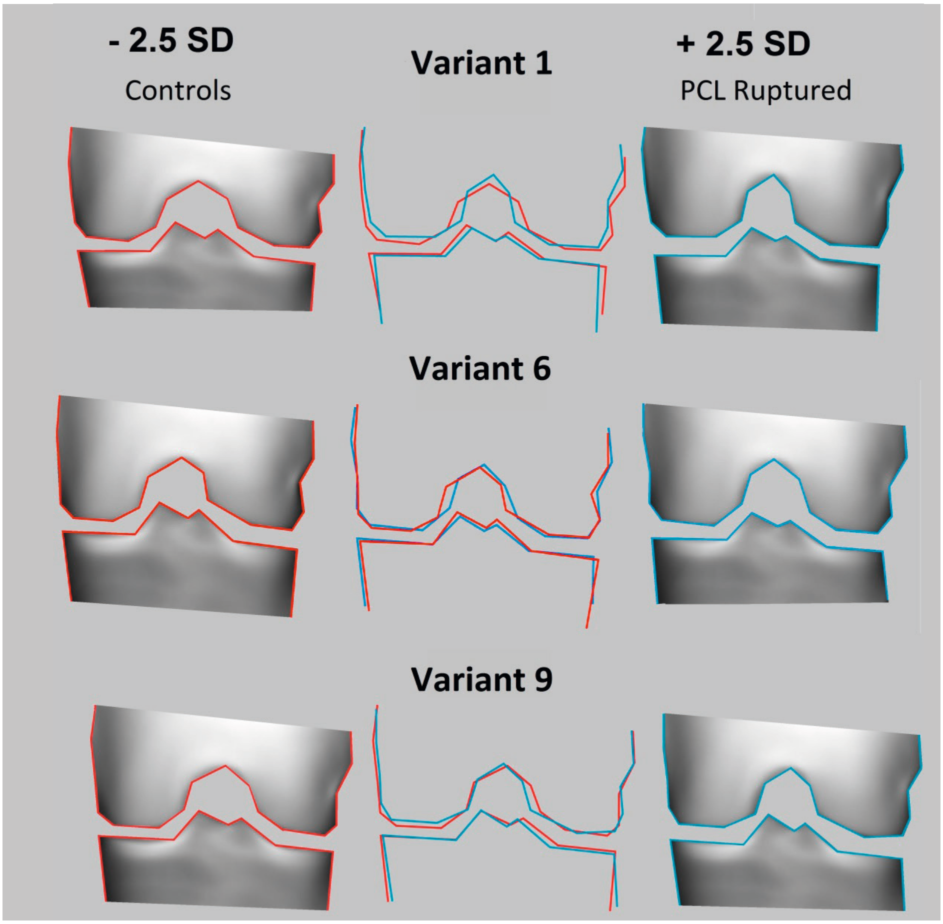

Figure 2: Graphic outcomes of statistical shape modelling: five variants that are significantly different for patients with intact and ruptured posterior cruciate ligament (PCL). On the left and right side are standard deviation scores of -2.5 and 2.5, respectively, and in the middle is the overlay of both sides.

Variant 1 showed a variation in flexion and extension in the knee. Patients with a PCL injury had, on average, more flexion in the knee than those without a PCL injury.

Variant 2 is a variation in the rotation of the tibia. Patients with a negative standard deviation in variant 2 had a Blumensaat line that crossed at a steep angle with the midline of the femur. Patients with a positive standard deviation seemed to have a larger angle with the midline of the femur (Fig. 3). We assumed that this could be explained by a variation in knee flexion during the taking of the radiograph. In addition, patients with a negative standard deviation seemed to have a narrower tibia compared with patients who scored a positive standard deviation in variant 2. Patients with a PCL injury scored higher (positive standard deviation) on variant 2 than patients who did not have a PCL injury (negative standard deviation).

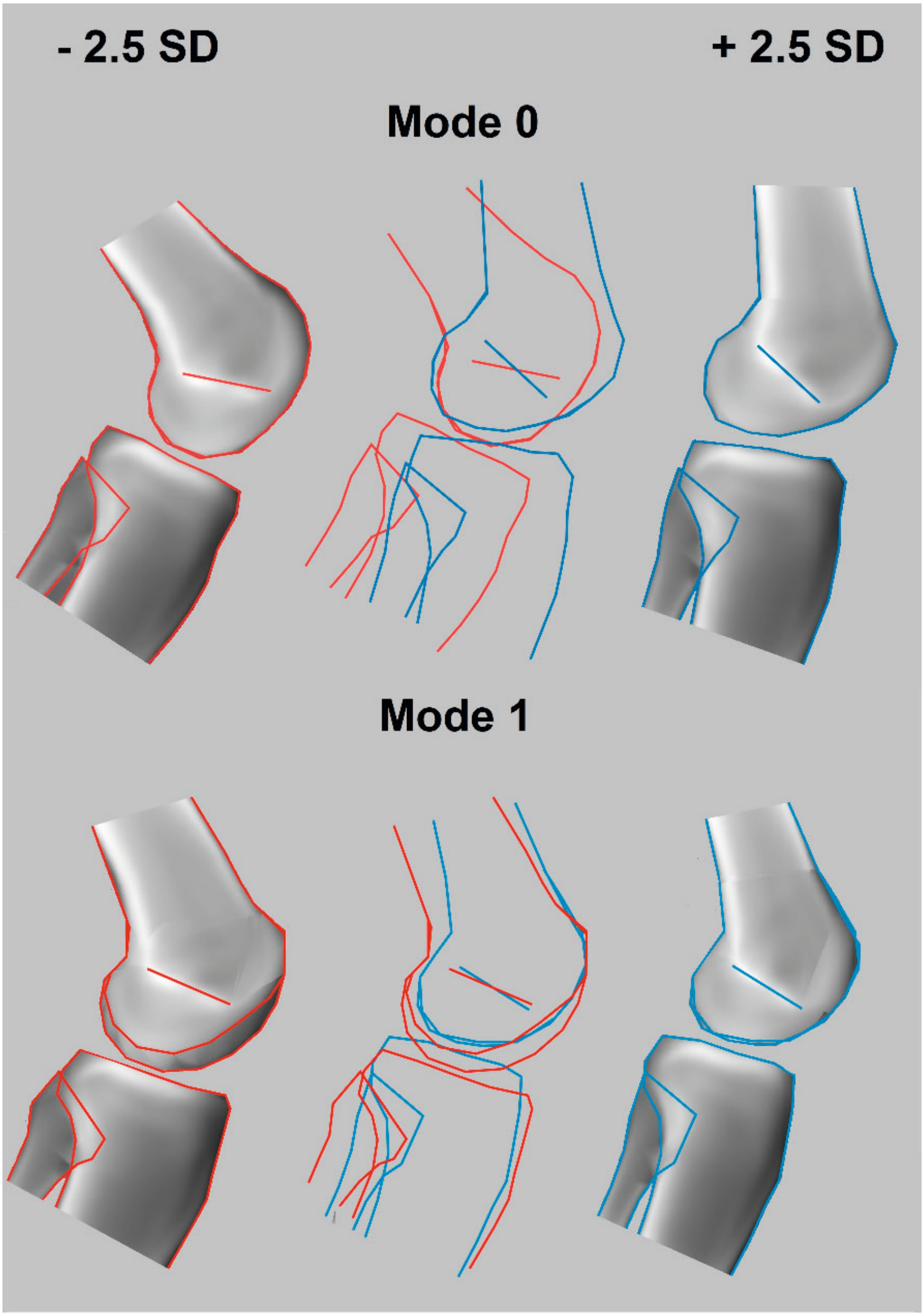

Figure 3 Graphic outcomes of statistical shape modelling: variation in flexion of the knee when the radiograph is taken. On the left and right side are standard deviation scores of -2.5 and 2.5, respectively, and in the middle is the overlay of both sides.

DISCUSSION

The main finding of the present study is that there are significant differences in bony morphology on the AP view and Rosenberg view radiographs between patients with a ruptured PCL and those without. A smaller and more sharply angled intercondylar notch and a wider tibial eminence are related to PCL rupture. Our research showed these findings in two different radiological projections. Although the differences in the AP view were subtler than in the Rosenberg view, they reinforce one another. Not all hospitals have a Rosenberg view radiograph of the knee as part of their standard work-up, so to make this research more accessible for different clinical settings, we think that the AP and Rosenberg view findings are equally important.

Previous research has shown that patients with a smaller intercondylar notch also have a smaller PCL and a smaller ACL. [17,18] A smaller PCL can resist less force than a larger PCL, so combined with our present study, it is possible that a patient with a smaller intercondylar notch also has a smaller PCL resulting in an increased risk of rupture. An alternative explanation is that a smaller intercondylar notch causes impingement on the PCL. Triantafyllidi et al [19] showed that the PCL occupies most of the space of the intercondylar notch in flexion, possibly resulting in impingement on the PCL in this position.

The findings on the lateral view are explained by the variation in the position of the knee when the radiograph is taken. This difference is thought to be the result of differences in flexion and extension (variant 1) and rotation (variant 2) during the acquisition of the radiograph. When we examined the different variants in our consensus meeting, we viewed 3D images and moving animations of the shape variants and found the differences to be more clearly visible than on 2D images.

Research into the risk factors for sustaining a PCL rupture is lacking. To the best of our knowledge, this is the first study to show that there are anatomical differences between patients with a PCL rupture and those without. Our results could be used in further research into the risk factors for PCL ruptures and perhaps, in the near future, could help to identify individual patients who are at greater risk of sustaining a PCL rupture. Finding risk factors is essential if we want to be able to prevent this from happening. Even if the midterm results after nonoperative management of a PCL injury are reasonably good, [12] Kang et al [20] showed that PCL deficiency is a factor leading to the degeneration of the patellofemoral joint in the long term.

Because of the low prevalence of PCL injuries, screening only for higher risk of sustaining a PCL injury would probably not be cost-efficient. However, more risk factors have been found for different sports injuries to the knee, such as an ACL injury. Screening and prevention programs could be combined to find and help patients at risk of different types of knee injury.

Numerous studies into the bony morphology of the knee have focused on patients with an ACL rupture. [21-37] Recent research has found significant differences in the shape of the knee between patients with an ACL rupture and control patients. The findings of this study34 were consistent with the findings in our present study. The morphology of the intercondylar notch plays an important role in the rupture of both the PCL and ACL.

We specifically included patients after a knee injury and compared PCL and non-PCL trauma patients. This makes the two selected groups of patients more comparable than if we had selected healthy controls without an injury. Radiographs were used for assessing the shape of the knee. The benefit of radiographs is that they are widely available and relatively inexpensive. At our hospital, patients with an injured knee all have radiographs of the knee, so the results of this study are reproducible and can be generalized. A drawback of the use of radiographs is that we cannot assess the shape of the articular surface, including cartilage, which plays an important role in the shape of the knee.

An advantage of statistical shape modelling is that the variants represent relative variation in shape, independent of differences in the size of the joint. In this way, the method reduces errors caused by variation in magnification or the size of the patient's knee.

This study shows that differences in the shape of the knee are related to the presence of a PCL rupture after injury. A smaller and more sharply angled intercondylar notch and a more flattened tibial eminence are related to PCL rupture. This suggests that the shape of the knee is a risk factor for sustaining a PCL rupture.

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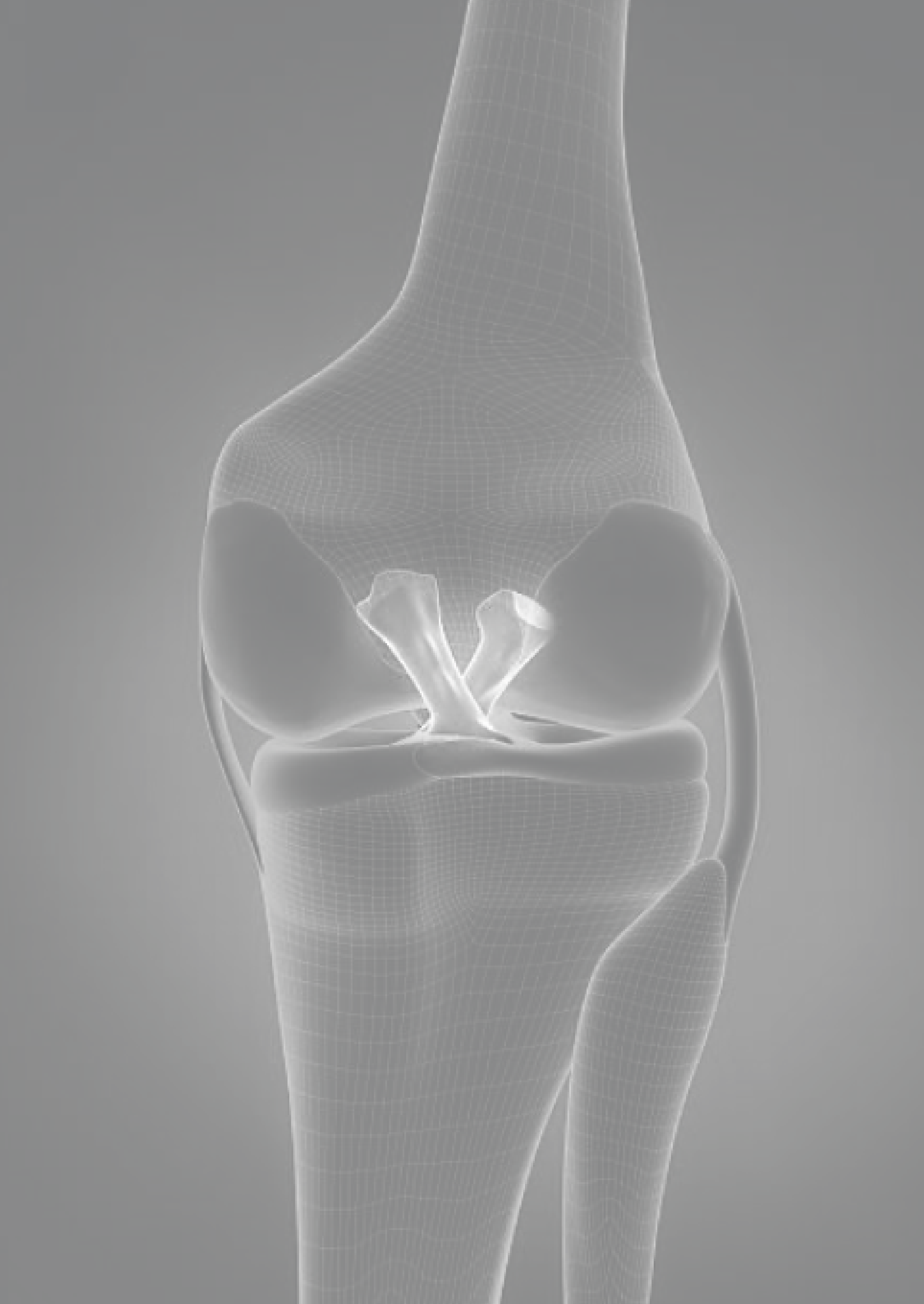

Chapter 5

Smaller intercondylar notch size and smaller ACL volume increase posterior cruciate ligament rupture risk

Van Kuijk KSR, Reijman M, Bierma-Zeinstra SMA, Meuffels DE

ABSTRACT

Purpose

Little is known about risk factors for sustaining a posterior cruciate ligament (PCL) rupture. Identifying risk factors is the first step in preventing a PCL rupture from occurring. The morphology of the knee in patients who ruptured their PCL may differ from that of control patients.

The hypothesis was that the intercondylar notch dimensions, 3-D volumes of the intercondylar notch and the 3-D volumes of both the ACL and the PCL were correlated to the presence of a PCL rupture.

Methods

The magnetic resonance imaging (MRI) scans of 30 patients with a proven PCL rupture were compared to 30 matched control patients with proven intact ACL and PCL. Control patients were selected from patients with knee trauma during sports but without cruciate ligament injury. Patients have been matched for age, height, weight, BMI, and sex. The volumes of the intercondylar notch and both the ACL and PCL were measured on 3D reconstructions. Secondly, the bicondylar width, the notch width, and the notch width index were measured for all subjects. The relationship between our measurements and the presence of a PCL rupture was analyzed.

Results

The results show a significant difference in the volumes of the intercondylar notch and the ACL between patients with a ruptured PCL and control patients. Patients with a PCL rupture have smaller intercondylar notch volumes and smaller ACL volumes. There were no significant differences in the bicondylar width, notch width, and notch width index. In the control patients, a significant correlation between the volume of the PCL and the volume of the ACL was found (0.673, $p<0.001$).

Conclusion

Patients with a PCL rupture have smaller intercondylar volumes and smaller ACL volumes when compared to control patients. Secondly, patients with smaller ACL volumes have smaller PCL volumes. This study shows, for the first time, that there are significant size and volume differences in the shape of the knee between patients with a PCL rupture and control patients.

INTRODUCTION

Injuries to the posterior cruciate ligament (PCL) occur in approximately 1–4% of all sport-related traumatic knee injuries, depending on the type of sport [14, 17]. With the growing number of athletes and especially competitive athletes [10], the absolute number of PCL injuries is growing and is likely to keep on growing in the next couple of years [3, 11].

In the short term, a PCL rupture, in most cases, causes pain and posterior laxity and reduces an individual's ability to take part in sports. In the long term, deficiency of the PCL results in abnormal kinematics and increased contact pressures in the medial and patellofemoral compartments of the knee and may increase strain on the posterolateral knee structures, placing them at risk of subsequent injury [9, 25]. Long-term studies have found that degenerative changes after PCL injury occur primarily in the medial and patellofemoral compartments [2, 6, 8, 17, 20]. PCL injuries are still often overlooked during primary care [18, 23], resulting in delayed diagnosis and delayed treatment. Therefore, risk factors need to be identified. Recently, van Kuijk et al. found that the size and shape of the intercondylar notch and the tibial eminence are related to the risk of sustaining a PCL rupture [13]. This study is conducted on plain radiographs. The knee, however, is a 3-Dimensional, complex joint, best analyzed on MRI. However, until this date, no studies using MRI have been conducted to investigate the morphological features of the PCL-deficient knee. It might be possible that the shape of the intercondylar notch has a positive correlation with the soft tissue moving through it, such as the PCL.

Therefore, the purpose of this study was to investigate if the volumes of the cruciate ligaments, the sizes of the intercondylar notch, and the intercondylar notch dimension are related to the risk of sustaining a PCL rupture.

MATERIAL AND METHODS

The institutional ethics review board of the Erasmus MC, Rotterdam, approved this study (MEC-2017-422).

Patient selection

Patients with a PCL rupture and control patients were selected from patients visiting our outpatient clinic of the Erasmus Medical Centre, Rotterdam, The Netherlands, between January 2003 and May 2014. Patients and controls had to be practicing pivoting sports competitively during the time of injury. Patients were only included if they had an isolated PCL rupture, confirmed by MRI or arthroscopy. Controls were selected from patients who had sustained a meniscal tear or a combined medial collateral ligament and meniscus injury and had an intact PCL and intact ACL confirmed by MRI or arthroscopy. Patients were excluded if they had radiographic evidence of knee osteoarthritis Kellgren and Lawrence score two or higher because secondary bone formation could change the notch shape and decrease or alter the volume. Patients were matched for age, height, weight, BMI, and sex. The institutional ethics review board approved this study.

MRI protocol and segmentation MR images were obtained using MRI scanners with a magnetic field strength of 1.0, 1.5, or 3.0 Tesla.

The MRI sequences used are sag PD, sag T2 FS, Cor PD FS, Coronal T2 TSE, axial T2 FS, and axial PD. The patients' legs were positioned neutrally. To assess PCL injury, and the measurements in the knee described below, we used sagittal and coronal proton density-weighted turbo spin-echo (TSE) sequences (slice thickness 1 mm, repetition time (TR)/echo time (TE), 2700/27 ms), and the coronal T2-weighted TSE sequence with fat saturation (slice thickness 1 mm, TR/TE 5030/71 ms).

ACL and PCL volume measurements

The volumes of the ACL in both groups, and the PCL in the controls, were obtained from sagittal T1-weighted series. Osirix software (open-source medical imaging software for MacOS X [Apple, Cupertino, CA]; OsiriX, Geneva, Switzerland) was used to manually outline the ACL and PCL. This method was tested and found to be reliable and accurate in previously conducted research[28]. The software calculated the volume as the sum of the surface multiplied by the slice thickness (1 mm), the volumes were presented in two decimals. (see Fig. 1). Furthermore, the correlation between the size of the ACL and the PCL in control patients was analyzed.

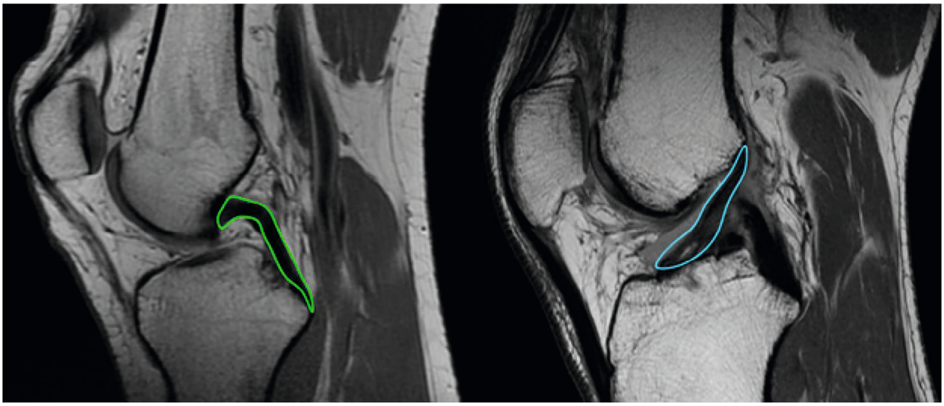

Figure 1: Sagittal view MRI of the knee, in which the PCL (left, green) and the ACL (right, blue) are outlined.

Femoral notch measurements

The boundaries of the intercondylar notch were measured according to Van Eck et al., who previously described the boundaries of the intercondylar notch [4]. The proximal border of the notch is defined as the image in which both femoral condyles were first clearly visible (Fig. 2A). The distal border of the notch is defined as the last image in which the condyles were continuous (Fig. 2B).

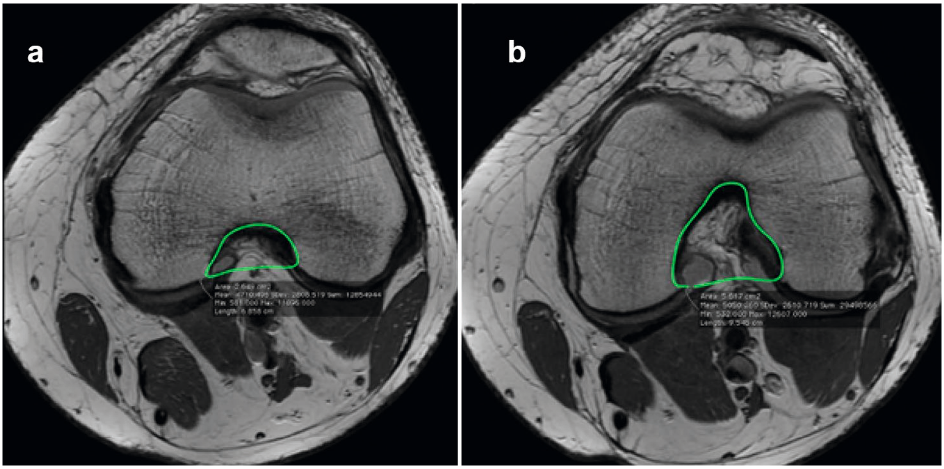

Figure 2: Axial MRI image of the knee, **A** most proximal, **B** most distal of the intercondylar notch

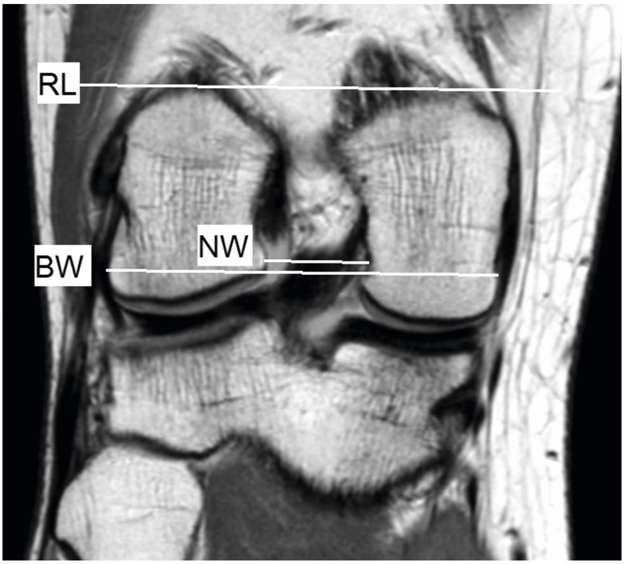

Figure 3: Coronal MRI of the knee, with the described measurements. RL reference line, NW notch width, BW bicondylar width

Additionally, the notch width index (NWI) was measured according to the method first described by Staeubli et al. [21] and later modified by Whitney et al. [26]. A reference line (RL) is defined as a tangent to the posterior subchondral aspect of both femoral condyles. All femoral widths are measured parallel to this reference line. In the coronal plane, the following measurements were applied: bicondylar width (BW) and notch width outlet (NW). The notch width index was calculated by dividing the NW by the BW (Fig. 3).

A T2 coronal plane was used in each patient to measure BW and NW. The slice chosen in every knee was the plane in which the ACL and PCL cross one another as close as possible to the midsubstance of the ACL [26]. This point was typically found on the first slice anterior to the appearance of the roof of the intercondylar notch.

Statistical analysis

The independent-sample t-test was used to assess whether or not the volume of the intercondylar notch and the volumes of the ACL and PCL and the bicondylar width, the notch width, and the notch width index were significantly related to the presence of a PCL rupture. The results were not corrected for height, weight, BMI, age, and sex, since we matched our cases with our patients on those factors. A value of 0.05 was chosen as the level of significance.

The reliability of the measurements performed in this study was established using interclass correlation coefficients (ICCs). Twenty-eight MRI scans were randomly selected to be assessed a second time, two weeks after initial measurements. The observer did not know the values of previous measurements. A post hoc power analysis was performed, showing that the current study with 30 patients included in each group, had a power of 94.9%. The calculation showed that 28 patients in the control group and 28 patients with a PCL rupture were needed to reach sufficient power. With 30 patients, the power was considered excellent.

The study population consisted of two groups of 30 patients matched for age, height, weight, BMI, and sex. There were six females (20%) in each group. The demographic data for each group are shown in Table 1.

Table 1 Characteristics of the patients. Data presented as mean with ± SD. BMI = Body Mass Index

	PCL injured (n=30)	PCL intact (n=30)
Age (years)	40 ± 13	38 ± 12.0
Length (cm)	180 ± 11	179 ± 9
Weight (kg)	80.3 ± 12	82.5 ± 12
BMI	24.3 ± 2.1	25.6 ± 3.0
Female, N (%)	6 (20%)	6 (20%)
Mean time between trauma and radiograph, mths (SD)	12.6 ± 16	6.9 ± 10

RESULTS

Measurements

Table 2 shows the means for the BW, NW, NWI, the volumes of the PCL and ACL, and the intercondylar sizes. A significant difference in the sizes of the intercondylar notch (p=0.001) between patients with a PCL rupture and the control patients were found. Secondly, a significant difference between the volumes of the ACL (p = 0.039) in patients with a PCL rupture and patients with intact PCLs was found.

5

Table 2: Overview of measurements of the Bicondylar Width (BW), the Notch Width (NW), the Notch Width Index (NWI), the intercondylar volumes and the cruciate ligament volumes. Measurements presented in mean with ± SD.

	PCL injured (n=30)	PCL intact (n=30)	p-value
BW (mm)	7.8 ± 0.7	8.1 ± 0.5	(n.s.)
NW (mm)	2.1 ± 0.4	2.2 ± 0.3	(n.s.)
NWI	0.3 ±0.1	0.3 ± 0.1	(n.s.)
Intercondylar volumes (cm^3)	7.0 ± 2.2	8.6 ± 1.2	**0.001**
PCL volumes (cm^3)	-	2.2 ± 0.4	
ACL volumes (cm^3)	1.1 ± 0.3	1.3 ± 0.3	**0.039**

Patients with a PCL rupture had smaller intercondylar sizes (7.0 cm3 ± 2.2 compared to 8.6 cm3 ± 1.2) and smaller volumes of the ACL (1.1 cm3±0.3 compared to 1.3 cm3±0.3), when compared to patients with an intact PCL.

There were no significant differences in the bicondylar width, notch width, and notch width index. The correlation between the size of the PCL and the ACL in the control patients was found to be a positive correlation of 0.7. Meaning patients with smaller volumes of the PCL are more likely to have smaller volumes of the ACL.

When looking at sex, the intercondylar sizes (p=0.02) and the volumes of the ACL in males were significantly larger than in the controls (p=0.01). For the females, only the intercondylar volumes were significantly different between patients and controls (p=0.001) (Table 3).

The ICCs were considered excellent with values of 0.906 for BW (95% CI 0.807–0.955), 0.993 for NW (95% CI 0.984–0.997), and 0.952 for NWI (95% CI 0.899–0.977).

Table 3 Descriptives of measurements divided between males and females and between controls and injured patients. Measurements presented in mean with ± SD.

	Males			**Females**		
	PCL injured (n=24)	**PCL intact (n=24)**	**P-value**	**PCL injured (n=6)**	**PCL intact (n=6)**	**P-value**
BW (mm)	79.8 ± 5.7	82.3 ± 3.6	(n.s.)	71.3 ± 5.4	73.9 ± 4.1	(n.s.)
NW (mm)	20.8 ± 3.4	22.1 ± 2.4	(n.s.)	21.2 ± 4.5	21.3 ± 3.0	(n.s.)
NWI	26.0 ± 3.9	26.9 ± 2.8	(n.s.)	29.5 ± 4.7	28.8 ± 3.7	(n.s.)
Intercondylar volumes (cm^3)	7.5 ± 2.2	8.8 ± 1.1	**0.015**	5.0 ± 0.9	8.0 ± 1.3	**0.001**
PCL volumes (cm^3)	-	2.3 ± 0.4	-	-	1.7 ± 0.4	-
ACL volumes, controls only (cm^3)	1.2 ± 0.3	1.4 ± 0.3	**0.013**	1.0 ± 0.2	1.0 ± 0.3	(n.s.)

DISCUSSION

The most important findings of this study are that patients with a PCL rupture had smaller intercondylar sizes and smaller ACL volumes. To our knowledge, this is the first study to find anatomical risk factors for sustaining a PCL rupture. In a recent study on plain radiographs of the knee, van Kuijk et al. found that the shape of the intercondylar notch plays an important role in the PCL-deficient knee [13]. With this current study, using MRI reconstructions of the intercondylar notch and the volumes of the PCL and ACL, it becomes clearer what specific anatomical features contribute to these findings on 2D plain radiographs.

Possibly, patients with smaller ACL volumes are also at greater risk of sustaining a PCL rupture. The absolute mean difference was 17 cubic millimeters, making it a statistically significant difference. Although the absolute difference is relatively small, raising the question if this would be clinically important, it is a difference of more than a 10% in volume. Our opinion is, that more than 10% difference in size would be clinically relevant, and as stated, it was statistically different too. A positive correlation between the volumes of the PCL and the ACL was found, and although the sample size is small, it can be assumed that patients with smaller ACL volumes had smaller PCL volumes. Smaller PCLs can withhold less force and are more prone to rupture [15, 24]. Furthermore, the size of the PCL (and of the ACL) is correlated with the size of the intercondylar notch [16, 22]. It is well-accepted that the volumes of the intercondylar notch, the PCL, and the ACL are all positively correlated. A question still unresolved is whether patients with smaller cruciate ligaments and smaller intercondylar notches rupture their ligaments because of the relatively smaller force they can withhold, or because of chronic or acute damage because of notch impingement to the cruciate ligaments [1, 5, 19, 27]. However, notch impingement may play a lesser role in the risk of sustaining a PCL rupture, because of the anatomical position of the PCL posterior in the knee.

When comparing males to females, we find a similar result, with the note that we only have a small group of females, thus the statistical power of these results is low.

It is difficult to compare the results of this study to previously conducted research since this study is the first to have investigated the volumes of the intercondylar notch and the volumes of the PCL and ACL in correlation with a PCL rupture. Research is abundant into the intercondylar notch and the ACL deficient knee (see Supplemental File) [12, 24, 26, 28]. These studies found similar results in the ACL-deficient knee as we have found in the PCL-deficient knee. This current study, therefore, adds important new information, proving the importance of the volumes of the cruciate ligaments and the sizes of the intercondylar notch.

The risk factors in the current study are possibly modifiable (for example, during surgery with notch plasty), it is uncertain if changing the notch dimension, can reduce the risk for future PCL rupture, and notch plasty results are debated in the literature.

A limitation is the low number of patients included in the study. Ideally, more patients would have been included, to have more power, although the study has adequate power. However, few patients have a sports-related isolated PCL rupture. Because the consequences of this type of injury are severe, we are confident that research into PCL rupture is necessary.

Degenerative changes in the knee could result in osteophyte formation and narrowing of the intercondylar notch. These changes happen more often after PCL rupture. This could mean that the results found were based on post-traumatic degenerative changes. Therefore, patients with Kellgren and Lawrence grade 2 or more were excluded, reducing this possible bias as much as possible.

While prevention programs are implemented for preventing an ACL rupture during sports [7], it has not been investigated if these programs or comparable programs can help to reduce the incidence of PCL ruptures. However, for preventing a disease or injury in general, risk factors must first be identified, and that is, in our opinion, the clinical relevance of our study. We are convinced, this study is an important first step in identifying risk factors, and we hope that we have inspired researchers to further investigate the results found. This study shows, for the first time, that there are significant differences in the shape of the knee between patients with a PCL rupture and control patients.

CONCLUSION

This study shows that patients with a smaller intercondylar size and a smaller volume of the ACL are more prone to sustain PCL rupture. This is an important first step in identifying patients at risk for a PCL rupture. Identifying patients at risk is useful information if, in the future, the risk of individuals sustaining a PCL rupture might be reduced.

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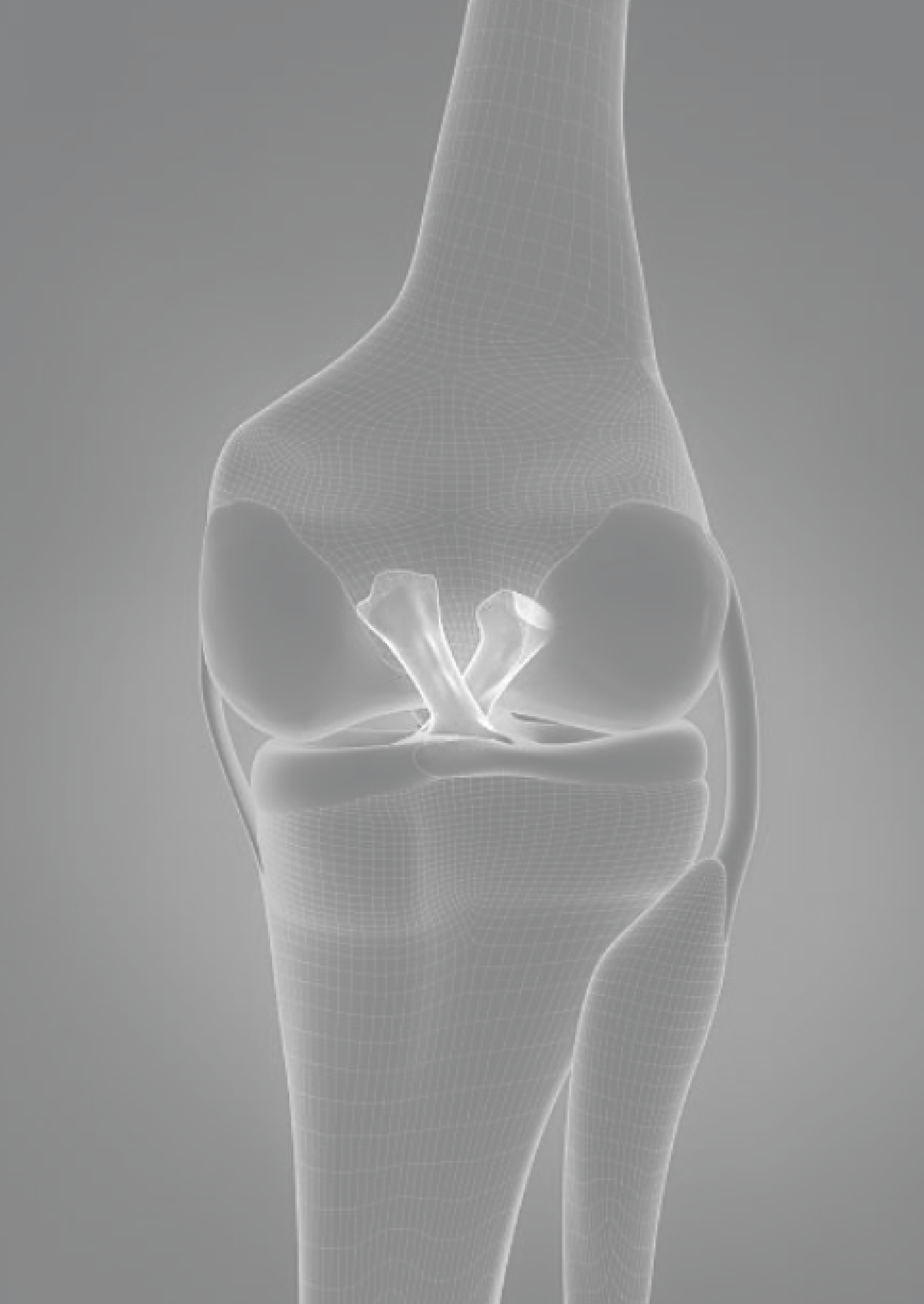

Chapter 6

Knee shape might predict clinical outcome after an anterior cruciate ligament rupture

Eggerding V, Van Kuijk KSR, Van Meer BL, Bierma-Zeinstra SMA, van Arkel E, Waarsing JH, Reijman M, Meuffels DE

ABSTRACT

Aim

We have investigated whether the shape of the knee can predict the clinical outcome of patients after an anterior cruciate ligament rupture.

Methods

We used statistical shape modelling to measure the shape of the knee joint of 182 prospectively followed patients on lateral and Rosenberg view radiographs of the knee after a rupture of the anterior cruciate ligament. Subsequently, we associated knee shape with the International Knee Documentation Committee subjective score at two years follow-up.

Results

The mean age of patients was 31 years (21 to 51), the majority were male (n = 121) and treated operatively (n = 135). We found two modes (shape variations) that were significantly associated with the subjective score at two years: one for the operatively treated group (p = 0.002) and one for the non-operatively treated group (p = 0.003). Operatively treated patients who had higher subjective scores had a smaller intercondylar notch and a smaller width of the intercondylar eminence. Nonoperatively treated patients who scored higher on the subjective score had a more pyramidal intercondylar notch as opposed to one that was more dome-shaped.

Conclusion

We conclude that the shape of the femoral notch and the intercondylar eminence is predictive of clinical outcome two years after a rupture of the anterior cruciate ligament.

INTRODUCTION

Rupture of the anterior cruciate ligament (ACL) is a common sports-related injury. The annual incidence is estimated at five per 10 000 persons in the general population.1 ACL rupture can lead to complaints of instability in the short term, which negatively influences the quality of life and level of sporting activity. In the long term, an ACL rupture is associated with an increased risk of osteoarthritis, which varies from 13% to 48%, depending on secondary injuries.2

At present clinical outcome after an ACL rupture is not predictable.3 Additional injuries to the knee might forecast a less successful outcome after an ACL rupture according to a population-based register.4 However, these supplementary injuries cannot be used to give an individual patient a clear prediction of their expected clinical outcome. The availability of objective predictors would aid the provision of accurate information for patients as to what they might expect.

A study of 100 patients by Fridén et al5 demonstrated that a more spherical shape of the femoral condyles was predictive of failure of non-operative treatment. However, conventional radiographs were used with lines drawn on them by the researcher. This manual method provided a low inter-observer correlation coefficient6 and they had no patient-reported outcome measures (PROMs), basing their end point on whether patients underwent an ACL reconstruction. Another measure of anatomical shape is the tibial slope.7 Using the same patients and outcome measures, Kostogiannis et al7 found that reconstructed knees were over-represented where there were extremely low tibial slope angles.

The shape of the knee can be assessed using radiographs and generally after a knee injury, a radiograph will have been obtained. Because of this widespread availability and low cost, it would be very useful if the radiographs could be used to predict outcomes after an ACL rupture.

Our objective was to evaluate whether the shape of the knee on the presenting radiographs can predict the clinical outcomes of patients after an ACL rupture.

PATIENTS AND METHODS

Patients were identified from two previously conducted prospective studies at the Erasmus MC Department of Orthopaedic Surgery; the KNee osteoArthritis anterior cruciate Ligament Lesion (KNALL)8 and the Computer Assisted Surgery for Anterior Cruciate Ligament injury (CAS-ACL) study.9

The KNALL is a prospective observational study of 154 patients with a recent ACL rupture, who were treated either operatively or non-operatively. The inclusion period of the KNALL study was from January 2009 to November 2010 with a follow-up period of two years.

The CAS-ACL study is a double-blinded randomized clinical trial of 100 patients, for whom ACL reconstruction was indicated. The study compared computer assisted ACL reconstruction with conventional ACL reconstruction.9 The inclusion period of the CAS-ACL study was from January 2007 to November 2009, with a follow-up period of two years.

Radiographs, patient characteristics, and International Knee Documentation Committee (IKDC)-subjective score10 at baseline and at the two years follow-up were obtained. Both studies were approved by the medical ethics committee and written consent was obtained from all patients.

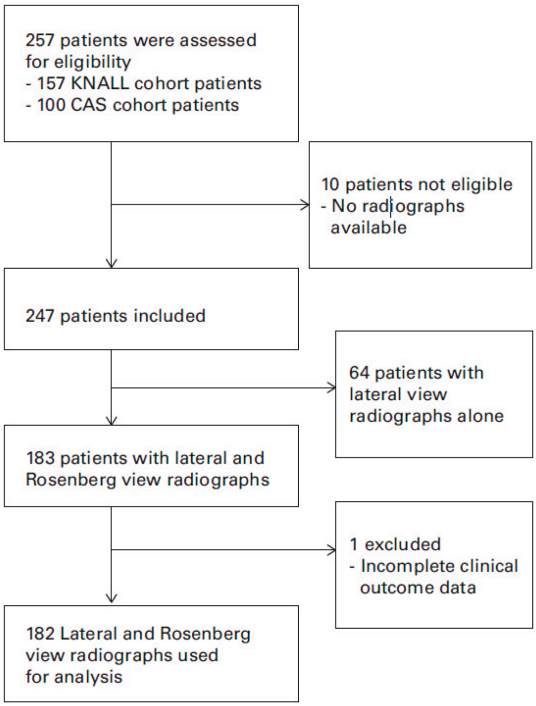

Figure 1: Flowchart of patients included in the study (KNALL, KNee osteoarthritis anterior cruciate Ligament Lesion; CAS, computer-assisted surgery).

For the present study, we selected those patients for whom we had lateral and Rosenberg view11 radiographs, IKDC- subjective score and two years of follow-up. The combination of the KNALL study and the CAS-ACL study created a database of 257 patients. Of these patients, a total of 182 fulfilled the inclusion criteria, of whom 135 had been treated operatively (74.2%) and 47 non-operatively (Fig. 1).

All participants had a complete primary ACL rupture and a mean age of 31 years (21 to 51) in the absence of any injury to the posterior cruciate ligament. The demographic data, time to reconstruction, and IKDC-subjective scores of the patients are provided in Table I.

The radiological measurements were performed on non-weight bearing, standard lateral and Rosenberg view radiographs. The Rosenberg view is a weight-bearing posterior-anterior radiograph taken at 45° flexion of the knee.11

With statistical shape modelling (SSM)12 it is possible to quantify the general shape of the knee joint on the radiographs. This method is unique because it deconstructs nearly all variation in shape into a limited number of quantitative measures that each describes distinct shape variants. In a recent study by our group,13 SSM was employed to see whether knee-shape variants were associated with the development of osteoarthritis. From the radiographs, we outlined the shape of the distal femur and the proximal tibia and fibula with the use of SSM software (ASM tool kit, Manchester University, Manchester, United Kingdom). 12 The shapes were defined by 60 landmarks on the lateral view and 25 landmarks on the Rosenberg view, which were placed along the contour of the bone in the image. Each point was placed at the same location in each image to allow comparison between shapes. The researcher who placed the points was blinded to the clinical outcome of the patient.

Principal component analysis was used to transform the set of point coordinates into the statistical shape model, which comprises a number of shape variants (modes) that together explain 95% of the variation in the shape of the knees in the study population.

The description of a definition of a mode was determined at a consensus meeting, which consisted of an orthopedic surgeon with extensive experience in treating ACL ruptures (DEM), an expert on statistical shape modelling (JHW), and the first two authors of this study (VE, KSRvK). Intraobserver reliability was assessed by randomly selecting 26 knees which were annotated a second time after four weeks.

Our primary outcome score was the IKDC-subjective score at two-years follow-up. The IKDC-subjective Knee Form was designed to measure symptoms and limitations in function and sporting activity due to impairment of the knee for every knee-related injury. 14,15 In a review of available outcome measurements for ligament injuries of the knee, Johnson and Smith16 and Van Meer et al10 found that the IKDC-subjective knee form is the preferred measurement tool for monitoring patients after an ACL rupture, particularly in the short-term.

Statistical analysis.

The association between separate modes with the IKDC-subjective score at two-year follow-up was analyzed using linear regression analyses. We performed a separate analysis for the operatively and non-operatively treated patients. The IKDC-subjective score was used as a dependent variable and the different modes as independent variables. We selected all the modes with a p-value < 0.05 with the use of univariate analyses and considered them as modes, with a possible association with the IKDC-subjective score at two years. A p-value < 0.01 was considered significant. We adjusted for known confounders for the IKDC-subjective score such as BMI, age, and gender17-19 and the IKDC-subjective score at inclusion. The reliability of the positioning of the landmarks was tested by assessing the intra-class correlation coefficient (ICC) with a two-way random model for absolute agreement. All statistical analyses were performed with IBM SPSS Statistics v.20.0 (IBM, Armonk, New York).

RESULTS

There was no statistical difference in mean IKDC-subjective after two years between the operatively treated and the non-operatively treated group of patients, 85.9 (SD 13.5) and 85.4 (SD 12.7), respectively (p = 0.835) (Table I).

Table I. Patient characteristics and clinical outcome. Data shown as mean value (range) (IKDC, international Knee Documentation Committee)

	Operative (n=134)	**Non-Operative (N=48)**	**p-value**
Age	30	33	0.012
Weight (KG)	77	78	0.677
Length (cm)	178	175	0.062
BMI	24	25	0.209
Female sex %	28.2	37	0.331
Time to reconstruction (months)	17 (range 1-180)	-	-
IKDC subjective form (baseline)	57.3 (range 19.5-93.1)	58.8 (range 18.4-97.7)	0.617
IKDC subjective form (2 years follow up)	85.9 (range 36.8-100)	84.9 (range 51.7-100)	0.835

Table II. Modes of the Rosenberg radiograph and correlation with clinical outcome. P-values are corrected for confounders for the International Knee Documentation Committee score (mean body mass index, age, gender and IKDC-subjective score at baseline)

	Non-operatively treated patients		Operatively treated patients	
	R2	**p-value**	**R2**	**p-value**
Mode 9			0.153	0.002
Mode 12			0.094	0.045
Mode 14			0.101	0.032
Mode 15	0.357	0.003		
Mode 20			0.092	0.050
Mode 21			0.093	0.047
Mode 22			0.118	0.014

The SSM provided 20 modes for the lateral radiographs (mode 0 to mode 19) and 28 modes for the Rosenberg view (mode 0 to mode 27). Tables II and III represent the modes and their correlation coefficients with $p < 0.05$. The intra-observer ICC was considered good, with a mean of 0.805 (0.48 to 0.97), 89% above 0.7; the ICC was below 0.7 for only three modes.

6

Table III. Modes of the lateral radiograph and correlation with clinical outcome. P-values are corrected for confounders for the International Knee Documentation Committee (IKDC) score (mean body mass index, age, gender and IKDC-subjective score at baseline)

	Non-operatively treated		Operatively treated	
	R^2	**p-value**	**R^2**	**p-value**
Mode 4			0.108	0.020
Mode 6			0.116	0.013
Mode 7			0.103	0.026
Mode 8			0.093	0.042
Mode 10			0.095	0.039
Mode 17	0.249	0.041		

With multivariate analysis, we found five modes with $p < 0.05$ for the lateral view which had an association with the IKDC-subjective scores (Mode 4: $p = 0.02$; mode 6: $p = 0.013$; mode 7: $p = 0.026$; mode 8: $p = 0.042$; mode 10: $p = 0.039$). For the Rosenberg view, we found five modes with $p < 0.05$ which had an association with the IKDC-subjective scores (mode 9: $p = 0.002$; mode 12: $p = 0.045$; mode 14: $p = 0.032$; mode 21: $p = 0.047$; mode 22: $p = 0.014$). In the univariate analyses, only mode 9 on the Rosenberg view was significantly predictive of the clinical outcome at two years ($p = 0.002$). Mode 9 describes the width of the intercondylar eminence and the width of the intercondylar notch, the variation in shape for mode 9 is shown in Figure 2. Patients with a smaller intercondylar eminence and a smaller intercondylar notch scored higher on the IKDC-subjective at two years.

We found one mode with $p < 0.05$ for the lateral view which had an association with the IKDC-subjective score (mode 17: $p = 0.041$). For the Rosenberg view, we found two modes with $p < 0.05$ which had an association with the IKDC-subjective scores (mode 5: $p = 0.019$; mode 15: $p = 0.003$). In the univariate analyses, only mode 15 on the Rosenberg view was significantly predictive of the clinical outcome at two years ($p = 0.003$). Mode 15 describes the shape of the intercondylar notch with the variation demonstrated in Figure 3. Patients with a pyramid-shaped intercondylar notch, similar to the A shape as described by Van Eck et al20 scored higher on the IKDC-subjective score at two years compared with a more dome-shaped intercondylar notch.

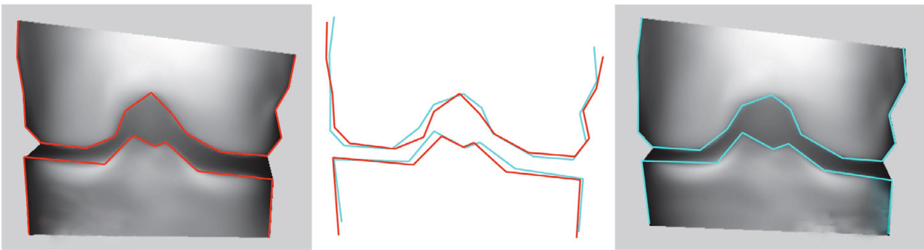

Figure 2: Digital images of the extreme shape variables for mode 9 represented as -2.5 standard deviation (SD) (left) and +2.5 SD (right).

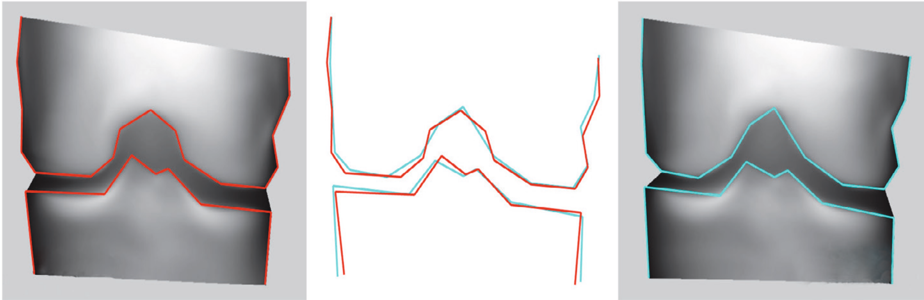

Figure 3: Digital images of the extreme shape variables for mode 15 represented as -3.0 standard deviations (SD) (left) and +3.0 SD (right).

DISCUSSION

The main finding of this prospective cohort study was that two specific shape variants of the knee are predictive of clinical outcome two years after an ACL rupture; mode 9 in the operatively treated group and mode 15 in the non-operatively treated group. Mode 9 represents a variation in the width of the intercondylar notch and the intercondylar eminence. A smaller intercondylar notch and a smaller intercondylar eminence predicted a better clinical outcome for patients who underwent operative reconstruction on the IKDC-subjective score at two years follow-up. Mode 15 represents a variation in the steepness of the intercondylar notch in the non-operatively treated group.

A possible explanation for our finding is that patients with a smaller intercondylar notch also had a smaller size of their native ACL.18 In this way, the graft used in ACL reconstruction bears more resemblance to the native ACL. Consistent with this idea is that patients with a larger notch have a relatively smaller graft compared with their native ACL and there is more of a mismatch between graft and notch size. Several studies in the past suggested that a larger graft is less likely to fail.21-23

An explanation for the fact that mode 15 can predict clinical outcome after non-operative treatment for patients after ACL rupture, is that patients with a pyramid-shaped notch have a larger contact area between the femur and tibia. In this way, the femur and tibia have a more intrinsically stable construction and such a patient may be able to reach a higher level of function despite the ligament rupture.

Our method to assess the shape of the knee with SSM creates modes. These modes are a combination of variations in different aspects of the shape. The advantage of SSM is that it objectively creates a set of shape variants that explain 95% of the variation.24 Nevertheless, it is not possible with SSM to extract the factor that contributes the greatest amount to the mode. It is possible that if we only take one contributing factor out of mode, then any correlation is lost.

Previous studies also focused on other anatomical variants thought to be predictive of outcome after an ACL rupture, such as the tibial slope and the sphericity of the femoral condyle on the lateral radiograph.5,7 Our study could not confirm the influence of these shape variants on clinical outcome. On the lateral view radiograph, no mode was predictive of clinical outcome after an ACL rupture. The difference between our findings and the previously published studies might be explained by the use of different outcome measures and another method is used to assess the shape of the knee. Previous studies used reconstruction of the ACL as an outcome measure, whereas we used a validated PROM.

The strengths of this study are the use of a large group of prospectively followed patients and the use of radiographs for depicting the shape of the knee. The benefits of the use of radiographs are that they are widely available and relatively inexpensive.

A limitation of this study is that the knee is a complex three-dimensional joint, of which some shape variations are attributable to a combination of the lateral and the Rosenberg projections. We tried to fully outline the important contours of the femur, tibia, and fibula aided by the placement of the landmarks. An advantage of SSM is that the various modes represent relative variation in shape, independent of differences in the size of the joint, such that the method reduces errors caused by variation in magnification.

In conclusion, this study demonstrates that two shape variants can predict a better score on the IKDC-subjective score at two years, one for the operatively treated group and one for the non-operatively treated group. Our results suggest that in the future, clinicians will identify the shape of the knee when informing patients with an ACL rupture about what they might expect their clinical outcome to be.

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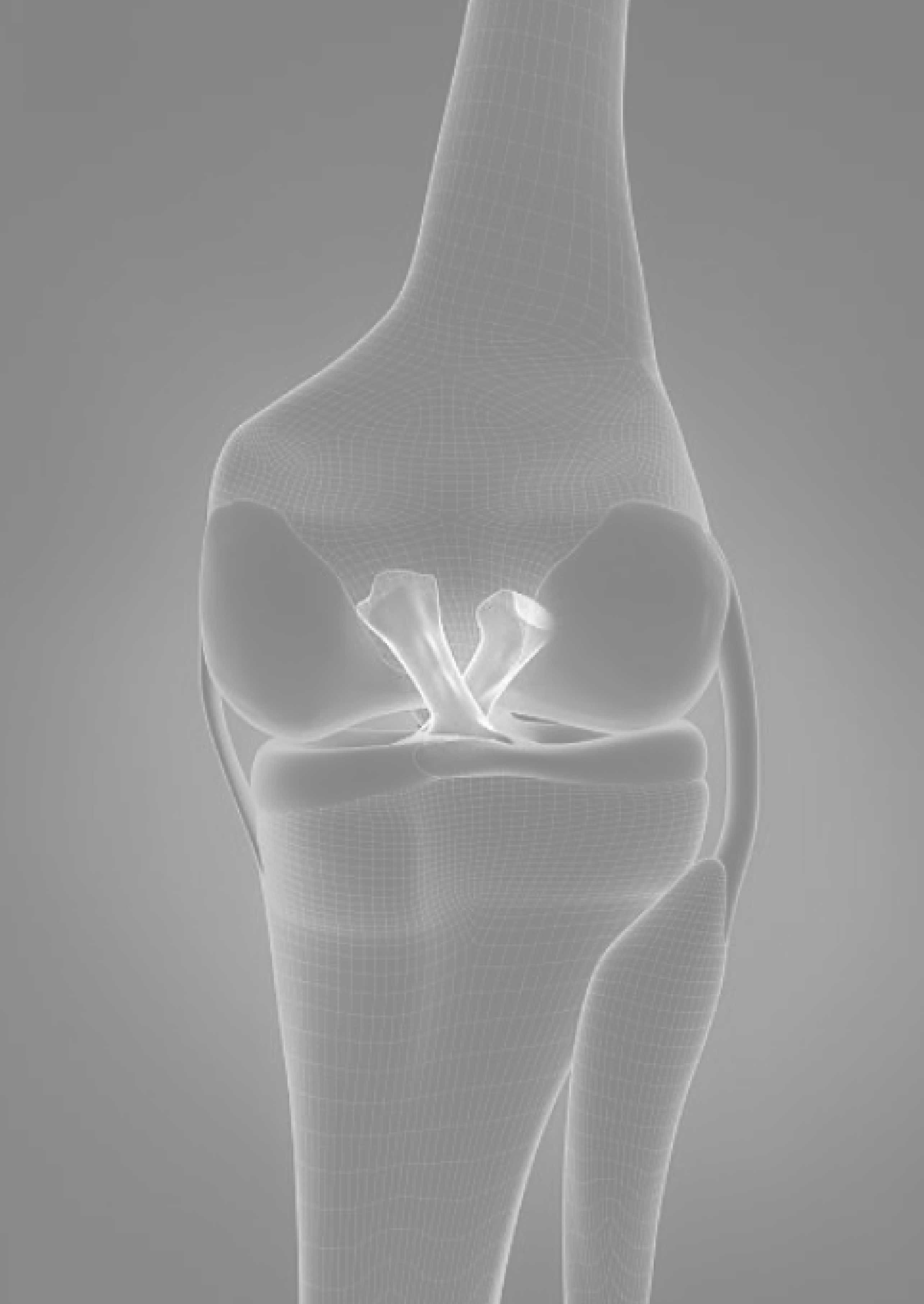

Chapter 7

General discussion

GENERAL DISCUSSION

In this chapter, I will discuss all shape variants found in this thesis related to anterior cruciate ligament (ACL) rupture and posterior cruciate ligament (PCL) rupture, and give an overview of the implications for daily practice. Furthermore, I will give my opinion for future research on shape variants of the knee and cruciate ligament ruptures. Lastly, I will outline how shape variants of the knee can be used now and in the nearby future for the prevention of cruciate ligament ruptures, for example in patient selection and patient-specific counselling.

My goal was to identify anatomical landmarks in patients, who are at greater risk for sustaining cruciate ligament rupture and thereby make it possible to identify high-risk groups for cruciate ligament rupture and its subsequent prevention. The first half of this thesis focuses on finding risk factors for sustaining an ACL injury in athletes, the second part focuses on finding risk factors for sustaining a PCL rupture. Hopefully, this will make it easier in the future to select only those patients who are at greater risk for sustaining a cruciate ligament injury. This could make injury prevention programs more efficient and cost-effective. In all the studies included in this thesis, we used the shape, volumes, and dimensions of the knee to identify patients who are at greater risk for sustaining a CL rupture, and compared these values to control groups of patients with knee trauma but without a CL rupture.

Anatomical variance in the shape of the knee between patients with a cruciate ligament injury and control patients.

In this thesis, two different methods were used to assess the shape of the knee, and to compare the shape variants in the ACL and PCL ruptured knee with a control group who had knee trauma, but had intact cruciate ligaments. First, the shape of the knee and dimensions of the knee were assessed using a self-learning program Statistical Shape Modeling (SSM) [25]. A large group of patients was selected retrospectively, who had suffered an isolated ACL rupture (**chapter 2**) or PCL rupture (**chapter 4**) and compared them to an evenly large, matched group of patients who had suffered knee trauma but did not injure their cruciate ligament. Secondly, in **chapter 3** and **chapter 5**, MRI with 3D reconstructions was used to measure the following dimensions of the shape of the knee: the volume of the ACL, the volume of the PCL, the volume of the intercondylar notch, the intercondylar notch width, bicondylar notch width, and the notch width index. We chose these measurements because these were found to be independent risk factors, following the results of chapter 2 and chapter 4. The result that we present in this thesis, are found on conventional x-rays and are confirmed on 3D MRI reconstructions. Both independent methods, using two very different imaging techniques, produced comparable results leading to stronger conclusions. One of the most important findings is that in both the ACL ruptured knee, and in the PCL ruptured knee, the role of the intercondylar notch is very prominent. When assessing the shape of the knee on conventional x-rays, patients with a ruptured cruciate ligament have smaller intercondylar notches when compared to patients who did not have a ruptured cruciate ligament. Furthermore, patients with a ruptured cruciate ligament also had a more pyramid-shaped intercondylar notch and a smaller tibial eminence. The results of our studies are consistent with studies in the past into the ACL ruptured knee, which has also found the notch width and femoral notch size to be related to ACL rupture [7, 20, 24]. However, these previously conducted studies were primarily focused on anterior-posterior X-rays, while we used the Rosenberg view X-rays. For the PCL ruptured knee, evidence was lacking. Our group is the first to investigate the shape of the knee in a PCL ruptured knee. Comparing these results to the literature is therefore difficult. Our results show that on conventional x-rays, a smaller and pointier intercondylar notch is related to a higher risk of sustaining an ACL and a PCL rupture. In chapters 3 and 5 we further investigated these findings on 3D reconstructions of the knee. Again, we found that the intercondylar notch plays an important role. The volume of the intercondylar notch of patients with a cruciate ligament rupture was significantly lower when compared to patients with intact cruciate ligaments. The notch width and notch width index were significantly smaller in the cruciate ligament ruptured knee as well. The study of van Diek et al [23] found no differences in morphology between patients with an ACL rupture and a control group in measurements with MRI. However, another MRI study performed by Whitney et al [28] found a decreased femoral notch width to be related to ACL rupture. The difference between our study and that of van Diek et al, could be due to differences in methods and smaller group sizes where we used a larger group of patients and controls. Few studies have focused on the volume of the intercondylar notch, while previous studies showed the importance of the shape of the intercondylar notch in relation to the ACL [6, 21]. In chapter 5, patients with a PCL rupture had smaller ACL volumes. Secondly, we found a positive correlation between the volumes of the PCL and the ACL in both chapters 3 and 5.

Some (cadaver) studies have shown that the size of the cruciate ligaments is related to the size of the intercondylar notch [5, 29]. The results of this thesis confirm and empower these results. Furthermore, smaller cruciate ligaments can withhold less force [15], possibly this is one of the reasons why persons with a smaller intercondylar notch, and thus a smaller, weaker cruciate ligament, are more prone to cruciate ligament rupture. Another interesting hypothesis is that a smaller, pointier notch shape gives impingement on the ACL and PCL, giving repeated micro traumata [8, 29], or one macro trauma, and thus increasing the risk of a cruciate ligament rupture.

Another interesting topic is the differences between males and females. We know that females are at greater risk of sustaining a CL rupture. In this current thesis, no significant difference was found in the relative size (length and weight corrected) of the intercondylar notch, nor in the relative notch width index between males and females, differences in absolute size were found, but when corrected to length and weight, not significant.

Worth noting is that however a smaller intercondylar notch and a smaller tibial eminence are related to sustaining a cruciate ligament rupture, these shape variants are showing better results in subjective performance after an ACL reconstruction. In **chapter 6** we compared the shape of the knee with the outcome of the IKDC scores 2 years after an ACL rupture, in a large group of patients (n=182). Operatively treated patients who had higher subjective scores had a smaller intercondylar notch and a smaller width of the intercondylar eminence. Non-operatively treated patients who scored higher on the subjective score had a more pyramidal intercondylar notch as opposed to one that was more dome-shaped. We concluded that the shape of the femoral notch and the intercondylar eminence is predictive of clinical outcome two years after a rupture of the anterior cruciate ligament. When comparing these results to the current literature, no similar studies have been performed to date. Off course, a lot of research has been done in the prediction of outcomes after ACL reconstruction, but no shape variants have been identified to be a predictor of outcomes after ACL reconstruction until now. However, it could be that a smaller intercondylar notch is a risk factor for sustaining an ACL rupture, and this same smaller intercondylar notch is giving a better outcome after reconstruction. Perhaps this is because an ACL graft better fits in a smaller intercondylar notch, resulting in for example better proprioception after reconstruction.

Strengths and limitations

While to some readers it might not come as a surprise that the results on conventional x-rays are also found on MRI 3D reconstructions of the knee, making this one of the main strengths of this thesis. We confirmed with two different radiological modalities (X-rays and MRI) that the shape of the knee is related to the risk of sustaining a cruciate ligament rupture. The fact that these results are similar makes the correlation stronger. In addition, it makes it easier to select patients who are at greater risk, because not all patients have an MRI of the knee done, while most patients do get an x-ray when visiting the emergency department or the orthopedic surgeon, and in most professional sports organizations, medical screening of athletes is comprised of solely knee x-rays. Furthermore, many patients have gotten an x-ray of the knee with unrelated complaints, which can be used for counseling for the prevention of other injuries. In our clinical practice, of each 100 patients with an x-ray of the knee, 30 patients go on to receive an MRI of the knee. This means that more patients have x-rays available than MRI, making selecting patients easier via x-rays, but when MRI is available, both can and perhaps should be used. X-rays and MRIs give different information about the structures in the knee and have different pros and cons, combining them gives the most complete information. Even if patients have an x-ray or MRI for unrelated complaints, advice can be given for preventing cruciate ligament ruptures.

Our studies are unique in the sense that we used SSM, a hypothesis-free software, to find shape variants to be associated with the risk of sustaining an ACL rupture. To our knowledge, in chapters 2 and 4 we are the first ones to use these methods to find shape variants. Being hypothesis-free, we did not exclude any shape variant, and we assessed the shape of the knee entirely in relation to sustaining an ACL rupture.

A limitation of this thesis could be the design of the studies, where we performed our measurements after the ligament rupture occurred. Potentially, the shape of the knee changes after a ligament rupture, making it unsure if the results found in our studies are the reason why the patients ruptured their CL, or that the results found are merely the result of the rupture. We avoided this by only selecting patients without radiological signs of OA, and all patients with a cruciate ligament rupture had their x-rays obtained within 3 months after the rupture, reducing the risk of remodeling of the knee, while research shows that degenerative changes in the knee are found not sooner than 6-12 months after cruciate ligament rupture[17, 22]. Remodeling of the notch after a cruciate ligament injury could especially be of influence for our results, because osteophyte formation could potentially narrow the notch, giving false results. That is why we were extra careful excluding patients with signs of OA. Another limitation of these methods could be that the knee is a complex 3D form, and x-rays are only 2D projections. However as discussed before, our results are confirmed in 3D MRI reconstructions.

For chapters 2, 3, and 4 we used large groups of patients and compared them to equally large groups of control patients. However, a limitation in this thesis is the number of patients included in chapter 5. We did a post-hoc power analysis, showing the study had excellent power. However, ideally, we would have included more patients to have more power, but only a few patients have a sports-related isolated PCL rupture. Because the consequences of this type of injury are severe, more research into PCL rupture is necessary.

For all studies included in this thesis, we used different groups of patients and different control patients, making the results more generalizable.

Implementations and proposed future research

An ACL injury is an acute injury that is painful, mobility debilitating in the first weeks. In at least half of the patients, it will give secondary instability complaints, and all will have an increased risk of developing post-traumatic osteoarthritis (PTOA) with numbers as high as 12-27% after two years and 50–90% after 15 years follow up [26, 27]. ACL reconstruction surgery is not preventive of the long-term consequences such as osteoarthritis, but also the return to pre-injury sports level is compromised with only 60% returning to their pre-injury sports level[16]. For PCL ruptures, little information is available about the long-term effect but some studies showed earlier degenerative changes in the PCL ruptured knee than in healthy control patients [9, 12]. Patients with a PCL rupture are on average younger when receiving a total knee arthroplasty [19] than control patients without a PCL rupture. This shows that both ACL and PCL rupture give significant burdens, both in the acute setting, and in the long-term. With the growing number of athletes and especially of competitive athletes [13], the absolute number of ACL and PCL ruptures is growing and is likely to keep on growing in the next couple of years[4, 14], with an annual increasing incidence rate of 2.3%[2]. The best way to prevent PTOA and to prevent sports level loss is to prevent the initial rupture from happening. Two main things are crucial to achieving this. First, risk factors need to be identified. A lot of research is focused on risk factors for sustaining an ACL rupture. It is known that females have a four to six times greater risk, compared to males [10, 18]. Other risk factors are showing conflicting evidence in the literature. For example, quadriceps force, valgus knee alignment, and posterior tibial slope [3]. For PCL ruptures, little to no evidence is available when it comes to risk factors. Especially in sports-related ruptures, evidence is lacking. Secondly, when persons are recognized who are at greater risk for sustaining an ACL or PCL rupture, we have to be able to influence these risk factors to decrease the number of ACL and PCL ruptures. In the last couple of years, much research is done on ACL prevention programs. A recently published systematic review showed that ACL injury can be reduced by as much as 53% when injury prevention programs are implemented [11]. In this review, eight original papers were analyzed, but these studies only selected very specific groups of patients, for example only females. Not one of these studies made a selection within these groups.

An interesting sequel would be to compare the differences in bony morphology between patients with and without a re-rupture after ACL and PCL reconstruction. This could help the clinician in giving the patient individualized information on the risk of re-rupture. With the growing numbers of patients with cruciate ligament rupture and the growing number of MRIs of the knees that are performed these days, the results of our study could have important implications for the treatment and prevention of re-ruptures. For example, notch plasty during cruciate ligament reconstruction could potentially be an interesting procedure to decrease the chance of notch impingement. Adjusting the size of the graft used in reconstruction surgery is also an interesting aspect for future research. Individualizing the size of the graft, compatible with the size of the notch, could help to reduce the re-rupture rate, which causes major health and economic issues [1]. Furthermore, as discussed in the introduction of this thesis, more and more studies focus on ACL prevention programs. A well-designed prospective study selecting patients who are more at risk for an ACL rupture would be a very interesting future research project. While prevention programs are implemented for preventing an ACL rupture during sports [11], it has not been investigated if these programs or comparable programs can help to reduce the incidence of PCL ruptures. Meta-analysis of multiple trials might shed light on this issue. Because of the low prevalence of PCL injuries, screening only for a higher risk of sustaining a PCL injury would probably not be cost-efficient. However, in this thesis, the same risk factors have been found for ACL and PCL injuries. Screening and prevention programs could be combined to find and help patients at risk of different types of knee injury.

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SUMMARY

Patients with an anterior cruciate ligament (ACL) rupture or a posterior cruciate ligament (PCL) rupture, have a significant health burden; both for the patients themselves, and for the general health system. With significant, short and long-term consequences. Loss of mobility, loss of sports activity, increased risk of early osteoarthritis, and not returning to their pre-injury sports capability are just some of the consequences. Therefore, preventing cruciate ligament (CL) ruptures is both in the interest of patients, and in the interest of the general health care systems. To prevent CL ruptures, risk factors need to be identified. The overall aim of this thesis is to find risk factors related to the shape of the knee, which can be used to select patients at risk for a CL rupture.

In chapter 2 we compared the lateral and Rosenberg view X-rays of 168 prospectively followed patients with a ruptured ACL to a control group with intact ACLs, matched for gender, after knee trauma. We used statistical shape modeling software to examine knee shape and find differences in shape variants between both groups. In the Rosenberg view X-rays, we found five shape variants to be significantly different between patients with an ACL rupture and patients with an intact ACL but with knee trauma. Overall, patients who had ruptured their ACL had smaller, flatter intercondylar notches, a lower lateral tibia plateau, a lower medial spike of the eminence, and a smaller tibial eminence compared to control patients. We concluded that in general, patients with an ACL rupture have smaller intercondylar notches and smaller tibial eminences in comparison to patients with an intact ACL after knee trauma.

In chapter 3 we retrospectively compared Magnetic resonance imaging (MRI) scans of 121 patients with a proven ACL rupture to 92 control patients with proven intact ACLs and PCLs. Patients were selected for age, weight, height, and sex (by manual selection). We measured the volumes of the intercondylar notch and ACL and PCL, the bicondylar width (BW), the notch width (NW), and the notch width index (NWI). Second, we compared the result between males and females. Patients with an ACL rupture had, on average, a smaller NW (P<.001), a smaller NWI (P<.001), smaller intercondylar volumes (P<.001), and smaller volumes of the PCL (P<.001). Secondary results showed that females have on average a smaller NW (P<.001), smaller volumes of the intercondylar notch (P<.001), ACL (P=.004) and PCL (P<.001). However, the NWI was not significantly different between the sexes (P=0.508). We concluded that a smaller notch dimension, smaller volumes of the intercondylar notch, and smaller volumes of the PCLs are related to the presence of an ACL rupture. Secondary, females have smaller volumes of the intercondylar notch, ACLs and PCLs, but do not have a smaller NWI when compared to males.

In chapter 4 statistical shape modelling software was used to assess the shape of the knee and determine any difference in anatomical landmarks. We compared the anteroposterior (AP), lateral, and Rosenberg view radiographs of 94 patients with a ruptured PCL to a control group of 168 patients matched by age, sex, and body mass index (BMI), but with an intact PCL after a knee injury. We found shape variants on the AP and Rosenberg view radiographs to be significantly different between patients who tore their PCL and those with an intact PCL after a knee injury. Overall, patients who ruptured their PCL have smaller intercondylar notches and smaller tibial eminences than control patients. This chapter showed that differences in the shape of the knee are associated with the presence of a PCL rupture after injury. A smaller and more sharply angled intercondylar notch and a more flattened tibial eminence are related to PCL rupture. This suggests that the morphology of the knee is a risk factor for sustaining a PCL rupture.

In chapter 5 our goal was to investigate if the morphology of the knee in patients who ruptured their PCL may differ from that of control patients. The hypothesis was that the intercondylar notch dimensions, 3-D volumes of the intercondylar notch, and the 3-D volumes of both the ACL and the PCL were correlated to the presence of a PCL rupture. The magnetic resonance imaging (MRI) scans of 30 patients with a proven PCL rupture were compared to 30 matched control patients with proven intact ACL and PCL. Control patients were selected from patients with knee trauma during sports but without cruciate ligament injury. Patients have been matched for age, height, weight, BMI, and sex. The volumes of the intercondylar notch and both the ACL and PCL were measured on 3D reconstructions. Secondly, the bicondylar width, the notch width, and the notch width index were measured for all subjects. The relationship between our measurements and the presence of a PCL rupture was analyzed. The results show a significant difference in the volumes of the intercondylar notch and the ACL between patients with a ruptured PCL and control patients. Patients with a PCL rupture have smaller intercondylar notch volumes and smaller ACL volumes. There were no significant differences in the bicondylar width, notch width, and notch width index. In the control patients, a significant correlation between the volume of the PCL and the volume of the ACL was found (0.673, $p<0.001$). We concluded that patients with a PCL rupture have smaller intercondylar volumes and smaller ACL volumes when compared to control patients. Secondly, patients with smaller ACL volumes have smaller PCL volumes. This study shows, for the first time, that there are significant size and volume differences in the shape of the knee between patients with a PCL rupture and control patients.

In chapter 6 we investigated whether the shape of the knee can predict the clinical outcome of patients after an anterior cruciate ligament rupture. We used statistical shape modelling to measure the shape of the knee joint of 182 prospectively followed patients on lateral and Rosenberg view radiographs of the knee after a rupture of the anterior cruciate ligament. Subsequently, we associated knee shape with the International Knee Documentation Committee subjective score at two years follow-up. The mean age of patients was 31 years (21 to 51), the majority were male (n = 121) and treated operatively (n = 135). We found two modes (shape variations) that were significantly associated with the subjective score at two years: one for the operatively treated group ($p = 0.002$) and one for the non-operatively treated group ($p = 0.003$). Operatively treated patients who had higher subjective scores had a smaller intercondylar notch and a smaller width of the intercondylar eminence. Non-operatively treated patients who scored higher on the subjective score had a more pyramidal intercondylar notch as opposed to one that was more dome-shaped. We concluded that the shape of the femoral notch and the intercondylar eminence is predictive of clinical outcome two years after a rupture of the anterior cruciate ligament.

Finally, in chapter 7, the general discussion, some of the key findings of the studies in this thesis are further discussed. Furthermore, we gave an overview of our studies, and how they contributed to the current practice. The strengths and limitations were discussed. To conclude, recommendations for practice and future research were presented.

NEDERLANDSE SAMENVATTING

Patiënten met een voorste kruisband (VKB) ruptuur of een achterste kruisband (AKB) ruptuur, hebben een aanzienlijke gezondheidslast; zowel voor de patiënten zelf, als voor de gezondheidzorg. Met aanzienlijke gevolgen op zowel korte- als lange termijn. Verlies van mobiliteit, verlies van sportactiviteiten, een verhoogd risico op vroege artrose en het niet terugkeren naar de sportmogelijkheden van voor de blessure zijn slechts enkele van de gevolgen. Daarom is het voorkomen van kruisbandrupturen zowel in het belang van de patiënten als in het belang van de algemene gezondheidszorg. Om kruisband rupturen te voorkomen, moeten risicofactoren geïdentificeerd worden. Het algemene doel van dit proefschrift is het vinden van risicofactoren gerelateerd aan de vorm van de knie, die gebruikt kunnen worden om patiënten te selecteren die risico lopen op een kruisband ruptuur.

In hoofdstuk 2 hebben we de laterale en Rosenberg view röntgenfoto's van 168 prospectief gevolgde patiënten met een gescheurde VKB vergeleken met een controlegroep met intacte VKB's, gematched op geslacht, nadat ze een knietrauma doorgemaakt hebben. We gebruikten software om de vorm van de knie te identificeren en verschillen in vormvarianten tussen beide groepen te vinden. Op de Rosenberg view röntgenfoto's vonden we vijf vormvarianten die significant verschilden tussen patiënten met een VKB-ruptuur en patiënten met een intacte VKB, maar met een doorgemaakt knietrauma. In het algemeen hadden patiënten met een gescheurde VKB kleinere, vlakkere intercondylaire notches, een lager lateraal tibiaplateau, een lagere mediale piek van de eminentia en een kleinere tibiale eminentia in vergelijking met de controle patiënten. Hieruit concludeerden wij dat in het algemeen, patiënten met een VKB-ruptuur kleinere intercondylaire notches en kleinere tibiale eminentia's hebben in vergelijking met patiënten met een intacte VKB na knietrauma.

In hoofdstuk 3 vergeleken we retrospectief Magnetic Resonance Imaging (MRI) scans van 121 patiënten met een bewezen VKB-ruptuur met 92 controle patiënten met bewezen intacte kruisbanden. De patiënten werden geselecteerd op leeftijd, gewicht, lengte en geslacht (door handmatige selectie). We hebben de volumes van de intercondylaire notches en de volumes van de VKB en AKB gemeten, evenals de de bicondylaire breedte (BW), de notch width (NW), en de notchwidth-index (NWI). Vervolgens vergeleken we de resultaten tussen mannen en vrouwen. Patiënten met een VKB-ruptuur hadden, gemiddeld, een kleinere NW ($P<.001$), een kleinere NWI ($P<.001$), kleinere intercondylaire volumes ($P<.001$) en kleinere volumes van de AKB ($P<.001$). Secundaire resultaten toonden aan dat vrouwen gemiddeld een kleinere NWI ($P<.001$), kleinere volumes van de intercondylaire notch ($P<.001$), VKB ($P=.004$) en AKB ($P<.001$) hebben. De NWI was echter niet significant verschillend tussen de geslachten (P=0.508). Wij concludeerden dat een kleinere notch dimensie, kleinere volumes van de intercondylaire notch en kleinere volumes van de AKB's gerelateerd zijn aan de aanwezigheid van een VKB-ruptuur. Secundair hebben vrouwen kleinere volumes van de intercondylaire notch, VKB's en AKB's, maar niet een kleinere NWI, in vergelijking met mannen.

In hoofdstuk 4 werd Statistical Shape Modelling (SSM) software gebruikt om de vorm van de knie te beoordelen en eventuele verschillen in anatomische punten te bepalen. We vergeleken de anteroposterior (AP), laterale en Rosenberg view röntgenfoto's van 94 patiënten met een gescheurde AKB, met een controlegroep van 168 patiënten gematched op leeftijd, geslacht en body mass index (BMI), maar met een intacte AKB na een knieletsel. Vormvarianten op de AP en Rosenberg röntgenfoto's verschilden significant tussen patiënten die hun AKB gescheurd hadden en patiënten met een intacte AKB na een knieletsel. Over het algemeen hebben patiënten die hun AKB gescheurd hebben kleinere intercondylaire notches en kleinere tibiale eminentia's dan controle patiënten. Dit hoofdstuk toonde aan dat verschillen in de vorm van de knie geassocieerd zijn met de aanwezigheid van een AKB-ruptuur na letsel. Een kleinere en meer scherp gehoekte intercondylaire notch en een meer afgeplatte tibiale eminentia zijn gerelateerd aan een AKB-ruptuur. Dit suggereert dat de morfologie van de knie een risicofactor is voor het oplopen van een AKB-ruptuur.

In hoofdstuk 5 was ons doel om te onderzoeken of de morfologie van de knie bij patiënten die een AKB-ruptuur hebben opgelopen kan verschillen van die van controle patiënten. De hypothese was dat de intercondylaire notch afmetingen, de 3-D volumes van de intercondylaire notch en de 3-D volumes van zowel de ACL als de PCL gecorreleerd waren aan de aanwezigheid van een AKB ruptuur. De MRI-scans van 30 patiënten met een bewezen AKB-ruptuur werden vergeleken met 30 gematchte controle patiënten met bewezen intacte kruisbanden. De controlepatiënten werden geselecteerd uit patiënten met een knietrauma tijdens het sporten maar zonder kruisbandletsel. De patiënten werden gematched op leeftijd, lengte, gewicht, BMI en geslacht. De volumes van de intercondylaire notch en zowel de VKB als de AKB werden gemeten op 3D reconstructies. Vervolgens werden de bicondylar width (BW), de notchwidth (NW), en de notchwidth-index (NWI) gemeten bij alle proefpersonen. De relatie tussen onze metingen en de aanwezigheid van een AKB-ruptuur werd geanalyseerd. De resultaten tonen een significant verschil in de volumes van de intercondylaire notch en de volumes van de VKB tussen patiënten met een gescheurde AKB en controle patiënten. Patiënten met een AKB-ruptuur hebben kleinere intercondylaire notch volumes en kleinere VKB-volumes. Er waren geen significante verschillen in de BW, NW en NWI. Bij de controle patiënten werd een significante correlatie tussen het volume van de AKB en het volume van de

VKB gevonden (0.673, $p<0.001$). Wij concludeerden dat patiënten met een AKB-ruptuur kleinere intercondylaire volumes en kleinere VKB-volumes hebben in vergelijking met controle patiënten. Ten tweede, patiënten met kleinere VKB-volumes hebben kleinere AKB-volumes. Deze studie toont voor het eerst aan dat er significante grootte- en volumeverschillen zijn in de vorm van de knie tussen patiënten met een AKB-ruptuur en controle patiënten.

In hoofdstuk 6 hebben we onderzocht of de vorm van de knie de klinische uitkomst van patiënten na een voorste kruisband ruptuur kan voorspellen. We gebruikten SSM om de vorm van het kniegewricht te meten van 182 prospectief gevolgde patiënten op de laterale en Rosenberg view röntgenfoto's van de knie na een ruptuur van de voorste kruisband. Vervolgens brachten wij de knievorm in verband met de subjectieve score van het International Knee Documentation Committee (IKDC) na twee jaar follow-up. De gemiddelde leeftijd van de patiënten was 31 jaar (21 tot 51), de meerderheid was man ($n = 121$) en operatief behandeld ($n = 135$). Wij vonden twee modi (vormvariaties) die significant geassocieerd waren met de subjectieve score na twee jaar: één voor de operatief behandelde groep ($p = 0{,}002$) en één voor de niet-operatief behandelde groep ($p = 0{,}003$). De operatief behandelde patiënten die een hogere subjectieve score hadden, hadden een kleinere intercondylaire notch en een kleinere breedte van de intercondylaire eminentia. Niet-operatief behandelde patiënten die hoger scoorden op de subjectieve score hadden een meer piramidale intercondylaire notch in tegenstelling tot een notch die meer koepelvormig was. Wij concludeerden dat de vorm van de femur notch en de intercondylaire eminentia voorspellend is voor de klinische uitkomst twee jaar na een ruptuur van het voorste kruisbandletsel.

Tenslotte worden in hoofdstuk 7, de algemene discussie, enkele van de belangrijkste bevindingen van de studies in dit proefschrift nader besproken. Verder werd een overzicht gegeven van onze studies, en hoe deze hebben bijgedragen aan de huidige kennis. De sterke punten en beperkingen werden besproken. Ter afsluiting werden aanbevelingen voor de praktijk en toekomstig onderzoek gepresenteerd.

PHD PORTFOLIO SUMMARY

Name PhD student: K.S.R. van Kuijk
Promotor: Prof. Dr. S.M.A. Bierma-Zeinstra
Copromotor: Dr. D.E. Meuffels

Activities concerning PhD orthopaedics	Date	ECTS
NOV 2015	5-2-2015	1
Oral presentation NOV	5-2-2015	1
OARSI meeting	29-3-2015	0,5
Presentation shoulder ETZ	13-1-2016	0,3
NOV 2016	28-1-2016	1
PICO feet compression	2-3-2016	0,3
NVA	8-4-2016	0,5
Oral presentation NVA	8-4-2016	1
Oral presentation NVA	8-4-2016	1
Science meeting ETZ	15-4-2016	0,5
PhD meeting Rome	5-6-2016	1
PhD meeting Rome	10-6-2016	1
Editor 4Bone; 1 year	1-10-2016	5
Presentation MRI ETZ	16-11-2016	0,3
Good clinical practice course	17-5-2019	1
Scientific integrity	21-6-2020	1
Review artikcle KSSTA	13-4-2021	0,3
ESSKA Milan Oral presentation	10-5-2021	1
ESSKA Milan poster presentation	11-5-2021	1

Activities concerning Residency radiology	Date	ECTS
Refereeravond radiologie EMC	15-2-2018	0,1
Critical appraised Topic Radiologie: Kraakbeendikte knie op MRI	16-4-2018	0,3
Refereeravond radiologie EMC	19-4-2018	0,1
Radiologen dagen 2018	24-5-2018	1
Refereeravond radiologie EMC	28-6-2018	0,1
Critical appraised Topic Radiologie: Thoracale endometriose	2-7-2018	0,3
MMV congres 2018	12-8-2018	0,5
Refereeravond radiologie EMC	8-11-2018	0,1
AAV bestuur Asz, 1 jaar lang	1-12-2018	5
Refereeravond radiologie ASZ	31-1-2019	0,2
Radiologen dagen 2019	16-5-2019	1
Critical appraised Topic Radiologie: Bakerse cyste	28-5-2019	0,3
Critical appraised topic radiologie: COVID CT	23-3-2020	0,3
Onderwijs geven co-assistenten 5 middagen	1-6-2020	1
Sandwichcursus	10-11-2020	0,3
Sandwichcursus	11-11-2020	0,3
Critical appraised topic radiologie: Osteonecrose	19-11-2020	0,3
Refereeravond radiologie	19-11-2020	0,1
Sandwichcursus	4-2-2021	0,3
Sandwichcursus	5-2-2021	0,3
Radiologendagen	20-5-2021	0,3
Sandwichcursus	16-6-2021	0,3
Sandwichcursus	17-6-2021	0,3
EUSOBI congress	1-10-2021	0,5
Sandwichcursus	10-11-2021	0,3
Sandwichcursus	8-2-2022	0,3
Radiologen dagen 2022	19-5-2022	0,3
Sandwichcursus	21-6-2022	0,3
Radiopaedia congress 2022	10-7-2022	0,6

LIST OF PUBLICATIONS

This list includes all publications in this thesis

van Kuijk KSR, Eggerding V, Reijman M, van Meer BL, Bierma-Zeinstra SMA, van Arkel E, Waarsing JH, Meuffels DE.
Differences in Knee Shape between ACL Injured and Non-Injured: A Matched Case-Control Study of 168 Patients.
J Clin Med. 2021 Mar 2;10(5):968. PMID: 33801168.

van Kuijk KSR, Reijman M, Bierma-Zeinstra SMA, Meuffels DE.
Anterior Cruciate ligament rupture is related to the shape and volume of the intercondylar notch and the size of the cruciate ligaments assessed on MRI.
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van Kuijk KSR, Reijman M, Bierma-Zeinstra SMA, Waarsing JH, Meuffels DE.
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CURRICULUM VITAE

Koen van Kuijk is geboren in Breda, in 1991. Zijn middelbareschooltijd bracht hij door in Breda, waar hij aan het Onze Lieve Vrouwelyceum zijn gymnasiumdiploma heeft gehaald. In zijn examen jaar is hij ook Nederlands kampioen geworden met hockey. Hierna begon hij in 2009 aan zijn opleiding geneeskunde in Rotterdam, waar hij toen ook is gaan wonen. Tijdens de opleiding kwam hij al vroeg in aanraking met de orthopedie, wat hem altijd trok. Daarom is hij in zijn 4^{e} jaar van de opleiding begonnen met een keuze onderzoek op de afdeling orthopedie, onder de begeleiding van Duncan en Vincent. Hier ontwikkelde hij zijn interesse in de wetenschap, waardoor hij verder is gegaan met het opzetten van zijn onderzoekslijn. In zijn laatste jaar van de geneeskunde opleiding nam hij deel aan het klinisch excellentie jaar van de orthopedie.

In 2016 behaalde hij op 24-jarige leeftijd zijn artsendiploma. Hij ging aan de slag als assistent chirurgie en later orthopedie in het IJsselland ziekenhuis. Na goed overwegen, en veel gesprekken bleek dat de radiologie beter bij hem past dan de orthopedie. In 2018 is Koen begonnen met de opleiding radiologie in het Albert Schweitzerziekenhuis in Dordrecht, onder de begeleiding van Dr. Nienke Katier. In december van 2022 is de opleiding tot radioloog voltooid.

Naast zijn opleiding tot radioloog, is Koen altijd bezig gebleven met zijn onderzoeken. Dit heeft geleid tot dit proefschrift. Zijn onderzoeken mocht hij presenteren op multipele congressen, waaronder meermaals op het NOV congres (Nederlandse Orthopedische Verenging), meermaals het NVA congres (Nederlandse vereniging van Arthroscopie) en meermaals het ESSKA congres (European Society for Sports Traumatology, Knee Surgery and Arthroscopy) . Daarnaast is hij op wetenschapsstage geweest in Rome onder begeleiding van Dr. Giovanni di Giacomo.

Na het afronden van dit proefschrift, en het behalen van zijn opleiding tot radioloog, mag Koen 1 januari 2023 starten als MSK en Mamma radioloog in het AZ Monica te Antwerpen. Op naar een nieuw hoofdstuk en nieuw avontuur!

DANKWOORD

Na heel wat jaren, komt aan mijn promotietraject een einde, maar niet aan mijn onderzoeksperiode. De jaren zijn voorbij gevlogen. Mijn eerste kennismaking met wetenschappelijk onderzoek, dateert uit 2013 tijdens mijn keuzeonderzoek op de afdeling orthopedie, waar dit thesis rechtstreeks uit voortvloeit. Al die tijd heb ik in mijn vrije tijd – naast mijn reguliere werkzaamheden als AIOS-radiologie – gewerkt aan dit onderzoek. Op vrije dagen, in weekenden en avonden, compensatiedagen en tijdens nachtdiensten altijd maar weer schrijven, onderzoek doen, analyses doen, artikelen insturen, overleggen, bijschaven en weer opnieuw schrijven.

Dat dit niet altijd makkelijk of vanzelf gaat en een zeer leuke, maar ook zeer tijdrovende periode geweest is, moge duidelijk zijn. Zonder de hulp van een hele grote groep fijne mensen was dit promotietraject nooit tot stand gekomen. Niet alleen mensen die mij inhoudelijk geholpen hebben bij het onderzoek, maar ook de mensen in mijn persoonlijke omgeving die mij gesteund hebben, gemotiveerd hebben en geaccepteerd hebben dat ik hieraan wilde werken. Bij al deze mensen wil ik graag stilstaan, en hen bedanken.

Duncan, dr. Meuffels, mijn copromotor, hartelijk bedankt voor alles wat je voor mij gedaan en betekend hebt de afgelopen jaren. Jouw begeleiding, adviezen, tips en hulp hebben in mij het beste naar boven gehaald. Jouw motivatie is eindeloos en ook hoe je mij altijd wist te enthousiasmeren – zelfs in wat moeilijkere perioden – is bijzonder knap. Na een ‘peptalk’ van jou heb ik er altijd weer met frisse moed tegenaan gekund.

Ik blijf het verbazingwekkend vinden hoe snel jij altijd reageert op mijn e-mails, zelfs in jouw vakantietijd of in de avonduren. Ik heb enorm veel respect voor de hoeveelheid uren die je steekt in je werk, je betrokken- en bevlogenheid bij de onderzoekslijnen en het feit dat je daarnaast ook nog een gezin hebt. Sommige mensen lijken meer uren in een dag te hebben dan anderen en jij bent daar één van. Ik heb de afgelopen jaren ontzettend veel van je mogen leren. Ik hoop dat we onze samenwerking nog vele jaren mogen voortzetten, ondanks dat ik radioloog geworden ben en geen orthopeed. Ik ben tenslotte skelet radioloog geworden met een reden ;).

Sita, professor dr. Bierma-Zeinstra, mijn promotor, hoewel wij niet dagelijks contact hebben gehad, was ook jij een grote inspiratiebron en een zeer welkome hulp in dit traject. Je bent altijd scherp geweest en had vaak goede ideeën om een publicatie te behalen. Je bent een fijn baken van rust geweest en had een realistische kijk op de te nemen stappen. Ik voel me vereerd dat jij mijn promotor bent!

Vincent, inmiddels dr. Eggerding, bij jou mocht ik de eerste meters maken als onderzoeker. Toentertijd nog als student-onderzoeker, die er heilig van overtuigd was dat hij orthopeed wilde worden. Dank voor je begeleiding en hulp. En ook meer recent nog, voor je hulp en adviezen bij mijn overstap naar onze Zuiderburen. Dat we beiden maar een hele leuke en fijne carrière in België tegemoet gaan!

Max, dr. Reijman, jij bent zeer belangrijk geweest in de beginfase van mijn onderzoek carrière. Tientallen malen gingen mijn opzetten, stukken en uiteindelijk publicaties, heen en weer tussen ons om een zo'n goed mogelijk artikel neer te zetten. Je kritische blik vond ik in het begin soms lastig – al durfde ik dat nooit uit te spreken – totdat ik doorhad dat deze kritische blik de stukken echt beter maakte. Daarnaast was je scherp op de methodiek en analyses. In het begin, samen met Vincent, hebben we vaak gelachen en gegierd om de prestaties van Feyenoord en de betere prestaties van Ajax. Dankjewel!

Beste Erwin, dankjewel voor je hulp bij het opstarten van de benodigde programma's om mijn resultaten te behalen. Zonder jou had ik nooit gebruik kunnen maken van Statistical Shape modelling. Bedankt ook voor je hulp bij de analyses en voor je hulp als statisticus.

Beste dr. Van Meer, beste Belle, dankjewel dat ik gebruik mocht maken van je databases van de KNALL-studie. Ook bedankt voor je hulp bij het publiceren van de artikelen.

Beste medeauteurs, welke ik nog niet apart genoemd heb, dank jullie wel voor de hulp bij het publiceren en helpen bij het onderzoek. Het is voor iedereen kostbare tijd om te investeren in het publicatieproces en dat iedereen daar altijd maar tijd voor vrijmaakt vind ik ontzettend mooi en fijn.

Beste Nienke, dr. Katier, mijn radiologie opleidster. Ontzettend bedankt voor de steun die jij mij hebt geboden tijdens de afgelopen jaren als AIOS-radiologie. Tijdens ieder voortgangsgesprek – en ook daarnaast – kwam mijn onderzoek weer even ter sprake en iedere keer vroeg je mij hoe en waarmee jij mij kon helpen of ondersteunen. Van jou heb ik altijd alle ruimte gekregen als ik voor een afspraak in het kader van mijn onderzoek eerder weg moest, of als ik een keer een onderzoeksdag wilde opnemen wanneer er een deadline naderde of submission moest gebeuren. Daarnaast ben ik je ontzettend dankbaar voor je rol als opleidster in het Albert Schweitzer ziekenhuis. Vanaf het begin al hebben we een goede klik en in die 5 jaar kon ik me geen betere opleidster wensen! Ontzettend veel dank hiervoor.

Daarnaast wil ik de overige leden van de opleidersgroep uit het Albert Schweitzer bedanken en alle radiologen uit het EMC. Ook zij waren altijd begripvol en stonden altijd voor mij klaar om dingen voor mij te faciliteren indien nodig. Dat maakt het leven als onderzoeker en promovendi een stuk makkelijker!

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Via deze weg wil ik al mijn vrienden bedanken. Jullie zijn al jaren een steun en toeverlaat en zonder jullie zou ik het ook nooit hebben kunnen voltooien. Jullie zorgden altijd voor de leuke, soms nodige ontspanning en leuke momenten. Hard werken kan alleen als je ook af en toe stoom kan afblazen en kan ontspannen. Dank jullie wel!

Papa, mama. Dankzij jullie ben ik de medische kant op gegaan. Door jullie verhalen en belevenissen heb ik uiteindelijk gekozen voor de studie geneeskunde en alles wat daaruit voortvloeit. Ik ben ontzettend trots dat jullie mijn ouders zijn. Betere ouders kan ik mij niet wensen! Altijd geïnteresseerd en altijd vrolijk als ik iets over mijn onderzoek kwam vertellen of uitlegde. Een liefdevolle omgeving is niet vanzelfsprekend, maar zo ontzettend fijn en waardevol! Dat we nog zo vaak met de hele familie samen zijn is iets waarvan ik hoop dat we dat nog vele jaren blijven doen, ook straks in België.

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Lieve schoonouders, Margaret, Mick en ook oma Riet, jullie hebben mij zo warm ontvangen in jullie gezin. Ook waren jullie erg betrokken bij mijn promotie en carrière, waarvoor ontzettend veel dank. Ook voor jullie is onze volgende stap, werken en wonen in België, een enorme verandering, waarbij ik ook nog eens jullie enige kind kaap. Zonder jullie steun kan dit niet, en dat wij die dan ook onvoorwaardelijk van jullie krijgen is ontzettend mooi om te zien!

Tot slot, Nadja, mijn lieve vrouw. Wat wij samen hebben opgebouwd is echt indrukwekkend. Zoveel liefde, steun en vertrouwen. De vele uren die we beiden werken, vereisen soms een hele logistieke onderneming om alles in goede banen te leiden en elkaar niet mis te lopen, maar nooit hoor ik hier een verkeerd woord over. Ook niet over de nachtdiensten, weekenden en feestdagen die ik soms moet werken. We vinden altijd tijd voor elkaar. Gelukkig vinden we het beiden ook heel belangrijk om naast ons werk samen stoom af te blazen; *'work hard, play hard'*. Een betere thuisbasis kan ik mij niet wensen. Jij geeft mij ontzettend veel kracht, energie en haalt het beste in mij naar boven, waardoor ik kan doen wat ik doe. We gaan een ontzettend mooie en fijne toekomst tegemoet.