ANATOMIC ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

CURRENT EVIDENCE AND FUTURE DIRECTIONS

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Anatomic anterior cruciate ligament reconstruction

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for my family,
you are my everything

happiness is only true when shared

1 / one abstract

Injury to the anterior cruciate ligament (ACL) is one of the most common orthopedic diagnoses. It is also one of the most researched areas in orthopedic surgery, with well over eleven thousand publications. Despite this, the solution for the best reconstructive technique is still not known and patients suffer from their injury in both the short- and the long-term.

An assessment of the outcomes was performed on randomized clinical trials. In terms of rehabilitation, a postoperative knee brace did not affect the clinical outcome and closed kinetic chain exercises produced less anteroposterior laxity and better subjective outcomes than open kinetic chain exercises. In terms of graft type, the patellar tendon graft produced initially more anterior knee pain and kneeling pain than the hamstring tendon graft. Moreover, the harvest site affected muscle strength initially and the hamstring tendon graft produced more tunnel widening. In terms of surgical technique, double-bundle ACL reconstruction produced less rotatory laxity than single-bundle. Finally, bioabsorbable screws and titanium screws produced equal clinical outcome.

An analysis and systematic review was performed on studies of primary ACL reconstruction. This analysis revealed that most therapeutic studies were of a low level of evidence and that the most common study type was case series. The three most common represented journals were Arthroscopy, Knee Surgery Sports Traumatology Arthroscopy and The American Journal of Sports Medicine. Furthermore, there was a correlation between the journals' impact factor and the mean level of evidence and there was a higher mean level of evidence over time.

Anatomic ACL reconstruction is currently one of the modern techniques for ACL reconstruction. This shift in paradigm has created confusion about the term "anatomic". Two systematic reviews assessed surgical data from studies claiming anatomic ACL reconstruction. The reviews revealed substantial under-reporting, making it difficult to do valid interpretations of the outcomes. A current concepts article was therefore published, outlining the concepts of anatomic ACL reconstruction, including principles and a definition: the functional restoration of the ACL to its native dimensions, collagen orientation and insertion sites. Ultimately, a scoring system was developed for the objective grading of surgical methods in studies of anatomic ACL reconstruction. This scoring system was subsequently implemented in studies comparing single- and double-bundle ACL reconstruction, which revealed means of the score well below a proposed minimum. In summary, a thorough analysis and review of what constitutes an anatomic ACL reconstruction was done, and an assessment was performed on studies comparing single- and double-bundle ACL reconstruction and studies claiming anatomic ACL reconstruction.

2 / two
swedish abstract

Främre korsbandsskador är ett av de vanligaste tillstånden inom ortopedi. Det är även ett forskningsintensivt område, med över 11 000 publicerade artiklar. Trots detta är den optimala operationsmetoden vid främre korsbandsrekonstruktion fortfarande inte klarlagd.

En omfattande översikt av randomiserade kliniska studier visade att en postoperativ ortos inte påverkade det kliniska utfallet och att closed kinetic chain-övningar medförde mindre anteroposterior laxitet och bättre subjektivt utfall än open kinetic chain-övningar. Vad gäller valet av sengraft, medförde rekonstruktion med patellarsena högre andel främre knäsmärta och smärta vid knästående jämfört med rekonstruktion med hamstringssenor. På platsen för det skördade graftet påverkades muskelstyrkan i initialskedet och ett graft av hamstringssenor orsakade mer vidgning av bentunneln. Operationsmetoden påverkade också utfallet; rekonstruktion med dubbla korsbandsskänklar medförde mindre rotatorisk laxitet jämfört med en enkel skänkel. När det gäller fixationsmetod så visade det sig att det kliniska utfallet inte skiljer sig mellan biologiskt absorberbara skruvar respektive titanskruvar.

I en systematisk litteraturöversikt avseende primär rekonstruktion av det främre korsbandet, påvisades att de flesta interventionsstudier höll låg vetenskaplig kvalitet och att de flesta studier var fallserier. De tre mest representerade tidskrifterna var Arthroscopy; Knee Surgery, Sports Traumatology, Arthroscopy och The American Journal of Sports Medicine. Tidskriftens impact factor korrelerade till den genomsnittliga evidensnivån; dessutom påvisades en trend mot en allt högre evidensnivå över tid.

Anatomisk rekonstruktion av det främre korsbandet tillhör de senaste operationsmetoderna. Tekniken har emellertid orsakat begreppsförvirring avseende termen ”anatomisk”. Genom två systematiska litteraturöversikter bedömdes anatomisk främre korsbandsrekonstruktion, dock påvisades omfattande underrapportering av data, vilket komplicerade tolkningen av utfallen. En översiktsartikel publicerades därför med avsikt att klargöra principer och definiera konceptet anatomisk främre korsbandsrekonstruktion: att funktionellt återskapa det främre korsbandet i dess ursprungliga dimensioner, kollagenriktning och infästning. Slutligen utvecklades en metod för att objektivt gradera kirurgiska tillvägagångssätt vid anatomisk korsbandsrekonstruktion. Denna gradering användes sedan i studier som jämförde enkel respektive dubbel skänkelrekonstruktion, vilket visade medelvärden klart under en föreslagen miniminivå. Sammanfattningsvis gjordes en noggrann genomgång av innebörden av anatomisk främre korsbandsrekonstruktion samt en utvärdering av studier som jämförde enkel och dubbel skänkelrekonstruktion respektive anatomisk korsbandsrekonstruktion.

3 / three
list of papers

This thesis is based on the following studies.

THEMES 1 – 2
Clinical outcome and level of evidence

1. **Treatment of anterior cruciate ligament injuries with special reference to surgical technique and rehabilitation: an assessment of randomized controlled trials**

   Andersson D, Samuelsson K, Karlsson J.

   Arthroscopy, 2009; 25(6): 653-85

2. **Treatment of anterior cruciate ligament injuries with special reference to graft type and surgical technique: an assessment of randomized controlled trials**

   Samuelsson K, Andersson D, Karlsson J.

   Arthroscopy, 2009; 25(10): 1139-74

3. **Systematic review on level of evidence in anterior cruciate ligament reconstruction**

   Samuelsson K, Desai N, McNair E, van Eck CF, Petzold M, Fu FH, Bhandari M, Karlsson J.

   Submitted to The American Journal of Sports Medicine

THEME 3

Anatomic anterior cruciate ligament reconstruction

4. **Anatomic single- and double-bundle anterior cruciate ligament reconstruction, part 2: clinical application of surgical technique**

Karlsson J, Irrgang JJ, van Eck CF, Samuelsson K, Mejia HA, Fu FH.

The American Journal of Sports Medicine, 2011; 39(9): 2016-26

5. **Systematic review on cadaveric studies of anatomic anterior cruciate ligament reconstruction**

van Eck CF, Samuelsson K, Vyas SM, van Dijk CN, Karlsson J, Fu FH.

Knee Surg Sports Traumatol Arthrosc., 2011; 19(S1): 101-8

6. **"Anatomic" anterior cruciate ligament reconstruction: a systematic review of surgical techniques and reporting of surgical data**

van Eck CF, Schreiber VM, Mejia HA, Samuelsson K, van Dijk CN, Karlsson J, Fu FH.

Arthroscopy, 2010; 26(9): 2-12

7. **Anatomic anterior cruciate ligament reconstruction scoring system: development and validation**

van Eck CF, Gravare-Silbernagel K, Samuelsson K, Musahl V, van Dijk CN, Karlsson J, Irrgang JJ, Fu FH.

Submitted to The American Journal of Sports Medicine

8. **Anatomic anterior cruciate ligament reconstruction scoring system: a systematic review on single- versus double-bundle**

Samuelsson K, Desai N, Ahldén M, van Eck CF, Fu FH, Musahl V, Karlsson J.

Manuscript

4 / four abbreviations

AARSS	Anatomic ACL Reconstruction Scoring System
ACL	Anterior Cruciate Ligament
AM	Anteromedial
AP	Anteroposterior
CKC	Closed Kinetic Chain
CS	Case Series
CSS	Case Control Study
EBM	Evidence-Based Medicine
HT	Hamstring Tendon
IKDC	International Knee Documentation Committee
MA	Meta-analysis
MRI	Magnetic Resonance Imaging
OKC	Open Kinetic Chain
OA	Osteoarthritis
PCL	Posterior Cruciate Ligament
PCS	Prospective Comparative Study
PL	Posterolateral
PROM	Patient Reported Outcome Measures
PT	Patellar Tendon
RCS	Retrospective Comparative Study
RCT	Randomized Clinical Trial
ROM	Range Of Motion
SR	Systematic Review

5 / five definitions

Bias	A systematic error or deviation in results or inferences from the truth. The main types of bias arise from systematic differences in the groups that are compared (selection bias), the care that is provided, exposure to other factors apart from the intervention of interest (performance bias), withdrawals or exclusions of people entered into a study (attrition bias) or how outcomes are assessed (detection bias).
Case-control study	A study that compares people with a specific disease or outcome of interest (cases) to people from the same population without that disease or outcome (controls), and which seeks to find associations between the outcome and prior exposure to particular risk factors
Case series	A study reporting observations on a series of individuals, usually all receiving the same intervention, with no control group
Cohort study	An observational study in which a defined group of people (the cohort) is followed over time. The outcomes of people in subsets of this cohort are compared, to examine people who were exposed or not exposed (or exposed at different levels) to a particular intervention or other factor of interest
Confidence interval	A measure of the uncertainty around the main finding of a statistical analysis. It is usually reported as 95% CI, which is a range of values within which it is possible to be 95% sure that the true value for the whole population lies
Confounder	A factor that is associated with both an intervention (or exposure) and the outcome of interest
Content validity	Asks if the measurement accurately assesses what it is purported to measure
Criterion validity	Psychometric property of an outcome instrument assessing its relationship to an accepted, "gold standard" instrument
External validity	The extent to which results provide a correct basis for generalizations to other circumstances

Face validity	Asks if the measurement appears to be intuitively correct
Factor analysis	Statistical method for analyzing relationships between a set of variables to determine underlying dimensions
Heterogeneity	Differences in treatment effect across studies
Hierarchy of evidence	A classification system which categorizes the hierarchy of research designs as levels of evidence from level 1 to 5
Inter-observer agreement	The assessment of agreement across two or more observers
Inter-rater reliability	The degree of stability exhibited when a measurement is repeated under identical conditions by different raters. Reliability refers to the degree to which the results obtained by a measurement procedure can be replicated
Internal consistency	Psychometric property of an outcome instrument regarding the degree to which individual items are related to each other
Internal validity	The extent to which the design and conduct of a study are likely to have prevented bias
Linear regression	A form of statistical analysis where one variable can predict the other and the dependent variable is a continuous variable whose relationship to the independent variable is linear
Meta-analysis	A systematic review that uses quantitative methods to summarize results
Post-hoc test	A form of statistical analysis which examines data for patterns that were not hypothesized before the experiment was conducted
Power	Probability of finding a significant association when one truly exists (1 – probability of type-II error)
Prognostic factor	Demographic or co-morbidity characteristic that tends to occur along with outcome of the condition
Prospective	Forward in time
Random effects	A model used to give a summary estimate of the magnitude of effect in a meta-analysis that assumes that the studies included are a random sample of a population of studies addressing the question posed in the meta-analysis
Randomization	When the investigator has no control over the intervention

	group to which a participant is assigned; a process to ensure a prognostic balance between groups in a randomized trial
Randomized clinical trial	The gold standard of experimental trials; level 1 evidence. Patients are randomly assigned to two or more treatment arms and followed prospectively over time
Reliability	The consistency of the results produced by an instrument
Retrospective	Backward in time
Risk factor	A variable associated with an increased risk of disease or infection
Sensitivity	Percentage of patients with an outcome who are classified as having positive results
Specificity	Percentage of patients without an outcome who are classified as having negative results
Student's t test	A parametric statistical test that examines the difference between the means of two groups of values
Systematic review	A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies
Two-tailed	A statistical measurement where both sides of a probability curve are assessed
Type I error	A conclusion that a treatment works, when it actually does not work. The risk of a Type I error is often called alpha. In a statistical test, it describes the chance of rejecting the null hypothesis when it is in fact true (also called false positive)
Type II error	A conclusion that there is no evidence that a treatment works, when it actually does work. The risk of a Type II error is often called beta. In a statistical test, it describes the chance of not rejecting the null hypothesis when it is in fact false (also called false negative)
Validity	The degree to which a result (of a measurement or study) is likely to be true and free of bias (systematic errors)

6 / six
preface

It all began with my own ACL tear. As a high level competing athlete in the Swedish National Judo Team, I had the opportunity and the privilege to be treated by Drs. Jón Karlsson and Sveinbjörn Brandsson. The surgeons enrolled me in a study and reconstructed my ACL. Soon after, I realized that there was a great deal of hard work ahead, as my knee was never the same. After my comeback, I suffered a re-tear in my reconstructed knee. My competing days were over.

Dr. Karlsson and I started our research during my last year in medical school. Due to my own injury, we focused on ACL injury and its treatment. We planned my thesis and divided it into two parts: evidence-based clinical outcomes for ACL reconstruction and an assessment of the level of evidence. During our research, an interest developed in the new techniques in ACL reconstruction, namely double-bundle and anatomic ACL reconstruction. At the same time, contact was initiated by Dr. Freddie H. Fu from the University of Pittsburgh Medical Center (UPMC). This was an honor and a privilege, as Dr. Fu is a world-renowned orthopedic surgeon and researcher. Dr. Fu sent Dr. Carola van Eck, at that time a postgraduate research associate, to meet with us and discuss collaboration. The idea from the UPMC was to evaluate so-called anatomic studies and build a scoring system. We found the whole project very interesting and gladly agreed to collaborate. Dr. van Eck showed directly that she was a committed researcher and a very hard worker. When the collaboration ended, we realized that the collaborative studies were of such importance and quality that, if they were included in my thesis, they would lift it to a new level. In agreement with Dr. Fu, we chose to exclude two previously planned studies and include the new studies as a new theme.

During this journey, we have found a new friend and mentor in Dr. Fu, who has clearly shown why he is as renowned as he is. It is difficult to find a more inspiring, energetic, ingenious and generous doctor. Dr. van Eck defended her thesis in Amsterdam after two very productive years as a research associate. It has been a pleasure to work with her. Several visits have been made to UPMC and we have been received by an unmatched hospitality, especially from Drs. van Eck, Musahl and Fu. We are definitely looking forward to future collaborations in all forms.

My whole research project and this thesis have been completed due to one person, one of my best friends and my mentor, Dr Jón Karlsson. There are no words to describe my gratitude to him.

7 / seven
introduction

7.1 history

The history of the ACL is filled with anecdotes and turns. The development has been magnificent from the first mention of the cruciate ligaments in 3000 BC by Papirus, an Assyrian in Egypt, to today's modern anatomic ACL reconstruction. [1]

The first to describe the subluxation of the knee was probably Hippocrates, a Greek from the island of Kos (460-377 BC), who was unaware of the cruciate ligament but related the symptoms to a ligamentous injury in the knee joint. [2] About 200 years later, another Greek, named Galen from Pergamon (201-131 BC), was the first to describe the anatomy in the knee thoroughly and named the cruciate ligaments after their appearance as 'ligamenta genu cruciate'. [3] Galen also discovered how important the ligaments were for the stabilization of the knee and to restrain it from abnormal motion.

After these three pioneers, nothing was reported in scientific circles for more than 2,000 years. In 1836, Wilhem Weber (1804-1891), Professor of Physics in Göttingen, and his brother Eduard Weber (1806-1871), Professor of Anatomy and Physiology in Leipzig, showed that transection of the ACL resulted in the abnormal antero-posterior movement of the tibia and thereby also gave an early description of anterior drawer sign. The Weber brothers were also the first to describe the distinct bundles of the ACL and their tension patterns. This was followed by Amadeé Bonnet (1809-1858), Professor of Surgery at Lyon University, who published the three signs indicative of ACL rupture, 'in patients who have not suffered a fracture, a snapping noise, hemarthrosis, and loss of function are characteristic of ligamentous injury in the knee'. [4, 5] Furthermore, Bonnet also described the subluxation of the knee after ACL injury and is therefore one of the first to describe the pivot-shift phenomenon. Furthermore, he proposed conservative treatment of the ACL and designed a hinged brace for those with recurring instability.

The first description of what is now known as the Lachman test is from 1875 by the Greek Georgios C. Noulis (1849-1915); "… fix the thigh with one hand; with the other hand hold the lower leg just below the knee with the thumb in front and the fingers behind; then, try to shift the tibia forward and backward…". [1]

Four years later, the French surgeon Paul Segond (1851-1912) from Paris provided a description of the signs for an ACL rupture; "strong articular pain, frequent accompanying pop, rapid joint effusion and abnormal anterior-posterior movement of the knee on clinical examination". Segond also described the pathognomic Segond fracture, one should bear in mind that this was presented before the discovery of roentgen. [1]

The first two known cases of ACL repairs were performed with the use of silk suture in 1895 by Sir Arthur Mayo-Robson of Leeds (1853-1933) and in 1900 by William Battle of St. Thomas in London (1855-1936). [1] This was the start of the surgical approach of the ACL and its long and winding road up to today's modern arthroscopic anatomic ACL reconstruction.

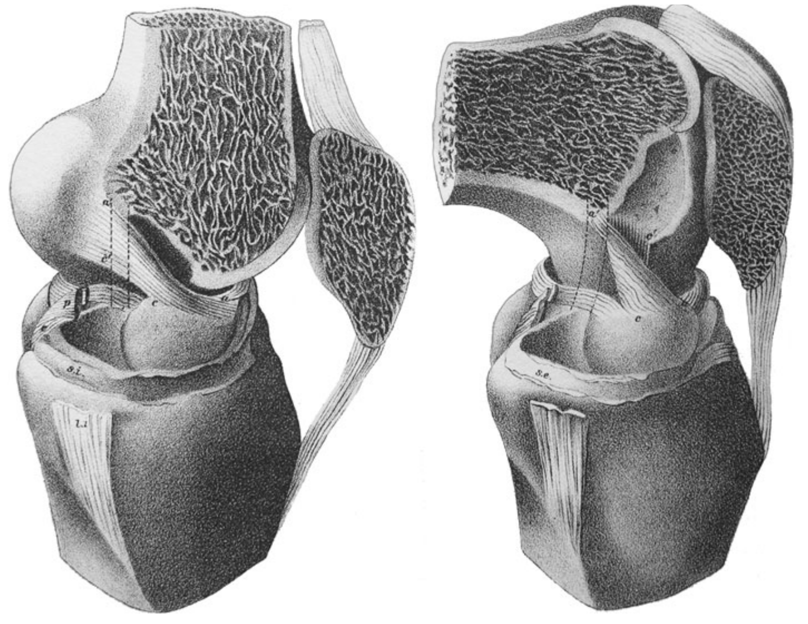


figure 1

Illustration from "Mechanics of the human apparatus" by the Weber brothers. It clearly shows the ACLs pattern in both knee extension and flexion. Printed with kind permission from Springer Verlag.

7.2 epidemiology

Injury to the ACL is very common among athletes and the incidence is suggested to be around 35 per 100,000 inhabitants worldwide and 80 per 100,000 in Sweden. [6, 7] About 3,330 primary ACL reconstructions were reported in

2010 to the Swedish National ACL Registry, which indicates that approximately 50% of the ACL injuries are reconstructed. The median age for an ACL reconstruction is 27 years and 40% of the patients are women. [7] Reports from the Multicenter Orthopedic Outcomes Network (MOON) in the USA show that the median age is 23 years and 48% of the patients are women. [8]

7.3 etiology

The mechanism of injury is usually a combination of hyperextension and rotation or flexion, external rotation and valgus. An isolated tear in the PL bundle can occur when the knee is hyperextended and the PL bundle is taut, while an isolated tear in the AM bundle can occur when landing on a flexed and externally rotated knee (the AM bundle is tightened to its maximum at 45-60 degrees). [9, 10] Most ACL tears occur as a result of non-contact injuries and the three most common activities in Sweden are soccer (43%), floor ball (13%) and alpine skiing (9%) for both men and women. [7] In the USA, the three most common sports are basketball (20%), soccer (17%) and American football (14%). [8]

7.4 anatomy

The ACL consists of multiple non-parallel collagen fibers and is surrounded by a synovial sheet. The major blood supply originates from the central geniculate artery. The ACL originates from the posteromedial surface of the lateral femoral condyle and inserts distally on the anterior aspect of the medial tibia. Functionally, the ACL consists of at least two bundles which display different characteristics. The bundles are named after their insertion site on the tibia: the anteromedial (AM) and the posterolateral (PL) bundle. The AM bundle is approximately 3.5 cm long and 0.5 cm wide and the PL bundle is about half the length.

On the femur, the footprint of the ACL is shaped like an oval. [11, 12] The mean size of the footprint is 18 mm in length and 11 mm in width. [11] This area is about 3.5 times larger than the midsubstance cross-sectional area. [11, 12] The position of the bundles varies depending on the flexion of the knee, as the bundles are inserts on the posterior part of the femoral condyle. When the knee is extended, the footprint is more vertical and the AM bundle inserts proximally, while the PL bundle inserts distally. When the knee is flexed, the footprint is more horizontal and the AM bundle inserts posteriorly, while the PL bundle inserts anteriorly.

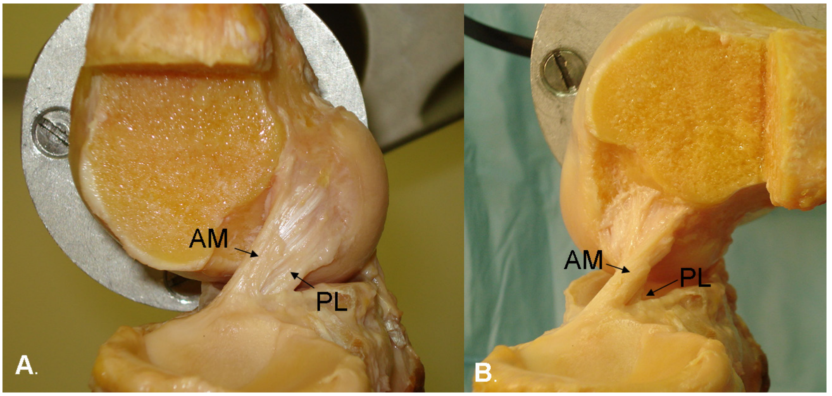


figure 2

Pictures showing the relations of the bundles and the oval femoral footprint in both extended (A) and flexed (B) position.

On the femur, there are two bony landmarks that denote the femoral insertion sites for each bundle, the lateral intercondylar ridge and the lateral bifurcate ridge. The lateral intercondylar ridge forms the anterior border of the femoral footprint and the lateral bifurcate ridge is located between the two bundles and is perpendicular to the former ridge. [12] Both ridges play an important role during ACL reconstruction, as they aid the surgeon in the placement of the graft in both acute and chronic ACL-deficient patients. [13]

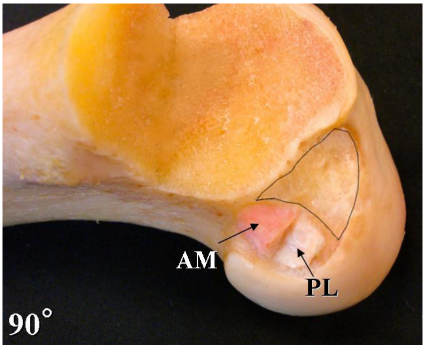


figure 3

Picture showing the femoral footprint for each bundle.

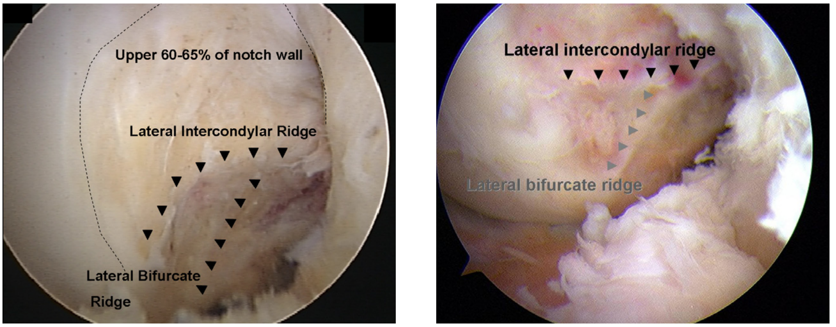


figure 4

Arthroscopic pictures of the right knee in 90° flexion, showing the lateral intercondylar ridge that forms the anterior border of the femoral footprint and the lateral bifurcate ridge located between the two bundles.

On the tibia, the footprint of the ACL varies in shape from oval to triangular. [11] The tibial footprint is the largest part of the ACL and it is 350% larger than the midsubstance ACL and 120% larger than the femoral footprint. [11] The AM bundle can be confluent with the anterior horn of the lateral meniscus and is centered 13-17 mm from the anterior tibial edge. [14] The PL bundle can be confluent with the posterior root of the lateral meniscus and is centered 20-25 mm from the anterior tibial edge and 7-8 mm anterior to the PCL. [14]

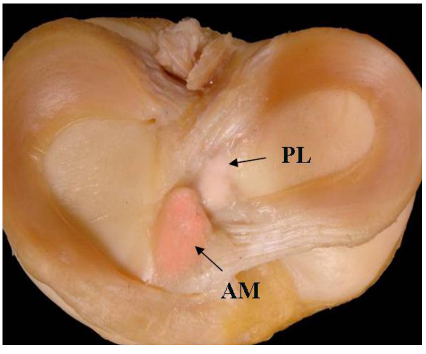


figure 5

Picture showing the tibial footprint for each bundle.

In midsubstance, the shape is oval and ranges in size from 7-12 mm. The course is anterior-medial. The ACL is tilted 26 degrees forward in the long axis and rotates 90 degrees externally before it inserts on the tibia.

The two bundles have different tensile properties due to the complex anatomy of the ACL. The AM bundle is taut throughout knee flexion and tightened to its maximum at 45-60 degrees. [12] The PL bundle is tightened to its maximum when the knee is extended. [12] Consequently, the PL bundle plays an important role when the knee is near extension, while the same thing applies to the AM bundle when the knee is in flexion. Thus, one part of the ACL will always be taught during the knees ROM.

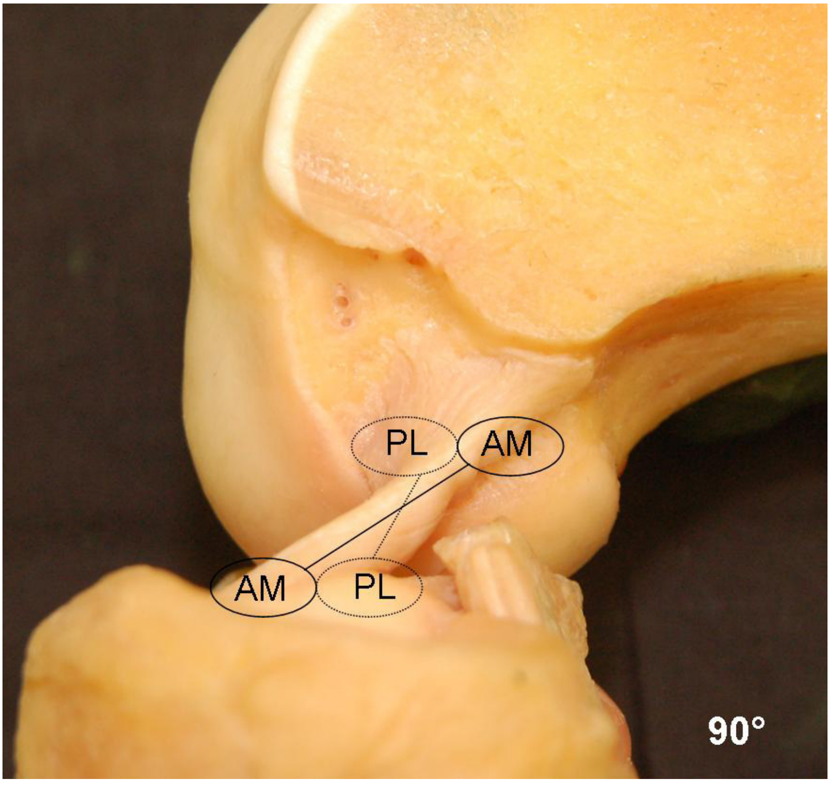


figure 6

Picture showing the crossing pattern for both bundles when the knee is in 90° flexion.

Due to the orientation of the AM bundle, almost vertical in the coronal plane, it is suggested that it is only able to withstand little rotational tibial force. Instead, the PL bundle is thought to control tibial rotation more effectively, as it is almost horizontally oriented. However, it appears that both the bundles work in a synergistic way during the range of motion to stabilize the knee under both antero-posterior and rotational tibial loads. [15, 16]

7.5 morbidity

Anterior cruciate ligament injury is functionally disabling, predisposes the knee to further injury and leads to the early onset of degenerative changes such as osteoarthritis in the knee. These changes are primarily attributable to the loss of the essential function of the ACL; to prevent the anterior displacement of the tibia relative to the femur and to restrain internal rotation and valgus angulation. However, the ACL is not merely a mechanical stabilizer of the knee. It also has important proprioceptive properties. It contains different sets of mechanoreceptors that provide the central nervous system with afferent information about the position of the joint via the tibial nerve. After an ACL rupture, recurring episodes of joint instability ("giving way") are associated with meniscus injury, damage to the joint cartilage and abnormal osseous metabolism.

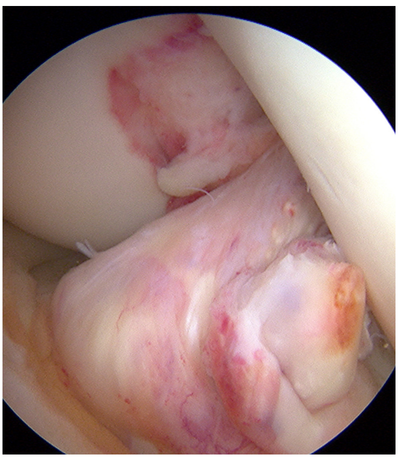
7.6 treatment perspectives

7.6.1 healing

An injury to a ligament usually causes a local hematoma, which eventually forms a fibrinogen mesh that permits inflammatory cells to transmigrate. Fibroblasts and stem cells are attracted via chemotaxis and granulation tissue forms and subsequently become organized. The fibroblasts of the granulation tissue eventually reorganize and finally form a scar. However, this is not possible in a complete ACL rupture for biochemical reasons, with a hostile environment towards chemotaxis and a longer healing process due to the slow proliferation of ACL fibroblasts, and for mecahnical reasons. [17] The ACL is an intra-articular and extra-synovial ligament that is lined with a vascularized synovial lining. In the event of a complete rupture, it causes the blood to diffuse into the knee joint and is therefore unable to create a fibrinogen mesh. Only with an intact synovial lining is it possible for the ACL to heal. [18] Furthermore, it is technically difficult to repair the ruptured ACL remnants surgically without the use of augmentation due to the fiber orientation and the amount of strain that is put on the ACL during knee motion.

7.6.2 partial tears

Partial tears of the ACL might have the capacity to heal and may therefore present the orthopedic surgeon with a difficult decision. There is no general consensus on what constitutes a partial tear with the capacity to heal. Noyes et al. looked at partial ACL ruptures and noted the progression of the tear in the majority of their patients. [19] The amount of damage to the ACL is difficult to assess by direct observation. Arthroscopic probing of the ACL, in combination with an accurate physical examination, appears to be the most accurate method to determine the degree of injury. [20]



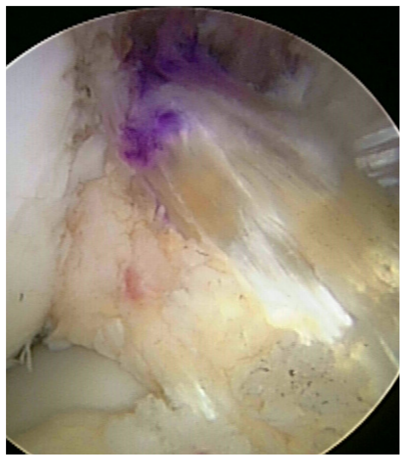


figure 7
Arthroscopic picture showing an isolated tear of the PL bundle with an intact AM bundle.

figure 8
Arthroscopic picture showing an intact PL bundle and a reconstructed AM bundle.

Partial tears can also be a complete isolated AM or PL bundle rupture. An isolated bundle rupture can be reconstructed using the anatomic ACL reconstruction approach, in which the damaged bundle is reconstructed by the utilization of a graft.

7.6.3 primary repair and augmentation

Several clinical attempts at a primary repair of the ACL have been made, but almost all report disheartening long-term results, in spite of encouraging short-term outcomes. [21, 22] This has led orthopedic surgeons to consider different augmentation techniques that would theoretically not only promote healing but also prevent elongation and rupture. Even though augmentation in combination with primary repair resulted in better outcomes than primary repair alone, there is no evidence that augmentation is superior to traditional reconstruction. [23, 24] The incapacity of the ruptured ACL to heal and the discouraging results from primary repair without or with different augmentation devices has led orthopedic surgeons to perform ACL reconstruction instead of repair.

7.7 technical and surgical perspectives

7.7.1 open versus arthroscopic

The technique for ACL reconstruction has been substantially developed since the start of arthroscopically assisted reconstruction, which was initially performed by Dandy in 1980. [25] Before the arthroscopic revolution, ACL reconstruction was performed as open arthrotomy with the goal of restoring the normal anatomy of the ACL. Even though arthrotomy is a more traumatic operation and has fewer theoretical advantages than arthroscopic ACL reconstruction, studies reported only modest improvements in early symptoms [26-29]. The change towards minimally invasive techniques and the increased knowledge of the ACL and its functions led to an increase in arthroscopically assisted ACL reconstructions worldwide, as well as the start of non-anatomic ACL reconstructions.

7.7.2 one versus two incisions

Initially, arthroscopically assisted ACL reconstruction was performed using a two-incision technique, also called the rear-entry technique, in which the femoral bone tunnels were drilled outside-in. However, at the beginning of 1990s, there was a trend towards the one-incision technique, also called the endoscopic, all-inside or transtibial technique, in which the femoral bone tunnels were drilled inside-out. The potential benefits of the new one-incision technique were; shorter operating time, lower costs, improved cosmesis, less postoperative pain and potentially faster rehabilitation. Several orthopedic surgeons were concerned that the new technique would yield less optimal femoral tunnel placement and a greater risk of posterior wall breakout. This was contested by advocates of one-incision ACL reconstruction who proposed notchplasty or the use of an anteromedial portal to improve the visualization of the posterior femur. Clinical studies comparing the two techniques found only minimal and divergent differences between the two techniques [30-34], except for the study by Panni et al. [35], which found more vertical femoral tunnel placement in the one-incision group. This was, however, contested by Harner et al. [32] who reported no difference in femoral tunnel placement. Although the study did not specifically quantify and measure femoral tunnel angles, both studies placed the femoral tunnels in the same o'clock position and used transtibial guides for drilling the femoral tunnel.

For almost a decade, one-incision ACL reconstruction with transtibial femoral tunnel drilling was the gold standard ACL reconstruction and its use is still widespread. During this period, several surgical principles were further developed and widely utilized; they included isometry, the o'clock reference and notchplasty. All three principles, together with transtibial femoral tunnel drilling, promoted non-anatomic ACL reconstruction.

7.7.3 isometry

Isometric graft placement means that the distance between the femoral and tibial attachments is constant during motion in the knee joint. [36] The isometric placement evolved from several well-grounded theories in which the main theory was that a tendon that is elongated more than 4% under repetitive motion will be irreversibly stretched. [37] Moreover, isometric graft placement was thought to produce better functional knee joint movement and clinical studies revealed positive effects of isometric placement. [38] However, the native ACL is not isometric but has a complex, non-uniform, multiple-bundle fiber anatomy. Furthermore, the best isometry for a femoral tunnel is high in the femoral notch and points close to the proximal end of Blumensaat's line. [37, 39] This localization differs from the lower positioned femoral footprint of the native ACL. An in-vitro study found that placement of the femoral graft in the femoral footprint of the native ACL resulted in closer knee joint kinematics than the isometric femoral position. [39] Isometric placement is therefore a poor substitute for correct anatomy and for this reason orthopedic surgeons today try to respect the normal anatomy and achieve an anatomic placement of the ACL graft.

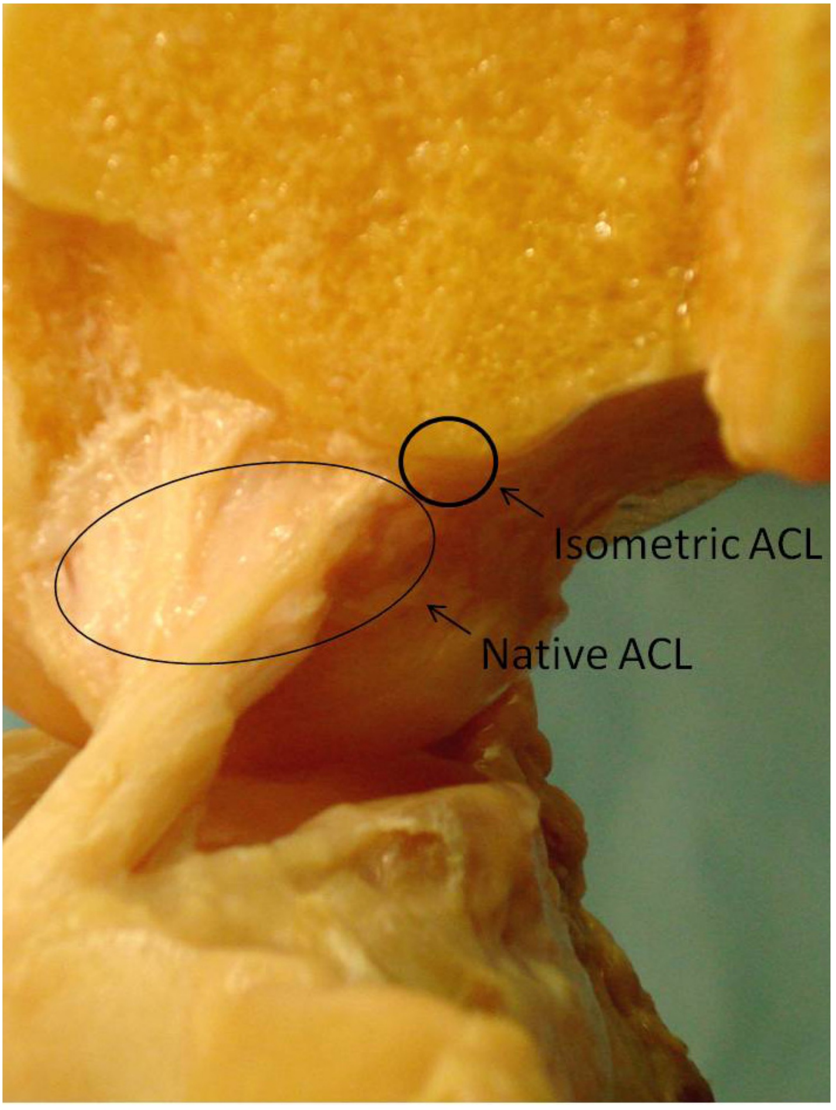


figure 9

Picture showing the localization of the isometric ACL placement and the relation to the native femoral ACL footprint.

7.6.4 o'clock position

The reference to the o'clock position for the placement of the femoral tunnel was developed in the infancy of arthroscopic knee surgery. It is now familiar to orthopedic surgeons worldwide. The o'clock reference was originally developed to be determined on radiographs with the knee in extension and is in this manner quite reliable. [40] It was not until later that it was also utilized for arthroscopic measurements, not taking into consideration that the knee is flexed in this situation. [41] Even though it is easy to use the o'clock position as a reference, there are several limitations; it refers to a two-dimensional structure and therefore neglects the depth of the notch, its position varies with knee flexion and it is not universally employed due to the asymmetric anatomy of the notch and therefore actually denotes different points on the femur for different orthopedic surgeons. [42] Due to its interpersonal variance and limitations, the o'clock position makes it impossible to assess the surgical data and therefore also outcomes in research papers. For this reason, any reference to the o'clock position is not reproducible and present-day orthopedic surgeons should utilize other means of documenting bone tunnel position.

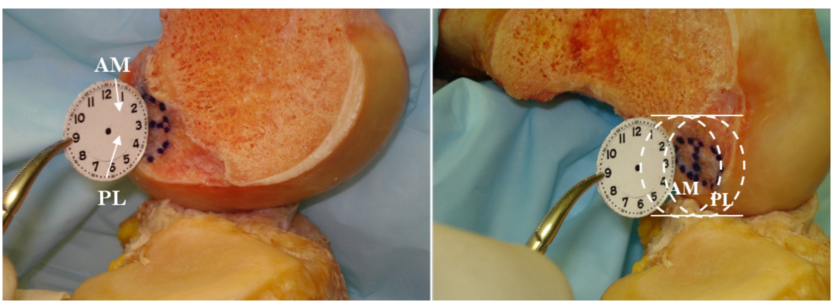


figure 10

The o'clock reference points to different positions depending on the knee flexion angle. To the left, the knee is extended and to the right the knee is in 90 degrees flexion.

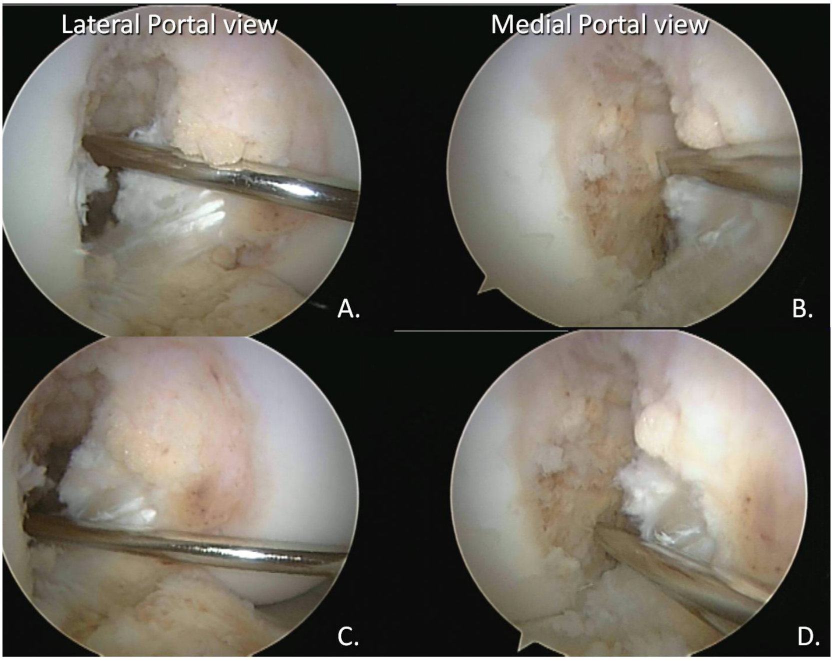


figure 11

Arthroscopic pictures showing the differences in o'clock position depending on portal.

Pictures A and B shows the same position with a probe, through a lateral and a medial arthroscopic portal. In the lateral portal (A) the o'clock position is approximately 10 o'clock and it appears as it is in the femoral ACL footprint. However, when changing to the medial portal (B) one can see that the placement of the probe is too dorsal and outside the femoral ACL footprint.

Pictures C and D shows the same position with a probe, through a lateral and a medial arthroscopic portal. In the lateral portal (C), the o'clock position is approximately 9 o'clock and thus maybe too inferior. However, when changing to the medial portal (D) one can see that the placement of the probe is in the center of the femoral ACL footprint.

7.6.5 notchplasty

Notchplasty and/or roof plasty were widely introduced and utilized at the start of the arthroscopically assisted ACL reconstruction. It aimed to assist the orthopedic surgeon in providing a better view of the posterior part of the notch and creating clearance for the graft to prevent impingement with the lateral wall and the roof of the notch. To resolve the issue of visualization, several orthopedic surgeons promote adding an accessory medial working portal. This significantly improves the visualization for both the femoral and tibial insertion sites and therefore renders the usage of notchplasty for visualization purposes unnecessary. [43] Impingement will not occur if the ACL is reconstructed in an anatomic fashion and this should be clear due to the fact that the native ACL does not impinge. Impingement is therefore not an indication for notchplasty in anatomic ACL reconstruction, unless there are central osteophytes or deviating anatomy. Furthermore, notchplasty not only removes osseous landmarks of major importance for the correct placement of bone tunnels, it also displaces the ACL graft abnormally laterally and therefore changes the kinematics of the ACL graft, which yields abnormal graft forces. [44] Finally, there are indications of regrowth and overgrowth of the notchplasty site. [45] The use of notchplasty is therefore outdated and its utilization is an indication of a faulty surgical technique, mainly misplaced portals and non-anatomic graft placement.

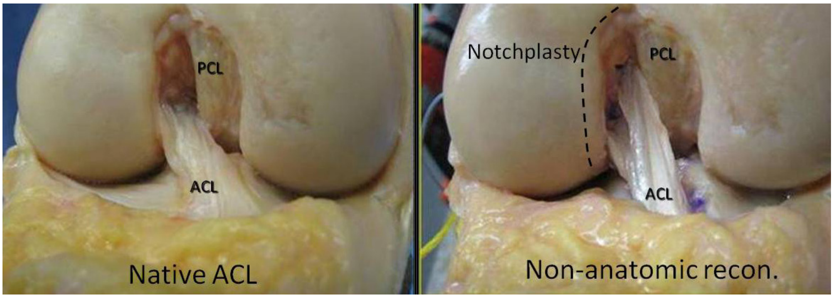


figure 12

Picture of native ACL to the left and a non-anatomic double-bundle ACL reconstruction to the right. The dotted area shows the area that is removed when performing a notchplasty. Notchplasty can be necessary in a non-anatomic ACL reconstruction as it can impinge; however, this is not the case for the native ACL or in anatomic ACL reconstruction.

7.7.6 anatomic acl reconstruction

At the beginning of the twenty-first century, the understanding of the native ACL and its kinematics expanded quickly and new recommendations were developed with regard to the placement of bone tunnels. The emphasis was now placed on anatomic graft placements to re-create normal physiologic graft tensions. Studies confirmed almost normal knee joint kinematics when the bone tunnels were in the center of the native ACL footprint. [46-50] A complete anatomic reconstruction denotes several prerequisites that have been defined, such as the functional restoration of the ACL to its native dimensions, collagen orientation and insertion sites. The purpose and thought behind the anatomic ACL reconstruction is that the native ACL is the best solution and can therefore act as a blueprint. For this reason, all reconstructions that aim to recreate as much as possible of the native ACL function should also yield the best clinical outcomes. Hopefully, this will also promote long-term knee health, including chondroprotective biomechanics, thus preventing osteoarthritis.

7.7.7 three-portal technique

One-incision arthroscopically assisted ACL reconstruction introduced the drilling of the femoral tunnel through a tibial tunnel, the so-called transtibial technique. The positive aspects of the transtibial technique are that it is simple and does not require the knee to be flexed beyond 90° when the femoral tunnel is drilled. Orthopedic surgeons and other researchers started to criticize the transtibial technique and suggested that it failed to place the bone tunnels in the center of the native ACL footprint, especially in the femur. Several disadvantages were identified, where the most serious limitation is the dependence of the two tunnels on one another since the femoral tunnel is drilled through the tibial tunnel. This restrictive link can cause an inaccurate and non-anatomic femoral tunnel position that is too high and deep in the intercondylar notch. [51-53] Together with a usually more posteriorly placed tibial tunnel, this produces a non-anatomic vertical ACL graft which reduces anteroposterior laxity but might fail to reduce rotatory laxity. [49, 54] The medial portal technique with an accessory medial portal was developed to facilitate visualization and unrestricted femoral tunnel drilling. [51, 52, 55, 56] Using the medial portal technique, the femoral tunnel is drilled independently of the tibial tunnel through the anteromedial or the accessory medial portal. This facilitates the anatomic placement of the ACL graft and therefore increases the success rate of the reconstruction. Furthermore, the medial portal technique offers other advantages. It allows the easy preservation of remaining intact ACL fibers which in turn aids the isolated reconstruction of the AM or PL bundle. There are few restrictions relating to graft type, graft fixation or instrumentation. [57] Moreover, it allows a new anatomic femoral tunnel in revision cases where the tibial tunnel is anatomic but the femoral tunnel is vertical. [58] Finally, it allows for a parallel femoral socket and interference screw placement which reduce the risks of divergent screw placement.

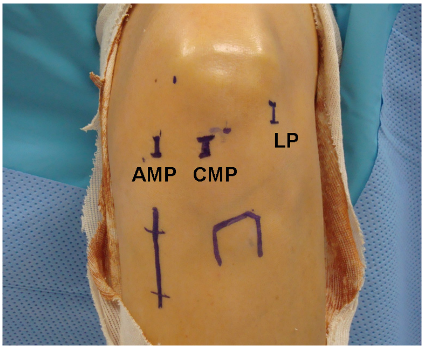


figure 13
Picture taken before ACL reconstruction with markings for arthroscopic portals. LP= Lateral portal, CMP = Central medial portal and AMP = Accessory medial portal.

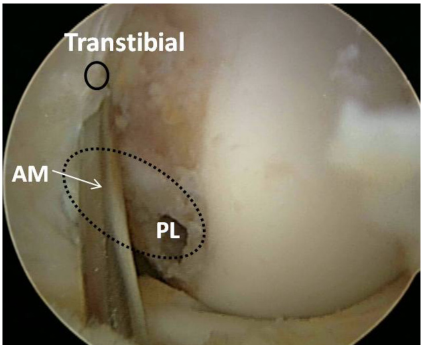


figure 14
Arthroscopic picture through the medial portal showing a transtibial guide. The guide is too high and outside the native femoral ACL footprint (dotted area). The insertion sites for the AM and the PL bundle are also shown.

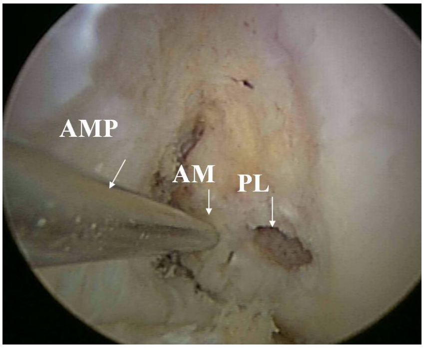
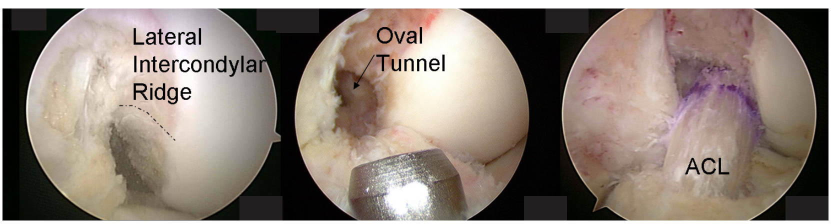


figure 15
Arthroscopic picture showing a probe through the accessory medial portal (AMP) that can reach the native femoral ACL footprint and the insertion sites for both AM and PL bundles.

7.6.8 single and double-bundle

Reconstruction of the ACL has traditionally focused on replacing the AM bundle of the ACL, so-called single-bundle reconstruction. Even though it reduces AP laxity, studies have also shown that it does not to fully restore rotatory laxity. [49, 54] This led to the further development of the surgical technique and the start of the double-bundle reconstruction. The theory is that double-bundle reconstruction more closely mimics the normal function of the native ACL and therefore yields better functional results.

However, it is vital to understand that double-bundle reconstruction is not the same as anatomic ACL reconstruction and it could still result in a non-anatomic ACL reconstruction. It is merely a step closer to anatomic ACL reconstruction. Biomechanical studies have shown that double-bundle reconstruction is more successful in restoring rotatory stability and normal knee kinematics. [49] The interesting question is whether this results in an improved clinical outcome?



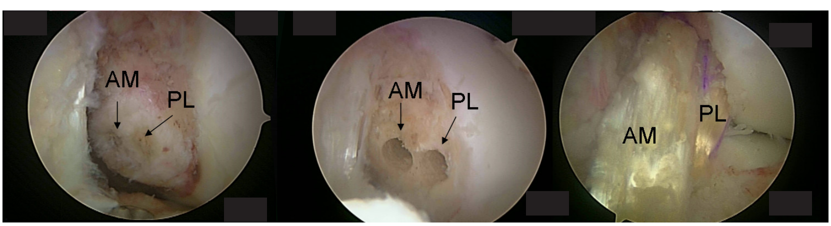


figure 16

Arthroscopic picture showing anatomic single-bundle ACL reconstruction.

figure 17

Arthroscopic picture showing anatomic double-bundle ACL reconstruction.

Artificial grafts

Different artificial grafts have been tested for various methods of ACL reconstruction; however, none has shown satisfactory mid-term to long-term results. [21, 59, 60] We are unaware of any studies with positive results involving artificial grafts and, for this reason; we do not recommend any utilization of prosthetic components in the ACL graft.

Allografts

The major theoretical advantage of allografts compared with autografts is the reduction in harvest site morbidity, with intact flexor and extensor mechanisms in the knee joint. However, allografts were initially seldom used, due in particular to the possible risk of disease transmission, inferior tensile properties and low availability. These issues have been resolved thanks to improved sterilization techniques and availability has increased to match the rise in demand. Furthermore, studies show that allografts revascularize after implantation and clinical studies show results comparable to those produced by autografts. [61, 62] However, as one might deduce, graft healing is slower for the allograft. [63] The traditional indications for allografts have been athletes who do not want any harvest site symptoms or functional deficits and people with revision ACL reconstruction and multiple ligament reconstructions. Nowadays, the indications have broadened and the use of allografts has expanded. For the right patient, an allograft is a good substitute for an autograft; however, the latter will always be superior to the allograft in terms of healing and graft implementation.

figure 18

Picture of a doubled tibialis anterior allograft prepared for ACL reconstruction.

Patellar tendon graft

The PT graft has traditionally been the "gold standard" for ACL reconstruction for almost three decades. Its main advantage is that it has bone plugs on both ends of the graft and this facilitates graft implementation and fixation. This in turn is the most likely explanation for the success rate seen in long-term follow-ups, as well as the patients' early return to sports activities. Advocates of the PT graft have also indicated that the PT graft produces less knee joint laxity than the HT graft. In addition, it is easy preoperatively to assess the thickness of the graft with MRI and therefore create a better foundation for the orthopedic surgeon before the ACL reconstruction. This is in contrast to the hamstring tendon, in which the lengths of the tendons are known first after harvest. This puts the surgical skill of the orthopedic surgeon even more to the test. The PT graft has lost ground during the past decade and is now secondary to hamstring tendon grafts. In Sweden, the quadrupled HT graft was used in 98% of all ACL reconstructions in 2010. [7] The reasons are probably mostly based on the harvest site morbidity.

figure 19

Picture of a patellar tendon graft prepared for ACL reconstruction.

Hamstring tendon graft

The quadrupled HT graft has increased in popularity during the past decade, most likely as a result of its low rate of postoperative morbidity, with fewer donor-site complications than the PT graft. Furthermore, biomechanical studies have shown that the quadrupled hamstring graft is not only much stronger than the PT graft, 4590 N compared with 2977 N, but also much stiffer, 861 N/mm compared with 620 N/mm. [64] In spite of this, there are several concerns when it comes to HT grafts and the majority reflect on the fact that the graft has soft tissue-to-bone fixation and the negative effect on the hamstring muscles in terms of muscle strength in deep flexion and internal rotation. Studies have confirmed that soft tissue to bone has a longer healing time than bone-to-bone; however, it is still unclear whether this has any effect in clinical high level studies. The HT graft is an excellent graft that provides the orthopedic surgeon with a range of options. It is thought to be equivalent to the PT graft and it is a valid option for both single- and double-bundle ACL reconstruction.

figure 20

Picture of a quadrupled semitendinosus and gracilis tendon graft prepared for ACL reconstruction.

Quadriceps tendon graft

The quadriceps tendon is an excellent graft option for ACL reconstruction and it has several advantages. It can easily be harvested with or without a patellar bone block, it is more often sufficient for both single- and double-bundle reconstruction than the PT graft and it has less anterior knee pain and numbness than the PT graft. [65] Furthermore, the quadriceps tendon graft has excellent biomechanical properties which can probably be attributed to its larger cross-sectional area compared with the PT graft and therefore also makes it a splendid graft option in revision cases with expanded bone tunnels. [64] Moreover, the residual muscle strength in the extensor mechanism is actually less impaired after a central third quadriceps tendon harvest compared with a PT harvest. [66] Finally, as with the patellar tendon, the quadriceps tendon can be measured preoperatively with MRI and, as such, it provides an excellent preoperative assessment of the patient. However, the quadriceps tendon is most commonly almost double the size of the patellar tendon and it is therefore a much more eligible graft option. The quadriceps tendon is a graft option that is at least equivalent to the PT graft and it provides the orthopedic surgeon with a range of options including a preoperative assessment of the tendon thickness.

figure 21

Picture of a quadriceps tendon graft prepared for ACL reconstruction.

7.9 graft fixation

7.9.1 pins versus screws

Cross pins and interference screws are common equipment in every orthopedic surgeon's surgical toolbox and standard devices for soft-tissue graft fixation in ACL reconstruction. A number of concerns have been raised about soft tissue-to-bone fixation in hamstring tendon grafts, especially in terms of graft slippage and micromotion. Cross pins are theoretically advantageous due to high failure load but, most importantly, the fixation is closer to the joint, which might reduce micromotion in the graft, thereby preventing tunnel widening. Biomechanical studies have shown that interference screws and cross pins (RIGIDfix) experience increased graft slippage compared with Bio-Transfix. [67]

7.9.2 bioabsorbable versus metal screws

Bioabsorbable screws have gained in popularity primarily as a result of their main theoretical advantage; they resolve after an unspecified time and thus cause no interference with future MRI and knee surgery. Furthermore, they should reduce the risk of late hematogenous infection to a "locus minoris resistentiae", as is the case with metal. The disadvantages of bioabsorbable screws are the risk of breakage at insertion and higher costs.

7.10 evidence–based medicine

Modern medicine, both in the clinical setting and in the field of research, is characterized by a need for well-founded information on diagnosis, treatment, prevention and prognosis for numerous patients with countless conditions and diseases. This has formed the basis of a shift in the general conception of the nature of scientific endeavour.

In 1986, Sackett et al. proposed a system for grading different levels of medical evidence and introduced the concept of evidence-based medicine. [68] It was described as "the conscientious, explicit, and judicious use of the current best evidence in making decisions about the care of individual patients". Historically, the philosophical origin of EBM extends back to mid-19th century Paris and earlier. [69]

As a concept and practice, EBM has woven its way into the fabric of most if not all fields of medicine today and orthopedic surgery is no exception. Two fundamental principles exist that form the backbone of presumed sound evidence: internal and external validity. Internal validity describes the contingent relationship between two variables; in the case of medicine, these variables are intervention/exposure and the resultant outcome. The presence of internal validity is in turn quantified by three main factors, the power of a study, subject allocation and blinding. External validity refers to the consistency or replicability of results within a given population or setting.

There are multiple version of the hierarchy for level of evidence and none that is unanimously used. However, there is a consensus on the strength from different study types relative to each other. The most common grading system and the one used in this thesis can be found at the Oxford Centre for Evidence-Based Medicine website, www.cebm.net. The system categorizes a study from one to five on the basis of its design and as one of four different types on the basis of its content. Based on this, the paradigm of EBM has proposed a hierarchy of study designs in ascending order of bias control whereby the presence of three vital features, each in itself contributing to such bias control, raises the strength of the studies within the hierarchy and thereby its level of evidence. These features are randomization, prospective follow-up and, finally, replication of evidence. The scale is built according to a hierarchy in which Level I is the highest level of evidence, which includes high quality randomized clinical trials, and Level V, which is the lowest level of evidence, so-called expert opinions. The higher the level of evidence, the more reproducibility and applicability to the general patient there is. Levels of evidence are important not only in determining whether one study is of higher quality than another, they also give the reader an immediate sense of how much weight the results of the study should be given. Thus, it is more likely to find a final answer to a research question the higher you move up the hierarchy. The grading system is widely accepted and utilized by most orthopedic journals as it ensures that the best available evidence is used in patient care. It has become the foundation of evidence-based medicine.

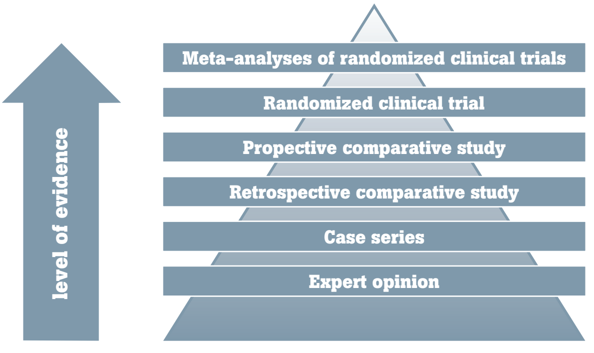


figure 22

The hierarchy of evidence.

7.11 the need for evidence-based practice in acl reconstruction

Thousands studies have been published on ACL reconstruction, most likely due to the high incidence of the injury, difficulty in restoring the normal anatomy of the ACL and the genuine interest among orthopedic surgeons to help their patients. Considering the vast amount of studies, a quick assessment of the studies of ACL reconstruction reveals disappointingly few studies of good quality and with a high level of evidence. Clearly, there is a need for the identification of the highest level of evidence that can be used as clinical guidelines. Furthermore, an evaluation of the current status regarding the distribution of the level of evidence is essential, as this has never been done before when it comes to ACL reconstruction.

7.12 the need for a definition of anatomic acl reconstruction

The shift in paradigm from isometric transtibial ACL reconstruction to anatomic ACL reconstruction has created confusion about what constitutes a true anatomic reconstruction. The term is used interchangeably for different types of reconstruction and several studies claim anatomic reconstruction. The debut of double-bundle ACL reconstruction also led to the use of the term “anatomic” double-bundle ACL reconstruction. Anatomic ACL reconstruction and double-bundle ACL reconstruction are not synonyms. Double-bundle ACL reconstruction means that both bundles of the ACL are reconstructed; however, this can still be performed in a non-anatomic fashion. Moreover, the surgical differences and the reporting of surgical data in studies claiming “anatomic” ACL reconstruction create a very difficult situation when assessing and pooling the outcomes of the studies. This confusion has also led to the need for a definition of what constitutes an anatomic ACL reconstruction. This definition, together with a scoring system, enables an evaluation of potential benefits of anatomic ACL reconstruction and creates an opportunity to compare and pool outcomes from studies.

8 / eight themes

8.1 theme 1: clinical outcome

This theme consists of two systematic reviews outlining the highest level of evidence in selected RCTs for the treatment of ACL injuries. The systematic reviews focused on surgical techniques, rehabilitation schedules and graft options. A detailed descriptive analysis and assessment of the outcomes were performed.

8.2 theme 2: level of evidence

This theme consists of three systematic reviews outlining the level of evidence in ACL reconstruction. Two systematic reviews clarify the relative strengths and weaknesses of selected RCTs in ACL reconstruction with special emphasis on the quality of the included studies. One systematic review identified the distribution of level of evidence in studies of primary ACL reconstruction. Moreover, evaluations of the level of evidence over time and factors related to level of evidence were performed.

8.3 theme 3: anatomic acl reconstruction

This theme consists of one current concept paper (literature review and expert opinion), three systematic reviews and one original article. In the current concept paper, an outline of the history of the surgical technique in ACL reconstruction, including the principles and outline of what constitutes an anatomic ACL reconstruction, was presented. Two systematic reviews assessed the reporting of surgical data in clinical and cadaver studies claiming "anatomic" ACL reconstruction. Thereafter, a scoring system for anatomic ACL reconstruction was developed and validated (original paper). An implementation of the scoring system using a systematic review methodology was then performed on clinical studies comparing single- and double-bundle ACL reconstruction.

9 / nine
aims

This research aimed at clarifying clinical outcomes with the highest level of evidence and the current status of evidence in ACL reconstruction today. Furthermore, the future directions of ACL reconstruction, so-called anatomic ACL reconstruction, are thoroughly reviewed and a scoring system has been developed and implemented.

9.1 overall aims

The overall aims are divided into three content areas.

1. To examine the clinical outcomes in ACL reconstruction based on the highest level of evidence in clinical trials, RCTs
2. To determine the quality of clinical trials and the distribution of the level of evidence in ACL reconstruction
3. To identify the need for a definition of anatomic ACL reconstruction, to present the concept and create a scoring system

9.2 specific aims

9.2.1 theme 1

Paper 1 To investigate and assess the current evidence from RCTs of ACL injuries, with special reference to the choice of surgical techniques and certain aspects of rehabilitation [Systematic Review]

Paper 2 To investigate and assess the current evidence from RCTs of ACL injuries, with special reference to graft type and surgical technique [Systematic Review]

9.2.2 theme 2

Papers 1 - 2 To clarify the relative strengths and weaknesses of selected RCTs, resolve literature conflicts and evaluate the need for further studies [Systematic Reviews]

Paper 3 To categorize the study type and level of evidence of studies of primary ACL reconstruction and to correlate the level of evidence with the impact factor for the journal and evaluate the level of evidence over time and geographic distribution [Systematic Review]

9.2.3 theme 3

Paper 4 To analyze and summarize the history of the ACL reconstruction and to present the anatomic ACL reconstruction concept [Current Concepts, Literature Review, Expert Opinion]

Paper 5 To assess the current basic science studies of anatomic ACL reconstruction, evaluating the reconstructive methods applied, in order to determine whether the data are sufficient to define the surgical technique as anatomic [Systematic Review]

Paper 6 To investigate and assess studies published on anatomic double-bundle ACL reconstruction that provides a description of the surgical technique. A descriptive analysis of the reporting of a variety of surgical data was performed. [Systematic Review]

Paper 7 To develop and validate a scoring system for evaluating anatomic ACL reconstruction. This scoring system is intended to be applicable for grading ACL reconstruction procedures for individual patients and for reviewing the description of surgical methods in published studies of anatomic single- and double-bundle ACL reconstruction and for peer reviews of these papers. [Original Paper]

Paper 8 To apply and evaluate the anatomic ACL reconstruction scoring system in clinical trials comparing single-bundle and double-bundle ACL reconstruction [Systematic Review]

10 / ten methods

10.1 systematic reviews

This thesis primarily utilized systematic reviews to address the relevant research questions.

10.1.1 terminology

The terminology for describing both systematic reviews and meta-analyses has changed and evolved over time. Today, it is essential to use the definition given by the Cochrane Collaboration: "A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies". [70]

10.1.2 level of evidence

Well-conducted systematic reviews and meta-analyses of high-quality homogeneous RCTs are the highest ranked studies in the hierarchy of level of evidence (Level 1a). The main advantage of meta-analyses is that they can increase the sample size of the included studies. Furthermore, meta-analyses can have a higher level of evidence than the individual included studies, as a meta-analysis utilizes new statistical methods that can resolve any eventual previous downgrading of the included RCTs. Systematic reviews, on the other hand, do not generally have a higher level of evidence than the lowest ranked level of the included studies.

10.1.3 limitations

It is vital to understand that the quality of the included studies reflects directly on the quality of the systematic review or meta-analysis. Moreover, errors are possible in both systematic reviews and meta-analyses, as they are retrospective and observational; for this reason, the quality and validity rely heavily on appropriate scientific methods to reduce systematic error. Some of the more common errors in systematic reviews are several types of reporting bias in the included studies that may affect both the conduct and the interpretation. A review of 300 systematic reviews reported that the quality was inconsistent and that readers should not accept SRs uncritically. [71] Guidelines have been developed to address these issues and to minimize suboptimal reporting. The two most common are the Cochrane Guidelines and the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement. [72, 73] The latter is an updated version of the QUOROM (QUality Of Reporting Of Meta-analyses) statement, which was published in 1996. The conducted systematic reviews follow these guidelines.

There is also a "best before date" for systematic reviews, as new studies are published continuously. A study that monitored 100 SRs found that 7% needed updating at the time of publication, another 4% within a year and another 11% within two years. The figures were even higher in rapidly-changing medical fields. [74] It is therefore vital to update and create new systematic reviews continuously.

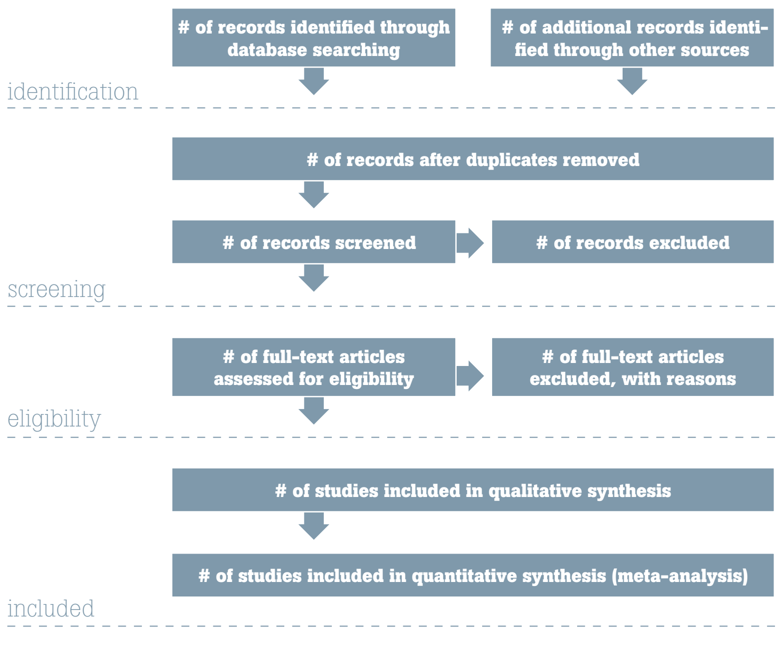


figure 23

Flow of information through the different phases of systematic review.

table 1

PRISMA checklist of items to include when reporting a systematic review (with or without meta-analysis).

Section/Topic	#	Checklist item
Title		
Title	1	Identify the report as a systematic review, meta-analysis, or both.
Abstract		
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
Introduction		
Rationale	3	Describe the rationale for the review in the context of what is already known.
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).
Methods		
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., web address), and, if available, provide registration information including registration number.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, induplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).

Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
Results		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
Discussion		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
Funding		
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

10.1.4 implementations

Lately, there has been an increase in the popularity of both meta-analyses and systematic reviews in medicine. [71] There are several reasons for this increase. Professional healthcare providers, including orthopedic surgeons, utilize them to keep up to date with today's fast-moving, modern medical research. Systematic reviews provide a very efficient way of keeping up to date with the highest level of evidence within the clinicians' content area. Several institutes and clinics use them as a baseline when creating clinical guidelines. In Sweden, this is routinely done by the Swedish Council on Health Technology Assessment (SBU). The SBU has the mandate of the Swedish Government comprehensively to assess healthcare technology from medical, economic, ethical and social standpoints.

10.2 developing a score

The scoring system for anatomic ACL reconstruction was developed in a four-step process.

10.2.1 step 1: item generation

Three senior orthopedic surgeons and authors with extensive clinical experience in ACL reconstruction created an item list they thought would either facilitate or inhibit anatomic ACL reconstruction. This list contained variables that could be used in the scoring system.

10.2.2 step 2: item reduction and face validity

A panel of international experts on ACL reconstruction was selected for aid in item reduction and to evaluate face validity. The panel evaluated each item according to importance (1 = not important, 2 = somewhat important, 3 = very important, 4 = extremely important) and performance when reconstructing an ACL (1 = never, 2 = sometimes, 3 = more often than not and 4 = always). The panel was also asked for their opinion regarding tunnel placement and suggest new items for the revised list. The items were then evaluated and included for the revised item list if they received an importance score of 3 or 4 by at least 75% of the experts, or if the median score was 3 or higher. Furthermore, a senior author was given the choice to veto any item.

10.2.3 step 3: item validity

After step 2, the validity of the revised list needed to be performed. A total of 959 peer reviewers were contacted from four high-impact orthopedic sports medicine journals; The American Journal of Sports Medicine (AJSM), Arthroscopy, The Journal of Bone and Joint Surgery – Series A and Knee Surgery, Sports Traumatology, Arthroscopy (KSSTA). An electronic invite to participate in an anonymous online survey was sent to all peer reviewers. The peer reviewers were asked to evaluate each item in the modified list with regard to importance (as previous scale) and performance when peer review of a manuscript on anatomic ACL reconstruction (as previous scale). The peer reviewers were also given the opportunity to suggest new items for the final list. Items were included for the final item list according to the same set of rules for step 2.

10.2.4 step 4: finalization and testing for reliability and validity

The final scoring system was based on the results from steps 1 to 3. Twenty de-identified methods sections from papers with different approximations of anatomic ACL reconstruction were selected. These sections were scored by the senior authors according to their expertise on the degree of "anatomicness" on a four-point scale (1 = non-anatomic, 2 = somewhat anatomic, 3 = almost anatomic, 4 = completely anatomic). Each of the four authors then selected two experts to score five of the selected papers, each using the scoring system. As a result, each paper was rated twice by two different experts, as eight experts performed 40 ratings. A statistical analysis was then performed to determine the reliability and internal consistency of the final scoring system.

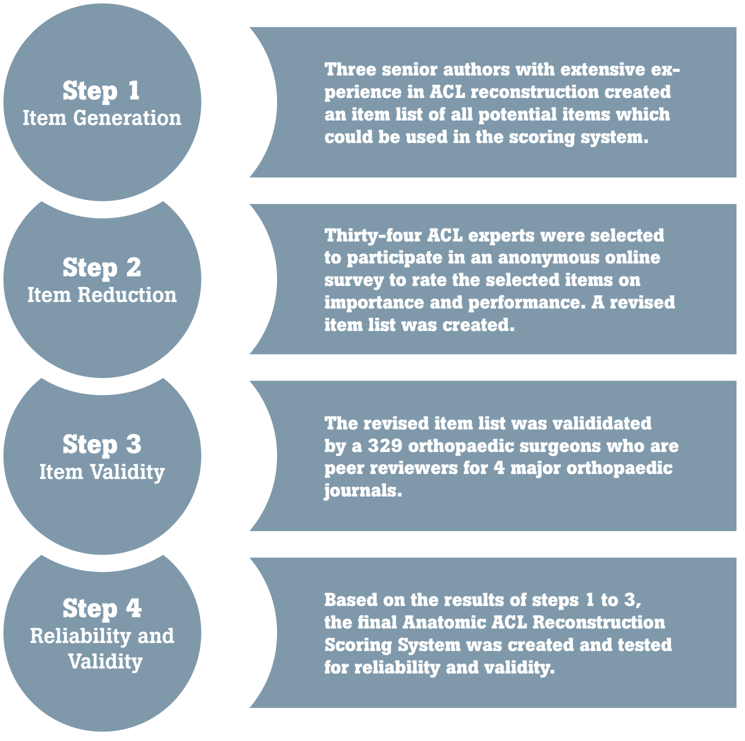


figure 24

The four-step process in which the anatomic ACL scoring system was developed.

11 / eleven
summary of papers

11.1 theme 1 - 2: clinical outcome and level of evidence

11.1.1 paper 1

Treatment of anterior cruciate ligament injuries with special reference to surgical technique and rehabilitation: an assessment of randomized controlled trials

Introduction

There are a huge number of studies of ACL reconstruction and few of them are RCTs. Assessments of the outcomes of these RCTs are therefore essential, together with a qualitative evaluation. Two systematic reviews were therefore made to investigate and assess the current evidence in RCTs on ACL injuries and to conduct a qualitative analysis of the included studies. This first systematic review focused on surgical technique and rehabilitation.

Methods

A PubMed database search using the keywords "Anterior Cruciate Ligament" was made. The search was limited to only RCTs published in English during the period January 1995 to March 2009. Articles relating to surgical technique and rehabilitation were obtained. The studies were screened and a subsequent quality appraisal was performed based on the CONSORT Statement.

Results

Seventy RCTs from the 271 in the electronic search were selected and included in this systematic review.

Surgical technique

Initial graft tension and the use of a ligament augmentation device did not affect clinical outcome. Bioabsorbable screws and titanium screws produced an equal clinical outcome, regardless of graft type. Cross-pin and interference screws were comparable means of fixating the HT graft and possibly the PT graft. A well-designed RCT is needed to demonstrate the benefits of the transcondylar screw. A more rigid HT graft complex generated less tunnel widening; however, there was no correlation with clinical outcomes. Fifty percent of ACL-injured patients developed radiographic signs of osteoarthritis, regardless of treatment. Meniscectomy further increased the risk. The eventual advantages of early reconstruction need to be evaluated by future studies.

Rehabilitation

The use of a postoperative knee brace did not affect the clinical outcome after ACL reconstruction and did not reduce the risk of subsequent intra-articular injury.

It remains to be clarified whether there are any differences in early versus late ACL reconstruction, accelerated versus non-accelerated and home-based versus supervised rehabilitation protocols. Closed kinetic chain exercises produced less pain and laxity, while promoting a better subjective outcome than OKC exercises after patellar tendon ACL reconstruction. Open kinetic chain exercises produced greater quadriceps femoris muscle strength without further compromising knee laxity in ACL-deficient patients.

Quality assessment

A total of thirteen percent of the trials did not have adequate randomization. Thirty-three percent of the trials did not present the randomization process. Seventy percent of the trials did not have a sample size calculation. Sixty-eight percent of the trials in which no significant differences between study groups could be demonstrated did not have a sample size calculation. Thirty-nine percent of the trials had sample sizes of less than 50 patients. Ninety-four percent of the trials had a short-term follow-up.

Conclusions

The most important finding in this systematic review was without doubt the qualitative weaknesses found in the study design of the included studies. In many cases, these studies are the final resort for orthopedic surgeons when creating guidelines and evaluating their clinical efforts. It is therefore of great importance that future studies with a higher qualitative level are performed with a long-term follow-up and preferably according to some form of guidelines. The identified qualitative limitations were therefore transferred to the assessment of outcome measurements and, as a result, several topics were left unanswered. In terms of rehabilitation, we found that the postoperative knee brace did not affect clinical outcomes and that CKC exercises produced less pain and fewer laxity differences. For this reason, the utilization of a brace should be considered individually and not in general and CKC exercises should be focused on after ACL reconstruction. Furthermore, we found that half the ACL-injured patients developed radiographic signs of osteoarthritis and that meniscectomy further increased the risk. This clearly demonstrates the need for the evolution of the surgical technique for ACL reconstruction.

table 2

Overview of limitations of the included studies [from Paper 1].

Limitation	Quantity	Percentage (%)
Inadequate randomization	9	13
No randomization method is presented	23	33
No sample size calculation	49	70
Number of trials with no significant differences among study groups	41	59
Number of trials with no significant differences among study groups, which did not have a sample size calculation	28	68
No blinding	4	6
No blinding stated	22	31
Sample size 0 – 49	27	39
Sample size 50 – 99	29	41
Less than 80% follow-up	5	7
Gender bias	29	41
Unknown gender ratio	12	17
Multiple surgeons	20	29
Unknown number of surgeons	14	20

table 3

Overview of follow-up of the included studies [from Paper 1].

Follow-up	Quantity	Percentage (%)
≥ 10 years	1	1.5
5 – 9 years	3	4
4 years	1	1.5
3 years	1	1.5
2 years	26	37
20 months	2	3
18 months	1	1.5
1 year	15	21
6 - 11 months	4	6
≤ 6 months	16	23

Treatment of anterior cruciate ligament injuries with special reference to graft type and surgical technique: an assessment of randomized controlled trials

Introduction

There are a huge number of studies of ACL reconstruction and few of them are RCTs. Assessments of the outcomes of these RCTs are therefore essential, together with a qualitative estimation. Two systematic reviews were therefore made to investigate and assess the current evidence from RCTs on ACL injuries and to conduct a qualitative analysis of the included studies. This second systematic review focused on graft type and surgical technique.

Methods

A PubMed database search using the keywords "Anterior Cruciate Ligament" was performed. The search was limited to only RCTs published in English during the period January 1995 to March 2009. Articles relating to surgical technique and rehabilitation were obtained. The studies were screened and a subsequent quality appraisal was made based on the CONSORT Statement.

Results

Thirty-nine RCTs from the 271 in the electronic search were selected and included in this systematic review.

Graft type

There were no differences between the PT graft and HT graft in terms of laxity, clinical outcome, time of return to sports, patella-femoral crepitations, one-leg-hop test, ROM, thigh muscle circumference and anterior knee sensory deficit. The PT graft produced more anterior knee pain and kneeling pain than the HT graft, but the difference appeared to disappear with time. The harvest site affected muscle strength initially but not over time. There were a possible correlation between the development of osteoarthritis and the PT graft. The HT graft produced more tunnel widening than the PT graft. However, there was no correlation between tunnel widening and clinical outcome or laxity. Harvesting both the semitendinosus and gracilis was associated with inferior knee flexion at higher angles, as compared with the harvest of only the semitendinosus. Furthermore, harvesting both tendons reduced hamstring muscle strength for approximately one year; however, this needs to be validated. There were no differences between the PT graft and the HT graft with bone block in terms of clinical outcome and laxity; however, this finding needs to be confirmed.

Surgical technique

There were no differences in clinical outcome between single- and double-bundle ACL reconstructions. However, double-bundle ACL reconstruction produced less rotatory laxity.

Qualitative assessment

Forty-four percent did not have adequate randomization. Thirteen percent did not present the randomization process. Sixty-four percent did not have a sample size calculation. Twenty percent of the trials in which no significant differences between study groups could be shown did not have a sample size calculation. None had sample sizes of less than 50 patients. Sixty-nine percent had a short-term follow-up.

Conclusions

The key findings from this systematic review were that there were several weaknesses in the design of the included studies. These limitations caused a problem when pooling the outcomes of the studies. Furthermore, the qualitative limitations resulted in issues when attempting to draw conclusions. In terms of graft type, it appears that most of the differences that were found, such as anterior knee pain, pain on kneeling and strength deficits after tendon harvest, relate to harvest site morbidity. These are all logical and somewhat expected outcomes. This also applies to the tunnel widening seen in ACL reconstructions with HT grafts. Another finding is that double-bundle ACL reconstruction produced less rotatory laxity than single-bundle reconstruction. This is not surprising, as it is the theorized advantage that has already been reported in biomechanical studies. The question of whether it is advantageous in the long-term still remains to be answered

table 4

Overview of limitations of the included studies [from Paper 2].

Limitation	Quantity	Percentage (%)
Inadequate randomization	17	44
No randomization method is presented	6	15
No sample size calculation	25	64
Number of trials with no differences among study groups	7	18
Number of trials with no differences among study groups, which did not have a sample size calculation	5	20
No blinding	4	10
No blinding stated	15	38
Sample size 0 – 49	0	0
Sample size 50 – 99	27	69
Sample size ≥ 100	12	31
Less than 80% follow-up	4	10
Gender bias	7	18
Unknown gender ratio	17	44
Multiple surgeons	7	18
Unknown number of surgeons	7	18

table 5

Overview of follow-up of the included studies [from Paper 2].

Follow-up	Quantity	Percentage (%)
≥ 10 years	0	0
5 – 9 years	8	21
3-years	3	8
31 months	1	3
2-years	17	44
19 months	1	3
18 months	2	5
1 year	4	10
≤ 6-months	3	8

Systematic review on level of evidence in anterior cruciate ligament reconstruction

Introduction

Modern medicine in the clinical setting and in the field of research is characterized by a need for well-grounded information. Although there are a large number of studies of ACL reconstruction, there are indications that most have a low level of evidence. However, there is no proper assessment of the status in terms of the level of evidence of these studies. For this reason, a systematic review was conducted with the aim of categorizing the study type and level of evidence of studies of ACL reconstruction by applying the level of evidence rating system, proposed by the Oxford Centre for Evidence-based Medicine.

Methods

An electronic search was made using the PubMed, Embase and Cochrane Library databases. Studies published from January 1995 to August 2011 were included. Therapeutic studies written in English that reported on isolated primary ACL reconstruction with clinical outcome measurements related to the reconstruction were included. Categorization and implementation of the level of evidence were performed. The correlation between the level of evidence and the impact factor of the journal was analyzed, together with linear regression models to reveal any significant trends over time.

Results

Seven thousand one hundred and fifty-four studies were analyzed, of which 1510 were included. Analysis of the study types revealed that case series (494; 32.7%) were the most frequent study type, followed by expert opinions (440; 29.1%). The most common clinical trials were, in descending order: retrospective comparative studies (214; 14.2%), randomized clinical trials 9.2% (139), prospective comparative studies 7.6% (115) and case-control studies 3.6% (54). Systematic reviews and meta-analyses represented only 2.3% (35) and 1.3% (19) respectively. Single-bundle studies were the most common studies (1,333; 88.3%), followed by double-bundle (98; 6.5%) and single-bundle versus double-bundle (79; 5.2%). There was a general increase in the absolute numbers of higher level of evidence studies over time and studies in general. The journals Arthroscopy, KSSTA and the AJSM accounted for 43.5% (657) of the included studies. These three journals represented the largest number of studies in all calculations. Arthroscopy had the largest number of publications in general and in level 4 and 5 studies, whereas the AJSM had the smallest number of the three. The AJSM had the largest number of level 1 and 2 studies in general. The total mean level of evidence for the top three journals was 3.77 for Arthroscopy, 3.43 for KSSTA and 3.03 for the AJSM. The mean level of evidence calculated without level 5 studies was 3.15 for Arthroscopy, 3.20 for KSSTA and 2.9 for the AJSM. There was a significant correlation between the impact factor of the journal and the mean level of evidence of the journal and the proportion of high level of evidence studies (level 1 and 2).

There was a significant trend towards a higher mean level of evidence over time. The USA had the largest number of publications and accounted for 36.2% (547) of all the studies. Sweden had most RCTs, followed by Italy and the USA.

Conclusions

The key findings from this systematic review were that most therapeutic studies of primary ACL reconstruction had a low level of evidence. This was an expected finding; however, it is promising that there was also a significant trend towards a higher mean level of evidence over time. Another finding was the positive correlation between the journals' impact factor and the mean level of evidence. This correlation was also found with the proportion of high level of evidence studies. It appears that the impact factor is a reliable tool for gauging the level of evidence of primary ACL reconstruction studies in journals

table 6

Frequencies of the included studies [from Paper 3].

Study Type	Frequency	Percentage (%)
Case Series	494	32.7
Expert Opinion	440	29.1
Retrospective Comparative Study	214	14.2
Randomized Clinical Trial	139	9.2
Prospective Comparative Study	115	7.6
Case Control Study	54	3.6
Systematic Review	35	2.3
Meta-analysis	19	1.3
Total	1510	100

table 7

Distribution of study types for the top 5 countries [from Paper 3]

Country		MA	SR	RCT	PCS	RCS	CSS	CS	EO	Total
United States	n	11	16	15	19	74	18	133	261	547
	*	2.0	2.9	2.7	3.5	13.5	3.3	24.3	47.7	100
	#	57.9	45.7	10.8	16.5	34.6	33.3	26.9	59.3	36.2
Japan	n	0	0	14	15	19	7	57	24	136
	*	0	0	10.3	11.0	14.0	5.2	41.9	17.7	100
	#	0	0	10.1	13.0	8.9	13.0	11.5	5.5	9.0
Italy	n	0	1	15	18	8	2	37	26	107
	*	0	0.9	14.0	16.8	7.5	1.9	34.6	24.3	100
	#	0	2.9	10.8	15.7	3.7	3.7	7.5	5.9	7.1
United Kingdom	n	0	3	4	3	5	3	39	21	78
	*	0	3.9	5.1	3.9	6.4	3.9	50.0	26.9	100
	#	0	8.6	2.9	2.6	2.3	5.6	7.9	4.8	5.2
Sweden	n	0	2	17	8	12	2	30	5	76
	*	0	2.6	22.4	10.5	15.8	2.6	39.5	6.6	100
	#	0	5.7	12.2	7.0	5.6	3.7	6.1	1.1	5.0

* = percentage of the countries' studies
# = percentage of the total studies
RCS = Retrospective Comparative Study , CSS = Case-Control Study, CS = Case Series, EO = Expert Opinion

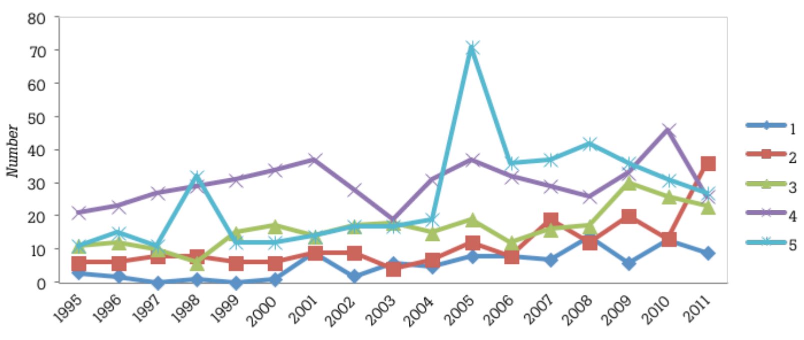


figure 25

Studies categorized according to level of evidence over time [from Paper 3].

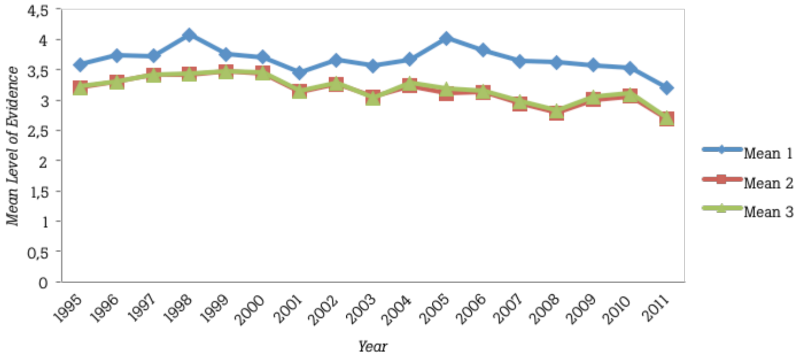


figure 26

The mean level of evidence over time [from Paper 3]. Mean 1 = All studies included, Mean 2 = Expert opinions excluded, Mean 3 = Only clinical studies.

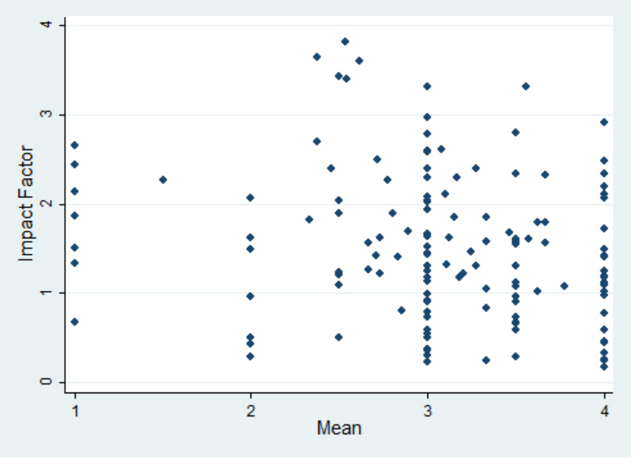


figure 27

Scatter plot for the correlation between the impact factor for journals with 10 or more included studies and the mean level of evidence calculated for clinical trials [from Paper 3].

11.2 theme 3: anatomic acl reconstruction

11.2.1 paper 4

Anatomic single- and double-bundle anterior cruciate ligament reconstruction, part 2: clinical application of surgical technique

Introduction

With the introduction of the arthroscopic technique, a two- and subsequently one-incision technique was applied. The new one-incision technique introduced drilling of the femoral tunnel through the tibial tunnel. With time, studies found that this traditional arthroscopic transtibial single-bundle reconstruction did not fully restore the rotational stability of the knee joint. Lately, a more anatomic approach to reconstructing the ACL has been proposed. Anatomic ACL reconstruction attempts to replicate normal anatomy, restore normal kinematics and protect long-term knee health. Although double-bundle ACL reconstruction has been shown to result in better rotational stability in both biomechanical and clinical studies, it is vital to differentiate between anatomic and double-bundle ACL reconstruction. The latter is merely a step closer to reproducing the native anatomy of the ACL; however, it can still be done non-anatomically. To evaluate the potential benefits of reconstructing the ACL in an anatomic fashion, we need accurate, precise and reliable outcome measurements. These include dynamic stereo radiography, T2 MRI mapping of cartilage and the quantification of graft healing on MRI. Furthermore, there is a need for a consensus on the patient-reported outcome measurements that should be used, in order to facilitate the homogeneous reporting of outcomes. A current concepts paper that focused on different aspects of anatomic ACL reconstruction was therefore produced.

Conclusions

The current concepts paper reported on the concepts in anatomic ACL reconstruction. The principles, surgical technique descriptions for anatomic single- and anatomic double-bundle reconstruction, the pearls and pitfalls, post-operative evaluation, rehabilitation and clinical outcome are thoroughly analyzed and presented. Finally, current trends in the literature were discussed.

Systematic review on cadaveric studies of anatomic anterior cruciate ligament reconstruction

Introduction

Basic science studies are often used as templates in the development and optimization of surgical techniques. This is also the case when it comes to the development of anatomic ACL reconstruction. However, these papers often lack the necessary data in the methods section to ascertain whether the proposed surgical technique is anatomic. These limitations create difficulty extrapolating the results to a clinical setting. We therefore planned and executed a systematic review with the aim of evaluating basic science studies of anatomic ACL reconstruction.

Methods

A systematic electronic search was performed using the PubMed and Embase databases. Studies that were published from January 1995 to April 2009 were included. Only basic science studies of human cadavers that reported "anatomic" ACL reconstruction and were written in English were included. Variations in surgical technique and the reporting of surgical descriptions were assessed.

Results

Eighteen studies from the 1097 in the electronic search were included in this systematic review. The most frequently reported items were fixation methods in the femur and tibia, graft type and tension patterns. Visualization of the insertion sites and placement of the tunnels in the footprint were reported in half to two thirds of the studies. Measurements of the insertion site and the dimensions of the intercondylar notch and visualization of the ridges were not reported in any study. Notchplasty and radiographic documentation were grossly under-reported. Other surgical data were reported in two thirds of the studies at best. There was a large variation in the reported surgical techniques between the included studies.

Conclusions

The key findings from this systematic review were that most variables in the surgical technique description were so poorly reported that any attempt to recreate the reconstruction or pool the outcomes would be difficult, to say the least. This finding should not be taken lightly, as many basic science studies are used both for guidance when creating clinical trials and as references. So, to provide literature that matches the current high level of medical research, authors are encouraged to report their surgical technique in a detailed manner, similar to high-level clinical trials.

table 8

Reporting of surgical data in included studies [from Paper 5].

Item	Reported (%)	Not reported (%)
Use of an accessory medial portal	27.8	72.2
Visualization of the tibial insertion site	61.1	38.9
Visualization of the femoral insertion site	66.7	33.3
Visualization of the lateral intercondylar and bifurcate ridge	0	100
Measuring the tibial insertion site	0	100
Measuring the femoral insertion site	0	100
Measuring the dimensions of the femoral intercon-dylar notch	0	100
Performing wall or notchplasty	5.6	94.4
Use of o'clock face for femoral tunnel position	50	50
Flexion angle during femoral drilling	22.2	77.8
Placement of the tibial tunnel in ACL footprint	66.7	33.3
Placement of the femoral tunnel in ACL footprint	55.6	27.8
Proof of tunnel placement provided	55.6	27.8
Placement of the tibial tunnel at fixed distance from another anatomic structure	44.4	55.6
Placement of the tibial tunnel at fixed distance from another anatomic structure	38.9	61.1
Graft type that was used	94.4	5.6
Use of fluoroscopy	11.1	88.9
Use of navigation	11.1	88.9
Tibial fixation method	100	0
Femoral fixation method	100	0
Use of a different tension pattern for the anterome-dial and posterolateral bundle graft •	78.6	21.4
Use of post-operative radiography	16.7	83.3
Use of post-operative MRI	0	100
Use of post-operative CT scan	0	100
Use of post-operative 3-dimensional CT scan	0	100

• For double-bundle techniques only

table 9

Proof of tunnel placement in the native ACL footprint [from Paper 5].

	Shown † (%)	Not shown (%)
Diagram	72.2	27.8
Pictures	0	100
Radiographs	11.1	88.9
MRI	0	100
CT	11.1	88.9
3D CT	5.6	94.4
Other	11.1	88.9
Multiple of the above	11.1	88.9

† % of papers that use this methods to show their tunnel positions.

"Anatomic" anterior cruciate ligament reconstruction: a systematic review of surgical techniques and reporting of surgical data

Introduction

The terms "anatomic" and "double-bundle ACL reconstruction" have been used interchangeably. This confusion in linguistic terms has created a dilemma, as anatomic ACL reconstruction is not the same as double-bundle ACL reconstruction. The latter can still be performed in a non-anatomic fashion. We therefore planned and executed a systematic review with the aim of evaluating the surgical data in published studies of anatomic double-bundle ACL reconstruction.

Methods

A systematic electronic search was made using the PubMed and Embase databases. Studies that were published from January 1995 to April 2009 were included. The selection criteria were studies that reported on a surgical technique for "anatomic double-bundle ACL reconstruction" on skeletally mature living human subjects and were written in English. The data that were collected and analyzed included a variety of surgical data.

Results

Seventy-four studies from the 1097 in the electronic search were included in this review. The most frequently reported items were fixation methods in the femur and tibia, graft type and placement of the tunnels in their footprint. Visualization of the insertion sites, proof of tunnel placement, use of o'clock reference, flexion angle during drilling, tension pattern and use of an accessory medial portal were reported in half to three quarters of the studies. Measurements of the insertion site and the dimensions of the intercondylar notch, visualization of the ridges, individualization of surgery and performance of notchplasty were grossly under-reported. The greatest variety was seen in knee flexion angle during femoral tunnel drilling and the tensioning pattern of the grafts.

Conclusions

The most important findings from this systematic review were that there was gross under-reporting of specific surgical technique data. This under-reporting has extensive effects in the research on anatomic ACL reconstruction, as it is difficult to recreate the reconstruction, pool the outcomes or extrapolate them to a clinical setting. We therefore encourage authors to report their surgical technique in a specific, standardized fashion.

table 10

Reporting of surgical data in included studies [from Paper 6].

Item	Reported (%)	Not reported (%)
Use of an accessory medial portal	51.4	48.6
Visualization of the tibial insertion site	77.0	23.0
Visualization of the femoral insertion site	70.3	29.7
Visualization of the lateral intercondylar and bifurcate ridge	12.2	87.8
Measuring the tibial insertion site	4.1	95.9
Measuring the femoral insertion site	4.1	95.9
Measuring the dimensions of the femoral intercondylar notch	1.4	95.9
Performing wall or notchplasty	12.2	87.8
Use of o'clock face for femoral tunnel position	60.8	39.2
Flexion angle during femoral drilling	59.5	40.5
Placement of the tibial tunnel in ACL footprint	85.1	14.9
Placement of the femoral tunnel in ACL footprint	81.1	18.9
Proof of tunnel placement provided	71.6	28.4
Placement of the tibial tunnel at fixed distance from another anatomic structure	35.1	64.9
Placement of the tibial tunnel at fixed distance from another anatomic structure	35.1	64.9
Individualization of surgical technique based on patient characteristics	4.1	95.9
Graft type that was used	91.9	8.1
Use of fluoroscopy	10.8	89.2
Use of navigation	10.8	89.2
Tibial fixation method	89.2	10.8
Femoral fixation method	94.6	5.4
Use of a different tension pattern for the anteromedial and posterolateral bundle graft	52.7	47.3
Use of post-operative radiography	18.9	81.1
Use of post-operative MRI	5.4	94.6
Use of post-operative CT scan	2.7	97.3
Use of post-operative 3-dimensional CT scan	2.7	97.3

table 11

Proof of tunnel placement in the native ACL footprint [from Paper 6].

	Shown † (%)	Not shown (%)
Diagram	74.3	25.7
Arthroscopic pictures	55.4	44.6
Radiographs	17.6	82.4
MRI	2.7	97.3
CT	4.1	95.9
3D CT	4.1	95.9
Other	5.4	94.6
Multiple of the above	64.9	35.1
† % of papers that use this methods to show their tunnel positions.		

11.2.4 paper 7

Anatomic anterior cruciate ligament reconstruction scoring system: development and validation

Introduction

Previous systematic reviews of surgical data have provided very limited descriptions of the surgical procedure in anatomic ACL reconstruction. There were also large variations in the techniques for the procedure. We therefore developed and validated a scoring system to grade anatomic ACL reconstruction procedures for individual patients, as well as for a review of the description of surgical methods in published studies and for a peer review of these papers.

Methods

The scoring system was developed according to a four-step process. In the first step, three senior authors generated a list of all the potential items that could be used in the scoring system. These items were used in the next step for reduction and validation; 34 international experts were selected to participate in an anonymous online survey to rate the selected items in terms of importance and performance, using a score of 1-4. The results were then verified in terms of item validity in the third step. This was done by surveying a large sample of 959 orthopedic surgeons who are peer reviewers for four major orthopedic journals. Items were included in the final scoring system if they received an importance score of 3 or 4 from at least 75% of the survey participants. Lastly, the scoring system was validated, tested for reliability and all the included items were tested for internal consistency.

Results

The survey response rate was 79% (27/34) for the international ACL experts and 40% (329/959) for the peer reviewers. The final anatomic ACL reconstruction scoring system included 17 items with a maximum score of 23 points. Validity testing produced an r of 0.63 (p=0.003), reliability testing produced an ICC of 0.65 and the Cronbach's alpha for internal consistency was 0.82.

Conclusions

This large survey-based study of anatomic ACL reconstruction resulted in a valid and reliable tool for objectively grading the surgical methods described in studies of anatomic ACL reconstruction. The scoring system can be used as a building block for the future development of anatomic ACL reconstruction and it can aid in everything from the reporting of surgical data when writing papers to the assessment of these papers.

table 12

Internal consistency of the items [from Paper 7].

Item no.	Item description	Cronbach's alpha
	All Items combined	0.82
1	Individualization	0.81
2	30-degree scope	0.83
3	Accessory medial portal	0.80
4	Direct visualization femoral insertion site	0.79
5	Measuring femoral insertion site	0.81
6	Visualization lateral intercondylar ridge	0.80
7	Visualization lateral bifurcate ridge	0.81
8	Femoral tunnel in insertion site	0.81
9	Transportal drilling	0.80
10	Direct visualization tibial insertion site	0.81
11	Measuring tibial insertion site	0.81
12	Tibial tunnel in insertion site	0.80
13	Femoral fixation documentation	0.80
14	Tibial fixation documentation	0.81
15	Knee flexion angle during drilling	0.80
16	Graft type documentation	0.82
17	Graft tension documentation	0.80
18	Documentation of tunnel position	0.82

table 13

Results of survey of ACL expert panel [from Paper 7].

	Importance			Performance/ performing			
Item	**Mean**	**Median**	**% ≥ 3**	**Mean**	**Median**	**% ≥ 3**	**P value**
Direct visualization femoral insertion site	3.85	4	100	3.78	4	96.3	ns
Femoral tunnel in insertion site	3.78	4	100	4	4	100	ns
Tibial tunnel in insertion site	3.56	4	96.3	4	4	100	0.008
Flexion angle during drilling	3.48	4	92.6	2.63	3	59.2	0.005
Individualization	3.41	4	85.2	3.44	4	88.9	ns
Direct visualization tibial insertion site	3.67	4	76.4	3.67	4	92.6	ns
30-degree scope	3.15	3	81.4	3.89	4	96.3	<0.001
Visualization lat int. ridge	2.96	3	74	3.26	3	81.4	0.046
Femoral fixation	2.70	3	62.9	4.00	4	100	< 0.001
Graft type	2.56	3	59.3	3.89	4	96.3	< 0.001
Transportal drilling	2.85	3	59.2	2.96	4	63.0	ns
Tibial fixation	2.67	3	59.2	3.93	4	96.3	< 0.001
Visualization lat bifurcate ridge	2.56	3	55.6	2.81	3	66.7	0.035
Appropriate graft tension	2.67	3	55.6	3.15	4	74.1	ns
Post-op X-ray	2.37	2	44.4	3.11	4	63.0	0.002
Accessory medial portal	2.22	2	40.7	2.37	2	40.7	ns
Measuring tibial insertion site	2.22	2	37.0	2.15	2	37.0	ns
Femoral tunnel at fixed distance	2.30	2	37.0	2	2	48.1	ns
Post-op CT/3D CT	2.11	2	33.3	1.67	2	14.8	0.012
Measuring femoral insertion site	2.19	2	29.6	2.04	2	29.6	ns
Tibial tunnel at fixed distance	2.04	2	29.6	2	2	33.3	ns
Measuring notch	2.00	2	25.9	1.70	2	11.1	0.011
Clock reference	1.81	2	18.5	2.19	2	29.6	0.008
Transtibial drilling	1.52	1	14.8	1.85	1	29.6	0.003
Flexible drill	1.56	1	11.1	1.33	1	7.4	ns
Fluoroscopy or navigation	1.56	1	7.4	1.44	1	11.1	ns
Post-op MRI	1.56	1	7.4	1.63	1	14.8	ns
70-degree scope	1.33	1	7.4	1.33	1	7.4	ns
Notchplasty	1.56	1	7.4	1.96	2	11.1	0.005

table 14

Comparison of survey results between reviewers and experts [from Paper 7].

	Reviewer n =329	Expert n=27	Mann Whitney
Item	**Median**	**Median**	**P value**
Individualization	3	4	0.034
30-degree scope	3	3	0.197
Accessory medial portal	2	2	0.998
Direct visualization femoral insertion site	4	4	0.001
Measuring femoral insertion site	2	2	0.582
Visualization lateral intercondylar ridge	3	3	0.775
Visualization lateral bifurcate ridge	2	3	0.421
Femoral tunnel in insertion site	4	4	0.327
Transportal drilling	3	3	0.300
Direct visualization tibial insertion site	4	4	0.049
Measuring tibial insertion site	2	2	0.954
Tibial tunnel in insertion site	4	4	0.860
Femoral fixation documentation	3	3	0.002
Tibial fixation documentation	3	3	0.001
Knee flexion angle during drilling	3	4	0.000
Graft type documentation	4	3	0.000
Graft tension documentation	3	3	0.019
Suitable documentation			
Diagram or drawing	38	30	
Arthroscopic picture	70	52	
Radiograph	32	59	
MRI	16	7	
CT	24	48	

Anatomic anterior cruciate ligament reconstruction scoring system: a systematic review of single- versus double-bundle

Introduction

A scoring system has recently been developed and validated to aid in the evaluation of the anatomic degree of ACL reconstruction techniques and to facilitate the comparison of studies of this topic. This scoring system has not yet been implemented in a clinical study except in its development. Furthermore, so far no minimum level for what constitutes an anatomic ACL reconstruction has been defined. For this reason, a proposed minimum score of 14 was used. In this systematic review, we aimed to apply and assess the AARSS in clinical studies comparing single- and double-bundle ACL reconstruction.

Methods

A systematic electronic search was made using the PubMed, Embase and Cochrane Library databases. Studies published from January 1995 to August 2011 were included. Studies written in English that report on comparisons of single- and double-bundle ACL reconstructions with clinical outcome measurements related to the reconstruction were included. The items from the AARSS were recorded for both the single- and double-bundle group in each included study.

Results

Seven thousand one hundred and fifty-four studies were analyzed, of which 52 were included. Randomized clinical trials (20; 39%) were the most frequent study type and most studies were published in 2011 (17; 33%). The most commonly reported items calculated for both groups were graft type (104; 100%), tibial and femoral fixation method (102; 98%), knee flexion angle during drilling (84; 81%) and placement of the tibial tunnel at the ACL insertion site (75; 72%). Measurements of the ACL insertion sites, the visualization of bony landmarks on the femur and individualization were poorly reported. The highest level of documentation used for ACL tunnel position for both groups was most often one dimensional, i.e. drawing, notes or o'clock reference. The double-bundle ACL reconstruction was generally more thoroughly reported. The means for the AARSS were 8.5 ± 3.6 for the single-bundle group and 10.7 ± 3.7 for the double-bundle group. Both means were below the proposed required minimum score of 14 for anatomic ACL reconstruction.

Conclusions

The key findings from this systematic review were that there was an under-reporting of variables in the surgical data for both the single- and double-bundle groups. Moreover, the means in the AARSS were well below the proposed minimum level of 14 points set by the authors. This under-reporting could create difficulties when comparing and pooling the results of scientific studies. In the future, comparisons between clinical trials of anatomic ACL reconstruction could be facilitated by the utilization of tools such as the AARSS, e.g. anatomic ACL reconstruction can be used if the score is the maximum. For this reason, future research should focus on improving surgical techniques and their documentation.

table 15

Items from the anatomic ACL scoring system and the frequency of the reported data [from Paper 8].

Anatomic ACL Score Items		§	Single-Bundle		Double-bundle		Total	
			n	%	n	%	n	%
Individualization of the surgery for each patient		1	1	2	1	2	2	2
Use of a 30 degrees arthroscope		1	3	6	4	8	7	7
Use of an accessory medial portal		1	4	8	15	29	19	18
Direct visualization of the femoral ACL insertion site		2	19	37	27	52	46	44
Measuring the femoral ACL insertion site dimensions		1	0	0	0	0	0	0
Visualizing the lateral intercondylar ridge		1	2	4	4	8	6	6
Visualizing the lateral bifurcate ridge		1	0	0	1	2	1	1
Placing the femoral tunnel(s) in the femoral ACL insertion site		2	17	33	29	56	46	44
Transportal drilling of the femoral ACL tunnel(s)		1	16	31	22	42	38	37
Direct visualization of the tibial ACL insertion site		2	19	37	24	46	43	41
Measuring the tibial ACL insertion site dimensions		1	0	0	0	0	0	0
Placing the tibial tunnel(s) in the tibial ACL insertion site		2	33	63	42	81	75	72
Documenting of femoral fixation method		1	51	98	51	98	102	98
Documenting of tibial fixation method		1	51	98	51	98	102	98
Documenting knee flexion angle during femoral tunnel drilling		1	15	29	26	50	41	39
Documenting graft type		1	52	100	52	100	104	100
Documenting knee flexion angle during graft tensioning		1	38	73	46	88	84	81
Highest level of documentation used for ACL tunnel position	*	0	29	56	25	48	54	52
	#	1	13	25	17	33	30	29
	¤	2	10	19	10	19	20	19

§ = Points for each item.
* = Drawing, diagram, surgical note, dictation, or o'clock face reference.
# = Arthroscopic pictures, radiographs, 2D MRI, or 2D CT.
¤ = 3D MRI, 3D CT, or navigation

table 16

Cross table with frequencies calculated for placement of tunnels in insertion sites and certain surgical techniques [from Paper 8].

		Placing the tunnel(s) in the ACL insertion site															
		Single-bundle								Double-bundle							
		Tibia				Femur				Tibia				Femur			
		No		Yes		No		Yes		No		Yes		No		Yes	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Direct visualization of the tibial ACL insertion site	No	13	25	20	38	30	58	3	6	8	15	20	38	19	37	9	17
	Yes	6	12	13	25	5	10	14	27	2	4	22	42	4	8	20	38
Direct visualization of the femoral ACL insertion site	No	12	23	21	40	30	58	3	6	8	15	17	33	19	37	6	12
	Yes	7	13	12	23	5	10	14	27	2	4	25	48	4	8	23	44
Transportal drilling of the femoral ACL tunnel(s)	No	13	25	23	44	28	54	8	15	7	13	23	44	16	31	14	27
	Yes	6	12	10	19	7	13	9	17	3	6	19	37	7	13	15	29
Use of an accessory medial portal	No	18	35	30	58	34	65	14	27	8	15	29	56	17	33	20	38
	Yes	1	2	3	6	1	2	3	6	2	4	13	25	6	12	9	17

12 / twelve discussion

12.1 theme 1: clinical outcome

There have been numerous clinical studies of ACL reconstruction; however, few of these studies constitute a high level of evidence. When faced with this vast number of studies, one cannot help but feel that it is difficult to obtain a real grasp of what is actually known. There are some systematic reviews that attempt to answer specific questions. However, they are overwhelmed by other studies and regular updates of the reviews are therefore vital. There is no doubt that any clinician or researcher can prove any point he or she wishes, due to the dispersion and number of studies. However, such an unsystematic and eclectic choice of literature would be in contrast to EBM. One should always try to find the highest level of evidence available that is reproduced and validated when stating a reference. If the highest level of evidence does not support the hypothesis, do not "go digging" for a lower level of evidence in support of your statement, instead of reconsidering your thinking. Of course, this does not mean that one should not disregard the evidence that is available. Questioning the evidence of today is one of the most important driving forces for progress in the research community and many of our beautiful hypotheses of today will be discarded by the cruel reality of tomorrow.

The aim with the systematic reviews included in this theme was to assess and summarize the evidence from RCTs. We hoped to create a high level of evidence reference that was as broad as possible so that it could be used for ACL reconstruction researchers in several areas. We chose not to use any quality scales or scores due to the issues associated with these scores; a study could have a high score yet still contain an inadequate method. The aim was therefore to adopt a descriptive approach, which explains the large size of the two systematic reviews and the meticulous reporting of each included study. Initially, there was actually only one systematic review which was divided into two parts, but in retrospect, it might have been beneficial to divide it still further.

It is important to point out that some of the topics in this theme have studies pooled together without an assessment of the surgical technique and bone tunnel placement of the reconstructed ACL. This could result in unfair comparisons when pooling the studies that have different surgical techniques. However, during the time frame for the creation of both systematic reviews and their included studies, many orthopedic surgeons utilized similar reconstructive techniques with few variations in bone tunnel placement. With this information in mind, care should be taken to translate all the results from the included studies to today's studies using modern anatomic ACL reconstruction.

Knee brace

The knee brace is a topic that generates many different opinions. The rationale of a knee brace is to protect the healing graft during rehabilitation. The criticisms are that the knee brace limits the patient's mobility and movement in the limb and therefore also the rehabilitation. It should also be noted that there is a high market value for companies that sell these products. The possible advantages that are presented in our systematic review of RCTs [Paper 1] are of doubtful clinical importance and not convincing. In addition, a knee brace did not produce any reduction in the risk of subsequent intra-articular injury after ACL reconstruction. Of the eleven included studies, two were of excellent quality and they both had contradictory results. One reported higher Cincinnati score and more thigh hypotrophy in the braced patients and the other found no differences. [75, 76] Most of the studies failed to show any difference between the braced and non-braced knees. Furthermore, one study found that early brace-free rehabilitation caused an increase in bone tunnel diameter in patients with HT grafts; however, there were no differences in other measurements. A knee brace should therefore not be utilized universally after ACL reconstruction without further studies that clearly demonstrate a positive correlation with a measurable clinical outcome.

Timing of rehabilitation

The immobilization of any joint in the human body causes adverse effects and it is especially detrimental to all the structures in the knee. It is well known in orthopedic surgery that all joints require mobilization with ROM exercises almost regardless of injury and surgery type. These thoughts have been implemented in the rehabilitation protocols after ACL reconstruction and the early start of rehabilitation has therefore been proposed. The criticism of early rehabilitation is that it might cause the irreversible elongation of the reconstructed ACL graft and possible graft failure. The RCTs included in our systematic review [Paper 1] did not provide a uniform answer. Of the six included studies, two reported positive effects and one negative effects of early rehabilitation. These studies had either severe limitations or very small differences without any clear clinical relevance. No clear conclusion can therefore be drawn from the included studies. It would be interesting to assess the effects on early rehabilitation with tendon allografts and compare this with autografts with or without bone blocks. Intuitively, one could hypothesize that the bone-to-bone interface and autografts heal more rapidly than allografts with a tendon-to-bone interface. Future studies are needed to ascertain when the postoperative rehabilitation should start. This time frame could differ greatly depending on the graft used, surgical technique and the patient.

Supervision of rehabilitation

Every orthopedic surgeon knows the importance of rehabilitation with physiotherapy for their patients and ACL reconstruction is no exception. The ultimate goal for rehabilitation after reconstruction is to restore ROM, knee stability, muscle strength and neuromuscular control. The rehabilitation protocol needs to be of high quality to meet these demands. It is therefore important to know if a rehabilitation protocol can be executed at home with the same effect on the clinical outcome as supervised rehabilitation. Seven RCTs were included in our systematic review [Paper 1] that assessed home-based versus supervised rehabilitation. Only two of these studies found superior clinical outcomes for a subgroup, males, compared with non-supervised males. These results were not replicated in any of the other studies. Even if the majority of the studies did not find any differences, we felt it was premature to draw a conclusion from the included studies. The findings are therefore inconclusive when it comes to whether one rehabilitation protocol is superior to another. At present, clinicians should therefore provide their patients with the rehabilitation program that works best with their clinic and patients.

Kinetic chain exercises

Open kinetic chain exercises are performed with the distal segment of an extremity free from the ground. On the other hand, CKC exercises are performed with the distal segment secured to the ground, where movement in one joint produces movement in all the other joints in the extremity. The current rehabilitation of choice is CKC as they appear to resemble functional movements of daily life and promotes the co-contraction of muscles of the thigh, thereby improving tibial stability. This is vital for the ACL-reconstructed knee. In our systematic review of RCTs [Paper 1], eight of the studies compared OKC and CKC exercises. One well-designed study favored CKC exercises in terms of pain, laxity, satisfaction and return to sport. One study found that OKC exercises produced greater quadriceps strength in ACL-deficient patients. Finally, one study found that a combination of the two exercises was superior to only CKC exercises in terms of quadriceps strength and return to sports. A conclusion cannot readily be drawn on the basis of these studies; however, it appears that the CKC exercises produce less pain and laxity and better subjective outcomes than OKC exercises after ACL reconstruction with PT grafts. However, OKC exercises might produce greater quadriceps strength in ACL-deficient patients. This still needs to be proven by a well-designed, high-quality RCT, as there are several limitations to the included studies. Furthermore, none of the included studies utilized HT grafts, which is naturally a severe limitation due to the increasing attraction of this graft and the fact that it heals with a tendon-to-bone interface. Perhaps there are greater differences between the exercise modalities in patients reconstructed with HT grafts.

12.1.2 surgical technique

Graft tensioning

The advocates of the initial graft tensioning procedure believe that an under-tensioned graft may result in increased laxity and that an over-tensioned graft may result in graft failure, fixation failure or a restricted range of knee motion. An evaluation of the effect of initial graft tension is very complex since it requires consideration of the type of graft, the position of the knee during the tensioning procedure, the magnitude of tension applied and the placement of the graft. Six RCTs in our systematic review [Paper 1] assessed the effect of initial graft tension. The studies are divergent, as different graft types and tensioning forces were used. Four of the studies, including one of high quality, reported no difference. Two studies found differences in favor of pre-tensioned grafts; however, the studies either had severe limitations or failed to find any subjective or clinical differences. This specific issue is complex and difficult to evaluate, but it appears that the utilization of initial graft tensioning does not affect the clinical outcome, irrespective of graft type.

Bioabsorbable screws

The advantage of bioabsorbable screws lies in their disappearance, thereby causing little or no interference in the future. This advantage has caused bioabsorbable screws to grow in popularity. The RCTs included in our systematic review [Paper 1] compared metal screws with two types of bioabsorbable screw, the poly L-lactic acid (PLLA) and the polyglyconate (PGA) screw. Of the nine included studies, two were of high quality and they reported significantly wider bone tunnels in the PLLA groups; however, there were no differences regarding clinical outcome measures. There were also no differences in clinical outcomes in any of the other included studies which were ranked as being of low quality. At present, there are therefore no clear clinical advantages or disadvantages to bioabsorbable screws. The choice between the screw types should therefore be based on other outcomes, such as cost, tunnel widening and the probability of future surgical knee procedures.

Cross-pins

Cross-pin fixation has previously been a major fixation method in ACL reconstruction in Sweden; however, its use has been reduced substantially. [7] This decrease is most likely due to new surgical techniques with anatomic femoral placement and three-portal drilling instead of transtibial. These new techniques have also most likely led to an increase in the use of suspensory fixation methods. The advantages of cross-pins lie in their high failure load and fixation closer to the joint compared with suspensory fixation. The rationale is that they stabilize and counteract movements of the graft in the bone tunnel, thereby creating a more stable graft-to-bone interface which will prevent bone tunnel enlargement. Furthermore, RIGIDfix cross-pins might have yet another potential advantage as it will yield less foreign body reaction due to its smaller size. Of the three RCTs included in our systematic review [Paper 1], none reports any significant differences between cross-pins and interference screws. Two studies were classified as level 1 and one as level 2 due to qualitative failings. The fixation method should therefore be based on the surgeon's preference, together with individualized surgery for each patient.

Graft fixation and tunnel widening

It is widely hypothesized that the HT graft, together with suspensory fixation, runs a greater risk of developing bone tunnel widening compared with a PT graft. The proposed mechanism for this effect is the increased elasticity in the graft implant complex during physiologic load. The mechanisms that are involved are called the windshield-wiper and the bungee-cord effect. Both are selfexplanatory. Three RCTs were included in our systematic review [Paper 1]. The conclusions from these studies confirmed that there was an increase in tunnel widening; however, there was no correlation with clinical outcomes including laxity. Moreover, the utilization of a periosteal flap reduced tunnel widening. However, the studies lacked sample size analysis and had other limitations which made it difficult to draw a firm conclusion. The future effects of bone tunnel widening are being discussed in the orthopedic research community. Does it matter? Even if there are no obvious effects on clinical outcome, it is certainly not advantageous in general, as it can jeopardize future surgery. However, there are naturally risks associated with aperture fixation as well. The fixation type should therefore be based on other factors.

Augmentation

The level of interest in different augmentation techniques has gone up and down. At the beginning of the 1980s, a braid called the Kennedy Ligament Augmentation Device (LAD) (3M, St. Paul, Minnesota, USA) was introduced. The LAD consisted of a polypropylene braid that was sutured to a PT graft. The PT graft has to be reduced in size in order to fit in the bone tunnel together with the braid. The proposed advantages were that the braid would prevent graft elongation, thereby protecting the graft during rehabilitation, and reduce the risk of re-ruptures. No direct clinical advantages to a ligament augmentation device were reported in the six RCTs included in our systematic review [Paper 1]. Although all but one of the included studies were classified as level 1, they all failed to present a sample size calculation, thus making a type 2 error difficult to rule out. However, based on current knowledge, there are no obvious reasons for using a ligament augmentation device.

Non-surgical treatment

The long-term goal of ACL reconstruction is to promote knee health and reduce the risk of osteoarthritis. However, the indication for reconstruction in Sweden is a history of giving way episodes and not preventing future OA. Prior to the publication of our systematic review [Paper I], it had not been clearly shown that surgical treatment reduces the risk of post-traumatic OA. Two RCTs were included in our systematic review [Paper 1]. One of these two studies was the RCT with the longest follow-up in our systematic review series. [77] Even though the study has several methodical errors and utilizes ACL repair instead of reconstruction, it stands the test due to its unique long-term follow-up. The study assessed surgical repair with and without augmentation and non-surgical treatment with a 15-year follow-up. The authors reported a significant increase in meniscus injuries in the non-surgically treated group and that meniscectomy resulted in more osteoarthritic changes. It appeared that the most important factor for the development of post-traumatic osteoarthritis was a meniscus injury. This has previously been reported and reproduced for ACL reconstruction. [78] The question is whether ACL reconstruction protects the meniscus from further damage and whether meniscus injury is a strong predictor of OA; does ACL reconstruction protect the knee from OA?

The other study compared muscle strength and hop-test performance without finding any differences. The comparative groups were conservative therapy with exercise or ACL reconstruction. This study had several limitations and it is therefore not easy to draw a conclusion as the results need to be replicated. Furthermore, the primary objective of ACL reconstruction is not regaining muscle strength and therefore the relevance of the study is limited.

Timing of surgery

There has been a long and active debate on when to reconstruct the ACL. The advocates of early ACL reconstruction point to the fact that, the earlier the reconstruction is performed, the earlier the patient can return to sports and begin rehabilitation. Moreover, biomechanical studies have shown that knee kinematics are kept intact if the ACL is reconstructed within 10 weeks after injury. [79] On the other hand, delayed ACL reconstruction provides an opportunity for proper rehabilitation to regain range of motion, muscle strength and neuromuscular control to a feasible degree, while also giving the orthopedic surgeon time to assess the patient's activity level and determine the type of surgery needed. Two RCTs were included in our systematic review [Paper 1] of this topic. Both studies had qualitative limitations and only one reported positive findings in favor of early ACL reconstruction in one intermediate follow-up. It is obvious that there is not enough evidence or qualitative studies to draw a correct conclusion on this subject. On the other hand, if the ACL reconstruction is chondro- and/or meniscus protective, an early ACL reconstruction would naturally be favorable.

Single and double-bundle

Reconstruction of the ACL with two bundles instead of a single-bundle has a theoretical advantage as it resembles the native ACL and allows more complete footprint restoration and the separate tensioning of the two bundles. Interest in double-bundle ACL reconstruction has recently declined in Sweden, probably due to the anatomic single-bundle ACL reconstruction. [7] The evolution of the ACL reconstruction back to its basics, the restoration of original anatomy, is potentially promising. However, double-bundle ACL reconstruction that is performed in an anatomic fashion is more similar to the native ACL and therefore theoretically more advantageous.

AP laxity

Eight studies that compared four-strand single and double-bundle ACL reconstruction were included in our systematic review of RCTs [Paper 2]. Of these studies, only two found a positive correlation between AP laxity and the double-bundle groups. [80, 81] The study by Yasuda et al. was a pioneering study and it compared not only single and double-bundle reconstruction but also non-anatomic and anatomic double-bundle reconstruction. [81] The study found a difference in AP laxity in favor of anatomic double-bundle ACL reconstruction. In our systematic review, we stated that "perhaps the divergent results were caused by the incorrect placement of the double-bundle graft or just simply that the strength in the double-bundle technique was not correlated with less AP laxity". This statement still stands in accordance with today's knowledge.

Rotatory laxity

The main rationale for double-bundle ACL reconstruction is that biomechanical studies have shown that it is superior in controlling rotatory laxity. For this reason, the most important variable in the short-term is the effect on rotatory laxity. All but one study found that rotatory laxity was more reduced in the double-bundle group as compared with the single-bundle group. The study that did not find any differences in rotatory laxity had a more "horizontal" placement in the femoral bone tunnel of the single-bundle group. This placement might be more anatomic and this could explain the results. We asked ourselves whether the superiority of double-bundle reconstruction was not the double-bundle technique as such, but instead the placement of the femoral tunnel in conventional non-anatomic single-bundle ACL reconstruction which produces inferior results. A present-day RCT has shown that we were probably right. [82] Conventional non-anatomic single-bundle ACL reconstruction does produce inferior results compared with anatomic ACL reconstruction; however, this applies to double-bundle ACL reconstruction as well. [82] Our results were also confirmed in the most recent meta-analysis in this topic. [83]

Clinical outcome

The large majority of the studies on this specific topic did not reveal any difference, either in clinical outcome measurements of functionality, patient-reported outcome measurements, in muscle strength or range of motion. This could also be rephrased to say that there was only one study demonstrating a difference in favor of the double-bundle technique. This indicates that there are no differences in clinical outcome measurements or functionality in the short-term between the two reconstruction types. Does this demonstrate the shortcomings of studies with a short follow-up or could it be that patient satisfaction is not only dependent on post-operative knee laxity? On the other hand, the major advantage of double-bundle ACL reconstruction is thought to be the restoration of normal knee kinematics; for this reason, any clinical difference should appear in the long-term. Furthermore, it is difficult to find differences between two groups with a coarse outcome measure if one expects good short-term outcomes from both groups. This is often seen in studies of ACL reconstruction. The results are therefore not surprising, even if they are somewhat disheartening.

12.1.3 graft type

The choice of grafts has previously been a hot topic in ACL reconstruction and it is still a common research question. The PT graft has clear advantages as it has bone plugs at both ends with native tendon-to-bone fixation to each bone plug. This creates an exceptionally good interface with the bone tunnels. The concern when it comes to the quadruple HT graft is that it might be inferior to the PT graft in terms of residual laxity and laxity over time; although, the structural strength of the quadruple HT graft is superior to that of the PT graft and the soft tissue-to-bone interface of the HT graft has healed only weeks after the PT graft. [84]

AP laxity

The RCTs in our systematic review [Paper 2] report a reduction in the AP laxity postoperatively in all the studies but one. Furthermore, the vast majority of the included studies and, much more importantly, all but one of the mid-term studies found no difference in terms of AP laxity between the two graft types. The only mid-term study that found a difference did so as a result of knee arthrometer measurements with a quadriceps test. [85] This is not a common outcome and it is not used in any of the other RCTs; for this reason, the results are not entirely reliable. One qualitative study found an interim increment in AP laxity in women with HT grafts; however, this difference disappeared at the 2-year follow-up. This finding is perhaps related to the slower graft-implant healing process found with the HT graft. However, this is not supported by other studies. Finally, the two studies with the longest follow-up, 7 years, found no difference between the groups in terms of AP laxity. [86, 87] One of the 7-year follow-up studies was regarded as being of very high quality, while the other one had several limitations; however, both were classified as level 1. Furthermore, a possible reason for the difference in AP laxity found in the short-term between the two grafts might be the difference in fixation methods and healing. With the information available, no other conclusions can be drawn other than that there are no convincing differences in AP laxity between the two graft types in the mid-term.

Rotatory laxity

Reports have suggested that there is a correlation between patient satisfaction levels and pivot shift grades. [88, 89] Even more importantly, there are some suggestions that a positive pivot shift is a predictor of subsequent osteoarthritis. [90] However, there are no reliable, reproducible and easy-to-use tools for the objective, quantitative evaluation of rotatory laxity. As a result, the pivot shift test is heavily dependent on the clinician's subjective feeling and skill level. It is therefore difficult to compare studies based on pivot shift. The RCTs included in our systematic review [Paper 2] reveal a reduction in postoperative rotatory knee laxity in both groups. The vast majority of the studies, ten of twelve, found no difference in terms of rotatory laxity between the PT graft and the HT graft. One interesting study found that the combination of medial meniscectomy and quadrupled HT graft ACL reconstruction correlated with an increase in the prevalence of pivot shift glide. [91] This might indicate that there is a correlation between medial meniscectomy and degenerative osteoarthritis and that the pivot shift test is a predictor of subsequent osteoarthritis. Another very interesting finding was that the mean time from injury to operation was a predictor of a positive pivot shift test in one study. [92] This might indicate that ACL reconstruction should be performed without delay to minimize long-term complications. Regarding rotatory laxity there are; however, until now no evident differences between the PT and HT graft.

Patient-reported outcome measurements

Many researchers focus on clinical outcome measurements including subjective measurements. All the RCTs in our systematic review [Paper 2] included an assessment with at least one questionnaire. The questionnaires that were included were the IKDC score, Tegner activity score, Lysholm knee score, Cincinnati knee score and Kujala knee score. To summarize, there were few studies demonstrating a difference between the two graft types regarding clinical outcome, even if differences in objective outcome measures were found. This clearly underlines the controversy regarding which graft type is optimal or maybe we need more accurate and precise questionnaires?

Time of return to sports

For many patients, especially high-level competing athletes, the most important question is when they can return to their sport. It could be hypothesized that the PT graft is superior in this case due to its bone-to-bone interface. However, this was not clearly demonstrated by the RCTs in our systematic review [Paper 2]. A couple of studies found evidence that the PT graft was superior in this respect; however, they had severe limitations that made it impossible to rely on the data. The question is therefore still unanswered by high-quality studies. Logically, any graft with a bone block at the graft ends should be superior in terms of healing and resisting the effect of tension forces induced by early activities. This is probably the reason why high-level athletes in American football reportedly favor PT allografts.

Pain

It is easy to deduce that, due to the harvest site of the PT graft, the patient will have more anterior knee pain and pain when knee walking. The RCTs in our systematic review [Paper 2] were almost evenly divided regarding anterior knee pain and the majority found an increase in pain on kneeling in the PT graft group. It appeared that the difference between the two groups with regard to anterior knee pain was greatest between 3 and 8 months after ACL reconstruction and that it then decreased. Furthermore, mid-term studies reported that pain on kneeling diminished with time and that the two graft types had similar outcomes after 5 years, even if there were significant differences in short-term follow-ups. There is no question that the PT graft yields more pain on kneeling and anterior knee pain; however, it appears that it decrease with time. As a result, a careful assessment of the patient's sporting activities and hobbies is essential to enable the patient to cope with any future anterior knee pain. Examples of activities that can be jeopardized due to anterior knee pain are activities and sports with a high frequency of kneeling, such as judo and wrestling.

Muscle strength

Measurements of muscle strength are common as it is a variable of great concern, due to the fact that increased muscle strength stabilizes the knee joint and thus protects the reconstructed ACL. Autografts will naturally always affect muscle strength, at least initially. What is the effect on muscle strength in the mid-term after tendon harvest? Most of the RCTs in our systematic review [Paper 2] support the general hypothesis and found that the extensor strength was impaired after PT graft harvest and that the flexor strength was impaired after HT graft harvest. There was some evidence that the flexor strength was more impaired at higher angles after HT harvest. This implies that the hamstring muscles are vital for flexion at higher angles, a function that is not shared with other flexor muscles. [84, 93] Furthermore, there was evidence that muscle strength impairment was temporary and that there was a progressive recovery over time. Two studies found a correlation between this impairment and clinical outcome. [92, 94] However, there was no clear benefit between the two graft types when assessed with the one-leg-hop test. Although some studies found a difference between the two grafts in terms of the one-leg-hop test, the majority did not. The conclusion is that tendon harvest does affect muscle strength, especially initially.

Range of motion

Deficits in range of motion can be handicapping for any patient and a loss of motion of 5° or more is usually classified clinically relevant in this setting. Naturally, it would not be surprising if tendon harvest caused an initial ROM deficit in the range for the harvested muscle; however, what are the long-term results? The majority of the RCTs in our systematic review [Paper 2] did not find any differences between the two groups, although there were some studies showing extension deficits after PT harvest. Tendon harvest localization should therefore be tailored for individuals with high future functional demands, so that eventual loss of motion is minimized and the impact on their activities.

Anterior knee sensory deficit

One of the concerns in relation to PT harvest is the anterior knee sensory deficit that follows after iatrogenic injury to the infrapatellar nerve branch. There was evidence indicating an increase in the prevalence of anterior knee sensory deficit after PT harvest in the RCTs included in our systematic review [Paper 2]. Even if this was not confirmed by a mid-term follow-up study, it is logical that anterior knee sensory deficit is primarily a complication following PT harvest and not HT harvest. For this reason, it should be a factor to consider when individualizing ACL reconstructive surgery.

Osteoarthritis

The “holy grail” in terms of ACL reconstruction is to develop a reconstructive technique that reduces the risk of long-term complications and especially osteoarthritis. This is due to the simple fact that it is the most serious complication with deleterious effects on young, otherwise healthy patients. The question whether the graft type is a factor that can contribute to the risk factors for developing osteoarthritis has been debated. Short-term studies are naturally not quite relevant when assessing osteoarthritis; however, it might be a negative factor if a short-term study reveals radiographic signs of suspect incipient osteoarthritis e.g. osteophytes. The results of the RCTs included in our systematic review [Paper 2] are not easy to pool. None of the short-term studies found a difference between the two graft types regarding this specific issue. However, two out of four mid-term studies found an increased prevalence of incipient osteoarthritis in the PT graft groups; although, these studies had severe limitations making it difficult to draw a correct conclusion. On the other hand one could argue that there were no studies demonstrating higher incidence of osteoarthritis in the HT graft group, which might be beneficial, but one should be careful to draw conclusions from this material and we look forward to further high quality long-term RCTs that can answer this question. There is a very recent prospective comparative study (PCS) with 15 year follow-up that reported a lower rate of radiographic osteoarthritis in the HT graft group compared with the PT graft; thus supporting the superiority of the HT graft in this outcome. [95] Even though it is unique in terms of follow-up time, it is still only one study and a proper systematic review of all the PCSs is needed before a conclusion can be performed. Two included RCTs found very interesting results in assessments of osteoarthritis; there was a correlation between osteoarthritis and medial meniscus pathology, patients' age or the length of time from injury to reconstruction. [92, 94] This lends support to the previous discussion regarding non-surgical treatment and the timing of reconstruction. It appears that reconstruction should be performed without delay and that preservation of the meniscus is important preserving long-term knee health.

Tunnel widening

There are indications that the HT graft results in more tunnel widening than the PT graft. This has previously been discussed and the reason is simple; the PT graft has bone blocks at both ends. Furthermore, the mechanical explanations of the possible tunnel widening related to the HT graft are the wind-shield-wiper effect and the bungee-cord effect. These are based on the assumption that the graft moves inside the tunnel during knee motion, in either the transverse or the longitudinal direction. The question remains of whether there is any correlation with laxity and subjective assessment and tunnel widening. All seven RCTs included on this topic in our systematic review [Paper 2] found that tunnel widening was more common in the HT graft group. Moreover, the frequency and the amount of tunnel widening appeared to show minimal changes after 3 months and 1 year, indicating that tunnel widening occurs within this time span and stabilizes thereafter. Most importantly, tunnel widening did not correlate to the final result with respect to laxity or knee scores, indicating that tunnel widening has no implications for the clinical situation. Nevertheless, a reduction in tunnel widening is important when it comes to potential future knee surgery. For this reason, new, more rigid fixation techniques for HT grafts would be welcomed.

Gracilis harvest?

Several orthopedic surgeons advocate harvesting only the semitendinosus tendon. The reasons for this are not only to reduce harvest site morbidity but also the fact that the semitendinosus yields thicker grafts sufficient for a quadruple graft. Furthermore, the preservation of the gracilis tendon can theoretically enhance the development of a neotendon replacing the harvested semitendinosus tendon. However, only using the semitendinosus tendon might result in a too short quadrupled graft, thus having a shorter bone-tendon interface in the bone tunnels. This will create a situation in which the fixation will play a more vital role even after healing. Some orthopedic surgeons have solved this by using two fixation types in both the femur and the tibia, thereby creating a more rigid complex with higher load-failure tolerance. The RCTs in our systematic review [Paper 2] reveals that the semitendinosus and gracilis muscles play an important role at higher flexion angles and during internal rotation of the knee. Moreover, it appears that gracilis harvest had a greater impact on knee flexion, especially at higher flexion angles, and internal rotation. As a result, gracilis harvest yields more deficits and preservation of the tendon should be a goal that needs to be borne in mind.

12.2 theme 2: level of evidence

There is no doubt that evidence-based medicine has forever changed modern medicine both in the clinical setting and in the field of research. In an international survey from the British Medical Journal to the global medical community, the EBM concept was voted as one of the top 15 medical breakthroughs in the last 160 years. [96] This places a perspective on the importance and the geniality of EBM.

The number of studies of ACL reconstruction is overwhelming and searching for evidence relating to a certain question is therefore time-consuming, to say the least. For example, MEDLINE adds 4,500 records every day and a physician in any field needs to read 18 papers every day to keep up with his/her own field. [96] This is naturally not possible, so the question remains, how many publications are of high quality and clinically relevant? The numbers differ depending on the field, but 10% is a reported percentage. [96] Until now, the distribution of the study types for ACL reconstruction has not yet been assessed.

The aims of this theme were to clarify the distribution of studies of primary ACL reconstruction and categorize the studies according to study type and level of evidence. Moreover, an evaluation of the evidence over time and geographic distribution was performed, as well as a possible correlation in relation to the impact factor of the journals. Finally, a descriptive qualitative assessment of a selective sample of RCTs was performed. We thereby aimed to create a stepping stone in the qualitative assessment and an awareness of the study distribution on this very important topic.

It is important to mention on beforehand that the studies included in our systemic reviews [Papers 1-3] had strict inclusion criteria. This creates a subgroup analysis and the results are therefore only applicable to studies of therapeutic primary ACL reconstruction and can therefore not be generalized to studies of ACL reconstruction in general. We chose these limitations intentionally to minimize the complexity of the systematic reviews.

12.2.1 study characteristics

Study types

One of the key findings in our systematic review [Paper 3] was that most studies of primary ACL reconstruction had a low level of evidence. This outcome was not surprising, as the same finding is seen in other research areas as well. [96] The most common study type was case series, which accounted for approximately one third of the sample. It was naturally promising that case series were a couple of percent higher than expert opinions. However, this also meant that level 4 and 5 papers represented more than 60% of the sample, which is an unflatteringly high number. Consequently, fewer than 40% were left for higher level of evidence studies with a control group. It is to be hoped that, in the future, researchers who want to perform case series will take the opportunity to introduce a control group in their cohort to increase the level of evidence of the study and thereby also its applicability and validity.

In terms of prospective clinical studies, RCTs and PCSs represented approximately 9% and 8% respectively. This is also an expected number, in line with previous general assessments. However, even if both studies are generally of a higher level of evidence, they can still contain limitations that produce issues and difficulties when attempting to extrapolate the outcomes. These limitations were brought to light when the categorization of the RCTs revealed that only 63% of the studies were classified as level 1. This may be regarded by some as a good number as it is a majority; however, RCTs are by default level 1 studies and are degraded if limitations are found. It would therefore be true to say that more than a third of the RCTs had serious and obvious limitations that directly degraded the level of evidence.

Filtered information, such as systematic reviews and meta-analyses, represented only 3.6% of the sample. However, this is more than a fair amount if it is considered in relation to the prospective clinical trials. For this reason, even if the number of systematic reviews and meta-analyses is small, interest should still focus on creating more prospective comparative studies, preferably randomized.

Randomized clinical trials

A more thorough analysis of the quality of the RCTs was performed in our systematic review series [Papers 1-2]. As previously mentioned, RCTs can sometimes be afflicted with severe methodical errors. These demerits, such as improper randomization, no sample size calculation, no blinding and low follow-up, might render the results unreliable or even misleading. In general, there are four biases of principal interest that affect method quality; selection, detection (recording), performance and attrition (transfer) bias.

Selection bias

Selection bias occurs when two groups with different prognoses are compared, making the groups unequal. This causes an unfair comparison, like comparing apples with oranges. Selection bias is minimized through randomization and with strict inclusion and exclusion criteria. Little more than half of the RCTs had either an inadequate generation of allocation, e.g. case record number, date of birth, date of admission, admission number and alternating patients, or did not present randomization at all. The absence of proper randomization leads to different levels of susceptibility among patients, who subsequently might react differently to the treatment given. These trials should therefore be seen as only allocated trials rather than randomized.

Sample size calculations are vital to all comparative studies as they both ensure that the unknown characteristics are likely to be equally distributed between the two groups and establish the minimum number of patients needed to demonstrate a difference between the groups. Without this calculation, it is impossible to know if a type II error has occurred; or, put simply, if the absence of a significant difference is, in fact, a consequence of the true state of nature, or is attributable to poor study design. Sixty-eight percent of the RCTs had not performed a proper sample size calculation and 69% of the trials, where no differences could be demonstrated, had waived a sample size calculation. These numbers are unflattering, to say the least, and they cause a great deal of unreliability when assessing the results. The lack of a sample size calculation could be compensated for by a large sample size; however, only a quarter of the studies comprised more than 100 patients. This means that most studies have less than 100 patients, which is, without doubt, a small sample for most studies.

Detection bias

Detection bias, sometimes called recording bias, depends on who measures the data. To minimize detection bias, an unbiased observer other than the surgeon should be asked to perform the postoperative assessments. Ideally, this person should be blinded to the treatment that was received. Seven percent of the RCTs were not blinded and 34% did not state whether blinding was accomplished. Blinding is an essential part of science, as it minimizes potential placebo response, which makes the hypothesis more difficult to discard. Randomized clinical trials that do not clearly state and describe blinding are downgraded to level 2 and researchers should therefore focus on this important subject.

Performance bias

Performance bias, as well as detection bias, can be reduced by blinding both the patients and the treatment providers. An RCT which encompasses multiple surgeons will be biased, as it is impossible to perform surgery in an identical manner. Likewise, if multiple investigators, such as physical therapists and radiologists, are employed, additional performance bias will be introduced. However, it should be remembered that one-surgeon trials also introduce bias and, as a result, no method eliminates performance bias entirely and someone has to perform the surgery. Twenty-five percent of the RCTs utilized multiple surgeons and 19% did not state the number of surgeons employed. It can be argued, however, that multiple surgeons, in contrast to the discussion above, add strength to a trial if the results conclusively point in one direction and therefore do so irrespective of the performing surgeon.

Attrition bias

Attrition bias, sometimes called transfer bias, is regarded by some as a part of selection bias and refers to systematic differences between the comparison groups, which occur after treatment allocation. Attrition (loss of participants) includes dropouts, non-responders and protocol deviators. These losses can cause differences in the characteristics of the groups and change outcomes irrespective of the intervention. For this reason, the number of patients lost to follow-up is very important and the authors should present the numbers and the possible effects they might have on the results. In large trials, some patients will inevitably be lost to follow-up, but this number should never exceed 10% in order to retain a high level of quality and reliable results. Eight percent of the RCTs had less than 80% follow-up, which means that they will be regarded as lower quality randomized trials, i.e. level of evidence 2.

The follow-up period can be divided into three categories; short-term (< 5 years), mid-term (> 5 years) and long-term (> 10 years). There are some researchers that argue that the 5-year follow-up is sufficient to be regarded as a long-term follow-up. However, given the fact that most ACL-injured patients are young at the time of the index injury and therefore have considerable remaining life expectancy, 5 years almost constitute an insignificant period of time. Furthermore, the development of any degenerative changes in the knee joint takes time. Only one trial was classified as long-term and 10% as mid-term. The need for trials with a longer follow-up is therefore huge.

Journals

Three journals accounted for 43.5% of all the studies in our systematic review [Paper 3]; Arthroscopy, KSSTA and the AJSM. Arthroscopy had the most publications in general and the AJSM had the most publications with high level of evidence. This was also seen when assessing the mean level of evidence, as the AJSM had the lowest number of the three. None of these findings were surprising, as the above-mentioned journals are the three to which most authors involved in ACL research submit their manuscripts. The reason is simple; these journals focus on orthopedic sports injuries and most orthopedic surgeons with this interest therefore subscribe to these journals. So, for anyone wishing to deliver a message to this special group, the above-mentioned journals are preferable.

12.2.2 trends over time

Are we getting any better? This is a very interesting and valid question. There was a trend towards a higher level of evidence over time in terms of means in our systematic review [Paper 3] of level of evidence. However, the percentage of higher level of evidence studies did not differ significantly over time. The analysis also revealed an increase in absolute numbers for clinical trials, which is of course very promising. However, this obviously did not affect the percentage high level of evidence studies and the aim should therefore once again be to work towards a higher level of evidence when designing a study and to strive for a careful, qualitative design for the trial. Preferably, the guidelines, such as the CONSORT Statement, should be followed to avoid lowering the level of evidence from 1 to 2, which was the case for more than one third of the RCTs.

To answer the previous question; we are slowly getting better, but we are still far from perfect.

12.2.3 factors associated with level of evidence

Impact factor

The impact factor, which is provided by Thomson Reuters Journal Citation Reports®, is probably the most frequently used measurement tool for comparing the influence of journals. It measures the frequency with which an article in a journal has been cited in a specific time frame. There are several issues when interpreting the impact factor, as it is highly discipline dependent, it has no reliability as it is not reproducible and journals can adopt policies that increase their impact factor. [97] Our systematic review [Paper 3] of level of evidence found a positive correlation between the mean level of evidence and the proportion of high level of evidence studies with the impact factors of the journals. This has previously been reported, as a prior systematic review revealed that orthopedic journals with a higher impact factor are more likely to publish articles with a higher level of evidence. [98] It appears as though the impact factor is a reliable tool for gauging the level of evidence of primary ACL reconstruction studies in journals. However, care should always be taken when utilizing only one tool for measuring a scientific journal, as all tools have their weaknesses, as does the impact factor.

Geographic distribution

There are no prior studies that present the distribution of the studies in this category. As a result, the findings from our systematic review [Paper 3] are unique and not validated. The systematic review revealed that the USA had the absolutely highest number of publications, with a little more than one third of all publications. However, most studies had a low level of evidence and the USA had the highest number of both case series and expert opinions. The latter group represented almost half the countries' publications and approximately 60% of all publications in that category. The top four countries after the USA were Japan, Italy, the United Kingdom and Sweden. Sweden had the highest number of RCTs and the USA had the highest number of meta-analyses and systematic reviews. What are the reasons for this distribution? One very obvious reason for the large number of level 5 studies from the USA is simply that the search was performed using criteria that only included papers written in English. Consequently, a broader search would most likely produce different results in this area. Scandinavia's large number of RCTs can be partly explained by a culture of conducting RCTs and the easier recruitment of patients.

12.3 theme 3: anatomic acl reconstruction

The shift in paradigm from non-anatomic to anatomic ACL reconstruction is one of the most important modern inventions regarding the surgical technique for ACL reconstruction, and we are in the midst of this shift at the moment. This has not only changed the surgical technique, it has also placed emphasis on previous publications and their reporting of surgical data. Previous studies have not focused on the placement of the graft but more on graft types, fixation and rehabilitation. Many of the previous studies have subsequently been used as references for ACL reconstruction in general; hence, as a baseline for contemporary clinical research comparing the outcomes of different techniques. However, this is far from correct, as we first need to stratify the type of reconstructive surgery that has been performed and then draw a conclusion based on this. For example, if a study finds no differences in certain outcomes when comparing early versus delayed ACL reconstruction with a surgical technique that is non-anatomic the results should not be generalized and report that there is no difference between early and delayed ACL reconstruction in general. Instead, one should report that there were no differences in early or delayed non-anatomic ACL reconstruction. Furthermore, studies should not be pooled together without ascertaining the surgical technique. This is most easily exemplified in the summary of studies comparing single- and double-bundle ACL reconstruction. Both reconstructive techniques can be performed anatomically and non-anatomically; for this reason, the sample would be very heterogeneous if the studies were pooled together and the outcomes were extrapolated. These differences in surgical technique were noted and described in our previous systematic review [Paper 2], see the discussion on this topic. As a result, future systematic reviews and meta-analyses should divide the groups not only according to the number of bundles used but also according to the type of reconstructive method; anatomic or non-anatomic.

To aid in the solution of the above-mentioned issues, we planned five studies. Initially, we created a guideline and a current concepts paper on what constitutes anatomic ACL reconstruction [Paper 4] and to assess published studies claiming anatomic ACL reconstruction [Papers 5-6]. Furthermore, a scoring system for anatomic ACL reconstruction was developed for use in future studies [Paper 7]. This scoring system was also implemented in studies comparing single- and double-bundle ACL reconstruction [Paper 8].

12.3.1 the concepts

In the authors' opinion, anatomic ACL reconstruction is defined by four main principles presented in our current concepts paper [Paper 4]. These principles are applicable to anatomic single- and double-bundle ACL reconstruction, as well as augmentation, primary and revision surgery. [99]

First principle

Anatomic ACL reconstruction is naturally all about anatomy; as a result, the first principle lies in the restoration of insertion site anatomy. Both ACL remnants can be used as landmarks to indicate the optimal tunnel position. In the femur, there are two bony landmarks that can aid in the placement of the bone tunnel, the lateral intercondylar ridge and the lateral bifurcate ridge. The bone tunnels should be placed so that they attempt to replicate as much as possible of the native footprints in terms of both size and shape.

Second principle

The ACL consists of at least two functional bundles and the restoration of these bundles therefore plays an important part in the anatomic ACL reconstruction and is regarded as the second principle. The bundles can be restored as a single graft named anatomic single-bundle ACL reconstruction. However, the aim should be to restore as much as possible of the functional anatomy of the ACL.

Third principle

Attention should be paid to the native tension pattern in the third principle. This is naturally very difficult to achieve, as the native tension pattern of the ACL is very complex; some even say that each fiber should be regarded as a separate bundle. Reproducing this is obviously impossible; however, an attempt should be made to mimic as much as possible through either of the reconstructive technique.

Fourth principle

The fourth principle is individualization in which the reconstructive procedure is adjusted to match the patients' knee morphology and the native ACL anatomy of each patient. For example, the single-bundle procedure might be insufficient for a patient with a large femoral footprint. The main goal is to tailor the reconstructive procedure to comply with each patient's anatomic, biomechanical and functional demands.

12.3.2 reporting of surgical data

Many of the recently published studies have claimed anatomic ACL reconstruction, although it can be questioned whether these studies really are performing a reconstruction that is anatomic. Both our systematic reviews [Papers 5-6] revealed gross under-reporting of a variety of variables in the surgical data. It goes without saying that not reported does not necessarily mean not performed. Under-reporting has far-reaching effects in many ways. First, we do not know if many of the studies really have performed an anatomic ACL reconstructive procedure and this therefore creates restrictions in terms of interpretation. Second, pooling the studies will create a heterogeneous sample with possible severe limitations regarding the conclusions. This should not be misunderstood; a limited report of the surgical technique does not necessarily make the paper less valid; however, it clearly creates difficulties in the pooling of the studies. Third, future guidelines based on studies based with limited reported data will be jeopardized, to say the least. The anatomic ACL reconstruction has been performed in many different ways, as we do not yet know the best way to perform it or its long-term outcomes. So, in the future, authors should report their surgical technique in such a detailed manner that anyone could repeat the procedure.

12.3.3 scoring system

Development and validation

The purpose of the scoring system presented in Paper 7 was to develop a tool that could be used for grading ACL reconstruction procedures for individual patients, for reviewing the description of surgical methods in published studies of anatomic ACL reconstructions and for peer reviews of these papers. The development of the scoring system was based on a rigorous protocol. It was found to have good validity, acceptable levels of inter-tester reliability and good internal consistency. As a result, the final scoring system was found by both experts and a large sample of peer reviewers to provide an adequate representation of the degree to of anatomic ACL reconstruction.

In addition to assessing the surgical items, an evaluation was made of the preferred documentation for tunnel position. The survey participants recommended the following: radiographs (59%), arthroscopic pictures (52%), CT scans (48%), diagrams or drawings (30%) and MRI (7%). CT scans are theoretically advantageous as they produce high resolution and three dimensional images and have the ability clearly to depict the bone tunnels. [100, 101] However, CT is not recommended as standard care due to radiation dose and costs. This discrepancy between the best method and the recommended method is common in today's medicine. The scoring system was adjusted to take account of this and the items for evaluating tunnel position were weighed accordingly.

There are several strengths in terms of the methodology of the scoring system; it has a large number of survey participants, including experts and peer reviewers and the sample was international and homogeneous, as they were all physicians who performed peer reviews for orthopedic journals. The response rate was satisfactory, 79% for the expert panel and 40% for the peer reviewers. The peer reviewers' expertise in this area was not known; although some of the peer reviewers who did not participate informed us that they did not have sufficient expertise. This might have created a more homogeneous sample of the responders with more accurate survey results.

The anatomic ACL reconstruction scoring system is the first of its kind and represents a building block in the quantification and definition of anatomic ACL reconstruction. It is short, concise and easy to apply. This is naturally only the first version and it is expected that modifications of and improvements to the scoring system will be needed in order to produce an improved definition of what constitutes an anatomic ACL reconstruction. Regardless of this, it is recommended that reviewers utilize this checklist in the assessment of papers on anatomic ACL reconstruction.

Implementation

Following the development of the scoring system, a systematic review [Paper 8] was made of randomized clinical trials comparing single- and double-bundle ACL reconstruction. As there was no defined minimum level for what constitutes an anatomic ACL reconstruction, the authors proposed a minimum score of 14 based on their experience. The aim was to implement the anatomic ACL scoring system and evaluate the scores that were obtained. The results were similar as the previous systematic reviews [Papers 5-6], and an under-reporting and variance in the surgical data were found. The means including the standard deviation for the scoring system were 8.5 ± 3.6 for the single-bundle group and 10.7 ± 3.7 for the double-bundle group. The double-bundle groups were therefore more thoroughly reported, but both means were below the proposed required minimum score of 14 for anatomic ACL reconstruction. However, it is difficult to evaluate these results since this scoring system has not previously been implemented or reported. Although, anatomic ACL reconstruction can be assumed if the score is 23. The results of this systematic review shed some light on the difficulties involved in assessing studies on anatomic ACL reconstruction and extrapolating the outcomes. In the future, comparisons between clinical trials could be facilitated by implementing tools such as standardized clinical tests or standardized surgical procedures. The AARSS could be a valuable tool to assist in clinical outcome research. Future research should focus on improving surgical techniques and their documentation so that a proper evaluation of the new anatomic ACL reconstruction can be performed.

13 / thirteen conclusions

The research program for this thesis included one current concept study, one survey-based original study and six systematic reviews. The conclusions from these studies are presented and divided into respective theme.

13.1 theme 1: clinical outcome

Potential differences in clinical outcome between different treatment groups could not be verified in some of our systematic reviews. If we still believe that there are differences in clinical outcome between the different treatment groups, such as HT versus PT, why can we not verify this in clinical trials? One reason might be that the evaluation tools we use in the assessment of two methods that both seem to yield good clinical outcomes are not precise enough. This is seen not only in studies of ACL reconstruction but also in other research areas. More precise and refined assessment tools are therefore warranted. Moreover, the follow-up time is too short for many of the assessed outcome measurements. For example, the development of osteoarthritis takes several years, so assessing it after only a couple of years with regular radiographs is not the appropriate assessment tool or follow-up period. Studies with a long-term follow-up are therefore essential.

13.1.1 rehabilitation

- The utilization of a postoperative knee brace did not affect the clinical outcome, nor did it reduce the risk of subsequent intra-articular injury.
- CKC exercises produced less pain and laxity, while promoting a better subjective outcome than OKC exercises after PT graft reconstruction.
- OKC exercises produced greater quadriceps femoris muscle strength than CKC exercises without further compromising knee laxity in ACL deficient patients.
- There was not enough evidence to draw any conclusions on the following comparisons; early versus late ACL reconstruction, accelerated versus non-accelerated and home-based versus supervised rehabilitation protocols.

13.1.2 surgical technique

- The initial graft tensioning procedure and the use of a ligament augmentation device did not affect the clinical outcome.
- Bioabsorbable screws and titanium screws produced an equal clinical outcome, regardless of graft type.
- Cross-pin and interference screws were comparable means of fixating the HT graft and possibly the PT graft.
- A more rigid HT graft complex generated less tunnel widening.
- Fifty per cent of ACL injured patients developed radiographic signs of osteoarthritis, regardless of treatment. Meniscectomy further increased the risk.
- The possible advantages of early ACL reconstruction needs to be evaluated in future studies.
- There were no significant differences in clinical outcome between single- and double-bundle ACL reconstruction; however, double-bundle ACL reconstruction produced less rotatory laxity.

13.1.3 graft type

- There were no clear differences between the PT and HT grafts in terms of laxity, clinical outcome, time of return to sports, patella-femoral crepitations, one-leg hop test, ROM, thigh muscle circumference, and anterior knee sensory deficit.
- The PT graft produced more anterior knee pain and kneeling pain than the HT graft, but the difference appeared to disappear with time.
- Harvest site affected muscle strength initially.
- There was a possible correlation between the development of incipient osteoarthritis and the PT graft harvest and utilization; however, this needs to be confirmed by future high quality RCTs.
- The HT graft produced more tunnel widening than then PT graft; however, there was no correlation between tunnel widening and clinical outcome or laxity.
- Harvesting of both the semitendinosus and gracilis was associated with inferior knee flexion strength at higher angles, as compared with harvesting of only the semitendinosus. Moreover, harvesting both tendons reduced hamstring muscle strength for approximately one year; however, this needs to be validated in future studies.

13.2 theme 2: level of evidence

The findings in this area were mostly disheartening. Why are we not better? The answer is probably multifactorial. Many researchers would most likely want to produce higher quality research and a higher level of evidence; however, this can be difficult, as it probably takes more time and resources to do this. Moreover, the focus on higher quality studies and EBM is still fairly new. Finally, basic science and lower level of evidence studies are essential as they provide an initial first assessment and evaluation of a hypothesis and thereby become a building block for high level of evidence studies. However, we cannot allow ourselves to focus exclusively on performing these studies, as the need for long-term high-quality high level of evidence studies is huge.

13.2.1 study characteristics

- The most common study type was case series followed by expert opinions.
- Retrospective comparative studies were the most common clinical trials followed by RCTs.
- Systematic review and meta-analyses were rare.
- Most studies were on single-bundle ACL reconstruction.
- Most RCTs had severe limitations in terms of randomization, sample size calculations, blinding, follow-up rate and follow-up time.
- The journals Arthroscopy, KSSTA and the AJSM were most the most represented; among these Arthroscopy had the highest number of publications in general and the AJSM the lowest.
- The AJSM had the highest number of level 1 and 2 studies in general.

13.2.2 trends over time

- There was a general increase in absolute number of higher level of evidence studies over time and studies in general.
- There was a significant trend towards higher mean level of evidence over time; however, the percentage of higher level of evidence studies did not differ over time.

13.2.3 factors associated with level of evidence

- There was a significant correlation between the impact factor of the journal and mean level of evidence of the journal and the proportion high level of evidence studies.
- USA had the highest number of publications and represented more than one third of all publications.
- USA had most low level of evidence studies which represented almost half the countries publications.
- USA had the highest count systematic-review and meta-analysis
- Sweden had most RCTs followed by Italy and USA.

13.3 theme 3: anatomic acl reconstruction

All in all, we found that most studies did not provide enough surgical data to evaluate the reconstructive procedure. This is crucial as the presented outcomes are extrapolated by several to evaluate both the anatomic reconstructive technique and the comparison between the single and double-bundle ACL reconstruction. To aid future studies; the concepts and principles of anatomic ACL reconstruction was presented and a scoring system was developed.

- Anatomic ACL reconstruction is defined by four principles; restoration of: the insertion site anatomy, the functional bundles, and the native tension pattern, and individualization.
- There was a gross under-reporting of a variety of variables in surgical data of clinical and basic science studies claiming anatomic ACL reconstruction.
- An anatomic ACL reconstruction scoring system was developed to aid in the quantification and definition of this new reconstructive technique.
- The means in anatomic ACL reconstruction scoring system were well below a proposed required minimum score on studies comparing the single and double-bundle ACL reconstructive technique.

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future perspectives

With well over 11 000 published studies on the subject and more than 2 million ACL injuries worldwide annually, one would think that we now have the solution for how this injury can best be treated. Scrutinizing the literature it appears that we have not found the best solution, yet. Even though anatomic ACL reconstruction is promising, we have still not seen the long-term effects of this new reconstructive technique.

The publications of ACL reconstruction are diverse and heterogeneous. In many cases they represent a low level of evidence with or without serious limitations in terms of quality. Although, there are publications with high level of evidence and exceptional quality, it is obvious that we are far from perfect in terms of quality and level of evidence. Where should we start? With ourselves; focus should be to aim for the best and following a guide such as the updated CONSORT check list; even if this means that the amount of annually published studies will decrease. [102] Furthermore, medical journals should present the guidelines such as CONSORT or PRISMA check lists on their home page, and editors and peer reviewers, should give guidance to authors in writing quality papers and maybe have a narrower filter. Of course, this is just a couple of proposals on how to improve the quality of studies in order to answer important research questions at hand, which could guide orthopedic surgeons in their clinical practice.

How does the future reconstructive technique look? This is both an easy and a difficult question. The easy part is that we actually already have a master blueprint; the native ACL. This blueprint obviously is the best solution nature has, and it should be enough for us as well. Now to the difficult part, how much do we need to replicate of the anatomy to restore enough of the knee kinematics and protect long-term knee health? This question is still unanswered. The surgical procedure for anatomic ACL reconstruction has a steep learning curve and many pitfalls. Hence, we are in great need of more information regarding the outcomes of this reconstructive technique. In the future, more reliable, accurate, precise and validated outcome measures are therefore needed to evaluate the results. With the results we will be able to prove a possible superiority of the technique and create guidelines for the technique so that it can be tailored for each patient. It is most likely that certain individuals, young healthy high-level athlete with large knees would be benefitted by a closer replication of the native ACL than others. I truly believe that reconstructive techniques that intend to replicate the native anatomy as much as possible are the key to solve this yet unsolved injury.

Anatomy is the key

15 / fifteen acknowledgements

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16 / sixteen references

1. Schindler, O.S., Surgery for anterior cruciate ligament deficiency: a historical perspective. Knee Surg Sports Traumatol Arthrosc, 2011.
2. Hippocrates, On wounds in the head. In: the surgery fractures joints (trans: Whittington ET). The Loeb classical library, vol. III. William Heinemann, London & Harvard University Press, Cambridge, MA, 1928.
3. Galen, On the usefulness of the parts of the body. Clin Orthop Relat Res, 2003(411): p. 4-12.
4. Bonnet, A., Traite´ des maladies des articulations [Treatise on joint diseases]. Baillie`re, Paris, 1845.
5. Bonnet, A., Traite´ de therapautique des maladies articulaires [Treatise on the treatment of joint diseases]. Baillie`re, Paris, 1853.
6. Gianotti, S.M., et al., Incidence of anterior cruciate ligament injury and other knee ligament injuries: a national population-based study. J Sci Med Sport, 2009. 12(6): p. 622-7.
7. XBase, The Swedish National Knee Ligament Register: Annual Report 2010. 2011.
8. Magnussen, R.A., et al., Cross-cultural comparison of patients undergoing ACL reconstruction in the United States and Norway. Knee Surg Sports Traumatol Arthrosc, 2010. 18(1): p. 98-105.
9. Boden, B.P., et al., Mechanisms of anterior cruciate ligament injury. Orthopedics, 2000. 23(6): p. 573-8.
10. Boden, B.P., et al., Noncontact anterior cruciate ligament injuries: mechanisms and risk factors. J Am Acad Orthop Surg, 2010. 18(9): p. 520-7.
11. Harner, C.D., et al., Quantitative analysis of human cruciate ligament insertions. Arthroscopy, 1999. 15(7): p. 741-9.
12. Yasuda, K., et al., Anatomic single- and double-bundle anterior cruciate ligament reconstruction, part 1: basic science. Am J Sports Med, 2011. 39(8): p. 1789-99.
13. van Eck, C.F., et al., Does the lateral intercondylar ridge disappear in ACL deficient patients? Knee Surg Sports Traumatol Arthrosc, 2010. 18(9): p. 1184-8.
14. Petersen, W. and T. Zantop, Anatomy of the anterior cruciate ligament with regard to its two bundles. Clin Orthop Relat Res, 2007. 454: p. 35-47.
15. Zantop, T., et al., The role of the anteromedial and posterolateral bundles of the anterior cruciate ligament in anterior tibial translation and internal rotation. Am J Sports Med, 2007. 35(2): p. 223-7.
16. Amis, A.A., The functions of the fibre bundles of the anterior cruciate ligament in anterior drawer, rotational laxity and the pivot shift. Knee Surg Sports Traumatol Arthrosc, 2012.
17. Schreck, P.J., et al., Integrin display increases in the wounded rabbit medial collateral ligament but not the wounded anterior cruciate ligament. J Orthop Res, 1995. 13(2): p. 174-83.
18. Hefti, F.L., et al., Healing of the transected anterior cruciate ligament in the rabbit. J Bone Joint Surg Am, 1991. 73(3): p. 373-83.
19. Noyes, F.R., et al., Partial tears of the anterior cruciate ligament. Progression to complete ligament deficiency. J Bone Joint Surg Br, 1989. 71(5): p. 825-33.
20. Lintner, D.M., et al., Partial tears of the anterior cruciate ligament. Are they clinically detectable? American Journal of Sports Medicine, 1995. 23(1): p. 111-118.
21. Grontvedt, T., et al., A prospective, randomized study of three operations for acute rupture of the anterior cruciate ligament. Five-year follow-up of one hundred and thirty-one patients. J Bone Joint Surg Am, 1996. 78(2): p. 159-68.
22. Sandberg, R., et al., Operative versus non-operative treatment of recent injuries to the ligaments of the knee. A prospective randomized study. J Bone Joint Surg Am, 1987. 69(8): p. 1120-6.
23. Andersson, C., M. Odensten, and J. Gillquist, Knee function after surgical or nonsurgical treatment of acute rupture of the anterior cruciate ligament: a randomized study with a long-term follow-up period. Clin Orthop Relat Res, 1991(264): p. 255-63.
24. Odensten, M., J. Lysholm, and J. Gillquist, Suture of fresh ruptures of the anterior cruciate ligament. A 5-year follow-up. Acta Orthop Scand, 1984. 55(3): p. 270-2.
25. Dandy, D.J., Arthroscopic surgery of the knee. Br J Hosp Med, 1982. 27(4): p. 360, 362, 365.
26. Buss, D.D., et al., Arthroscopically assisted reconstruction of the anterior cruciate ligament with use of autogenous patellar-ligament grafts. Results after twenty-four to forty-two months. Journal of Bone and Joint Surgery - Series A, 1993. 75(9): p. 1346-1355.

27. Cameron, S.E., W. Wilson, and P. St Pierre, A prospective, randomized comparison of open vs arthroscopically assisted ACL reconstruction. Orthopedics, 1995. 18(3): p. 249-52.

28. Raab, D.J., et al., Comparison of arthroscopic and open reconstruction of the anterior cruciate ligament. Early results. Am J Sports Med, 1993. 21(5): p. 680-3; discussion 683-4.

29. Shelbourne, K.D. and J.H. Wilckens, Intraarticular anterior cruciate ligament reconstruction in the symptomatic arthritic knee. Am J Sports Med, 1993. 21(5): p. 685-8; discussion 688-9.

30. Hess, T., et al., Single-versus two-incision technique in anterior cruciate ligament replacement: influence on postoperative muscle function. Am J Sports Med, 2002. 30(1): p. 27-31.

31. Gerich, T.G., et al., One- versus two-incision technique for anterior cruciate ligament reconstruction with patellar tendon graft. Results on early rehabilitation and stability. Knee Surg Sports Traumatol Arthrosc, 1997. 5(4): p. 213-6.

32. Harner, C.D., et al., Anterior cruciate ligament reconstruction: endoscopic versus two-incision technique. Arthroscopy, 1994. 10(5): p. 502-12.

33. Brandsson, S., et al., Reconstruction of the anterior cruciate ligament: comparison of outside-in and all-inside techniques. Br J Sports Med, 1999. 33(1): p. 42-5.

34. Reat, J.F. and D.M. Lintner, One-versus two-incision ACL reconstruction. A prospective, randomized study. Am J Knee Surg, 1997. 10(4): p. 198-208.

35. Panni, A.S., et al., Clinical and radiographic results of ACL reconstruction: a 5- to 7-year follow-up study of outside-in versus inside-out reconstruction techniques. Knee Surg Sports Traumatol Arthrosc, 2001. 9(2): p. 77-85.

36. Amis, A.A. and T.D. Zavras, Isometricity and graft placement during anterior cruciate ligament reconstruction. The Knee, 1995. 2(1): p. 5-17.

37. Zavras, T.D., et al., A comparative study of 'isometric' points for anterior cruciate ligament graft attachment. Knee Surg Sports Traumatol Arthrosc, 2001. 9(1): p. 28-33.

38. Sommer, C., N.F. Friederich, and W. Muller, Improperly placed anterior cruciate ligament grafts: correlation between radiological parameters and clinical results. Knee Surg Sports Traumatol Arthrosc, 2000. 8(4): p. 207-13.

39. Musahl, V., et al., Varying femoral tunnels between the anatomical footprint and isometric positions: effect on kinematics of the anterior cruciate ligament-reconstructed knee. Am J Sports Med, 2005. 33(5): p. 712-8.

40. Yamazaki, J., et al., Radiographic description of femoral tunnel placement expressed as intercondylar clock time in double-bundle anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc, 2011. 19(3): p. 418-23.

41. van Eck, C.F., J.R. Romanowski, and F.H. Fu, Anatomic Single-Bundle Anterior Cruciate Ligament Reconstruction. Arthroscopy, 2009. 25(9): p. 943-946.

42. van Eck, C.F., et al., Anatomic Single- and Double-Bundle Anterior Cruciate Ligament Reconstruction Flowchart. Arthroscopy, 2010. 26(2): p. 258-268.

43. Cohen, S.B. and F.H. Fu, Three-portal technique for anterior cruciate ligament reconstruction: use of a central medial portal. Arthroscopy, 2007. 23(3): p. 325 e1-5.

44. Markolf, K.L., et al., Biomechanical effects of femoral notchplasty in anterior cruciate ligament reconstruction. Am J Sports Med, 2002. 30(1): p. 83-9.

45. May, D.A., et al., MR imaging findings in anterior cruciate ligament reconstruction: evaluation of notchplasty. AJR Am J Roentgenol, 1997. 169(1): p. 217-22.

46. Yasuda, K., et al., Anatomic reconstruction of the anteromedial and posterolateral bundles of the anterior cruciate ligament using hamstring tendon grafts. Arthroscopy, 2004. 20(10): p. 1015-25.

47. Loh, J.C., et al., Knee stability and graft function following anterior cruciate ligament reconstruction: Comparison between 11 o'clock and 10 o'clock femoral tunnel placement. 2002 Richard O'Connor Award paper. Arthroscopy, 2003. 19(3): p. 297-304.

48. Scopp, J.M., et al., The effect of oblique femoral tunnel placement on rotational constraint of the knee reconstructed using patellar tendon autografts. Arthroscopy, 2004. 20(3): p. 294-9.

49. Yagi, M., et al., Biomechanical analysis of an anatomic anterior cruciate ligament reconstruction. Am J Sports Med, 2002. 30(5): p. 660-6.

50. Yamamoto, Y., et al., Knee stability and graft function after anterior cruciate ligament reconstruction: a comparison of a lateral and an anatomical femoral tunnel placement. Am J Sports Med, 2004. 32(8): p. 1825-32.

51. Arnold, M.P., J. Kooloos, and A. van Kampen, Single-incision technique misses the anatomical femoral anterior cruciate ligament insertion: a cadaver study. Knee Surg Sports Traumatol Arthrosc, 2001. 9(4): p. 194-9.

52. Hantes, M.E., et al., Differences in graft orientation using the transtibial and anteromedial portal technique in anterior cruciate ligament reconstruction: a magnetic resonance imaging study. Knee Surg Sports Traumatol Arthrosc, 2009. 17(8): p. 880-6.

53. Dargel, J., et al., Femoral bone tunnel placement using the transtibial tunnel or the anteromedial portal in ACL reconstruction: A radiographic evaluation. Knee

Surgery, Sports Traumatology, Arthroscopy, 2009. 17(3): p. 220-227.

54. Woo, S.L., et al., The effectiveness of reconstruction of the anterior cruciate ligament with hamstrings and patellar tendon . A cadaveric study comparing anterior tibial and rotational loads. J Bone Joint Surg Am, 2002. 84-A(6): p. 907-14.

55. Gavriilidis, I., et al., Transtibial versus anteromedial portal of the femoral tunnel in ACL reconstruction: a cadaveric study. Knee, 2008. 15(5): p. 364-7.

56. Heming, J.F., J. Rand, and M.E. Steiner, Anatomical limitations of transtibial drilling in anterior cruciate ligament reconstruction. Am J Sports Med, 2007. 35(10): p. 1708-15.

57. Cha, P.S., A. Chhabra, and C.D. Harner, Single-bundle anterior cruciate ligament reconstruction using the medial portal technique. Operative Techniques in Orthopaedics, 2005. 15(2): p. 89-95.

58. Brophy, R.H., R.M. Selby, and D.W. Altchek, Anterior cruciate ligament revision: double-bundle augmentation of primary vertical graft. Arthroscopy, 2006. 22(6): p. 683 e1-5.

59. Murray, A.W. and M.F. Macnicol, 10-16 year results of Leeds-Keio anterior cruciate ligament reconstruction. Knee, 2004. 11(1): p. 9-14.

60. Moyen, B. and J.L. Lerat, Artificial ligaments for anterior cruciate replacement. A new generation of problems. J Bone Joint Surg Br, 1994. 76(2): p. 173-5.

61. Arnoczky, S.P., R.F. Warren, and M.A. Ashlock, Replacement of the anterior cruciate ligament using a patellar tendon allograft. An experimental study. J Bone Joint Surg Am, 1986. 68(3): p. 376-85.

62. Noyes, F.R. and S.D. Barber-Westin, Reconstruction of the anterior cruciate ligament with human allograft. Comparison of early and later results. J Bone Joint Surg Am, 1996. 78(4): p. 524-37.

63. Jackson, D.W., et al., A comparison of patellar tendon autograft and allograft used for anterior cruciate ligament reconstruction in the goat model. Am J Sports Med, 1993. 21(2): p. 176-85.

64. Noyes, F.R., et al., Biomechanical analysis of human ligament grafts used in knee-ligament repairs and reconstructions. J Bone Joint Surg Am, 1984. 66(3): p. 344-52.

65. Geib, T.M., et al., Anterior cruciate ligament reconstruction using quadriceps tendon autograft: intermediate-term outcome. Arthroscopy, 2009. 25(12): p. 1408-14.

66. Adams, D.J., A.D. Mazzocca, and J.P. Fulkerson, Residual strength of the quadriceps versus patellar tendon after harvesting a central free tendon graft. Arthroscopy, 2006. 22(1): p. 76-9.

67. Ahmad, C.S., et al., Mechanical properties of soft tissue femoral fixation devices for anterior cruciate ligament reconstruction. Am J Sports Med, 2004. 32(3): p. 635-40.

68. Sackett, D.L., Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest, 1986. 89(2 Suppl): p. 2S-3S.

69. Sackett, D.L., et al., Evidence based medicine: what it is and what it isn't. BMJ, 1996. 312(7023): p. 71-2.

70. Green S, H.J., Glossary of Terms in The Cochrane Collaboration, 2005, The Cochrane Collaboration: http://www.cochrane.org/sites/default/files/uploads/glossary.pdf.

71. Moher, D., et al., Epidemiology and reporting characteristics of systematic reviews. PLoS Med, 2007. 4(3): p. e78.

72. Moher, D., et al., Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med, 2009. 6(7): p. e1000097.

73. Higgins JPT, G.S.e., Cochrane Handbook for Systematic Reviews of Interventions, 2011, The Cochrane Collaboration: www.cochrane-handbook.org.

74. Shojania, K.G., et al., How quickly do systematic reviews go out of date? A survival analysis. Ann Intern Med, 2007. 147(4): p. 224-33.

75. Birmingham, T.B., et al., A randomized controlled trial comparing the effectiveness of functional knee brace and neoprene sleeve use after anterior cruciate ligament reconstruction. Am J Sports Med, 2008. 36(4): p. 648-55.

76. Risberg, M.A., et al., The effect of knee bracing after anterior cruciate ligament reconstruction. A prospective, randomized study with two years' follow-up. Am J Sports Med, 1999. 27(1): p. 76-83.

77. Meunier, A., M. Odensten, and L. Good, Long-term results after primary repair or non-surgical treatment of anterior cruciate ligament rupture: a randomized study with a 15-year follow-up. Scand J Med Sci Sports, 2007. 17(3): p. 230-7.

78. Oiestad, B.E., et al., Knee osteoarthritis after anterior cruciate ligament injury: a systematic review. Am J Sports Med, 2009. 37(7): p. 1434-43.

79. Isberg, J., et al., Will early reconstruction prevent abnormal kinematics after ACL injury? Two-year follow-up using dynamic radiostereometry in 14 patients operated with hamstring autografts. Knee Surg Sports Traumatol Arthrosc, 2011.

80. Muneta, T., et al., A prospective randomized study of 4-strand semitendinosus tendon anterior cruciate ligament reconstruction comparing single-bundle and double-bundle techniques. Arthroscopy, 2007. 23(6): p. 618-28.

81. Yasuda, K., et al., Clinical evaluation of anatomic double-bundle anterior cruciate ligament reconstruction procedure using hamstring tendon grafts: comparisons among 3 different procedures. Arthroscopy, 2006. 22(3): p. 240-51.

82. Hussein, M., et al., Prospective Randomized Clinical Evaluation of Conventional Single-Bundle, Anatomic Single-Bundle, and Anatomic Double-Bundle Anterior Cruciate Ligament Reconstruction: 281 Cases With 3- to 5-Year Follow-up. Am J Sports Med, 2011.

83. van Eck, C.F., et al., Single-Bundle Versus Double-Bundle Reconstruction for Anterior Cruciate Ligament Rupture: A Meta-Analysis—Does Anatomy Matter? Arthroscopy, 2012. 28(3): p. 405-424.

84. Aune, A.K., et al., Four-strand hamstring tendon autograft compared with patellar tendon-bone autograft for anterior cruciate ligament reconstruction. A randomized study with two-year follow-up. Am J Sports Med, 2001. 29(6): p. 722-8.

85. Zaffagnini, S., et al., Prospective and randomized evaluation of ACL reconstruction with three techniques: a clinical and radiographic evaluation at 5 years follow-up. Knee Surg Sports Traumatol Arthrosc, 2006. 14(11): p. 1060-9.

86. Ibrahim, S.A., et al., Clinical evaluation of arthroscopically assisted anterior cruciate ligament reconstruction: patellar tendon versus gracilis and semitendinosus autograft. Arthroscopy, 2005. 21(4): p. 412-7.

87. Lidén, M., et al., Patellar tendon or semitendinosus tendon autografts for anterior cruciate ligament reconstruction: a prospective, randomized study with a 7-Year follow-up. Am J Sports Med, 2007. 35(5): p. 740-8.

88. Yagi, M., et al., Double-bundle ACL reconstruction can improve rotational stability. Clin Orthop Relat Res, 2007. 454: p. 100-7.

89. Kocher, M.S., et al., Relationships between objective assessment of ligament stability and subjective assessment of symptoms and function after anterior cruciate ligament reconstruction. Am J Sports Med, 2004. 32(3): p. 629-34.

90. Jonsson, H., K. Riklund-Ahlstrom, and J. Lind, Positive pivot shift after ACL reconstruction predicts later osteoarthrosis: 63 patients followed 5-9 years after surgery. Acta Orthop Scand, 2004. 75(5): p. 594-9.

91. Aglietti, P., et al., Anterior cruciate ligament reconstruction: bone-patellar tendon-bone compared with double semitendinosus and gracilis tendon grafts. A prospective, randomized clinical trial. J Bone Joint Surg Am, 2004. 86-A(10): p. 2143-55.

92. Harilainen, A., E. Linko, and J. Sandelin, Randomized prospective study of ACL reconstruction with interference screw fixation in patellar tendon autografts versus femoral metal plate suspension and tibial post fixation in hamstring tendon autografts: 5-year clinical and radiological follow-up results. Knee Surg Sports Traumatol Arthrosc, 2006. 14(6): p. 517-28.

93. Beynnon, B.D., et al., Anterior cruciate ligament replacement: comparison of bone-patellar tendon-bone grafts with two-strand hamstring grafts. A prospective, randomized study. J Bone Joint Surg Am, 2002. 84-A(9): p. 1503-13.

94. Jansson, K.A., et al., A prospective randomized study of patellar versus hamstring tendon autografts for anterior cruciate ligament reconstruction. Am J Sports Med, 2003. 31(1): p. 12-8.

95. Leys, T., et al., Clinical Results and Risk Factors for Reinjury 15 Years After Anterior Cruciate Ligament Reconstruction: A Prospective Study of Hamstring and Patellar Tendon Grafts. Am J Sports Med, 2011.

96. Committee, I.S., et al., A practical guide to research: design, execution, and publication. Arthroscopy, 2011. 27(4 Suppl): p. S1-112.

97. Rossner, M., H. Van Epps, and E. Hill, Show me the data. J Cell Biol, 2007. 179(6): p. 1091-2.

98. Obremskey, W.T., et al., Level of evidence in orthopaedic journals. J Bone Joint Surg Am, 2005. 87(12): p. 2632-8.

99. Shen, W., et al., Application of the anatomic double-bundle reconstruction concept to revision and augmentation anterior cruciate ligament surgeries. J Bone Joint Surg Am, 2008. 90 Suppl 4: p. 20-34.

100. Kopf, S., et al., Nonanatomic tunnel position in traditional transtibial single-bundle anterior cruciate ligament reconstruction evaluated by three-dimensional computed tomography. J Bone Joint Surg Am, 2010. 92(6): p. 1427-31.

101. Forsythe, B., et al., The location of femoral and tibial tunnels in anatomic double-bundle anterior cruciate ligament reconstruction analyzed by three-dimensional computed tomography models. J Bone Joint Surg Am, 2010. 92(6): p. 1418-26.

102. Moher, D., et al., CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ, 2010. 340: p. c869.

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