

Risk factors for revision after anterior cruciate ligament reconstruction

Andreas Persson

Thesis for the degree of Philosophiae Doctor (PhD)
University of Bergen, Norway
2019

UNIVERSITY OF BERGEN



Risk factors for revision after anterior cruciate ligament reconstruction

Andreas Persson



Thesis for the degree of Philosophiae Doctor (PhD)
at the University of Bergen

Date of defense: 06.09.2019

© Copyright Andreas Persson

The material in this publication is covered by the provisions of the Copyright Act.

Year: 2019

Title: Risk factors for revision after anterior cruciate ligament reconstruction

Name: Andreas Persson

Print: Skipnes Kommunikasjon / University of Bergen

Contents

1.	SCIENTIFIC ENVIRONMENT AND FUNDING	6
2.	ACKNOWLEDGEMENTS	7
3.	TERMS AND ABBREVIATIONS	10
4.	ABSTRACT	12
5.	LIST OF PUBLICATIONS	13
6.	INTRODUCTION	14
6.1	THE KNEE – AN OVERVIEW	14
6.2	ANATOMY OF THE ANTERIOR CRUCIATE LIGAMENT	15
6.3	FUNCTION OF THE ACL	16
6.4	EPIDEMIOLOGY AND RISK FACTORS FOR ACL INJURY	16
6.5	INJURY MECHANISM	17
6.6	PREVENTION OF PRIMARY ACL INJURY	17
6.7	THE HISTORY OF ACL SURGERY, HIGHLIGHTING GRAFT CHOICE AND FIXATION	18
6.7.1	<i>The journey to the first ACL suture – at a glance</i>	18
6.7.2	<i>Fascia lata grafts</i>	19
6.7.3	<i>Hamstring tendon grafts</i>	19
6.7.4	<i>Patellar tendon grafts</i>	20
6.7.5	<i>Quadriceps tendon grafts</i>	21
6.7.6	<i>Allografts</i>	22
6.7.7	<i>Synthetic grafts</i>	22
6.8	MODERN TREATMENT OF AN ACL INJURY	24
6.8.1	<i>Non-operative treatment of ACL tear – physical rehabilitation</i>	25
6.8.2	<i>Arthroscopically assisted reconstruction of the ACL</i>	26
6.8.3	<i>The anatomic ACL reconstruction</i>	26
6.9	CURRENT GRAFT SELECTION	27
6.9.1	<i>Mechanical properties of grafts compared to the native ACL</i>	28
6.10	GRAFT FIXATION AND HEALING	29
6.11	PRINCIPLES OF GRAFT FIXATION	30
6.11.1	<i>Anatomical fixation / Aperture fixation</i>	30
6.11.2	<i>Non-anatomic / Suspensory fixation</i>	31
6.11.3	<i>Transfixation with cross-pins / Transfemoral fixation</i>	31
6.11.4	<i>Combination devices</i>	31
6.11.5	<i>Fixation device material</i>	31
6.11.6	<i>What fixation are used today?</i>	32
6.12	OUTCOME AFTER ACL RECONSTRUCTION	33
6.12.1	<i>Outcome measures</i>	33

6.12.2	<i>Return to sport and activity score</i>	33
6.12.3	<i>Subjective outcome</i>	33
6.12.4	<i>Failure rate</i>	34
6.12.5	<i>Post-injury osteoarthritis</i>	34
6.13	WHY IS THIS THESIS NEEDED?	35
7.	AIMS OF THESIS	36
	<i>The specific aims of the three papers were:</i>	36
8.	MATERIAL AND METHODS	37
8.1	THE SCANDINAVIAN KNEE LIGAMENT REGISTRIES	37
8.1.1	<i>The Norwegian National Knee Ligament Register</i>	37
8.1.2	<i>The Swedish and Danish national knee ligament registries</i>	38
8.2	STATISTICS	39
8.2.1	<i>Statistical analysis</i>	39
8.3	ETHICAL CONSIDERATIONS	39
9.	SUMMARY OF PAPERS	40
9.1	PAPER I	40
9.2	PAPER II	41
9.3	PAPER III	43
10.	DISCUSSION	44
10.1	METHODOLOGICAL CONSIDERATIONS	44
10.1.1	<i>Register studies as a method</i>	44
10.1.2	<i>Observational studies and randomized controlled trials</i>	45
10.1.3	<i>Revision surgery as endpoint</i>	46
10.1.4	<i>Possible hidden confounders</i>	48
10.2	RESULTS	49
10.2.1	<i>Patient age</i>	49
10.2.2	<i>Graft choice and fixation</i>	50
	<i>Graft healing</i>	53
	<i>Graft forces depends on tunnel positioning</i>	55
10.3	CLINICAL IMPLICATIONS	57
11.	CONCLUSIONS	58
11.1	PAPER I	58
11.2	PAPER II	58
11.3	PAPER III	59
12.	SUGGESTIONS FOR FURTHER RESEARCH	60
12.1	DATA QUALITY	60

12.2	CAUSE OF REVISION _____	60
12.3	SUBJECTIVE OUTCOME AFTER ACL RECONSTRUCTION _____	60
12.4	CONVERSION OF ACL RECONSTRUCTIONS TO TOTAL KNEE ARTHROPLASTY _____	61
12.5	INDICATION FOR REVISION SURGERY _____	61
12.6	REGISTER-RCT _____	61
13.	REFERENCES _____	62
14.	APPENDIX _____	80
	<i>Appendix 1 - Surgical form NNKLR 2004-2011</i> _____	80
	<i>Appendix 2 - Surgical form NNKLR 2012-</i> _____	82
15.	PAPERS I-III _____	84

1. Scientific environment and funding

This PhD project started in 2013, and was at the start funded by the Department of orthopedic surgery at Haukeland University Hospital in Bergen. Initially, I spent 60% of my time at the Norwegian National Advisory Unit on Arthroplasty and Hip Fractures who runs the Norwegian National Knee Ligament Register (NNKLR). I received further funding from the Norwegian Orthopaedic Association in 2014. In 2017, I relocated to Oslo and the project continued at the Department of Orthopedic surgery at Oslo University Hospital, Ullevål. The project was finalized with the help of funding from Sophies Minde Ortopedi AS, and as a fellow in Sports Traumatology at the Norwegian School of Sports Science funded by Smith & Nephew. Supervision was provided by colleagues at the departments of orthopaedic surgery at both Haukeland and Oslo University Hospital, in addition to the scientific staff at the NNKLR and the University of Bergen.



2. Acknowledgements

I have been working with this thesis since 2013, and it was carried out in collaboration with the following insititutes: The orthopedic department at Haukeland University hospital, the Norwegian National Knee Ligament Register and Oslo Sports Trauma Research center.

Many people have contributed directly or indirectly to the work of this thesis that I would like to thank. Without the support and encouragement of colleagues, friends and family, this would not have been possible. I would like to express my sincere gratitude to the following persons:

Jonas M. Fevang, my main supervisor, professor at the University of Bergen and current head of orthopedic department at Haukeland University hospital. I wish to thank you for your patience and steady guidance in scientific writing and thinking. Your initial effort and continous encouragement and support through this time has been essential. Your warm and humoristic attitude and friendly leadership has been invaluable and I'm deeply grateful.

Lars Engebretsen – my co-supervisor, professor at the University of Oslo and co-founder of Oslo Sports Trauma Research Center. You have been involved and helped in all aspects of this thesis. Initially and throughout the period, you have given immediate, positive and constructive feedback on my work. Your never-ending engagement, positivity and ability to conduct research is impressive. Special thanks for the help in my job situation during my relocation to Oslo and for the opportunities given during the last phase of this thesis.

Jan-Erik Gjertsen – my co-supervisor, associate professor at University of Bergen and former colleague at Orthopedic department at Haukeland University Hospital. You have contributed greatly to my early surgical skills, my scientific understanding and development, in addition to the help with any possible question that has landed in your inbox throughout this period. Your empathic attitude as a colleague and toward others is inspiring.

To my coauthors *Martin Lind, Jon Olav Drogset, Birgitte Espehaug, Randi M. Hole and Magnus Forssblad*, thank you for the help with data interpretation and improving the manuscripts. Special thanks to *Tone Gifstad* who did an extensive job to fuse and quality control the dataset used in paper III.

I would like to thank all former colleagues at the orthopedic department, Haukeland University hospital, for a friendly and collegial atmosphere. Special thanks to *Trude, Håvard, Truls, Jostein* and all others moving in and out of our shared office. *Knut Fjeldsgaard*, former leader of the NNKLR, and *Asle B. Kjellsen* introduced me to knee surgery. Thank you for your patience when I initially tried to find my way with the camera inside the knee joint and for the help as co-authors on the papers.

When starting my research I spent time at the registry, sharing office with *Håvard Dale*. Thank you for sharing tips how to organize the research in SPSS, and for your encouragement. It is still of great help. I would also like to thank the secretaries, statisticians, computer scientists and other staff of the registry to accommodate me and help with any practical or academic question. Special thanks to *Lise Bjordal Kvamsdal* for looking after me in general and to *Anne Marie Fenstad* for invaluable statistical help and guidance. *Ove Furnes* – former head of the orthopedic department at Haukeland University hospital, now leader of the Norwegian National Advisory Unit on Arthroplasty. I'm grateful that my repetitive job inquires lead to my initial opportunity to combine clinical work with research and for the valuable help with any research-related question.

I would also like to thank my current colleagues at the orthopedic department at Oslo University Hospital, Ullevål. *Sverre Løken, Ragnhild Støen, Berte Bøe, Tom Ludvigsen, Frode Mauroy, Marc Strauss* and *Gilbert Moatshe*. I'm very privileged having the opportunity to learn from your vast surgical and academic experience and to share interesting discussions on any topic that comes our way. This has definitely helped me in the final part of this period.

Dr. Rolf Elmros (1946 – 2016) – team doctor of our junior soccer team in Växjö BK during the 1990's and former clinician at Idrottskliniken, Växjö. With his warm,

humoristic and engaged personality, he affected his surroundings in many aspects. Thank you Rolf for introducing me to the field of sports medicine, often as a patient, and helping me with my first “scientific work” about knee injuries in high school. May your spirit continue to inspire!

I am lucky to have had a supporting and loving family throughout life. Thank you to my parents *Per* and *Janet Persson* who taught me what is really important, and to my younger siblings *André* and *Sophie* for being born. To my older and wiser sister *Louise* and partner *Andreas Benneche*, thank you for all support and laughs. To my wife and best friend *Kristina*. Thank you for your loving support and care in any situation we encounter. You are the greatest mum and role model for our two diamonds Maximilian and Lily.

3. Terms and abbreviations

ACL	Anterior cruciate ligament
ACLR	Anterior cruciate ligament reconstruction
AM	Anteromedial
AL	Anterolateral
Allograft	Transplant of tissue from one individual to another of the same species
Autograft	Transplant of tissue from the same individual
BC	Before Christ
BPTB	Bone-patellar tendon-bone
CACLR	Contralateral anterior cruciate ligament reconstruction
DB	Double-bundle
DNKLR	Danish National Knee Ligament Register
HA	Hydroxyapatite
HR	Hazard ratio
HT	Hamstring tendon
IKDC	International knee documentation committee
KOOS	Knee Injury and Osteoarthritis Outcome Score
LAD	Ligament augmentation device
MRI	Magnetic resonance imaging
MIS	Metal interference screw
NNAUHF	Norwegian National Advisory Unit on Arthroplasty and Hip Fractures
NNKLR	Norwegian National Knee Ligament Register
N	Newton
Nm	Newton meter
OA	Osteoarthritis
PEEK	Poly-ether-ether-ketone
PCL	Posterior cruciate ligament
PLA	Poly-lactic acid
PLLA	Poly-L-lactic acid

PROM	Patient reported outcome measure
PTS	Posterior tibial slope
QoL	Quality of life
QT	Quadriceps tendon
QTB	Quadriceps tendon-bone
RCT	Randomized controlled trial
SNKLR	Swedish National Knee Ligament Register
ST	Semitendinosus
TKA	Total knee arthroplasty
TT	Transtibial
Y	Years

4. Abstract

The overall aim of this thesis was to investigate risk factors for revision anterior cruciate ligament (ACL) reconstruction with a special attention to surgical technique (graft choice and choice of graft fixation) and patients' age and sex. Specific aims were to describe the usage of the most common grafts and fixations for ACLR in Norway and Scandinavia respectively. To answer these questions we used register data for patients with isolated ACL tear who had undergone ACL reconstruction (ACLR), with revision as the endpoint. We used data from the Norwegian National Knee Ligament Register (NNKLR) for all papers, and in addition, data from the Swedish and Danish National Knee Ligament Registries for paper III. In study I, 12,643 patients were included to evaluate the revision rate and risk factors for revision ACLR, primarily the influence of graft choice (patellar tendon [BPTB] or hamstring tendon [HT] graft). The patients' age and sex were included in the overall analysis. The revision rate was higher for HT compared with BPTB grafts at all follow-up times, and the adjusted revision risk were twice as high for HT compared with BPTB. Young age was the strongest predictor for revision of the investigated factors. In study II, we described the usage of fixation implants for 14,034 patients with BPTB and HT in Norway and investigated the revision risk for the most common combinations of fixations for BPTB and HT. We found combinations of fixation implants with a higher risk of revision when using HT, especially when suspensory fixation in the femur was used. In study III, we described the most common fixation methods for HT grafts used in 38,666 patients in Scandinavia, and investigated the influence of fixation method on the risk of revision. We found that similar graft fixation methods influenced the risk of revision as in study II. In conclusion, we found both surgical techniques and patient-specific factors that affect the revision rate and revision-risk after ACLR. Young age was the strongest predictor for further revision surgery. Patients reconstructed with HT had twice the risk of revision compared with BPTB, and certain fixation methods for HT had an increased risk of early and overall revision.

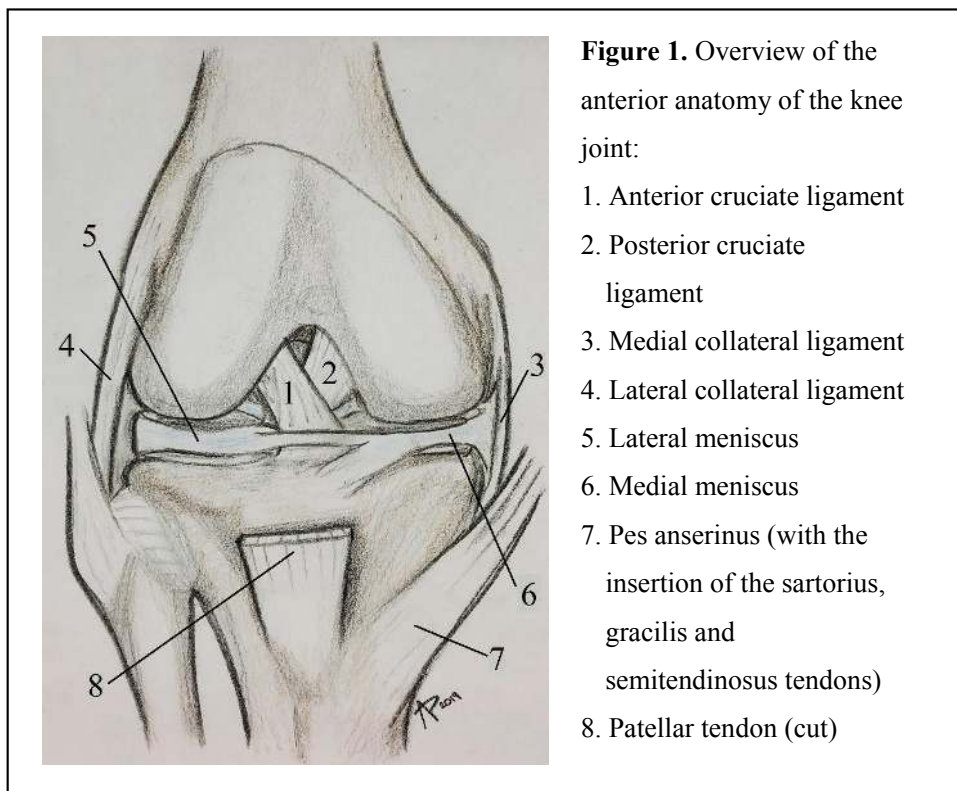
5. List of publications

- I Persson A, Fjeldsgaard K, Gjertsen JE, Kjellsen AB, Engebretsen L, Hole RM, Fevang JM. **Increased risk of revision with hamstring tendon grafts compared with patellar tendon grafts after anterior cruciate ligament reconstruction: a study of 12,643 patients from the Norwegian Cruciate Ligament Registry, 2004-2012.** Am J Sports Med. 2014 Feb;42(2):285-91.
- II Persson A, Kjellsen AB, Fjeldsgaard K, Engebretsen L, Espehaug B, Fevang JM. **Registry data highlight increased revision rates for endobutton/biosure HA in ACL reconstruction with hamstring tendon autograft: a nationwide cohort study from the Norwegian Knee Ligament Registry, 2004-2013.** Am J Sports Med. 2015 Sep;43(9):2182-8.
- III Persson A, Gifstad T, Lind M, Engebretsen L, Fjeldsgaard K, Drogset JO, Forssblad M, Espehaug B, Kjellsen AB, Fevang JM. **Graft fixation influences revision risk after ACL reconstruction with hamstring tendon autografts.** Acta Orthop. 2018 Apr;89(2):204-210.

6. Introduction

6.1 The knee – an overview

The knee is a hinged joint with three joint surfaces; the medial and lateral tibiofemoral joints and the patellofemoral joint. The tibiofemoral joint involves both rotation (flexion-extension, internal-external tibial rotation, medial-lateral opening of the joint space) and translation (anterior-posterior displacement, abduction-adduction, and compression-distraction). The patella slides in the trochlea of the distal femur in flexion-extension [1]. The tibiofemoral joint is stabilised dynamically by supporting musculature in addition to the main stabilising ligaments. Other stabilising anatomic structures includes the joint capsule, menisci, iliotibial tract and popliteus. An overview of the main structures of the knee joint is presented in Figure 1.



6.2 Anatomy of the anterior cruciate ligament

The anterior cruciate ligament (ACL) can be recognized from the 7th week of embryonal development, just after the posterior cruciate ligament (PCL) appears in the intercondylar notch. Although the ACL is intraarticular, it is completely extra-synovial as it develops from mesenchymal cells in the posterior joint capsule [2]. It is richly vascularized, mainly from the middle genicular artery and innervated with vasomotoric and mechanoreceptive nerve fibers originating from the tibial nerve [3]. The ligament consists primarily of collagen type I fibers, organized in parallel fascicles responsible for its main tensile strength. In addition, it consists of other types of collagens, cells and matrix components (glycosaminoglycans attracting water, glyco-conjugates and elastic components) [4].

Macroscopically the ACL runs between its bony insertions medially to the anterior horn of the lateral meniscus to the posterior inner wall of the lateral femoral condyle. The ACL is often described to consist of two distinct bundles, the anteromedial (AM) and posterolateral (PL), referring to its area of insertion on the tibia [3, 5, 6]. The AM bundle has its tibial insertion anteromedially in the tibial ACL footprint, wrapping medially around the PL to its insertion proximal to PL on the femur when the knee is in full extension. Some anatomical studies have also identified a third intermediate bundle [7, 8], similar to what is described in various animal species [9]. The femoral footprint can often be identified laying posterior of a bony ridge, the intercondylar ridge. Between the femoral insertion of the AM and PM bundle is the lateral bifurcate ridge, that together with the intercondylar ridge and the ACL remnants are crucial for identification of the correct position for the femoral tunnel in the anatomic ACL reconstruction. The main dense collagen fibers of the ACL inserts to bone with a direct insertion, through a fibrocartilaginous layer [10]. The two-bundle version of the ACL is widely acknowledged due to its direct correlation to the mechanical functions of the ligament. However, the variance of the tibial insertion morphology and size, and the inconsistency in reporting bundle-like structures in the anatomic literature highlights the inter-personal variation and makes the macroscopic bundle-appearance of the ACL controversial [11]. Some authors have reported that the ACL

had a C-shaped tibial insertion and a flat midsubstance “ribbon-like” shape, with a corresponding femoral insertion just posterior to the intercondylar ridge [11, 12]. The shape of the ACL in a transverse plane changes with the degree of flexion of the knee joint, but in general, it is larger in its anteroposterior aspect [13]. The anatomy and length of the ACL fibers shows an interpersonal variation, with a reported average length of 32-38 mm [5, 14].

6.3 Function of the ACL

The main biomechanical function of the ACL is to prevent anterior translation of the tibia in relation to the femur. In addition, it has a role as a stabilizer for internal rotation of the tibia. The individual contribution of the two functional bundles (AM and PL) of restraining anterior translation of the tibia changes with the flexion of the knee. The tension of the PL bundle significantly increases in extension, whereas the tension of the AM bundle increases in flexion [15, 16]. In a combined rotatory load of 10 Newton meter (Nm) valgus and 5 Nm internal tibial torque, the force on the PM bundle peaked at 15° knee flexion whilst the force on the AM bundle in 15° knee flexion was similar to that in 30° knee flexion in a cadaver study by Gabriel [16]. In total, the mechanical contribution of the PL bundle is largest close to full knee extension [17].

The previously mentioned nerve supply of the ACL contributes to the afferent part in knee proprioception activating supporting musculature around the knee, important for postural control [2, 4, 18].

6.4 Epidemiology and risk factors for ACL injury

The exact incidence of ACL injury in the population is unknown. The majority of the injuries to the ACL is thought to happen during physical activity, especially in competitive sports that include cutting movements and landings [19-22]. The incidence of clinically diagnosed ACL injuries has recently been found to be 68.6 per 100.000 person-years in a population-based cohort study in the United States, with a peak in incidence for 19-25 year old males and 14-18 year old females [23]. The

same age-specific pattern has been found in Norway, with females having a peak in ACL reconstruction at the age <20 years, whereas males have their peak incidence at the age 20-29 [24]. It is estimated that less than 50% of the patients with an ACL injury undergoes reconstructive surgery [25]. The overall incidence of ACL reconstructions in Scandinavia has been reported to be 32-38 per 100.000 inhabitants per year, whereas for the high risk population (age 16-29) an incidence of 85 per 100.000 inhabitants per year has been reported [21, 26]. Even though males are overrepresented in overall reported incidence of ACL injuries and reconstructions, females have been reported to have a higher risk of ACL injuries when exposed to sport activities in several studies [22, 27, 28]. Other potential risk factors for ACL injury are anatomical variants of the intercondylar notch, general joint laxity, and increased posterior tibial slope [29-31].

6.5 Injury mechanism

The majority of ACL injuries has been reported to happen in a non-contact situation, typically in a landing situation or during sudden deceleration while cutting [32-34]. The knee joint seems to be in particular risk for ACL injury when it is in close to full extension in combination with knee valgus and internal or external rotation of the tibia [32, 35]. It has also been reported that the force from the quadriceps muscle is straining the ACL, in particular between 15-30 degrees of flexion [36-38], and therefore could act as an additional shear force at the time of the ACL injury.

6.6 Prevention of primary ACL injury

Given the long-term negative effects of an ACL injury (discussed later in this thesis), the importance of prevention of the initial injury has been highlighted [39-41]. Several neuromuscular and proprioceptive training programs has been found effective to reduce the risk of ACL injuries in athletes, and a pooled risk ratio reduction of 0.38 was found comparing prevention with control in a recent systematic review [42]. The continuous compliance with the prevention programs seems important, as it was

found that the protective effects from the training programs was reversed when the participation compliance decreased [43].

6.7 The history of ACL surgery, highlighting graft choice and fixation

In order to understand and properly evaluate the studies conducted in any research field, it is important to be acquainted with the history. In ACL surgery research, different surgical techniques have been directly compared possibly introducing bias, which is important to acknowledge for the interpretation of the results.

6.7.1 The journey to the first ACL suture – at a glance

The existence of the cruciate ligaments has been known since the old Egyptian era, and the first known anatomic description is found in the first known written document of surgical treatments of injuries, the Edwin Smith Surgical Papyrus (3000 Before Christ [BC]). Hippocrates of Greece (460-370 BC), who was called “the father of modern medicine” also described the instability of an ACL deficient knee [44]. The name “genu cruciate” was given to the anatomical structure of the cruciate ligaments by the Greek physician Claudius Galen (201-131 BC) who emphasized their joint stabilizing role, but did not describe their function in detail [45]. It was not until the 19th century that the Weber brothers described the pathological anterior translation of the tibia in relation to the femur after transection of the ACL, nowadays used clinically to assess potential ACL tears in stability testing. At this time, most papers published by journals were case reports. In 1837, the Irish surgeon Robert Adams reported the first clinical case of ACL-related injury where a tibial spine fracture was found in a septic knee during autopsy 24 days after a knee injury sustained during wrestling [46].

In line with most surgery at this time, the first attempts of repairing ruptured ACLs must be considered as experimental. Sir Arthur William Mayo-Robson reported to have performed the first known bicruciate repair in 1895 using a direct suture technique with catgut. The patient reported his leg as “perfectly strong” at a 6-years follow-up visit [47]. In the 20th century, different methods with suturing technique to

achieve a direct repair were described. The famous Palmer suture technique of Ivar Palmer for primary repair of acute ACL injuries was explained in his thesis published in 1938 [48]. The technique was popular and laid ground for the treatment of acute ACL injuries in the years to come. The concept of primary suture was further described by Don O'Donoghue who, like Palmer, argued for the importance of early surgery for success of the repair [49].

6.7.2 Fascia lata grafts

When the clinicians acknowledged patients with chronic knee laxity, they realized they needed other treatment options than early repair. In 1917, Ernest William Hey Groves published a short case report with patients he had treated with an intra-articular technique of ACL reconstruction with an autologous ilio-tibial band graft.

He used a strip from the entire fascia lata

loosened from its tibial insertion, threaded through bored femoral and tibial tunnels, and the distal end of the graft sutured to the deep fascia and periosteum of the tibia (Figure 2) [50].

Together with Alwyn Smith, who further presented an ACL reconstruction technique based on Hey Groves description, but with the distal end of the graft further used for a MCL augmentation [51], the two are known as pioneers in ACL reconstruction with an anatomic approach to the drilling of the bony tunnels.

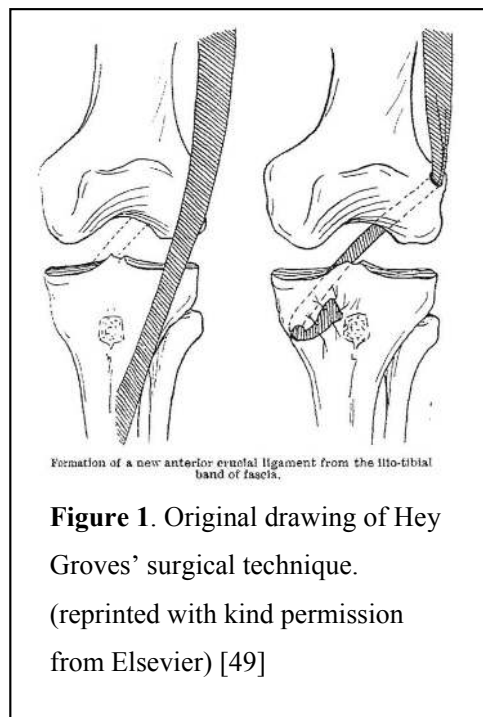


Figure 1. Original drawing of Hey Groves' surgical technique. (reprinted with kind permission from Elsevier) [49]

6.7.3 Hamstring tendon grafts

Surgery for stabilization of the knee-joint continuously developed, and in 1934 the Italian surgeon Riccardo Galeazzi used the same anatomic landmarks as Hey Groves for tunnel placement, but used a semitendinosus (ST) graft with a preserved

attachment in pes anserinus sutured to the periosteum of the lateral femoral condyle [52]. Several surgeons used the gracilis or the ST tendon with its proximal attachment to the muscle/tendon unit intact, giving the possibility of dynamic stabilization [53, 54]. In 1981, Brant Lipscomb published his experience with combining the gracilis with the ST tendon. He kept the distal attachment of the two tendons, sutured them together with a Bunnell-type suture and passed through bony channels “at the approximate site of origin of the anterior cruciate”. The graft was then fixed with sutures to the periosteum of the lateral femoral condyle with the knee at 75° flexion [55]. The principle of Lipscomb’s technique was further developed into today’s 4-6 strand hamstring tendon (HT) reconstruction techniques with a variety of fixation implants available.

6.7.4 Patellar tendon grafts

When considering the knee extensor complex as a source of graft for ACL surgery, Ernst Gold from Vienna was in 1928 the first to describe the usage of a strip from the medial patellar retinaculum and tendon attached distally at its original insertion. He passed the graft through a tibial tunnel and sutured it to the posterior cruciate ligament [56]. In 1936, Willis C. Campbell described a technique using tendinous tissue of the medial patellar tendon and quadriceps tendon with its original distal insertion, but through bony tunnels of both the tibia and femur drilled according to Hey Groves’ anatomic landmarks. He sutured the graft to the periosteum on the femoral side [46]. By 1963, Kenneth Jones was the first to report the use of a bone block from the patella. In addition to the bone block, he harvested the central third of the patellar tendon keeping the original patellar tendon insertion on the tibia intact. The procedure was popularly known as “the Jones procedure” [57]. Due to the short graft produced and the inability to position this anatomically at the femoral attachment, Helmut Brückner published a further modification in 1966 with the addition of a tibial tunnel to give the graft more length by shortening the distance to

its original distal insertion. The graft was fixed proximally with sutures attached to a metal button resting on cortical bone [45], a construct similar to the suspension devices used in modern ACL reconstruction.

Kurt Franke described the reconstruction technique with a free patellar tendon graft with bone blocks in both ends, the so-called bone-patellar tendon-bone (BPTB) graft. He used press-fixation in the femur and tibia with pieces of bone and published the first long-term clinical results in 1976 [58]. In 1982, William Clancy published his experience with free BPTB grafts. He fixed the grafts with sutures through drill-holes in the bone blocks tied over a plastic buttons or around staples (Figure 3). In addition, he made dynamic muscle transfers of the lateral hamstring attachment and pes anserinus to compensate for capsular laxity [59]. The reproducible good outcome and clearly described procedures lead to that Jones, Brückner, Franke and Clancy are typically credited for the increased popularity of ACL reconstruction with

BPTB graft that led to its status as “gold standard” in the later part of the 20th century.

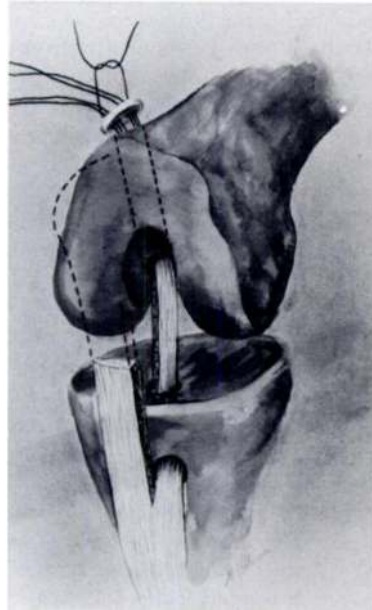


Figure 2. Initially, Clancy used the medial third of the patellar tendon keeping the distal attachment, which often left the graft too short. He later routinely used a free graft with a bone blocks in both ends. (reprinted with kind permission of Wolters Kluwer Health, Inc.) [58]

6.7.5 Quadriceps tendon grafts

Considering the graft site morbidity of the autologous BPTB and potential adverse effects such as patellar fracture, the quadriceps tendon (QT) was described as an alternative graft by Walter Blauth in 1984 [60]. In addition to the tendinous part of the quadriceps, he used a distal bone block from the upper part of the patella forming

a quadriceps tendon-bone (QTB) graft. The tendon part was divided in two for a double bundle reconstruction. One bundle was placed in a femoral tunnel and the other “over the top” around the lateral femoral condyle. The fixation in the tibia was accomplished through a press-fit fixation of the bone-block. The graft harvest was described as more demanding [61] and the graft did for some reason initially not gain as much popularity as other autografts. Recently, the outcomes of using the graft is being further evaluated and it is being used in both primary and revision reconstructions [61-64].

6.7.6 Allografts

The rationale of using an allograft instead of an autograft to avoid graft site morbidity seemed appealing and started a great interest in the 1980s. Based on successful reports of allografts in animal models [65], Konsei Shino presented in 1986 2-year results for 31 patients of whom 30 were considered as successfully treated as they had returned to sporting activities. They used freshly frozen tendon grafts from amputation specimen or fresh cadavers, stored at -80°C for at least 10 days, fixed in the femur and tibia with sutures tied over a button in addition to staples when the graft-length was sufficient [66]. The following years, several authors published good results using allografts. However, the risk of transmission of viral infections made an obvious impact on the popularity. In addition, sterilization methods used, especially irradiation, was found to alternate the collagen structure and biomechanical properties of the allograft [67]. Allografts remains popular today in some countries for primary reconstructions and in particular for revisions and multiligament reconstructions, despite that the failure rates have been reported to be higher compared with autografts [68, 69].

6.7.7 Synthetic grafts

The first experience made with a synthetic graft in ACL reconstruction was in the early 20th century using silk. Alwyn Smith, previously mentioned for his usage of fascia lata grafts, documented a patient treated with a silk graft for his chronic ACL deficiency. He fixed the fascia lata graft in the femur “by a wire keeper which was hammered into the bone”, probably similar to today’s staples, and in the tibia he

sutured the graft to the periosteum and the “infrapatellar tendon”. After 10 weeks of immobilization, increased passive movements was started and signs of synovitis began. In the 11th week “a small sinus appeared at the lower end of the wound”, together with rising temperature. The patient was revised, and Smith described that “the whole joint was extremely congested” He interpreted this as a foreign body reaction [51]. We can only speculate if this could possibly have been an intraarticular infection.

In 1914, Dr Edred M. Corner described an attempt of stabilizing a chronic ACL deficient knee in a 29-year-old healthy man with two loops of silver wire interlaced in the joint (Figure 4). He used a somewhat extensive approach to the knee joint, with a longitudinal incision and splitting patella in two to make access. However, Corner reported that the two wires broke, together with the “apparatus” (orthosis?) that was given to the patient to limit the joint motion. No further follow-up was reported [70].

Silk was used as a sort of augmentation device by Ludloff in 1927, as he wrapped it in a free fascia lata graft [71]. He avoided fixing the augmented graft nor proximally or distally with the idea that it would find its own tension equilibrium, and reported good outcome in a farmer presenting 5 months after the operation.

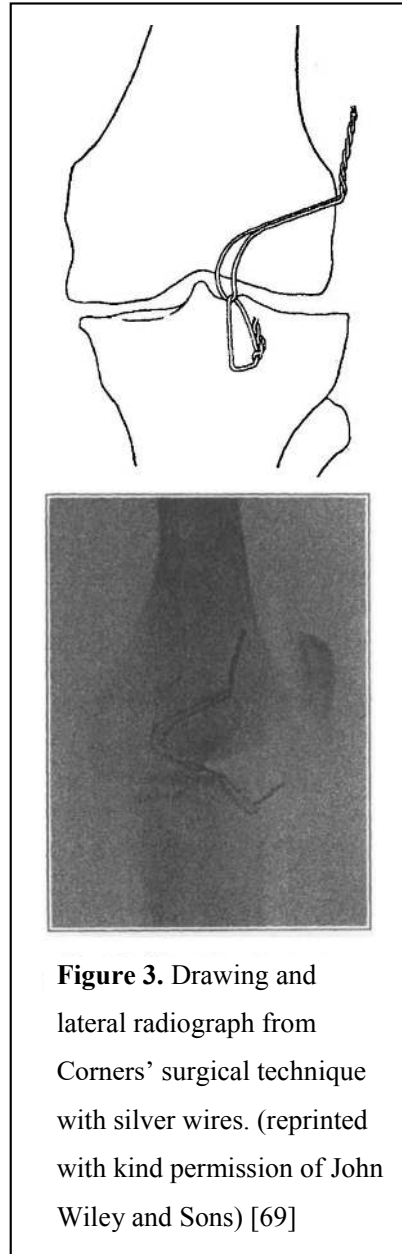


Figure 3. Drawing and lateral radiograph from Corners' surgical technique with silver wires. (reprinted with kind permission of John Wiley and Sons) [69]

A various of synthetic grafts was developed in the later 20th century, made out of Supramid®, Teflon®, Dacron®, GORE-TEX® as examples, either used in isolation or as an augmentation device. To surpass the imperfection of a single material, the industry also produced combination of materials with desirably characteristics (ABC®, Activated Biological Composite). The results were discouraging [72-74], with acceptable results in low as 14% of the patients after 9 years [75] with Dacron® grafts.

Jack Kennedy introduced the “Kennedy-LAD”, a polypropylene augmentation device in the 1970’s. The rationale was that it would share the load with the autogenous graft, “protecting the autogenous structure during its critical first year”. It was sutured together with autogenous tissue, and attached on the lateral femoral condyle in an “over the top” position [76]. In 1990, Lars Engebretsen published the results of a prospective randomized study with 2 years follow-up of 150 patients. The patients were treated with either Kennedy-LAD augmentation, primary repair with Palmer suture or reconstruction with a free mid-third BPTB graft. The groups had similar results after 1 year in terms of activity level. At 2 years follow-up, the BPTB group improved significantly, whereas the primary repair group worsened and the Kennedy-LAD group did not improve [77]. The following years the encouraging results with autologous free grafts reduced the interest for synthetic grafts, which was barely in use up until today.

However, the industry has lately developed and is pushing new methods of augmentation with synthetic grafts in combination with direct suture of the ACL or PCL [78]. Patient selection with these techniques of repair seems crucial [79-82]. Even though good short term-results have been reported [83], the long-term results and comparison to an ACL reconstruction in a randomized study is still missing.

6.8 Modern treatment of an ACL injury

Even though that the same grafts are used today as more than 50 years ago, new technology and research has improved the equipment available for the surgeon to perform a safe and reproducible procedure. In addition, the introduction of evidence-

based medicine protects the patients from experimental treatments. There has also been substantial work done mechanically testing the effect of different anatomical knee structures on knee stability, giving the surgeon a broader insight of the complex knee joint.

Nowadays, there are two main options for treatment of the ACL-deficient patients – surgical or non-surgical, both with physical rehabilitation. Whilst it seemed rather by chance who was surgically treated for an ACL injury 100 years ago, today's approach is to individualize the treatment dependent on several patient factors. It is somewhat widespread that high-level athletes, in particular performers of pivoting sports, are likely to profit from a stabilizing ACL reconstruction. Other concomitant injuries, such as meniscal lesions, can strengthen the indication for an early ACL reconstruction [84-86]. The higher risk of subsequent meniscal or chondral injuries in the non-reconstructed ACL deficient knee is also often held as an argument for early surgical reconstruction [87-90], as those injuries further worsen the prognosis substantially for premature osteoarthritis (OA) [91]. A common approach in Scandinavia for the average patient is to start initial rehabilitation with close follow-up. If the patient in the follow-up period reports instability symptoms or sustains subsequent meniscal or cartilage injuries, there is a relative indication for ACL reconstruction. With that, the patient has already started the rehabilitation, and the outcome after surgery might be better with the preoperative rehabilitation than without [92]. This strategy could be influenced by the results of Frobell et al's RCT comparing initial ACL reconstruction with rehabilitation alone and choice of later reconstruction. They found no difference between the groups at 5-year follow-up [93]. However, the study was criticized on several points [94, 95]. A recent Cochrane review concluded that there is a low-quality evidence that there is no difference between surgical and non-surgical treatment, and that further research is needed [96].

6.8.1 Non-operative treatment of ACL tear – physical rehabilitation

The primary goal of the rehabilitation program is to reestablish joint function in terms of joint mobility, neuromuscular control, and muscle strength. A physiotherapist should monitor the rehabilitation, either as a home-based or clinic-based program.

Similar to post-operative rehabilitation, it should consist of goal-based phases with appropriate test batteries before entering a new phase [97].

6.8.2 Arthroscopically assisted reconstruction of the ACL

Since David Dandy did the first reported arthroscopically assisted ACL reconstruction with a synthetic graft in 1980 [98], the arthroscopic technique has gradually replaced the open technique. Initially, a 2-incision technique was popular. A rear-entry guide was used to create the femoral tunnel with outside-in drilling through a skin incision on the distal lateral thigh. The second incision was made over the proximal tibia for graft harvest and preparation of the tibial tunnel [99]. When the offset guides became available, there was only need for one incision, the distal skin-incision, and the femoral tunnel could be drilled either through the tibial tunnel (transtibial technique [TT]), or through an anteromedial (AM) portal. In spite of the potential advantages of the one-incision technique being less invasive [100], most of the clinical studies at that time and a recent Cochrane review did not find any difference in outcome between the two techniques [99, 101-104]. Nevertheless, the 1-incision technique became more popular in the late 1990's and beginning of 2000, probably due to a shorter duration of surgery with less surgical trauma and scars [99].

6.8.3 The anatomic ACL reconstruction

The positioning of the femoral graft tunnel with the TT technique is severely limited as the reamer has to be inserted through the tibial tunnel. The femoral tunnel often ends up in a non-anatomical position, high in the intercondylar roof compared with the native ACL footprint [105-107]. In 1995, John B. O'Donnell for the first time described the advantages of using an accessory AM portal for reaming of the femoral tunnel. This technique was reported to achieve a more anatomical femoral tunnel position, to decrease the risk of interference screw divergence, graft laceration and "blow-out" of the posterior wall of the femoral tunnel [108]. Both cadaveric and clinical studies have shown that anatomical femoral tunnels gave better rotational stability, compared with tunnels from the TT technique [109-112]. The AM technique is considered the gold standard today.

To mimic the anatomical appearance of the ACL with two bundles, a double-bundle

(DB) technique with separate bone tunnels and grafts for the AM and PL bundle is in use. Mott et al published his DB technique already in 1983, an open reconstruction technique with a semitendinosus graft that he had used since 1978 as a salvage procedure [113]. It was not until Takeshi Muneta and Kazunori Yasuda presented early clinical results in the early 21th century that the arthroscopically assisted DB technique was further popularized [114, 115]. However, lack of consistency of superior results for the DB reconstruction and the reported complications with this more technically demanding procedure may explain its low popularity [116-120].

6.9 Current graft selection

The graft choice is likely to be dependent on surgeons' preference and local guidelines, in addition to recommendations in the current literature for different patient groups [121]. There are substantial differences in graft choice between countries – HT and BPTB autografts are the most popular choice in many European countries (Figure 5) while a larger proportion of allografts is used in some parts of the United States [122].



Figure 5. An 8 mm 4-strand HT graft attached to a 15 mm Endobutton CL Ultra (on top) and a 9 mm BPTB graft. (printed with patients' approval)

6.9.1 Mechanical properties of grafts compared to the native ACL

The ultimate graft should resemble the mechanical properties of the native ACL. The mechanical testing of grafts often describes the ultimate load to failure and is measured in Newton (N), whereas the stiffness of the graft is measured in force per unit elongation (N/mm). In a cadaver model with the knee at 30° flexion, the native ACL was found to have an ultimate load to failure of 2160 N with a stiffness of 242 N/mm in a laboratory test in young specimen by Woo et al [123]. The force was applied in an axis vertical along the ACL. Similar results were found by Rowden et al [124], but they had the tested cadaver knees at 60° flexion. Hamner et al tested human cadaveric 4-strand HT grafts in a testing machine applying axial tension, resulting in a load to failure of 2831 N and a stiffness of 456 N/mm [125]. To avoid graft slippage, they fixed the two ends of the grafts in clamps with chambers filled with dry ice. Ferretti et al reported similar results in a study with the same principle of graft fixation to the testing machine [126]. Before applying tensile force, they rotated, bent and translated the graft to imitate an in vivo loaded situation. Schatzmann et al investigated the mechanical properties for human cadaveric BPTB grafts and found an ultimate load to failure and stiffness of 1953 N and 423 N/mm respectively [127]. They also used a cryofixation method of the grafts to their testing machine, similar to Hamner et al. In a comparison between quadrupled HT and 10 mm BPTB grafts, Wilson et al found that the grafts had similar stiffness (HT: 238 N/mm, BPTB: 210 N/mm) but the HT had a higher maximum load to failure (2422 N versus 1784 N). For the BPTB grafts, they inserted two threaded pins through the boneblocks cemented into a metal casing, whereas they used cryofixation in clamps for the two ends of the HT grafts prior to testing.

The laboratory tests conducted vary slightly in methodology, which limits their direct comparability, but they provide some evidence of similarity between the native ACL and the mentioned grafts.

6.10 Graft fixation and healing

Although the grafts seems to have appropriate mechanical properties, it is suggested that the fixation of the graft is the most fragile part of the fixation-graft complex before sufficient graft-to-bone healing is achieved [128]. The time to sufficient graft healing in a human is not known since most studies on the topic are done in animal models [129]. Beynnon et al obtained the reconstructed and the normal knee from a patient who had a BPTB ACL reconstruction 8 months prior to his suicide. They found that the stiffness and ultimate load to failure of the graft was almost 90% to that of the normal ACL, suggesting an acceptable graft healing at that time [130]. In a recent systematic review of human studies presenting histological results, slower graft-to-bone healing was found with soft tissue grafts, and it is expected that an indirect tendon-to-bone insertion with histologic findings of Sharpey-like fibers exists from 10 months postoperatively [131]. Rodeo et al found in a dog model that the failure at pull-out no longer occurred in the tendon-bone interface after 12 weeks of healing of the extensor tendon in a tibial bone-tunnel. They found this to be correlated to the histological bony ingrowth of the tendon [132]. However, in humans, the total length of the incorporation and remodeling of the graft, the “ligamentization”, is unknown [133]. In a magnetic resonance imaging (MRI) study of patients with BPTB grafts signs of a revascularization process were still detectable 12 months postoperatively, suggesting that there was still an active healing process at that time [134]. Some authors have claimed that the graft does not reach maturity until 2-3 years postoperatively [135, 136].

It is paramount that the fixation of the graft allows for a safe graft healing during rehabilitation. The graft-fixation complex consists of a femoral graft-fixation site, a central tendinous component and a tibial graft-fixation site. An ideal graft-fixation complex should have the following characteristics

- The graft fixation technique should be user-friendly, allowing for a repetitive and safe fixation procedure
- The implants should be biocompatible
- Until sufficient graft healing, the graft-fixation complex should have

-
- Strength: enough to withstand peak forces without displacement
 - Stiffness: enough to resist significant load displacement
 - Resistance to slippage: enough to avoid graft-fixation displacement during cyclic loading

Most studies on fixation methods have been laboratory testing in models either using human cadaver, porcine or bovine knees, with varying study methods [137]. There is a debate whether an animal model is appropriate as differences have been found when investigating fixation properties in human and animal tissue [138]. In addition, the strength of the fixation is often dependent on the bone density of the specimen, and the results from old human cadavers might not be valid for the younger population undergoing ACL reconstruction [139, 140]. The setup of the biomechanical testing could also affect the results depending on the orientation of the specimen, whereas a force applied in the axis of the bone tunnel will put an ultimate test to the fixation point. These results might not be fully applicable to the “in vivo” environment where the direction of the force from the graft is oblique in relation to the femoral tunnel and fixation [141].

6.11 Principles of graft fixation

Fixation methods vary according to location and graft and we can categorize them according to their principle of fixation:

6.11.1 Anatomical fixation / Aperture fixation

When fixation of the graft occurs at the anatomical insert of the ACL / aperture fixation, an interference screw is typically used. The point of fixation is close to the joint-line, hence anatomic, and the interference screw compress the graft to bone. In terms of cyclic displacement and ultimate load to failure, most studies found acceptable findings for interference screws in both the tibia and femur [142-144]. However, concerns of increased graft slippage in cyclic loading in the tibia have been discussed [138, 144, 145].

6.11.2 Non-anatomic / Suspensory fixation

In the non-anatomic fixation / suspensory fixation, the graft is interlaced or looped into a rigid or adjustable polyester loop device, such as Endobutton (Smith & Nephew), or Tightrope (Arthrex). These are primarily implants for soft tissue grafts, where the ultimate fixation point, a metal button, rests on a cortical button. They are also in use for BPTB fixation, with the theoretical advantage of a 360° bone-to-bone healing between the bone block and the tunnel. Biomechanically, the traditional rigid suspensory devices have had good material properties [143], but lately the adjustable loop devices has been found to elongate in cyclic loading [146-148]. It is still uncertain if this affects the clinical results.

The graft can be fixed with sutures over a post, typically an AO screw with a washer on the tibia, or with a spiked clamp securing the graft to a non-anatomical point distal to the bone tunnel.

6.11.3 Transfixation with cross-pins / Transfemoral fixation

In transfixation with cross-pins, biodegradable or metal pins are inserted through the lateral or medial condyle to both pierce and fix the graft or for the graft to be looped upon. The fixation point will be close to the joint, but not anatomic. The piercing of the graft by cross-pins leads to a local expansion of the graft volume compressing the graft towards the bone tunnel, theoretically advantageous for graft healing.

6.11.4 Combination devices

Combination screw and sheet devices are only available for tibial fixation. There are several soft-tissue fixation implants that combines a screw and a sheet, but the principle of fixation is identical. The sheet is inserted into the tibial bone tunnel, often after dilatation, and thereafter the legs of the soft tissue graft are spread and the screw is centrally inserted within the sheet until flush with bone.

6.11.5 Fixation device material

The implants are either “biodegradable” or non-degradable. The non-degradable implants are traditionally made of titanium, but implants made out of plastic polymers such as polyetheretherketone (PEEK) thermoplastic are also available.

Degradable or bioabsorbable materials, often Poly-Lactic Acid (PLA) thermoplastic polymers, are supposed to disintegrate and eventually be replaced with bone. PLA can be derived from e.g. rice or wheat, and are not petroleum-based like other plastics. The polymers synthesized have hydrolytically unstable linkages in its backbone [149]. In living organisms, after hydrolysis, the remnant polymers (α -hydroxy acid) are incorporated in the tricarboxylic acid cycle of the cells. The hydrolysis and degradation of the material is dependent on many factors, such as the degree of crystallinity of the polymer, but it has also been shown that implants that are stressed might degrade faster [150]. A commonly used stereoisomer of PLA for graft fixation implants is Poly-L-Lactic Acid (PLLA). PLLA is a semi-crystalline polymer, giving it desirable strength and stiffness, and a theoretic degradation time of 12 to 16 months [151, 152]. Sometimes, the PLA polymer is combined with hydroxyapatite (HA), a natural element in bone, for a theoretically faster bone replacement.

The reported disadvantages of metal implants compared with non-metal were distortion of postoperative MRI, potential increased risk of laceration of the graft at insertion and problems with hardware removal at a later revision surgery [153]. On the other hand, several adverse effects have been reported with biodegradable screws, such as local pretibial irritation with cyst formation and screw breakage [154, 155]. In a MRI study, Drogset et al found that the disintegration of a PLLA screw 2 years postoperatively was two thirds of its original size, whereas Thompson et al found no radiological evidence of disintegration of the tibial PLLA interference screws 4 years after surgery, but complete resorption 10-16 years postoperatively [156].

6.11.6 What fixation are used today?

A recent international multi-register study found that the interference screw was the most commonly used fixation in the tibia, with varying material choice in Europe and bioabsorbable materials reported from a community-based ACL register in the United States. All national European registries reported that the most common femoral fixation technique was by a suspensory device, while the United States based register reported a metal interference screw to be most popular femoral fixation amongst the surgeons [122].

6.12 Outcome after ACL reconstruction

6.12.1 Outcome measures

It is paramount that the correct outcome measures are chosen in clinical studies to be able to detect the treatment effect in question [157]. In clinical ACL research, more than 54 outcome scores have been found to be in use for the ACL deficient knee [158]. Ahmad et al investigated the effect on citation probability the outcome measure had in highly cited articles. They recommended to combine instrumental and clinical testing, subjective outcome measures and to report graft failure as outcome measures [159]. Other studies highlighted the use of the Knee Injury and Osteoarthritis Outcome Score (KOOS) [160], especially the subscores “quality of life” (QoL) and “sport and recreation”, which were found to be most sensitive to changes in perceived knee function after ACL reconstruction [161, 162]. In addition, the KOOS QoL score <44, proposed as a measure of treatment failure by Frobell et al [163], has been found to be a risk factor for prospective graft failure [164].

6.12.2 Return to sport and activity score

The majority of patients undergoing ACL reconstruction are active in sports, recreational or professional, and have a wish to return to their pre-injury activity level. Ardern et al performed a meta-analysis and systematic review [165], reporting that 82% had returned to sports participation, of whom 64% returned to the preinjury activity level. The return-to-sport rate might vary between different sports and were found to be high for high-performance athletes, but the available literature on the topic was questioned and believed to be insufficient and of low quality [166].

6.12.3 Subjective outcome

In a systematic review of 11 randomized, controlled trials, with a minimum of 24 months follow-up, Lewis et al described baseline data for single bundle ACL reconstructions. They found a high patient-satisfaction (>90%), with most patients (74%) in the overall International Knee Documentation Committee [167] (IKDC) system grade A or B, corresponding to normal or near normal knee function. Most of the studies included reported a median Tegner score [168] at follow-ups to be ≥ 5 [91]. In

contrast, Ingelsrud et al conducted a cross-sectional register study of 598 patients, and found that only two thirds of the patients reported acceptable results 2 years postoperatively. Of the remaining third, 10% reported that they believe the treatment was a failure [169]. The discrepancy of reported patient-reported outcome between those studies might be influenced by what information the patients received preoperatively of the expected result.

6.12.4 Failure rate

The reported postoperative failure rates varies, possibly due to a heterogenic definition of failure between studies. From the results of systematic reviews, one can expect that between 3.5-7% of the autografts have failed at 2-year follow-up [91, 170]. In clinical trials with more than 10-years follow-up, most failures occurred the first 5 years, and the reported proportion of graft rupture varied between 5-17%. Half of the patients were in need of additional surgery in the index knee [171-175].

6.12.5 Post-injury osteoarthritis

The ACL injury has been found to lead to an increased risk of secondary meniscal tears, secondary OA, and a higher risk of undergoing a total knee arthroplasty (TKA) compared with an uninjured knee joint [176]. On long term, 10 to 20 years from injury, a 10-fold increased risk of OA has been reported compared to normal knee joints [177]. 20 years after ACLR, in total 42% of the patients had radiographic findings of OA in the knee in a prospective study by Risberg et al [178]. The authors accentuated that a majority of the patients (57%) with concomitant injuries (meniscal or cartilage lesions at the time of ACLR or subsequently during the follow-up) had radiographic OA at 20 year-follow up, whilst only 16% in the group of patients without.

Unfortunately, no treatment for an ACL injury has so far consistently been recognized to reduce the risk for developing knee OA [179]. Considering the potential protection from subsequent meniscal injuries and the increasing focus on meniscal repair at the time of reconstruction [180], it will be interesting to see if there will be a shift in indication for early ACL reconstruction in the future.

6.13 Why is this thesis needed?

As of 24th January 2019 searching for “ACL” on PubMed results in 23,942 hits, of whom 2,135 research items were published in 2018. Despite this, there is still a debate on surgical indication, best surgical technique, and surgical timing.

A universal outcome measure after ACL reconstruction has not been defined.

However, undergoing revision surgery after ACL reconstruction must be considered a robust outcome measure for failure. This thesis will try to further outline risk factors for revision ACL reconstruction, and hopefully provide another piece in the puzzle of joint preservation and better outcome after initial ACL reconstruction.

7. Aims of thesis

The overall objective of this thesis was to investigate the influence of surgical technique and patients' characteristics on the revision rate and risk of revision after primary ACLR.

The specific aims of the three papers were:

- To describe the yearly usage of HT and BPTB grafts in Norway (paper I)
- To investigate the influence of sex and age on the risk of revision (paper I)
- To compare the revision rates and revision risk for HT with BPTB grafts in Norway (paper I)
- To describe the most commonly used fixations for HT and BPTB grafts used in ACL reconstructions in Norway (paper II) and Scandinavia (paper III)
- To compare the revision rates and revision risk for the most common combinations of fixations of HT and BPTB grafts used in ACL reconstructions in Norway (paper II) and fixation methods in Scandinavia (paper III)

8. Material and methods

8.1 The Scandinavian knee ligament registries

8.1.1 The Norwegian National Knee Ligament Register

In 2004, Granan et al published an overview article describing the trends in ACL surgery in Norway. The authors had distributed a questionnaire asking for information on surgical treatment of cruciate ligament injuries at 83 hospitals in 2002, and they compared the result to a similar study from the 1980's. They found a great diversity of how the ACL reconstructed patients were treated, and suggested to start a register to monitor cruciate ligament reconstruction in Norway [25], similar to the Norwegian Arthroplasty Register (NAR) [181].

The Norwegian National Knee Ligament Register (NNKLR) received its authorization from the Norwegian Data Inspectorate in 2004, and was at the start the first of its kind in the world. It was initially a surgical register, but since 2017 patients treated non-operatively can be included in the register. All patients must sign an informed consent before information can be registered. Reporting to the register was previously voluntary for the surgeon, but has been compulsory since 2016. The register collects data through a paper form or through a secure web-based interface entered by the surgeon immediately after surgery, in addition to patient reported outcome measure (PROM). On the surgical form, patient- and injury-related information are described, in addition to information on the cruciate ligament injury with potential concomitant injuries, graft choice, fixation of grafts, meniscal and cartilage surgery and other surgical details. Patients' age and gender are automatically rendered through the patient's unique social security number, which also allows for linkage of index operation to potential subsequent surgery. Stickers with specific reference numbers delivered by the manufacturer of the implants used during the surgery are attached to the paper form. In the web-based interface, the implant barcodes are scanned and connected to the digital surgery form. The paper forms are sent to the register per mail where they are checked for completeness and potential errors. If necessary, the register returns the form to the hospital for completion. In the

digital form, if mandatory information is missing the form cannot be completed, ensuring data completeness.

The PROM data is collected preoperatively and at 2-, 5-, and 10-year follow-up through the KOOS questionnaire sent by mail. Lately, the patient can deliver the questionnaire electronically.

The Norwegian National Advisory Unit on Arthroplasty and Hip Fractures (NNAUAHF) (former NAR) runs the NNKLR, and the data is stored on a secure server. For later research, a depersonalized research file is distributed upon approval of the research application by the NNKLR's steering committee and leader of the NNAUAHF.

The compliance for reporting primary cruciate ligament reconstructions is investigated every second year and has been found to be 86% in 2008-2009 [182] and 84% in 2015-2016 [24]. Annual reports gives surgeons and departments feedback on their treatment practice.

8.1.2 The Swedish and Danish national knee ligament registries

The Swedish National Knee Ligament Register (SNKLR) and the Danish Knee Ligament Register (DNKLR) were started in 2005 and are similar to NNKLR in terms of data collection and processing, and follow-up of the patients. However, some differences exist. SNKLR have used a web-based protocol for data collection since the start. The reporting to the register is mandatory in Denmark since 2006 but voluntary in Sweden. Patient consent has not been necessary for SNKLR since the start, and for DNKRL since 2006.

Both registries collect preoperative PROM in form of KOOS; in addition to follow-up in SNKLR at 1, 2, and 5 years and in DNKLR at 1, 5, and 10 years postoperatively.

In addition, SNKLR asks patients to report EQ-5D as a complementary PROM preoperatively, and DNKLR collects data from clinical follow-up regarding knee stability, complications and Tegner functional score at 1-year follow-up.

The compliance for the surgical forms has been found to be 84-85% and >90% in DNKLR and SNKLR respectively [183-186].

8.2 Statistics

8.2.1 Statistical analysis

We performed the statistical analyses using SPSS version 21-22 (SPSS Inc, Chicago, Illinois). The significance level was set to 0.05 and all tests were 2-sided.

When comparing groups for possible differences, we used the Pearson chi-square test for categorical variables and the Mann-Whitney U test or independent Student t-test for continuous variables. For calculation of unadjusted revision rates and revision curves, Kaplan Meier estimation and survival curves were established [187].

Multivariable risk analyses including possible confounding factors were assessed with Cox regression analyses [188]. We used revision surgery as the endpoint for the Kaplan Meier estimates and Cox regression model. Clinical risk factors for inferior outcome were tested as possible confounding factors in univariable cox regression models, and entered into the multivariable analysis if the p-value<0.2. We tested the assumption of proportional hazard by evaluating the log-minus-log plot and Schoenfeld residuals [189], which were found suitable.

8.3 Ethical considerations

No further ethical evaluation through a committee was necessary for using the depersonalised data of the registries according to the authorization from the Data Inspectorate in Norway, the Patient Data Act in Sweden and the General Data Protection Regulation in Denmark.

9. Summary of papers

9.1 Paper I

Increased risk of revision with hamstring tendon grafts compared with patellar tendon grafts after anterior cruciate ligament reconstruction: a study of 12,643 patients from the Norwegian Cruciate Ligament Registry 2004-2012

Background: Graft choice for ACL reconstruction is controversial. HT and BPTB autograft are the most commonly used grafts and have shown similar subjective and objective outcomes.

Purpose: The objective of the study was to compare the revision rate between HT and BPTB used in ACLR in Norway and to estimate the influence of age and gender.

Methods: All patients with primary ACLRs without concomitant ligament injury registered in the Norwegian National Knee Ligament Register from 2004 through 2012 were included in the study. The cohort was stratified in age groups (15-19 years [y], 20-29 y, ≥ 30 y), and according to graft type (HT or BPTB). 1-, 2-, and 5-years revision rates were calculated using Kaplan Meier analysis. HRs for revision were calculated using multivariable Cox regression models.

Results: With a mean follow-up of 4.0 years, 12,643 primary ACLRs were identified, 3,428 PT and 9,215 HT, among which 69 revisions for PT and 362 revisions for HT were performed. The overall 5-year revision rate was 4.2%. HT had a higher revision rate at all follow-ups compared to BPTB. When adjusted for sex and age, HR for revision was 2.3 (95% CI, 1.8-3.0) for HT compared with BPTB. The HR for revision in the youngest age group was 4.0 (95% CI, 3.1-5.2) compared to the oldest. Sex had no influence on revision rate.

Conclusion: Patients treated with HT graft had twice the risk of revision compared to patients with BPTB graft. Young age was the most important risk factor for revision while patients' sex showed no effect. Further studies should be conducted to identify the cause of the increased revision rate found for HT.

9.2 Paper II

Registry data highlight increased revision rates for Endobutton/Biosure HA in ACL reconstruction with hamstring tendon autograft: a nationwide cohort study from the Norwegian Knee Ligament Registry, 2004-2013

Background: There are no studies analyzing if the risk of revision after ACLR is influenced by the graft fixation, and if this could explain the difference in revision risk found between HT and BPTB.

Purpose: To estimate the influence on the risk of revision and revision rates for the patients with the most commonly used combinations of fixation for HT's with BPTB's in Norway.

Methods: The study included all primary ACLRs registered in the Norwegian National Knee Ligament Register from 2004 through 2013 with no concomitant ligament injury, excluding patients with combinations of fixations used in less than 500 patients. 2-year revision rates were calculated using the Kaplan-Meier analysis. HRs for revision at 2 years were calculated using multivariable Cox regression models.

Results: 14,034 patients identified with a mean follow-up of 4.5 years, 3,806 patients with BPTB and 10,228 patients with HT. In patients with HT, five combinations of fixations in the femur/tibia met the inclusion criteria; Endobutton/RCI screw (Smith & Nephew) (n=2,339), EzLoc/WasherLoc (Zimmer Biomet) (n=1,352), Endobutton/Biosure HA (Smith & Nephew) (n=1,209), Endobutton/Intrafix (Smith & Nephew) (n=687), and TransFix II (Arthrex)/Metal interference screw (MIS) (n=620). For BPTB patients, the 2-year revision rate was 0.7 (95% CI, 0.4-1.0). For the HT patients the revision rate ranged from 1.5 (95% CI, 0.5-2.4) for TransFix II/MIS to 5.5% (95% CI, 4.0-7.0) for Endobutton/Biosure HA. In a multivariable cox regression, the HR for revision at 2 years was increased for all HT combinations compared with BPTB. The combinations Endobutton/Biosure HA and

Endobutton/Intrafix had the highest HR's of 7.3 (95% CI, 4.4-12.1) and 5.5 (95% CI, 3.1-9.9), respectively.

Conclusion: The fixation used in HT ACLR may influence the risk of revision significantly. None of the examined combination of fixations for HT had an equally low revision rate as BPTB.

9.3 Paper III

Graft fixation influences revision risk after ACL reconstruction with hamstring tendon autografts

Introduction: The hamstring autograft is one of the most common grafts used for ACL reconstruction and a large number of fixation methods are available.

Purpose: To describe the current use of fixation methods in Scandinavia, and to compare the risk of revision between various femoral and tibial fixation methods.

Methods: A total of 38,666 patients undergoing primary ACL reconstructions in the period 2004-2011 were included from the three Scandinavian national knee ligament registries. The median follow-up time was 3 years (range 0 to 8 years). Fixation devices that were used scarcely were grouped according to the point of graft fixation and implant design. To compare the risk of revision between various fixation methods, we applied the multiple Cox proportional hazard regression model. HRs were reported as the measure of effect.

Results: The present study included a total of 1,042 revision ACL reconstructions. Based on a Cox regression model stratified for country and adjusted for gender, age at surgery (five-year categories), activity at the time of primary injury, femoral fixation, and tibial fixation, we found a significantly lower risk of revision for the transfemoral fixation devices Rigidfix (DePuy Synthes) (0.69 (95% CI, 0.57-0.83)) and TransFix (Arthrex) (0.74 (95% CI, 0.58-0.93)) compared with the cortical device Endobutton. The same model showed that the retro interference screw (Arthrex) used for tibial fixation had a higher risk of revision (1.91 (95% CI, 1.27-2.87)) compared with a standard interference screw.

Conclusion: In view of the findings in the present study, both femoral and tibial fixation method of hamstring autografts seem to be of significance when evaluating risk of revision after ACL reconstruction.

10. Discussion

10.1 Methodological considerations

10.1.1 Register studies as a method

Prospective observational studies are primarily used to provide epidemiological data and to detect prognostic factors [190]. They are in general hypothesis generating, rather than proving causality between treatment and outcome. Prospective cohort studies on data derived from medical quality register have several strengths. Large sample size can make it possible to study rare endpoints, As the data already exists at the start of study, the costs for research can be cut. The dataset is aiming to be complete for the target population thereby limiting selection and attrition bias, and increasing the external validity. Further, data are collected prospectively and independently of future research, which reduce the risk of recall bias and differential misclassification. Finally, an extensive time-line for long follow-up and adjustment for possible confounders in risk analysis is possible [191, 192]. However, register-based studies have several limitations that are important to consider. The collected data was selected by the register, and not by the researcher. This limits the research topics, and possible confounding factors might not be recorded or considered leading to biased results, so called “hidden confounding”[193]. Even though the Scandinavian national knee ligament registers collect relevant clinical data, some data that could affect the outcome might be unavailable.

Another important factor to consider in register research is the data quality.

According to a literature review by Arts et al [194], the quality attributes of a medical register most often cited was “completeness” and “accuracy”. With completeness meaning compliance of reporting to the register, the Scandinavian registries have a compliance rate of over >84%, as previously mentioned. The compliance rate is calculated comparing data from the countries national patient administrative systems with the data in the registries. The compliance is acceptable, but the steering committees of all three registries continuously aim to improve it.

With completeness, one also includes the attribute that all available data that are *to be*

reported, *are* reported. This type of data quality is difficult to fully validate, as it is not sure that it will be found elsewhere, for instance in the patients' medical journal. The accuracy of register data, meaning the fact that variable values are correct, can be estimated with validation studies. All three registries have performed validation studies, of whom the study from NNKLR is currently being finalized. The data in the registers was compared to the "gold standard", the data in the medical journal. Both SNKRL and DNKRL [183, 195] found good validity for the key variables used in this thesis. In the validity study of DNKLR, data on some cartilage lesions were often missing. Therefore, they simplified the registration of those injuries in hope to improve the accuracy of this variable. This highlight the importance of data reporting guidelines and variable definitions.

Other possible limitations that could introduce bias in prospective observational studies is the misuse of data when large datasets are available. "Data dredging" is a term describing a systematic search in a dataset for possible statistically significant findings, prior to establishing a research question. In the NNKRL, this is avoided by the need for an approved study protocol prior to delivery of the predetermined data. The use of post-hoc analyses could also introduce possible bias, as an analysis not specified in the study protocol is performed on the dataset [196]. In paper I, the peer-reviewers asked us to investigate the influence of graft choice in the risk of contralateral ACL reconstruction and the influence of body mass index on the risk of revision. We described these analyses as sub-analyses in the manuscript. Potentially, we could have refused to make such analysis because of the introduction of multiple testing, and rather suggest performing a new study with those research questions. We should have labelled the sub analyses as post-hoc analysis in paper I and II, investigating the main outcome of the two different time-periods, as a co-author proposed this in the process of writing of the manuscripts. This also includes the last sub analysis of paper II, comparing the intratunnel and extratunnel femoral fixations only for HT patients.

10.1.2 Observational studies and randomized controlled trials

In medical research, the gold standard study design to evaluate the effect of a treatment on the outcome is the randomized controlled trial (RCT), and in particular

systematic reviews of well-planned RCTs [197]. The randomization process is the only mean to avoid unmeasured group differences and to avoid allocation of one group of patients to one of the treatments, biasing the results [198]. RCTs do have limitations. Often, the studies have narrow inclusion/exclusion criteria, limiting the external validity of the results. Further, RCTs are time-consuming and expensive. This limits the possible numbers of patients that are possible to include, making studies on rare endpoints, such as revision ACLR difficult.

Previously, Benzon et al published a comparison of the treatment effects of RCTs and modern observational studies [199]. They argued that the traditional view of observational studies finding stronger and sometimes faulty treatment effects compared to RCTs is biased because landmark papers have used old observational studies in the comparison. In their study, they compared the results from observational studies published after 1984 to corresponding RCTs, and found that the treatment effects derived from the two study designs were, in most cases, similar. Concato et al did a similar study, using only comparison of RCTs to observational studies that did not use historical controls, resulting in the same conclusion [200]. The studies were criticized [201, 202] and other comparative studies of the results from the two designs did not agree with their conclusion [203-205].

It is, however, clear that observational studies from good quality clinical registers offers new possibilities compared with data from administrative databases [206], and that they should be seen as a compliment to randomized controlled studies, especially when the outcome in question is difficult to investigate with a RCT. The use of standardized reporting guidelines for observational studies, such as “Strengthening the Reporting of Observational studies in Epidemiology” [207] or “Reporting of studies Conducted using Observational Routinely-collected health Data” [208], has been proposed to further facilitate the quality of reporting observational studies [209].

10.1.3 Revision surgery as endpoint

Of possible endpoints in ACL research, undergoing revision surgery is a hard endpoint, which involves both the surgeon and patient in the decision-making. It will

not include all subjective and clinical failures, as they will not all undergo revision surgery. Because of the large amount of included patients in register research, the proportion of treatment failures not meeting the endpoint revision will most likely be evenly distributed. The question is then; will patients' characteristics, surgeons practice or surgery procedures affect the likelihood of the patient to undergo revision surgery and induce a *selection* or *indication* bias?

For patients' characteristics such as young age, a high activity level, and participating in knee-demanding sports will probably increase the willingness to undergo revision surgery. We have adjusted for age in the analyses of all studies. Unfortunately, the activity level was not reported to the registries during the study period. Clinics and hospitals with preferred grafts and fixation methods might attract patients with a higher or lower activity level, affecting the revision risk and introducing a sample selection bias. Other patient variations that might affect outcome include psychological factors and somatic comorbidity, which would normally be equally distributed between groups.

Surgeons have different experience and the indication for revision surgery might vary between surgeons, hospitals, and regions - creating an indication bias. We reported data for the reader to assess the likelihood of this potential problem in study II, presenting the number of hospitals using the different combinations of fixations and in what volume. The risk of this indication bias will likely decrease the more hospitals that have contributed in the different groups. Unfortunately, it is difficult to form an adjustment variable for this factor with the dataset available. To investigate the potential heterogeneity of the indication for revision, it is possible to distribute a questionnaire to the reporting hospitals.

Considering the effect of surgical procedures on the overall decision-making, particular implants could be technically harder to revise, and leaving a larger bone-defect in the tibia or femur. This could make the surgeon reconsider proceeding with further surgery. In paper II and III, the less frequently revised TransFix and Rigidfix would probably be slightly more difficult to revise than a suspensory fixation. That is, if the implant needs to be removed. If the femoral tunnel is positioned high in the

notch, a more anatomical tunnel could be placed lower and therefore avoiding the old tunnel with the implant.

Revision ACLR is not considered in all clinical ACLR failure, mainly for recurrent instability. If instability develops early (<6 months), the causes were often reported to be technical errors, premature exposure of risk activities, biologic failure or excessively aggressive rehabilitation. At a late development of instability (>6 months post reconstruction), causes such as a repeat trauma, tunnel misplacement, concomitant ligament laxity or general joint laxity were reported [210].

Up until the 1990's, technical errors, especially tunnel misplacement, was reported to be the leading cause of failure or revision ACLR in reports [211, 212], while more recent studies attribute the majority of failures to traumatic reinjuries [213-216]. In most cases, the cause of failure is multifactorial. Even if a single factor was identified as the main cause of revision, other factors will often have contributed. For instance, in a traumatic reinjury, the graft might have been able to withstand the trauma if the graft tunnels were either more or less anatomic, and vice-versa; in a knee trauma with an existing non-anatomic femoral tunnel, one type of graft might be more likely to withstand a tear at that certain time-point. For further investigation, we can conduct a study where we split the endpoint revision into the categories reported to be the main cause, maybe finding differences between the grafts or fixation techniques. This could generate further hypotheses built on the findings from the present thesis. For the studies conducted, we assumed that the causes of revision were evenly distributed between the groups.

10.1.4 Possible hidden confounders

Several important factors that could affect the outcome and revision-risk were not collected by the registries:

- Rehabilitation protocol and compliance
- Posterior tibial slope (PTS): PTS has been identified both as a risk factor for initial ACL injury as well as for single and multiple revision surgeries [217-220]. Increased PTS increases the force in the ACL graft in vitro, possibly

disturbing graft healing and may increase the risk for traumatic graft rupture [221].

- HT graft diameter: Several studies have associated smaller hamstring autograft diameter with failure [222-224]. The NNKLR collects data of graft size; however, this data is not complete and has therefore not been included in the studies.
- The effect of transtibially drilled femoral graft tunnels compared with tunnels drilled from an accessory anteromedial portal; will be discussed below

10.2 Results

The main results of this thesis were that several factors influenced the revision-risk after ACL reconstruction. While the strongest predictor for revision was patients' age, we found that the influence of the choice of graft also was significant. We do not know the reason for that the patellar graft is superior to hamstring graft for the outcome revision, but the choice of graft fixation may play a major role. It is, however, not certain if there are other inherent factors for a hamstring graft that contributes to the investigated measure of failure.

10.2.1 Patient age

The patient age at the time of reconstruction was found to be the strongest risk factor for revision after ACL reconstruction in paper I. Compared with patients ≥ 30 years, patients aged 15-19 had four times increased risk for revision surgery. In line with our results, young age has been consistently reported as a risk factor for failure after ACLR [175, 218, 225, 226]. The fact that the patient is young at the time of reconstruction is often demanding for the surgeon. The young patient does not always have insight in the severity of the injury and focuses on the short-term functional outcome. Due to their young age, they can ignore guidelines for rehabilitation and postoperative restrictions to a greater extent than the older patient. It is debated whether the surgeons should continue to stabilize ACL deficient knee joints in young patients enabling them to resume the same risk activity that might lead to further knee injuries. An approach with advocating a change in exposure for risk activities is

perhaps the right way to go, independently if the young patient is treated surgically or not.

Another contributing explanation could be that the young patient has a higher demand for knee stability as they might be more active. They would therefore be more prone to undergo revision surgery when the reconstruction have failed compared to an older patient, who might instead accept a change in daily activities.

10.2.2 Graft choice and fixation

In paper I, the main results were an increased risk of revision for patients with HT grafts compared with BPTB grafts. The estimated 1, 2 and 5-year revision rates were 1.1, 2.8 and 5.1% and 0.3, 0.7 and 2.1% for patients with HT and BPTB grafts respectively. Since then, several other register studies have reported a higher risk of revision for HT grafts [69, 215, 227, 228]. In conclusion, there seems to be uniform results from national registries that HT has a higher revision rate in comparison to BPTB [229]. However, in the available literature of clinical studies comparing the two grafts, most independent studies and meta-analyses found no difference between the grafts. They often have other outcome measures than register studies, but the samples size are as usually small and could be insufficient for the research question to be answered.

Mohtadi et al conducted a single-surgeon double-blinded RCT including 330 patients allocated to either ACL reconstruction with BPTB, HT or double-bundle (DB) HT with a minimal loss-to follow-up (3%) at 2 years [230]. Their report was on anatomical reconstructions and they used AM technique in the DB group. However, they used TT technique for the BPTB and HT group, except for when they could not achieve a femoral tunnel in the anatomical ACL footprint. Primarily, they used Endobutton in the femur and biodegradable interference screws in the tibia for graft fixation in all groups. Baseline patient's characteristic were similar between the groups. In their primary outcome measure, PROM at 2 years, they found no differences between the techniques. However, they found more traumatic injuries in the HT group (n=7) compared with the PT group (n=3) (p=0.05). They conducted their power-calculation based on the minimal clinically important change in PROM, and conclusions made for their secondary outcome traumatic reinjury might be

subject to a type 1 error. Out of the 15 patients that underwent revision surgery, 12 patients required staged revisions. One can therefore question if the reconstructions really were anatomical. Freedman et al reported a significantly higher failure rate with HT grafts compared with PT grafts in a meta-analysis of articles published from 1966 to 2000 [231]. With the large time-span of the studies, there was a heterogeneity of surgical techniques, and the definition of graft failure varies between the studies. Biau et al conducted a meta-analysis including 423 patients from 6 RCTs published between 2000-2006 [232]. They found a lower odds ratio (0.46) for postoperative knee instability favouring PT. Postoperative positive pivot shift was reported to be a valid indicator for worse functional outcome [233], and it is likely that this also increases the risk for revision ACLR.

Increased anterior knee pain from the harvest site has been reported for BTPB [234-237]. Post-operative pain may be worse with BPTB grafts, and could affect the patients' choice when considering revision surgery biasing our results. The potential donor-site morbidity of HT grafts, however, should not be underestimated. The ST and gracilis tendons insert on the medial side of the proximal tibia, and can therefore dynamically stabilize valgus, for instance in a cutting movement [238]. They further dynamically acts as agonists to the ACL, reducing the shear forces in anterior tibial translation [239]. Toor et al recently conducted a cadaver study aiming to quantify the importance of the medial hamstrings to knee kinematics. They found that in the medial hamstring-deficient cadaver knee, anterior translation, internal rotation and valgus motion was increased, discussing its relevance to graft choice [240]. Even though that the tendons of ST and gracilis have been reported to regenerate into tendon-like structures in some patients [241, 242], the hamstring function might not be normalised [243]. Zebis et al found that preactivation found by EMG of the semitendinosus during a cutting manoeuvre was a protective predictor for primary ACL injury [244]. Consequently, the impaired medial hamstring function after harvest for ACLR [245-248] might contribute to the failure of HT reconstructions. Several authors have reported an increased risk of contralateral ACLR (CACLR) when using BPTB. Leys et al reported a 15-year follow-up comparing HT and BPTB reconstructions [175] where they found patient age less than 18 years and the usage

of a BPTB graft to increase the likelihood of undergoing subsequent ACLR. They have attributed the difference to possible decreased function of the index knee in the BPTB group, with more reliance on the contralateral side making it more susceptible for a new injury. Unfortunately, they had a substantial loss to follow-up after 15 years, and it was not a RCT. The reasoning is also contradicted by studies measuring patient-reported outcome, as they do not find differences between the grafts either in activity level and subjective scores [237]. An increased risk of ACLR for any of the two grafts was not found in a subanalysis in paper I.

In paper II and III, an increased risk of revision was found for the femoral fixation Endobutton, or suspensory devices/cortical fixation, when analysed together in comparison with transfemoral fixation. Tibial fixation had a significant impact, especially for the biodegradable screw BiosureHA in study II. In study III the Retro interference screw had a higher risk of revision, but due to the small group size and the lack of data on how many hospitals that had contributed to this group, the results may be biased. The combination of Endobutton/BiosureHA was used in 1209 patients from in total 11 Norwegian hospitals, of whom 6 hospitals reconstructed >50 patients of the patients during the study period. This is a reasonable group size, most likely including a variety of surgical techniques and postoperative rehabilitation protocols, thus making the assumption of the external validity of the results reasonable. However, it could be that there is a selection or indication bias for the subgroups in the study as previously discussed. A recent Cochrane review concluded that there is a very low evidence that more treatment failures may be associated to the use of biodegradable screws compared with metal interference screws, in agreement with our results.

Data from the DNKLR was used to investigate the revision-risk dependent on graft fixation by Eysturoy et al [249]. They found that, after 2-year follow-up, femoral suspensory fixation had a HR of 1.24, and femoral intratunnel transfixation had a HR of 0.83 compared with the mean HT reconstruction. The actual numbers in our results are not directly comparable, as we did not compare to the mean but to another fixation group. Our overall results are, however, the same with an increased revision-

risk when using a suspensory fixation/Endobutton on the femoral side.

We cannot explain why the hamstring autograft reconstructions, in particular with femoral suspensory fixation fail to a greater extent than BPTB reconstructions. Both the graft itself, suspensory devices, transfemoral cross-pin fixation, and aperture fixation have performed well in biomechanical studies [143], indicating that the graft-fixation complex has enough strength and stiffness for an accelerated rehabilitation program [250, 251]. In light of the findings in this thesis, one could seek answers in the process of biological healing of the graft, and the potential differences between the grafts and the effects the different fixation types might have on graft healing and the outcome.

Graft healing

Due to the invasive nature of harvesting biopsies in ACL reconstructed patients, most human studies have collected samples in the setting of revision surgery or other subsequent procedures such as meniscal surgery or cyclops/hardware removal. There is an inherent problem with investigating biopsies from failed reconstructions, where the force acting on the graft disappears after reinjury and possibly altering the continuous graft to bone healing until the day of biopsy [252].

Zaffagnini et al conducted two studies investigating the ultrastructural collagen fibre distribution of samples from the central parts of BPTB (n=10) and HT (n=8) grafts [253, 254]. With the aid of a transmission electron microscopy, they looked at the number of collagen fibrils and their mean diameter. They concluded that the grafts underwent changes mainly in the first two postoperative years as they found no further changes from that point up until 10 years postoperatively. The ultrastructure resembled, but never matched the native ACL.

Histological studies investigating the tendon to bone healing in the tunnels have shown a great heterogeneity for surgical techniques, graft fixation and rehabilitation protocols [131]. To our knowledge, there are only two studies describing histological findings of the graft-to-bone healing in human BPTB patients. Petersen et al reported on findings from 8 patients having received a BPTB graft 9-37 months before biopsy at revision surgery [255]. In the five patients where the graft was fixed with screws

both in the femur and tibia, the insertions of the graft resembled that of the native ACL. In the 3 patients that had the distal bone block fixed outside of the tunnel due to graft-tunnel mismatch, indirect tendon-to-bone healing were observed in the tibial tunnels. As the patellar tendon normally is longer than the native ACL, there is often a part in the proximal part of the tibial tunnel where the tendon will heal to bone like a soft-tissue graft. To investigate the healing of the BPTB graft in the entire tibial tunnel, Ishibashi et al used a coring reamer to obtain samples in 10 patients at revision surgery. They found that in the patients revised early (<1 year), there was granulation tissue between the tendon part of the graft and bone tunnel. In the patients revised late (>1 year), the granulation tissue was replaced with a thin fibrous tissue and the tendon parts of the grafts were adherent to the bone tunnel. They concluded that with BPTB grafts, the distal junction between the graft and bone was shifted from the bone plug early after ACL reconstruction to the proximal tunnel wall with time.

The native ACL inserts to bone in a direct connection with a zone of fibrocartilage gradually mineralized into bone. In all studies on humans available, the successful tendon-bone healing for HT grafts were described as an indirect ligament insertion with Sharpey-like fibres connecting the tendon graft directly to bone, not through a fibrocartilaginous transition zone. Chen et al reported on the tendon-to-bone healing and pull-out strength using a periosteum flap wrapped around a tendon graft in a rabbit model [256]. On the leg where a periosteum flap was used around the graft, they found a histological direct insertion between graft and bone and the pull-out strength was significantly higher. Whether these findings can be generalized to humans is not clear.

For samples examined in HT reconstructions, healing with an indirect insertion was reported when interference screws were used as fixation in the tibial tunnel [257-259] and femoral tunnel [260, 261]. When a suspensory fixation was used in the femur, either partial or complete tendon-to-bone healing were reported [255, 262]. However, Nebelung et al and Robert et al found that some patients had no sign of anchorage of the HT graft-to-bone. Interestingly, some of those patients were clinically stable [261, 262]. The authors discussed whether the stability of the construct was still relying on

the suspensory fixation, even though the patients had their ACL reconstructed up to 15 months before biopsy. It is difficult to believe that the ACLR in those patients would be able to withstand the same peak loads as those with a complete graft-to-bone healing, maybe prone to a sudden atraumatic failure.

When using a suspensory device, the point of fixation will be more proximal to the joint line in the femur, compared with transfemoral fixation and aperture fixation. This leads to increased graft-motion in the tunnel, the so-called “bungee-effect” [263], possibly disturbing the tendon-to-bone healing in soft-tissue grafts [261, 264]. The increased graft movement in the channel might also introduce synovial fluid in the graft tunnels, which in a rabbit model was found to have inhibitory effects on tendon-to-bone healing [265]. To overcome graft movement, synovial fluid influx, and to possibly enhance tendon-to-bone healing, hybrid fixation with a femoral interference screw in addition to a suspension device has been proposed and was found biomechanically superior compared with a suspension device alone in many studies [266-269].

Graft forces depends on tunnel positioning

A possible limitation in our studies is the drilling technique for creating the femoral tunnel. Several studies have found an increased risk of revision when using an anatomically placed femoral tunnel compared with a non-anatomic tunnel typically produced with TT drilling [270-272]. Even if DePuy Synthes has developed a femoral guide-frame intended to be used through the anteromedial portal for Rigidfix, most femoral tunnels in transfemoral fixation in study II and III are likely to have been drilled transtibially. In addition, some grafts with suspensory fixations were used in a transtibially-drilled tunnel. Thus, in the dataset from the Scandinavian registries, there will often, but not always, be an association between the fixation and the femoral drilling technique. Because of this association, the drilling technique was not used as a confounder in the conducted studies [273].

To further review this limitation, one should conduct a study including only patients where AM technique was used to compare the outcome for the two grafts. This could unfortunately be difficult for comparison between suspensory and transfemoral fixation due to the low usage and availability of transfemoral fixation for AM-drilled

tunnels. When drilling the femoral tunnel transtibially, there are limited possibilities of adjustment towards the femoral ACL footprint [106]. Biomechanical studies at time zero have reported better rotational stability for grafts placed centrally in the footprint [111, 274], but this comes with the cost of greater graft stress during knee range-of-motion [275]. In an animal model, the early graft healing was impaired in rats with a high force ACL reconstruction allowed mobilization compared to rats who had their knee-joint totally immobilised and rats with low force ACL reconstructions [264]. The authors conclude that the graft-to-bone healing in anatomical soft-tissue ACL reconstruction might benefit from an early immobilisation period, also advocated by an author from a similar animal study [276]. We believe that the findings from study I are likely to be caused by the security of the fixation of the BPTB grafts with interference screws and the predictable early bone to bone healing. Combining Endobutton with the degradable screw BiosureHA had a significantly increased risk of early revision for HT grafts in paper II. It is important to acknowledge that the properties of the biodegradable materials differ significantly dependent on the production protocol, and the interaction with biological factors such as local tissue pH values can alter the desired properties of the implant significantly [149]. As previously mentioned, mechanical stress can speed up degradation. It was hypothesized that this could be due to increased microcracks in the implant, increasing exposure to water. This could reduce the implant strength and stiffness prematurely and have an impact in anatomical reconstruction when there is a high stress to the graft-fixation complex.

In conclusion, we have found that there are differences in revision risks between the grafts and between fixation methods for HT. This may be due to differences in graft healing between the grafts and fixation methods, where the HT graft may not have the same predictable healing in the femoral tunnel as the BPTB graft. An initially restricted rehabilitation protocol and an additional aperture fixation in the femoral tunnel might enhance the healing and result of the HT graft.

10.3 Clinical implications

- ACL surgeons should counsel young patients adequately on the risk of re-injury and revision surgery
- BPTB seems to be a better general choice than HT for ACL reconstruction with today's techniques. This is especially emphasised for young patients, where we found the revision rate to be almost 10% at 5 years for HT. HT grafts could primarily be considered in patients with kneeling activities due to increased anterior knee pain with BPTB, but should be seen in light of the increased failure rate
- Graft fixation with metal interference screws for BPTB gives a predictable result
- For graft fixation in anatomical HT reconstructions, there are limited fixation methods available except suspensory and aperture fixation. An additional interference screw to suspensory femoral fixation or an initially restricted rehabilitation program may enhance graft healing and could improve the postoperative result for HT grafts in anatomical reconstructions

11. Conclusions

11.1 Paper I

- During the study period, HT grafts were most popular up until 2010 (84%), when BPTB usage increased
- The risk of revision in Norway was 2.3 times higher for patients treated with a HT compared with a BPTB
- The most influential risk factor for undergoing revision surgery was patients' age at primary reconstruction; compared with the patient group aged ≥ 30 y, patients aged 15-19 y and 20-29 y had a 4-fold and doubled risk of revision respectively
- Patients' sex did not influence the risk of revision
- The overall 2- and 5-year revision rates were 2.2 and 4.2% respectively. HT had higher revision rate at all follow-up times in all age groups compared with BPTB

11.2 Paper II

- During the study period, the most common femoral and tibial fixations used in Norway for HT grafts were Endobutton and RCI screw. For BPTB grafts, the vast majority were fixed with metal interference screws
- When using HT, patients with combinations of fixations with femoral fixation Endobutton had a significantly higher risk of early revision compared with other combinations of fixations. No combination of fixation for HT had equally low early revision risk as the average patient with BPTB
- The 2-year revision rates for the combinations of fixations with Endobutton varied between 3.5-5.5%, whereas the revision rates for the combinations EZLoc/WasherLoc and TransFix II/metal interference screw were found to be 2.2 and 1.5% respectively

11.3 Paper III

- During the study period, the most common femoral and tibial fixation used in HT ACL reconstructions in Scandinavia were Endobutton (36%) and interference screw (48%), respectively
- Compared with Endobutton, patients treated with Rigidfix and TransFix had 0.7 times lower overall risk of revision
- We found an increased overall risk of revision for patients treated with tibial fixation retro interference screw

12. Suggestions for further research

The present thesis have added knowledge in fields that could be difficult to achieve with other study designs and has contributed with several new hypotheses. There are still obvious questions to be answered in ACL research, some of those are possible to penetrate with valid register data but other research questions needs other study designs.

12.1 Data quality

In the process of working with the present thesis, the importance of data quality was acknowledged. This attribute has not previously been described for the NNKLR. We started the process of validating the accuracy of the register data, comparing it with data registered in the patient's medical journal, mid-term in this PhD project.

12.2 Cause of revision

The cause of revision is multifactorial, and certain patient's characteristics or surgical techniques might show specific patterns of failure dependent on time after primary reconstruction. With the existing data in the register, we can further penetrate this research question. We could potentially find differences in described failure mechanism, to generate further hypotheses for inherent failure mechanisms of the grafts or fixations.

12.3 Subjective outcome after ACL reconstruction

To further investigate the outcome between the grafts, and possible between fixation methods, the analysis of subjective outcome in form of KOOS is an important complement to the results of this thesis. In addition to using the subscales, one can perform analysis on separate questions in the KOOS that could highlight differences between the grafts not found in the overall subscales.

12.4 Conversion of ACL reconstructions to total knee arthroplasty

The ultimate failure for the ACL injured knee is a TKA, and this pathway is not well studied. By coupling individual data from the NNKLR to the NAR we can find the incidence and possibly important prognostic factors for this end-stage endpoint.

12.5 Indication for revision surgery

For the reporting hospitals to the NNKLR, there might be variations in decision-making for what patients with treatment failure that should be revised. This should be investigated to further elicit the risk of indication bias when using revision as the endpoint. As a side-effect, this study could create an important discussion and elicit the need for a national guideline for these patients.

12.6 Register-RCT

To surpass the general weakness for register studies of being observational, there has lately been proposed to introduce randomization into registries – the “registry-based RCT” [277]. By using randomization in the framework from an existing clinical register to allocate treatment, it is possible to follow the included patients within the collected register endpoints. This would result in low-cost and pragmatic prospective randomised trials that can prove causality with a great external validity. If embedded in the NNKLR, we can for example compare the following treatments:

- Graft choice – including only anatomic reconstructions, randomised to HT or BPTB. Due to the large sample size necessary, this design might provide the ultimate evidence for this question
- Fixation method – for hamstring tendon grafts, randomization between suspension device with or without an additional interference screw in the femur
- Non-operative treatment versus early reconstruction for an acute ACL injury

13. References

1. Noyes, F.R., E.S. Grood, and P.A. Torzilli, *Current concepts review. The definitions of terms for motion and position of the knee and injuries of the ligaments.* J Bone Joint Surg Am, 1989. **71**(3): p. 465-72.
2. Merida-Velasco, J.A., et al., *Development of the human knee joint ligaments.* Anat Rec, 1997. **248**(2): p. 259-68.
3. Arnoczky, S.P., *Anatomy of the anterior cruciate ligament.* Clin Orthop Relat Res, 1983(172): p. 19-25.
4. Duthon, V.B., et al., *Anatomy of the anterior cruciate ligament.* Knee Surg Sports Traumatol Arthrosc, 2006. **14**(3): p. 204-13.
5. Girgis, F.G., J.L. Marshall, and A. Monajem, *The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis.* Clin Orthop Relat Res, 1975(106): p. 216-31.
6. Kennedy, J.C., H.W. Weinberg, and A.S. Wilson, *The anatomy and function of the anterior cruciate ligament. As determined by clinical and morphological studies.* J Bone Joint Surg Am, 1974. **56**(2): p. 223-35.
7. Fujie, H., et al., *Mechanical functions of the three bundles consisting of the human anterior cruciate ligament.* Knee Surg Sports Traumatol Arthrosc, 2011. **19 Suppl 1**: p. S47-53.
8. Iwahashi, T., et al., *Assessment of the "functional length" of the three bundles of the anterior cruciate ligament.* Knee Surg Sports Traumatol Arthrosc, 2008. **16**(2): p. 167-74.
9. Tantisricharoenkul, G., et al., *Anterior cruciate ligament: an anatomical exploration in humans and in a selection of animal species.* Knee Surg Sports Traumatol Arthrosc, 2014. **22**(5): p. 961-71.
10. Iwahashi, T., et al., *Direct anterior cruciate ligament insertion to the femur assessed by histology and 3-dimensional volume-rendered computed tomography.* Arthroscopy, 2010. **26**(9 Suppl): p. S13-20.
11. Siebold, R., et al., *Flat midsubstance of the anterior cruciate ligament with tibial "C"-shaped insertion site.* Knee Surg Sports Traumatol Arthrosc, 2015. **23**(11): p. 3136-42.
12. Smigielski, R., et al., *Ribbon like appearance of the midsubstance fibres of the anterior cruciate ligament close to its femoral insertion site: a cadaveric study including 111 knees.* Knee Surg Sports Traumatol Arthrosc, 2015. **23**(11): p. 3143-50.
13. Harner, C.D., et al., *Comparative study of the size and shape of human anterior and posterior cruciate ligaments.* J Orthop Res, 1995. **13**(3): p. 429-34.
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. Amis, A.A. and G.P. Dawkins, *Functional anatomy of the anterior cruciate ligament. Fibre bundle actions related to ligament replacements and injuries.* J Bone Joint Surg Br, 1991. **73**(2): p. 260-7.
16. Gabriel, M.T., et al., *Distribution of in situ forces in the anterior cruciate ligament in response to rotatory loads.* J Orthop Res, 2004. **22**(1): p. 85-9.

17. Markolf, K.L., et al., *Contributions of the posterolateral bundle of the anterior cruciate ligament to anterior-posterior knee laxity and ligament forces*. Arthroscopy, 2008. **24**(7): p. 805-9.
18. Kennedy, J.C., I.J. Alexander, and K.C. Hayes, *Nerve supply of the human knee and its functional importance*. Am J Sports Med, 1982. **10**(6): p. 329-35.
19. Myklebust, G., et al., *Prevention of anterior cruciate ligament injuries in female team handball players: a prospective intervention study over three seasons*. Clin J Sport Med, 2003. **13**(2): p. 71-8.
20. Johnsen, M.B., et al., *Sport Participation and the Risk of Anterior Cruciate Ligament Reconstruction in Adolescents: A Population-based Prospective Cohort Study (The Young-HUNT Study)*. Am J Sports Med, 2016. **44**(11): p. 2917-2924.
21. Granan, L.P., et al., *The Scandinavian ACL registries 2004-2007: baseline epidemiology*. Acta Orthop, 2009. **80**(5): p. 563-7.
22. Walden, M., et al., *The epidemiology of anterior cruciate ligament injury in football (soccer): a review of the literature from a gender-related perspective*. Knee Surg Sports Traumatol Arthrosc, 2011. **19**(1): p. 3-10.
23. Sanders, T.L., et al., *Incidence of Anterior Cruciate Ligament Tears and Reconstruction: A 21-Year Population-Based Study*. Am J Sports Med, 2016. **44**(6): p. 1502-7.
24. NKLR, *Annual report 2018*. http://nrlweb.ihelse.net/eng/Rapporter/Report2018_english.pdf, 2018.
25. Granan, L.P., L. Engebretsen, and R. Bahr, *[Surgery for anterior cruciate ligament injuries in Norway]*. Tidsskr Nor Laegeforen, 2004. **124**(7): p. 928-30.
26. Granan, L.P., et al., *Development of a national cruciate ligament surgery registry: the Norwegian National Knee Ligament Registry*. Am J Sports Med, 2008. **36**(2): p. 308-15.
27. Gornitzky, A.L., et al., *Sport-Specific Yearly Risk and Incidence of Anterior Cruciate Ligament Tears in High School Athletes: A Systematic Review and Meta-analysis*. Am J Sports Med, 2016. **44**(10): p. 2716-2723.
28. Kaeding, C.C., B. Leger-St-Jean, and R.A. Magnussen, *Epidemiology and Diagnosis of Anterior Cruciate Ligament Injuries*. Clin Sports Med, 2017. **36**(1): p. 1-8.
29. Myer, G.D., et al., *The effects of generalized joint laxity on risk of anterior cruciate ligament injury in young female athletes*. Am J Sports Med, 2008. **36**(6): p. 1073-80.
30. Wang, Y.L., et al., *Association Between Tibial Plateau Slopes and Anterior Cruciate Ligament Injury: A Meta-analysis*. Arthroscopy, 2017. **33**(6): p. 1248-1259 e4.
31. Uhorchak, J.M., et al., *Risk factors associated with noncontact injury of the anterior cruciate ligament: a prospective four-year evaluation of 859 West Point cadets*. Am J Sports Med, 2003. **31**(6): p. 831-42.
32. Olsen, O.E., et al., *Injury mechanisms for anterior cruciate ligament injuries in team handball: a systematic video analysis*. Am J Sports Med, 2004. **32**(4): p. 1002-12.

33. Boden, B.P., et al., *Mechanisms of anterior cruciate ligament injury*. Orthopedics, 2000. **23**(6): p. 573-8.
34. Myklebust, G., et al., *Registration of cruciate ligament injuries in Norwegian top level team handball. A prospective study covering two seasons*. Scand J Med Sci Sports, 1997. **7**(5): p. 289-92.
35. Myklebust, G., et al., *A prospective cohort study of anterior cruciate ligament injuries in elite Norwegian team handball*. Scand J Med Sci Sports, 1998. **8**(3): p. 149-53.
36. Beynnon, B., et al., *The measurement of anterior cruciate ligament strain in vivo*. Int Orthop, 1992. **16**(1): p. 1-12.
37. Beynnon, B.D., et al., *The strain behavior of the anterior cruciate ligament during squatting and active flexion-extension. A comparison of an open and a closed kinetic chain exercise*. Am J Sports Med, 1997. **25**(6): p. 823-9.
38. Henning, C.E., M.A. Lynch, and K.R. Glick, Jr., *An in vivo strain gage study of elongation of the anterior cruciate ligament*. Am J Sports Med, 1985. **13**(1): p. 22-6.
39. Ardern, C.L., et al., *Prevention, diagnosis and management of paediatric ACL injuries*. Br J Sports Med, 2018. **52**(20): p. 1297-1298.
40. Ardern, C.L., et al., *2018 International Olympic Committee consensus statement on prevention, diagnosis and management of paediatric anterior cruciate ligament (ACL) injuries*. Br J Sports Med, 2018. **52**(7): p. 422-438.
41. Takeda, H., et al., *Prevention and management of knee osteoarthritis and knee cartilage injury in sports*. Br J Sports Med, 2011. **45**(4): p. 304-9.
42. Sadoghi, P., A. von Keudell, and P. Vavken, *Effectiveness of anterior cruciate ligament injury prevention training programs*. J Bone Joint Surg Am, 2012. **94**(9): p. 769-76.
43. Myklebust, G., A. Skjolberg, and R. Bahr, *ACL injury incidence in female handball 10 years after the Norwegian ACL prevention study: important lessons learned*. Br J Sports Med, 2013. **47**(8): p. 476-9.
44. Grammaticos, P.C. and A. Diamantis, *Useful known and unknown views of the father of modern medicine, Hippocrates and his teacher Democritus*. Hell J Nucl Med, 2008. **11**(1): p. 2-4.
45. Davarinos, N., J. O'Neill, and W. Curtin, *A Brief History of Anterior Cruciate Ligament Reconstruction*. Advances in Orthopedic Surgery, 2004. **Volume 2014**: p. 6 pages.
46. Schindler, O.S., *Surgery for anterior cruciate ligament deficiency: a historical perspective*. Knee Surg Sports Traumatol Arthrosc, 2012. **20**(1): p. 5-47.
47. Robson, A.W., *VI. Ruptured Crucial Ligaments and their Repair by Operation*. Ann Surg, 1903. **37**(5): p. 716-8.
48. Palmer, I., *On the injuries to the ligaments of the knee joint; a clinical study*. Acta Chir Scand 1938. **53**(Suppl 53).
49. O'Donoghue, D.H., *Surgical treatment of fresh injuries to the major ligaments of the knee*. J Bone Joint Surg Am, 1950. **32 A**(4): p. 721-38.
50. Hey Groves, E., *Operation for repair of the crucial ligaments*. Lancet, 1917. **190**: p. 674-675.

51. Smith, A., *The diagnosis and treatment of injuries to the crucial ligaments*. Br J Surg, 1918. **6**: p. 176-189.
52. Galeazzi, R., *La ricostituzione dei ligamenti crociati del ginocchio [Reconstitution of the cruciate ligaments]*. Atti e Memorie della Società Lombarda di Chirurgia, 1934. **13**: p. 302-317.
53. Lindemann, K., *Über den plastischen Ersatz der Kreuzbänder durch gestielte Sehnenverpflanzungen*. Z Orthop, 1950(79): p. 316-334.
54. Augustine, R.W., *The unstable knee*. Am J Surg, 1956. **92**(3): p. 380-8.
55. Lipscomb, A.B., R.K. Johnston, and R.B. Snyder, *The technique of cruciate ligament reconstruction*. Am J Sports Med, 1981. **9**(2): p. 77-81.
56. Gold, E., *Vollst indiger plastischer Ersatz des vorderen Kreuzbandes und funktionell-anatomische Wiederherstellung desselben*. Dtsch Z Chir, 1928. **123**: p. 120-126.
57. Jones, K.G., *Reconstruction of the Anterior Cruciate Ligament. A Technique Using the Central One-Third of the Patellar Ligament*. J Bone Joint Surg Am, 1963. **45**: p. 925-32.
58. Franke, K., *Clinical experience in 130 cruciate ligament reconstructions*. Orthop Clin North Am, 1976. **7**(1): p. 191-3.
59. Clancy, W.G., Jr., et al., *Anterior cruciate ligament reconstruction using one-third of the patellar ligament, augmented by extra-articular tendon transfers*. J Bone Joint Surg Am, 1982. **64**(3): p. 352-9.
60. Blauth, W., *Die zweizügelige Ersatzplastik des vorderen Kreuzbandes aus der Quadricepssehne*. Unfallheilkunde, 1984. **87**: p. 45-51.
61. Fulkerson, J.P. and R. Langeland, *An alternative cruciate reconstruction graft: the central quadriceps tendon*. Arthroscopy, 1995. **11**(2): p. 252-4.
62. Cavaignac, E., et al., *Is Quadriceps Tendon Autograft a Better Choice Than Hamstring Autograft for Anterior Cruciate Ligament Reconstruction?* Am J Sports Med, 2017: p. 363546516688665.
63. Eriksson, E., *Patellar tendon or quadriceps tendon grafts for ACL reconstruction*. Knee Surg Sports Traumatol Arthrosc, 2007. **15**(11): p. 1283.
64. Garofalo, R., A. Djahangiri, and O. Siegrist, *Revision anterior cruciate ligament reconstruction with quadriceps tendon-patellar bone autograft*. Arthroscopy, 2006. **garofalo22**(2): p. 205-14.
65. Shino, K., et al., *Replacement of the anterior cruciate ligament by an allogeneic tendon graft. An experimental study in the dog*. J Bone Joint Surg Br, 1984. **66**(5): p. 672-81.
66. Shino, K., et al., *Reconstruction of the anterior cruciate ligament by allogeneic tendon graft. An operation for chronic ligamentous insufficiency*. J Bone Joint Surg Br, 1986. **68**(5): p. 739-46.
67. Smith, C.W., I.S. Young, and J.N. Kearney, *Mechanical properties of tendons: changes with sterilization and preservation*. J Biomech Eng, 1996. **118**(1): p. 56-61.
68. Belk, J.W., et al., *Autograft Versus Allograft for Posterior Cruciate Ligament Reconstruction: An Updated Systematic Review and Meta-analysis*. Am J Sports Med, 2018. **46**(7): p. 1752-1757.

69. Maletis, G.B., M.C. Inacio, and T.T. Funahashi, *Risk factors associated with revision and contralateral anterior cruciate ligament reconstructions in the Kaiser Permanente ACLR registry*. Am J Sports Med, 2015. **43**(3): p. 641-7.
70. Corner, E., *The exploration of the knee-joint: With some illustrative cases*. Br J Surg, 1914. **2**(6): p. 191-204.
71. Ludloff, K., *Der operative Ersatz des vorderen Kreuzbandes am Knie*. Zentralbl Chir, 1927. **54**: p. 3162-3166.
72. Rütter, H., *Die Verwendung von Supramid in der operativen Orthopädie*. Z Orthop, 1949. **78**: p. 161-169.
73. Wilk, R.M. and J.C. Richmond, *Dacron ligament reconstruction for chronic anterior cruciate ligament insufficiency*. Am J Sports Med, 1993. **21**(3): p. 374-380.
74. Woods, G.A., P.A. Indelicato, and T.J. Prevo, *The Gore-Tex anterior cruciate ligament prosthesis. Two versus three year results*. Am J Sports Med, 1991. **19**(1): p. 48-55.
75. Maletius, W. and J. Gillquist, *Long-term results of anterior cruciate ligament reconstruction with a Dacron prosthesis. The frequency of osteoarthritis after seven to eleven years*. Am J Sports Med, 1997. **25**(3): p. 288-93.
76. Kennedy, J.C., et al., *Presidential address. Intraarticular replacement in the anterior cruciate ligament-deficient knee*. Am J Sports Med, 1980. **8**(1): p. 1-8.
77. Engebretsen, L., et al., *A prospective, randomized study of three surgical techniques for treatment of acute ruptures of the anterior cruciate ligament*. Am J Sports Med, 1990. **18**(6): p. 585-90.
78. Kohl, S., et al., *Dynamic intraligamentary stabilisation: initial experience with treatment of acute ACL ruptures*. Bone Joint J, 2016. **98-B**(6): p. 793-8.
79. Krismer, A.M., et al., *Factors influencing the success of anterior cruciate ligament repair with dynamic intraligamentary stabilisation*. Knee Surg Sports Traumatol Arthrosc, 2017.
80. van Eck, C.F., O. Limpisvasti, and N.S. ElAttrache, *Is There a Role for Internal Bracing and Repair of the Anterior Cruciate Ligament? A Systematic Literature Review*. Am J Sports Med, 2017: p. 363546517717956.
81. Smith, J.O., et al., *Paediatric ACL repair reinforced with temporary internal bracing*. Knee Surg Sports Traumatol Arthrosc, 2016. **24**(6): p. 1845-51.
82. Ahmad, S.S., et al., *Dynamic intraligamentary stabilization for ACL repair: a systematic review*. Knee Surg Sports Traumatol Arthrosc, 2018.
83. Buchler, L., et al., *Functional recovery following primary ACL repair with dynamic intraligamentary stabilization*. Knee, 2016. **23**(3): p. 549-53.
84. Marx, R.G., et al., *Beliefs and attitudes of members of the American Academy of Orthopaedic Surgeons regarding the treatment of anterior cruciate ligament injury*. Arthroscopy, 2003. **19**(7): p. 762-70.
85. Moksnes, H. and M.A. Risberg, *Performance-based functional evaluation of non-operative and operative treatment after anterior cruciate ligament injury*. Scand J Med Sci Sports, 2009. **19**(3): p. 345-55.

-
86. McRae, S.M., et al., *Survey study of members of the Canadian Orthopaedic Association on the natural history and treatment of anterior cruciate ligament injury*. Clin J Sport Med, 2011. **21**(3): p. 249-58.
 87. Snoeker, B.A., et al., *Risk factors for meniscal tears: a systematic review including meta-analysis*. J Orthop Sports Phys Ther, 2013. **43**(6): p. 352-67.
 88. Granan, L.P., et al., *Timing of anterior cruciate ligament reconstructive surgery and risk of cartilage lesions and meniscal tears: a cohort study based on the Norwegian National Knee Ligament Registry*. Am J Sports Med, 2009. **37**(5): p. 955-61.
 89. Richmond, J.C., J.H. Lubowitz, and G.G. Poehling, *Prompt operative intervention reduces long-term osteoarthritis after knee anterior cruciate ligament tear*. Arthroscopy, 2011. **27**(2): p. 149-52.
 90. Sanders, T.L., et al., *Is Anterior Cruciate Ligament Reconstruction Effective in Preventing Secondary Meniscal Tears and Osteoarthritis?* Am J Sports Med, 2016. **44**(7): p. 1699-707.
 91. Lewis, P.B., et al., *Systematic review of single-bundle anterior cruciate ligament reconstruction outcomes: a baseline assessment for consideration of double-bundle techniques*. Am J Sports Med, 2008. **36**(10): p. 2028-36.
 92. Failla, M.J., et al., *Does Extended Preoperative Rehabilitation Influence Outcomes 2 Years After ACL Reconstruction? A Comparative Effectiveness Study Between the MOON and Delaware-Oslo ACL Cohorts*. Am J Sports Med, 2016. **44**(10): p. 2608-2614.
 93. Frobell, R.B., et al., *Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial*. BMJ, 2013. **346**: p. f232.
 94. Levy, B.A., et al., *Treating ACL injuries in young moderately active adults*. BMJ, 2013. **346**: p. f963.
 95. Petersen, W., *Does ACL reconstruction lead to degenerative joint disease or does it prevent osteoarthritis? How to read science*. Arthroscopy, 2012. **28**(4): p. 448-50.
 96. Monk, A.P., et al., *Surgical versus conservative interventions for treating anterior cruciate ligament injuries*. Cochrane Database Syst Rev, 2016. **4**: p. CD011166.
 97. van Melick, N., et al., *Evidence-based clinical practice update: practice guidelines for anterior cruciate ligament rehabilitation based on a systematic review and multidisciplinary consensus*. Br J Sports Med, 2016. **50**(24): p. 1506-1515.
 98. Dandy, D.J. and P.F. O'Carroll, *Arthroscopic surgery of the knee*. Br Med J (Clin Res Ed), 1982. **285**(6350): p. 1256-8.
 99. Harner, C.D., et al., *Anterior cruciate ligament reconstruction: endoscopic versus two-incision technique*. Arthroscopy, 1994. **10**(5): p. 502-12.
 100. 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.
 101. Howell, S.M. and M.L. Deutsch, *Comparison of endoscopic and two-incision techniques for reconstructing a torn anterior cruciate ligament using hamstring tendons*. Arthroscopy, 1999. **15**(6): p. 594-606.

-
102. Rezende, F.C., et al., *One-incision versus two-incision techniques for arthroscopically assisted anterior cruciate ligament reconstruction in adults*. *Cochrane Database Syst Rev*, 2017. **12**: p. CD010875.
 103. 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.
 104. Karlsson, J., et al., *Comparison of arthroscopic one-incision and two-incision techniques for reconstruction of the anterior cruciate ligament*. *Scand J Med Sci Sports*, 1999. **9**(4): p. 233-8.
 105. Strauss, E.J., et al., *Can anatomic femoral tunnel placement be achieved using a transtibial technique for hamstring anterior cruciate ligament reconstruction?* *Am J Sports Med*, 2011. **39**(6): p. 1263-9.
 106. Kopf, S., et al., *Transtibial ACL reconstruction technique fails to position drill tunnels anatomically in vivo 3D CT study*. *Knee Surg Sports Traumatol Arthrosc*, 2012. **20**(11): p. 2200-7.
 107. Dargel, J., et al., *Femoral bone tunnel placement using the transtibial tunnel or the anteromedial portal in ACL reconstruction: a radiographic evaluation*. *Knee Surg Sports Traumatol Arthrosc*, 2009. **17**(3): p. 220-7.
 108. O'Donnell, J.B. and T.A. Scerpella, *Endoscopic anterior cruciate ligament reconstruction: modified technique and radiographic review*. *Arthroscopy*, 1995. **11**(5): p. 577-84.
 109. Harner, C.D., N.J. Honkamp, and A.S. Ranawat, *Anteromedial portal technique for creating the anterior cruciate ligament femoral tunnel*. *Arthroscopy*, 2008. **24**(1): p. 113-5.
 110. Sadoghi, P., et al., *Impact of tibial and femoral tunnel position on clinical results after anterior cruciate ligament reconstruction*. *Arthroscopy*, 2011. **27**(3): p. 355-64.
 111. Bedi, A., et al., *Transtibial versus anteromedial portal reaming in anterior cruciate ligament reconstruction: an anatomic and biomechanical evaluation of surgical technique*. *Arthroscopy*, 2011. **27**(3): p. 380-90.
 112. 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.
 113. Mott, H.W., *Semitendinosus anatomic reconstruction for cruciate ligament insufficiency*. *Clin Orthop Relat Res*, 1983(172): p. 90-2.
 114. 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.
 115. 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.
 116. Aga, C., et al., *Risk of Revision Was Not Reduced by a Double-bundle ACL Reconstruction Technique: Results From the Scandinavian Registers*. *Clin Orthop Relat Res*, 2017. **475**(10): p. 2503-2512.

-
117. Mascarenhas, R., et al., *Does Double-Bundle Anterior Cruciate Ligament Reconstruction Improve Postoperative Knee Stability Compared With Single-Bundle Techniques? A Systematic Review of Overlapping Meta-analyses*. *Arthroscopy*, 2015. **31**(6): p. 1185-96.
 118. Tiamklang, T., et al., *Double-bundle versus single-bundle reconstruction for anterior cruciate ligament rupture in adults*. *Cochrane Database Syst Rev*, 2012. **11**: p. CD008413.
 119. Asagumo, H., et al., *Anatomic reconstruction of the anterior cruciate ligament using double-bundle hamstring tendons: surgical techniques, clinical outcomes, and complications*. *Arthroscopy*, 2007. **23**(6): p. 602-9.
 120. Aga, C., et al., *No Difference in the KOOS Quality of Life Subscore Between Anatomic Double-Bundle and Anatomic Single-Bundle Anterior Cruciate Ligament Reconstruction of the Knee: A Prospective Randomized Controlled Trial With 2 Years' Follow-up*. *Am J Sports Med*, 2018. **46**(10): p. 2341-2354.
 121. Houck, D.A., et al., *Variance in Anterior Cruciate Ligament Reconstruction Graft Selection based on Patient Demographics and Location within the Multicenter Orthopaedic Outcomes Network Cohort*. *J Knee Surg*, 2018. **31**(5): p. 472-478.
 122. Prentice, H.A., et al., *Patient demographic and surgical characteristics in anterior cruciate ligament reconstruction: a description of registries from six countries*. *Br J Sports Med*, 2018. **52**(11): p. 716-722.
 123. Woo, S.L., et al., *Tensile properties of the human femur-anterior cruciate ligament-tibia complex. The effects of specimen age and orientation*. *Am J Sports Med*, 1991. **19**(3): p. 217-25.
 124. Rowden, N.J., et al., *Anterior cruciate ligament graft fixation. Initial comparison of patellar tendon and semitendinosus autografts in young fresh cadavers*. *Am J Sports Med*, 1997. **25**(4): p. 472-8.
 125. Hamner, D.L., et al., *Hamstring tendon grafts for reconstruction of the anterior cruciate ligament: biomechanical evaluation of the use of multiple strands and tensioning techniques*. *J Bone Joint Surg Am*, 1999. **81**(4): p. 549-57.
 126. Ferretti, A., et al., *Biomechanics of anterior cruciate ligament reconstruction using twisted doubled hamstring tendons*. *Int Orthop*, 2003. **27**(1): p. 22-5.
 127. Schatzmann, L., P. Brunner, and H.U. Staubli, *Effect of cyclic preconditioning on the tensile properties of human quadriceps tendons and patellar ligaments*. *Knee Surg Sports Traumatol Arthrosc*, 1998. **6 Suppl 1**: p. S56-61.
 128. Kurosaka, M., S. Yoshiya, and J.T. Andrish, *A biomechanical comparison of different surgical techniques of graft fixation in anterior cruciate ligament reconstruction*. *Am J Sports Med*, 1987. **15**(3): p. 225-9.
 129. Ekdahl, M., et al., *Graft healing in anterior cruciate ligament reconstruction*. *Knee Surg Sports Traumatol Arthrosc*, 2008. **16**(10): p. 935-47.
 130. Beynon, B.D., et al., *Evaluation of knee joint laxity and the structural properties of the anterior cruciate ligament graft in the human. A case report*. *Am J Sports Med*, 1997. **25**(2): p. 203-6.

-
131. Lu, H., et al., *Tendon Healing in Bone Tunnel after Human Anterior Cruciate Ligament Reconstruction: A Systematic Review of Histological Results*. J Knee Surg, 2018.
 132. Rodeo, S.A., et al., *Tendon-healing in a bone tunnel. A biomechanical and histological study in the dog*. J Bone Joint Surg Am, 1993. **75**(12): p. 1795-1803.
 133. Claes, S., et al., *The "ligamentization" process in anterior cruciate ligament reconstruction: what happens to the human graft? A systematic review of the literature*. Am J Sports Med, 2011. **39**(11): p. 2476-83.
 134. Ntoulia, A., et al., *Revascularization process of the bone--patellar tendon--bone autograft evaluated by contrast-enhanced magnetic resonance imaging 6 and 12 months after anterior cruciate ligament reconstruction*. Am J Sports Med, 2011. **39**(7): p. 1478-86.
 135. Rougraff, B., et al., *Arthroscopic and histologic analysis of human patellar tendon autografts used for anterior cruciate ligament reconstruction*. Am J Sports Med, 1993. **21**(2): p. 277-84.
 136. Sanchez, M., et al., *Ligamentization of tendon grafts treated with an endogenous preparation rich in growth factors: gross morphology and histology*. Arthroscopy, 2010. **26**(4): p. 470-80.
 137. Brand, J., Jr., et al., *Graft fixation in cruciate ligament reconstruction*. Am J Sports Med, 2000. **28**(5): p. 761-74.
 138. Magen, H.E., S.M. Howell, and M.L. Hull, *Structural properties of six tibial fixation methods for anterior cruciate ligament soft tissue grafts*. Am J Sports Med, 1999. **27**(1): p. 35-43.
 139. Brand, J.C., Jr., et al., *Interference screw fixation strength of a quadrupled hamstring tendon graft is directly related to bone mineral density and insertion torque*. Am J Sports Med, 2000. **28**(5): p. 705-10.
 140. Domnick, C., et al., *Anterior Cruciate Ligament Soft Tissue Graft Fixation in the Elderly: Is There a Reason to Use Interference Screws? A Human Cadaver Study*. Arthroscopy, 2017. **33**(9): p. 1694-1700.
 141. Harvey, A., N.P. Thomas, and A.A. Amis, *Fixation of the graft in reconstruction of the anterior cruciate ligament*. J Bone Joint Surg Br, 2005. **87**(5): p. 593-603.
 142. Aga, C., et al., *Biomechanical comparison of interference screws and combination screw and sheath devices for soft tissue anterior cruciate ligament reconstruction on the tibial side*. Am J Sports Med, 2013. **41**(4): p. 841-8.
 143. Kousa, P., et al., *The fixation strength of six hamstring tendon graft fixation devices in anterior cruciate ligament reconstruction. Part I: femoral site*. Am J Sports Med, 2003. **31**(2): p. 174-81.
 144. Kousa, P., et al., *The fixation strength of six hamstring tendon graft fixation devices in anterior cruciate ligament reconstruction. Part II: tibial site*. Am J Sports Med, 2003. **31**(2): p. 182-8.
 145. Scheffler, S.U., et al., *Biomechanical comparison of hamstring and patellar tendon graft anterior cruciate ligament reconstruction techniques: The impact*

-
- of fixation level and fixation method under cyclic loading.* Arthroscopy, 2002. **18**(3): p. 304-15.
146. Ahmad, S.S., et al., *Adjustable loop ACL suspension devices demonstrate less reliability in terms of reproducibility and irreversible displacement.* Knee Surg Sports Traumatol Arthrosc, 2018. **26**(5): p. 1392-1398.
 147. Nye, D.D., et al., *Biomechanical Comparison of Fixed-Loop and Adjustable-Loop Cortical Suspensory Devices for Metaphyseal Femoral-Sided Soft Tissue Graft Fixation in Anatomic Anterior Cruciate Ligament Reconstruction Using a Porcine Model.* Arthroscopy, 2017. **33**(6): p. 1225-1232 e1.
 148. Mickelson, D.T., et al., *Adjustable-Loop Femoral Cortical Suspensory Fixation for Patellar Tendon Anterior Cruciate Ligament Reconstruction: A Time Zero Biomechanical Comparison With Interference Screw Fixation.* Am J Sports Med, 2018. **46**(8): p. 1857-1862.
 149. Farah, S., D.G. Anderson, and R. Langer, *Physical and mechanical properties of PLA, and their functions in widespread applications - A comprehensive review.* Adv Drug Deliv Rev, 2016. **107**: p. 367-392.
 150. Athanasiou, K.A., et al., *Orthopaedic applications for PLA-PGA biodegradable polymers.* Arthroscopy, 1998. **14**(7): p. 726-37.
 151. Pietrzak, W.S., D.R. Sarver, and M.L. Verstynen, *Bioabsorbable polymer science for the practicing surgeon.* Journal of Craniofacial Surgery, 1997. **8**(2): p. 87-91.
 152. Middleton, J.C. and A.J. Tipton, *Synthetic biodegradable polymers as orthopedic devices.* Biomaterials, 2000. **21**(23): p. 2335-46.
 153. Shellock, F.G., et al., *MR imaging and metallic implants for anterior cruciate ligament reconstruction: assessment of ferromagnetism and artifact.* J Magn Reson Imaging, 1992. **2**(2): p. 225-8.
 154. Ramsingh, V., N. Prasad, and M. Lewis, *Pre-tibial reaction to biointerference screw in anterior cruciate ligament reconstruction.* Knee, 2014. **21**(1): p. 91-4.
 155. Watson, J.N., et al., *Bioabsorbable interference screw failure in anterior cruciate ligament reconstruction: A case series and review of the literature.* Knee, 2015. **22**(3): p. 256-61.
 156. Thompson, S.M., S. Fung, and D.G. Wood, *The Natural History of Biointerference Screw Cyst and New Bone Formation in Anterior Cruciate Ligament Reconstruction: 16-Year Follow-up.* Am J Sports Med, 2016. **44**(1): p. 113-7.
 157. Grimes, D.A. and K.F. Schulz, *An overview of clinical research: the lay of the land.* Lancet, 2002. **359**(9300): p. 57-61.
 158. Johnson, D.S. and R.B. Smith, *Outcome measurement in the ACL deficient knee--what's the score?* Knee, 2001. **8**(1): p. 51-7.
 159. Ahmad, S.S., et al., *Outcome measures in clinical ACL studies: an analysis of highly cited level I trials.* Knee Surg Sports Traumatol Arthrosc, 2017. **25**(5): p. 1517-1527.
 160. Roos, E.M. and L.S. Lohmander, *The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis.* Health Qual Life Outcomes, 2003. **1**: p. 64.

161. Ingelsrud, L.H., et al., *Meaningful Change Scores in the Knee Injury and Osteoarthritis Outcome Score in Patients Undergoing Anterior Cruciate Ligament Reconstruction*. *Am J Sports Med*, 2018. **46**(5): p. 1120-1128.
162. Wang, D., et al., *Patient-reported outcome measures for the knee*. *J Knee Surg*, 2010. **23**(3): p. 137-51.
163. Frobell, R.B., et al., *A randomized trial of treatment for acute anterior cruciate ligament tears*. *N Engl J Med*, 2010. **363**(4): p. 331-42.
164. Granan, L.P., et al., *Associations between inadequate knee function detected by KOOS and prospective graft failure in an anterior cruciate ligament-reconstructed knee*. *Knee Surg Sports Traumatol Arthrosc*, 2015. **23**: p. 1135-1140.
165. Ardern, C.L., et al., *Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play*. *Br J Sports Med*, 2011. **45**(7): p. 596-606.
166. Mohtadi, N.G. and D.S. Chan, *Return to Sport-Specific Performance After Primary Anterior Cruciate Ligament Reconstruction: A Systematic Review*. *Am J Sports Med*, 2018. **46**(13): p. 3307-3316.
167. Irrgang, J.J., et al., *Development and validation of the international knee documentation committee subjective knee form*. *Am J Sports Med*, 2001. **29**(5): p. 600-13.
168. Tegner, Y. and J. Lysholm, *Rating systems in the evaluation of knee ligament injuries*. *Clin Orthop Relat Res*, 1985(198): p. 43-9.
169. Ingelsrud, L.H., et al., *Proportion of Patients Reporting Acceptable Symptoms or Treatment Failure and Their Associated KOOS Values at 6 to 24 Months After Anterior Cruciate Ligament Reconstruction: A Study From the Norwegian Knee Ligament Registry*. *Am J Sports Med*, 2015. **43**(8): p. 1902-7.
170. Gabler, C.M., et al., *Comparison of Graft Failure Rate Between Autografts Placed via an Anatomic Anterior Cruciate Ligament Reconstruction Technique: A Systematic Review, Meta-analysis, and Meta-regression*. *Am J Sports Med*, 2016. **44**(4): p. 1069-79.
171. Bjornsson, H., et al., *A Randomized Controlled Trial With Mean 16-Year Follow-up Comparing Hamstring and Patellar Tendon Autografts in Anterior Cruciate Ligament Reconstruction*. *Am J Sports Med*, 2016. **44**(9): p. 2304-13.
172. Leiter, J.R., et al., *Long-term follow-up of ACL reconstruction with hamstring autograft*. *Knee Surg Sports Traumatol Arthrosc*, 2014. **22**(5): p. 1061-9.
173. Morgan, M.D., et al., *Fifteen-Year Survival of Endoscopic Anterior Cruciate Ligament Reconstruction in Patients Aged 18 Years and Younger*. *Am J Sports Med*, 2016. **44**(2): p. 384-92.
174. Sanders, T.L., et al., *Long-term rate of graft failure after ACL reconstruction: a geographic population cohort analysis*. *Knee Surg Sports Traumatol Arthrosc*, 2017. **25**(1): p. 222-228.
175. 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*, 2012. **40**(3): p. 595-605.

-
176. Sanders, T.L., et al., *Long-term follow-up of isolated ACL tears treated without ligament reconstruction*. *Knee Surg Sports Traumatol Arthrosc*, 2017. **25**(2): p. 493-500.
 177. Gillquist, J. and K. Messner, *Anterior cruciate ligament reconstruction and the long-term incidence of gonarthrosis*. *Sports Med*, 1999. **27**(3): p. 143-56.
 178. Risberg, M.A., et al., *Changes in Knee Osteoarthritis, Symptoms, and Function After Anterior Cruciate Ligament Reconstruction: A 20-Year Prospective Follow-up Study*. *Am J Sports Med*, 2016. **44**(5): p. 1215-24.
 179. 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.
 180. Seil, R. and R. Becker, *Time for a paradigm change in meniscal repair: save the meniscus!* *Knee Surg Sports Traumatol Arthrosc*, 2016. **24**(5): p. 1421-3.
 181. Engesaeter, L.B., et al., *[Artificial hip joints in Norway. A national registry of total hip arthroplasties]*. *Tidsskr Nor Laegeforen*, 1992. **112**(7): p. 872-5.
 182. Ytterstad, K., et al., *Registration rate in the Norwegian Cruciate Ligament Register: large-volume hospitals perform better*. *Acta Orthop*, 2012. **83**(2): p. 174-8.
 183. SNKLR, *Annual report*. <https://aclregister.nu/media/uploads/Annual%20reports/rapport2017.pdf>, 2017.
 184. Lind, M., F. Menhert, and A.B. Pedersen, *The first results from the Danish ACL reconstruction registry: epidemiologic and 2 year follow-up results from 5,818 knee ligament reconstructions*. *Knee Surg Sports Traumatol Arthrosc*, 2009. **17**(2): p. 117-24.
 185. Ahlden, M., et al., *The Swedish National Anterior Cruciate Ligament Register: a report on baseline variables and outcomes of surgery for almost 18,000 patients*. *Am J Sports Med*, 2012. **40**(10): p. 2230-5.
 186. DNKLR, *Annual report*. https://www.sundhed.dk/content/cms/0/4700_dkrk_aarsrapport_2018_til_offen_tligg%C3%B8rrelse.pdf, 2018.
 187. Kaplan, E.L. and P. Meier, *Nonparametric estimation from incomplete observations*. *J Am Stat Assoc*, 1958. **53**: p. 457-481.
 188. Cox, D.R., *Regression models and life tables*. *J Roy Stat Soc*, 1972. **34**: p. 187-220.
 189. Therneau, T. and P. Grambsch, *Modeling survival data: extending the Cox Model*. 1 ed. 2000: Springer-Verlag New York.
 190. Naylor, C.D. and G.H. Guyatt, *Users' guides to the medical literature. X. How to use an article reporting variations in the outcomes of health services. The Evidence-Based Medicine Working Group*. *JAMA*, 1996. **275**(7): p. 554-8.
 191. Thygesen, L.C. and A.K. Ersboll, *When the entire population is the sample: strengths and limitations in register-based epidemiology*. *Eur J Epidemiol*, 2014. **29**(8): p. 551-8.
 192. Sorensen, H.T. and S. Schulze, *Danish health registries. A valuable tool in medical research*. *Dan Med Bull*, 1996. **43**(5): p. 463.
 193. Moses, L., *Measuring effects without randomized trials? Options, problems, challenges*. *Med Care*, 1995. **33**.

-
194. Arts, D.G., N.F. De Keizer, and G.J. Scheffer, *Defining and improving data quality in medical registries: a literature review, case study, and generic framework*. J Am Med Inform Assoc, 2002. **9**(6): p. 600-11.
 195. Rahr-Wagner, L., et al., *Validation of 14,500 operated knees registered in the Danish Knee Ligament Reconstruction Register: registration completeness and validity of key variables*. Clin Epidemiol, 2013. **5**: p. 219-28.
 196. Dans, P., *Looking for answers in all the wrong places*. Ann Intern Med. , 1993. **119**: p. 855-857.
 197. Abel, U. and A. Koch, *The role of randomization in clinical studies: myths and beliefs*. J Clin Epidemiol, 1999. **52**(6): p. 487-97.
 198. Kunz, R. and A.D. Oxman, *The unpredictability paradox: review of empirical comparisons of randomised and non-randomised clinical trials*. BMJ, 1998. **317**(7167): p. 1185-90.
 199. Benson, K. and A.J. Hartz, *A comparison of observational studies and randomized, controlled trials*. N Engl J Med, 2000. **342**(25): p. 1878-86.
 200. Concato, J., N. Shah, and R.I. Horwitz, *Randomized, controlled trials, observational studies, and the hierarchy of research designs*. N Engl J Med, 2000. **342**(25): p. 1887-92.
 201. Barton, S., *Which clinical studies provide the best evidence? The best RCT still trumps the best observational study*. BMJ, 2000. **321**(7256): p. 255-6.
 202. Pocock, S.J. and D.R. Elbourne, *Randomized trials or observational tribulations?* N Engl J Med, 2000. **342**(25): p. 1907-9.
 203. Gotzsche, P.C. and O. Olsen, *Is screening for breast cancer with mammography justifiable?* Lancet, 2000. **355**(9198): p. 129-34.
 204. Hulley, S., et al., *Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group*. JAMA, 1998. **280**(7): p. 605-13.
 205. Rush, C.J., et al., *Association is not causation: treatment effects cannot be estimated from observational data in heart failure*. Eur Heart J, 2018. **39**(37): p. 3417-3438.
 206. Kuhn, J.E. and W.J. Mallon, *Quantitative Observational Database Research in the Journal of Shoulder and Elbow Surgery*. J Shoulder Elbow Surg, 2016. **25**(11): p. 1733-1734.
 207. von Elm, E., et al., *Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies*. BMJ, 2007. **335**(7624): p. 806-8.
 208. Benchimol, E.I., et al., *The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement*. PLoS Med, 2015. **12**(10): p. e1001885.
 209. Paxton, E.W., et al., *Are we throwing the baby out with the bath water?* J Shoulder Elbow Surg, 2017.
 210. Kamath, G.V., et al., *Revision anterior cruciate ligament reconstruction*. Am J Sports Med, 2011. **39**(1): p. 199-217.
 211. Carson, E.W., et al., *Revision anterior cruciate ligament reconstruction: etiology of failures and clinical results*. J Knee Surg, 2004. **17**(3): p. 127-32.

-
212. Brown, C.H., Jr. and E.W. Carson, *Revision anterior cruciate ligament surgery*. Clin Sports Med, 1999. **18**(1): p. 109-71.
 213. Magnussen, R.A., et al., *Patient demographics and surgical characteristics in ACL revision: a comparison of French, Norwegian, and North American cohorts*. Knee Surg Sports Traumatol Arthrosc, 2015. **23**(8): p. 2339-2348.
 214. Wegrzyn, J., et al., *Repeat revision of anterior cruciate ligament reconstruction: a retrospective review of management and outcome of 10 patients with an average 3-year follow-up*. Am J Sports Med, 2009. **37**(4): p. 776-85.
 215. Rahr-Wagner, L., et al., *Comparison of hamstring tendon and patellar tendon grafts in anterior cruciate ligament reconstruction in a nationwide population-based cohort study: results from the danish registry of knee ligament reconstruction*. Am J Sports Med, 2014. **42**(2): p. 278-84.
 216. Chen, J.L., et al., *Differences in mechanisms of failure, intraoperative findings, and surgical characteristics between single- and multiple-revision ACL reconstructions: a MARS cohort study*. Am J Sports Med, 2013. **41**(7): p. 1571-8.
 217. Grassi, A., et al., *Steep Posterior Tibial Slope, Anterior Tibial Subluxation, Deep Posterior Lateral Femoral Condyle, and Meniscal Deficiency Are Common Findings in Multiple Anterior Cruciate Ligament Failures: An MRI Case-Control Study*. Am J Sports Med, 2019: p. 363546518823544.
 218. Salmon, L.J., et al., *20-Year Outcomes of Anterior Cruciate Ligament Reconstruction With Hamstring Tendon Autograft: The Catastrophic Effect of Age and Posterior Tibial Slope*. Am J Sports Med, 2018. **46**(3): p. 531-543.
 219. Christensen, J.J., et al., *Lateral Tibial Posterior Slope Is Increased in Patients With Early Graft Failure After Anterior Cruciate Ligament Reconstruction*. Am J Sports Med, 2015. **43**(10): p. 2510-4.
 220. Lee, C.C., et al., *Does Posterior Tibial Slope Affect Graft Rupture Following Anterior Cruciate Ligament Reconstruction?* Arthroscopy, 2018. **34**(7): p. 2152-2155.
 221. Bernhardson, A.S., et al., *Tibial Slope and Its Effect on Force in Anterior Cruciate Ligament Grafts: Anterior Cruciate Ligament Force Increases Linearly as Posterior Tibial Slope Increases*. Am J Sports Med, 2019: p. 363546518820302.
 222. Magnussen, R.A., et al., *Graft size and patient age are predictors of early revision after anterior cruciate ligament reconstruction with hamstring autograft*. Arthroscopy, 2012. **28**(4): p. 526-31.
 223. Snaebjornsson, T., et al., *Graft Diameter as a Predictor for Revision Anterior Cruciate Ligament Reconstruction and KOOS and EQ-5D Values: A Cohort Study From the Swedish National Knee Ligament Register Based on 2240 Patients*. Am J Sports Med, 2017. **45**(9): p. 2092-2097.
 224. Spragg, L., et al., *The Effect of Autologous Hamstring Graft Diameter on the Likelihood for Revision of Anterior Cruciate Ligament Reconstruction*. Am J Sports Med, 2016. **44**(6): p. 1475-81.

-
225. Andernord, D., et al., *Patient predictors of early revision surgery after anterior cruciate ligament reconstruction: a cohort study of 16,930 patients with 2-year follow-up*. Am J Sports Med, 2015. **43**(1): p. 121-7.
 226. Faltstrom, A., et al., *Predictors for additional anterior cruciate ligament reconstruction: data from the Swedish national ACL register*. Knee Surg Sports Traumatol Arthrosc, 2016. **24**(3): p. 885-94.
 227. Gifstad, T., et al., *Lower risk of revision with patellar tendon autografts compared with hamstring autografts: a registry study based on 45,998 primary ACL reconstructions in Scandinavia*. Am J Sports Med, 2014. **42**(10): p. 2319-28.
 228. Maletis, G.B., et al., *Reconstruction of the anterior cruciate ligament: association of graft choice with increased risk of early revision*. Bone Joint J, 2013. **95-B**(5): p. 623-8.
 229. Svantesson, E., et al., *Factors associated with additional anterior cruciate ligament reconstruction and register comparison: a systematic review on the Scandinavian knee ligament registers*. Br J Sports Med, 2018.
 230. Mohtadi, N., et al., *A Randomized Clinical Trial Comparing Patellar Tendon, Hamstring Tendon, and Double-Bundle ACL Reconstructions: Patient-Reported and Clinical Outcomes at a Minimal 2-Year Follow-up*. Clin J Sport Med, 2015. **25**(4): p. 321-31.
 231. Freedman, K.B., et al., *Arthroscopic anterior cruciate ligament reconstruction: a metaanalysis comparing patellar tendon and hamstring tendon autografts*. Am J Sports Med, 2003. **31**(1): p. 2-11.
 232. Biau, D.J., et al., *Patellar tendon versus hamstring tendon autografts for reconstructing the anterior cruciate ligament: a meta-analysis based on individual patient data*. Am J Sports Med, 2009. **37**(12): p. 2470-8.
 233. Ayeni, O.R., et al., *Pivot shift as an outcome measure for ACL reconstruction: a systematic review*. Knee Surg Sports Traumatol Arthrosc, 2012. **20**(4): p. 767-77.
 234. Tan, S.H.S., L.B.P. Huh, and L. Krishna, *Outcomes of Anterior Cruciate Ligament Reconstruction in Females Using Patellar-Tendon-Bone versus Hamstring Autografts: A Systematic Review and Meta-Analysis*. J Knee Surg, 2018.
 235. Chee, M.Y., et al., *Outcome of Patellar Tendon Versus 4-Strand Hamstring Tendon Autografts for Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis of Prospective Randomized Trials*. Arthroscopy, 2017. **33**(2): p. 450-463.
 236. Poolman, R.W., et al., *Overlapping systematic reviews of anterior cruciate ligament reconstruction comparing hamstring autograft with bone-patellar tendon-bone autograft: why are they different?* J Bone Joint Surg Am, 2007. **89**(7): p. 1542-52.
 237. Mohtadi, N.G., et al., *Patellar tendon versus hamstring tendon autograft for anterior cruciate ligament rupture in adults*. Cochrane Database Syst Rev, 2011(9): p. CD005960.

-
238. Buchanan, T.S., A.W. Kim, and D.G. Lloyd, *Selective muscle activation following rapid varus/valgus perturbations at the knee*. Med Sci Sports Exerc, 1996. **28**(7): p. 870-6.
 239. Hewett, T.E., et al., *A review of electromyographic activation levels, timing differences, and increased anterior cruciate ligament injury incidence in female athletes*. Br J Sports Med, 2005. **39**(6): p. 347-50.
 240. Toor, A.S., et al., *The significant effect of the medial hamstrings on dynamic knee stability*. Knee Surg Sports Traumatol Arthrosc, 2018.
 241. Suijkerbuijk, M.A.M., et al., *Predictive Factors of Hamstring Tendon Regeneration and Functional Recovery After Harvesting: A Prospective Follow-up Study*. Am J Sports Med, 2018. **46**(5): p. 1166-1174.
 242. Cross, M.J., et al., *Regeneration of the semitendinosus and gracilis tendons following their transection for repair of the anterior cruciate ligament*. Am J Sports Med, 1992. **20**(2): p. 221-3.
 243. Suijkerbuijk, M.A.M., et al., *Hamstring Tendon Regeneration After Harvesting: A Systematic Review*. Am J Sports Med, 2015. **43**(10): p. 2591-8.
 244. Zebis, M.K., et al., *Identification of athletes at future risk of anterior cruciate ligament ruptures by neuromuscular screening*. Am J Sports Med, 2009. **37**(10): p. 1967-73.
 245. Arnason, S.M., et al., *Medial hamstring muscle activation patterns are affected 1-6 years after ACL reconstruction using hamstring autograft*. Knee Surg Sports Traumatol Arthrosc, 2014. **22**(5): p. 1024-9.
 246. Elias, A.R., C.D. Hammill, and R.L. Mizner, *Changes in quadriceps and hamstring cocontraction following landing instruction in patients with anterior cruciate ligament reconstruction*. J Orthop Sports Phys Ther, 2015. **45**(4): p. 273-80.
 247. Koutras, G., et al., *Comparison of knee flexion isokinetic deficits between seated and prone positions after ACL reconstruction with hamstrings graft: Implications for rehabilitation and return to sports decisions*. J Sci Med Sport, 2016. **19**(7): p. 559-62.
 248. Ortiz, A., C.E. Capo-Lugo, and H.L. Venegas-Rios, *Biomechanical deficiencies in women with semitendinosus-gracilis anterior cruciate ligament reconstruction during drop jumps*. PM R, 2014. **6**(12): p. 1097-106.
 249. Eysturoy, N.H., et al., *The Influence of Graft Fixation Methods on Revision Rates After Primary Anterior Cruciate Ligament Reconstruction*. Am J Sports Med, 2018. **46**(3): p. 524-530.
 250. Noh, J.H. and J.W. Lee, *One-Year Serial Follow-up Magnetic Resonance Imaging Study of RigidFix for Femoral Fixation in Anterior Cruciate Ligament Reconstruction*. Knee Surg Relat Res, 2017. **29**(3): p. 203-209.
 251. 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.
 252. Thomopoulos, S., G.M. Genin, and L.M. Galatz, *The development and morphogenesis of the tendon-to-bone insertion - what development can teach us about healing*. J Musculoskelet Neuronal Interact, 2010. **10**(1): p. 35-45.

-
253. Zaffagnini, S., et al., *Electron microscopy of the remodelling process in hamstring tendon used as ACL graft*. Knee Surg Sports Traumatol Arthrosc, 2010. **18**(8): p. 1052-8.
 254. Zaffagnini, S., et al., *Neoligamentization process of BTPB used for ACL graft: histological evaluation from 6 months to 10 years*. Knee, 2007. **14**(2): p. 87-93.
 255. Petersen, W. and H. Laprell, *Insertion of autologous tendon grafts to the bone: a histological and immunohistochemical study of hamstring and patellar tendon grafts*. Knee Surg Sports Traumatol Arthrosc, 2000. **8**(1): p. 26-31.
 256. Chen, C.H., et al., *Enveloping the tendon graft with periosteum to enhance tendon-bone healing in a bone tunnel: A biomechanical and histologic study in rabbits*. Arthroscopy, 2003. **19**(3): p. 290-6.
 257. Heyde, C.E., et al., *[Histological findings for human tibial bone-tendon healing after hamstring transplantation. Investigation of tibial insertion after reconstruction of anterior cruciate ligaments with hamstring transplantation near joint fixation using bioresorbable interference screws]*. Unfallchirurg, 2006. **109**(5): p. 377-82.
 258. Pinczewski, L.A., et al., *Integration of hamstring tendon graft with bone in reconstruction of the anterior cruciate ligament*. Arthroscopy, 1997. **13**(5): p. 641-3.
 259. Eriksson, K., L.G. Kindblom, and T. Wredmark, *Semitendinosus tendon graft ingrowth in tibial tunnel following ACL reconstruction: a histological study of 2 patients with different types of early graft failure*. Acta Orthop Scand, 2000. **71**(3): p. 275-9.
 260. Fankhauser, F., et al., *Tendon-to-bone healing of a quadrupled hamstring tendon graft fixed with biodegradable screws in an immature athlete: a radiologic, arthroscopic, histologic, and electromicroscopic investigation*. Arthroscopy, 2004. **20**(9): p. 992-7.
 261. Nebelung, W., et al., *Histological findings of tendon-bone healing following anterior cruciate ligament reconstruction with hamstring grafts*. Arch Orthop Trauma Surg, 2003. **123**(4): p. 158-63.
 262. Robert, H., et al., *Hamstring insertion site healing after anterior cruciate ligament reconstruction in patients with symptomatic hardware or repeat rupture: a histologic study in 12 patients*. Arthroscopy, 2003. **19**(9): p. 948-54.
 263. Hoher, J., H.D. Moller, and F.H. Fu, *Bone tunnel enlargement after anterior cruciate ligament reconstruction: fact or fiction?* Knee Surg Sports Traumatol Arthrosc, 1998. **6**(4): p. 231-40.
 264. Ma, R., et al., *Effect of Dynamic Changes in Anterior Cruciate Ligament In Situ Graft Force on the Biological Healing Response of the Graft-Tunnel Interface*. Am J Sports Med, 2018. **46**(4): p. 915-923.
 265. Sun, L., et al., *Inhibitory effect of synovial fluid on tendon-to-bone healing: an experimental study in rabbits*. Arthroscopy, 2012. **28**(9): p. 1297-305.
 266. Porter, M.D. and B. Shadbolt, *Femoral Aperture Fixation Improves Anterior Cruciate Ligament Graft Function When Added to Cortical Suspensory Fixation: An In Vivo Computer Navigation Study*. Orthop J Sports Med, 2016. **4**(9): p. 2325967116665795.

-
267. Oh, Y.H., et al., *Hybrid femoral fixation of soft-tissue grafts in anterior cruciate ligament reconstruction using the EndoButton CL and bioabsorbable interference screws: a biomechanical study*. Arthroscopy, 2006. **22**(11): p. 1218-24.
 268. Weimann, A., et al., *Initial fixation strength of a hybrid technique for femoral ACL graft fixation*. Knee Surg Sports Traumatol Arthrosc, 2006. **14**(11): p. 1122-9.
 269. Tsuda, E., et al., *The effect of soft-tissue graft fixation in anterior cruciate ligament reconstruction on graft-tunnel motion under anterior tibial loading*. Arthroscopy, 2002. **18**(9): p. 960-7.
 270. Rahr-Wagner, L., et al., *Increased risk of revision after anteromedial compared with transtibial drilling of the femoral tunnel during primary anterior cruciate ligament reconstruction: results from the Danish Knee Ligament Reconstruction Register*. Arthroscopy, 2013. **29**(1): p. 98-105.
 271. Tejwani, S.G., et al., *Femoral Tunnel Drilling Method: Risk of Reoperation and Revision After Anterior Cruciate Ligament Reconstruction*. Am J Sports Med, 2018. **46**(14): p. 3378-3384.
 272. Desai, N., et al., *Revision surgery in anterior cruciate ligament reconstruction: a cohort study of 17,682 patients from the Swedish National Knee Ligament Register*. Knee Surg Sports Traumatol Arthrosc, 2017. **25**(5): p. 1542-1554.
 273. Rothman, K., S. Greenland, and T. Lash, *Casual diagrams*, in *Modern Epidemiology*. 2008, Lippincott Williams & Wilkins. p. 183-200.
 274. Kondo, E., et al., *Biomechanical comparison of anatomic double-bundle, anatomic single-bundle, and nonanatomic single-bundle anterior cruciate ligament reconstructions*. Am J Sports Med, 2011. **39**(2): p. 279-88.
 275. Lubowitz, J.H., *Anatomic ACL reconstruction produces greater graft length change during knee range-of-motion than transtibial technique*. Knee Surg Sports Traumatol Arthrosc, 2014. **22**(5): p. 1190-5.
 276. Bedi, A., et al., *Effect of early and delayed mechanical loading on tendon-to-bone healing after anterior cruciate ligament reconstruction*. J Bone Joint Surg Am, 2010. **92**(14): p. 2387-401.
 277. Mathes, T., et al., *Registry-based randomized controlled trials merged the strength of randomized controlled trails and observational studies and give rise to more pragmatic trials*. J Clin Epidemiol, 2018. **93**: p. 120-127.

14. Appendix

Appendix 1 - Surgical form NNKLR 2004-2011

NASJONALT KORSBÅNDSREGISTER
 Nasjonalt Register for Leddproteser
 Helse Bergen HF, Ortopedisk klinikk
 Haukeland universitetssjukehus
 Mellandsbakken 11, 5021 BERGEN
 Tlf: 55 97 64 54

F.nr. (11 sifre)

Navn

Sykehus

(Skriv tydelig evt. pasientklirellapp - spesifiser sykehus.)

KORSBÅND

KORSBÅNDSOPERASJONER OG ALLE REOPERASJONER på pasienter som tidligere er korsbåndoperert.
 Alle klirellapper (med unntak av pasientklirellapp) settes i merket felt på baksiden av skjemaet.

(Bilateral operasjon = 2 skjema)

AKTUELLE SIDE (ett kryss) Høyre Venstre

MOTSATT KNE Normalt Tidligere ACL/PCL-skade

TIDLIGERE OPERASJON I SAMME KNE Nei Ja +

SKAEDATO FOR AKTUELL SKADE (mm.åå) | | | | |

AKTIVITET SOM FØRTE TIL AKTUELLE SKADE

<input type="checkbox"/> Fotball	<input type="checkbox"/> Annen lagidrett
<input type="checkbox"/> Håndball	<input type="checkbox"/> Motor- og bisport
<input type="checkbox"/> Snowboard	<input type="checkbox"/> Annen fysisk aktivitet
<input type="checkbox"/> Alpint (inkl. twin tip)	<input type="checkbox"/> Arbeid
<input type="checkbox"/> Annen skiaktivitet	<input type="checkbox"/> Trafikk
<input type="checkbox"/> Kampsport	<input type="checkbox"/> Fall/hopp/vold/lek
<input type="checkbox"/> Basketball	
<input type="checkbox"/> Annet	

AKTUELLE SKADE (Registrer alle skader - også de som ikke opereres)

ACL MCL PLC Med. menisk

PCL LCL Brusk Lat. menisk

Annet

YTERLIGERE SKADER (evt. flere kryss) Nei, hvis ja spesifiser under

Karskade Hvilken:

Nerveskade N. tibialis N. peroneus

Fraktur Femur Tibia Fibula

Patella Usikker

Ruptur i ekstensorapparatet Quadricepsenen Patellarsenen

OPERASJONSDATO (dd.mm.åå) | | | | |

AKTUELLE OPERASJON (ett kryss)

Primær rekonstruksjon av korsbånd

Revisjonskirurgi, 1. seanse

Revisjonskirurgi, 2. seanse

Annen knekirurgi (Ved kryss her skal andre prosedyrer fylles ut)

ÅRSÅK TIL REVISJONSREKONSTRUKSJON (evt. flere kryss)

Infeksjon Graftsvikt

Fiksasjonssvikt Nytt traume

Ubehandlete andre ligamentskader Smerte

Annet

ANDRE PROSEDYRER (evt. flere kryss) Nei, hvis ja spesifiser under

Meniskoperasjon Osteosyntese

Synovektomi Bruskoperasjon

Mobilisering i narkose Artroskopisk debridement

Fjerning av implantat Operasjon pga infeksjon

Benreseksjon (Notch plastikk) Bentransplantasjon

Osteotomi Artridese

Annet

GRAFTVALG

	ACL	PCL	MCL	LCL	PLC
<input type="checkbox"/> BPTB					
<input type="checkbox"/> Hamstring					
<input type="checkbox"/> Allograft					
<input type="checkbox"/> Direkte sutur					
<input type="checkbox"/> Annet					

GRAFTDIAMETER (oppgi største diameter på graftet)mm

Ved bruk av double bundle-teknikk: AM:.....mm PL:.....mm

TILGANG FOR FEMURKANAL

Anteromedial Transtibial Annet

FIKSASJON

Sett klirellapp på merket felt på baksiden av skjemaet

Skil mellom femur og tibia +

AKTUELL BEHANDLING AV MENISKLESJON

	Partiell reseksjon		Total reseksjon		Sutur		Syntetisk fiksasjon*		Menisk-transpl.		Trepnering		Ingen
	Medial	Lateral	Medial	Lateral	Medial	Lateral	Medial	Lateral	Medial	Lateral	Medial	Lateral	
Medial	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lateral	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

* Sett klirellapp på merket felt på baksiden

BRUSKLESJON (evt. flere kryss)

	Areal (cm ²) ≤2 >2	ICRS Grade*				Artrase		Behandlings-kode**						
		1 2 3 4				Ja	Nei	1	2	3	4	Spesifiser annet		
		1	2	3	4									
Patella MF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Patella LF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Trochlea fem.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Med. fem. cond.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Med. tib. plat.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Lat. fem. cond.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Lat. tib. plat.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

*ICRS Grade: 1 Nearly normal: Superficial lesions, soft indentation and/or superficial fissures and cracks; 2 Abnormal: Lesions extending down to <50% of cartilage depth; 3 Severely abnormal: Cartilage defects extending down >50% of cartilage depth as well as down to calcified layer; 4 Severely abnormal: Osteochondral injuries, lesions extending just through the subchondral boneplate or deeper defects down into trabecular bone.

**Behandlingskoder: 1 Debridement; 2 Mikrofraktur; 3 Ingen behandling; 4 Annet.

DAGKIRURGISK OPERASJON Nei Ja

PEROPERATIVE KOMPLIKASJONER Nei Ja, hvilke(n)

OPERASJONSTID (hud til hud)min

SYSTEMISK ANTIBIOTIKA

Nei Ja Profylakse Behandling

Medikament 1 Dosering Varighet timer

Eventuelt i kombinasjon med medikament 2

TROMBOSEPROFYLAKSE

Nei Ja: Første dose Preoperativt Postoperativt +

Medikament 1 Dosering opr.dag.

Medikament 2 Dosering videre Varighet dager

Anbefalt total varighet av tromboseprofylakse

NSAIDs

Nei Ja, hvilken type

Anbefalt total varighet av NSAIDs-behandling

HØYDEcm

VEKTkg

RØYK Nei Av og til Daglig

SNUS Nei Av og til Daglig

Legge:

Legen som har fylt ut skjemaet (navnet registreres ikke i databasen).

2002 5007 Bergen Grafisk AS - 10.0117

**RETTLEDNING**

- Registreringen gjelder primæroperasjon eller reoperasjon av korsbåndsrupstur (fremre og bakre).
- Registreringen gjelder også alle reoperasjoner på pasienter som tidligere er korsbåndsooperert.
- Ett skjema fylles ut for hvert kne som blir operert.
- Flere operasjoner i samme kne registreres på samme skjema.
- Aktuelle ruter markeres med kryss. I noen tilfeller skal det fylles inn et tall i rutene (Brusklesjon).
- Pasienten skal på eget skjema gi samtykke til registrering.

**KOMMENTARER TIL DE ENKELTE PUNKTENE****TIDLIGERE OPERASJON I SAMME KNE**

Forkortelser som er brukt under dette punktet og påfølgende punkter:

- ACL: Fremre korsbånd
- PCL: Bakre korsbånd
- MCL: Mediale kollateralligament
- LCL: Laterale kollateralligament
- PLC: Popliteus kompleks/bicepssene kompleks

SKADEDATO

Skriv inn skadedatoen så eksakt som mulig. Ved ny skade av tidligere operert korsbånd, skriv inn den nye skadedatoen.

FIKSASJON

Angi hvilken fiksasjonstype som er brukt ved å feste klistrelapp på baksiden. Husk å skille mellom femur og tibia.

GRAFTVALG

Forkortelser som er brukt under dette punktet:

- BPTB; Patellarsene autograft
- ST: Semitendinosus autograft
- STGR: Semitendinosus + gracilis autograft
- BQT: Sentral quadricepssene autograft
- BQT-A: Sentral quadricepssene allograft
- BPTB-A: Patellarsene allograft
- BACH-A: Achilles allograft

**PEROPERATIVE KOMPLIKASJONER**

Ved en eventuell ruptur av høstet graft e.l. skal det her nevnes hva som var det opprinnelige graftet. Andre peroperative komplikasjoner skal også fylles inn her.

SYSTEMISK ANTIBIOTIKAPROFYLAKSE

Her føres det på hvilket antibiotikum som er blitt benyttet i forbindelse med operasjonen. Det anføres hvor stor dose, hvor mange doser og profylaksens varighet. Hvis en f.eks. kun har gitt 2g Keflin 4 ganger operasjons dagen med 4 timers mellomrom dvs. 12 timer mellom første og siste dose, så angis det i skjema: Hvilken (A) Keflin Dose(A) 2g
Totalt antall doser 4 Varighet 12 timer.

Kopi beholdes til pasientjournalen, originalen sendes til Haukeland Sykehus.

Kontaktpersoner vedrørende registreringsskjema er

Professor Lars Engebretsen, Ortopedisk Senter, Ullevål Universitetssykehus, tlf.: 950 79 529,

e-post: lars.engebretsen@medisin.uio.no

Overlege Knut Andreas Fjeldsgaard, Haukeland Universitetssykehus, tlf.: 55 97 56 80,

e-post: knut.andreas.fjeldsgaard@helse-bergen.no

Sekretær i Nasjonalt Korsbåndregister, Ortopedisk avd., Helse Bergen:

Ruth G Wasmuth, tlf.: 55 97 64 50, faks: 55 97 37 49

e-post: rgth@helse-bergen.no



GRAFTFIKSASJON		MENISKFIKSASJON	
FEMUR	TIBIA	MEDIAL	LATERAL

Appendix 2 - Surgical form NNCLR 2012-

NASJONALT KORSBÅNDSREGISTER
 Nasjonalt Register for Leddproteser
 Helse Bergen HF, Ortopedisk klinikk
 Haukeland Universitetssykehus
 Mellandsbakken 11, 5021 BERGEN
 Tlf: 55976450

F.nr. (11 sifre).....
 Navn.....
 Sykehus.....
 (Skriv tydelig ev. pasient klistrelapp – spesifiser sykehus.)

KORSBÅND

KORSBÅNDSOPERASJONER OG ALLE REOPERASJONER på pasienter som tidligere er korsbåndoperert.
 Alle klistrelapper (med unntak av pasientklistrelapp) settes i merket felt på baksiden av skjemaet.

(Bilateral operasjon = 2 skjema)

AKTUELL SIDE (ett kryss) Høyre Venstre

MOTSATT KNE Normalt Tidligere ACL/PCL-skade

TIDLIGERE OPERASJON I SAMME KNE (ev. flere kryss)

ACL MCL PLC Medial menisk
 PCL LCL Brusk Lateral menisk
 Annet, spesifiser.....

SKADEDATO FOR AKTUELL SKADE (mm.åå) | | | | | | | |

AKTIVITET SOM FØRTE TIL AKTUELL SKADE

Fotball Kampsport Trafikk
 Håndball Basket Volleyball
 Alpin/Telemark Langrenn/turski Skateboard
 Snowboard Mosjonsaktiviteter Trampoline
 Ishockey/bandy/ rullerkeytter Friluftsliv Dans
 Racketsport Annet fritidsaktivitet Motocross
 Annet.....

AKTUELL SKADE (Registrer alle skader – også de som ikke opereres)

ACL MCL PLC Menisk
 PCL LCL Brusk
 Annet.....

YTERLIGERE SKADER (ev. flere kryss)

Karskade Hvilken:.....
 Nerveskade N. tibialis N. peroneus
 Fraktur Femur Tibia Fibula
 Patella Usikker
 Ruptur i ekstensorapparatet Quadricepsenenen Patellarsenenen

OPERASJONSDATO (dd.mm.åå) | | | | | | | |

AKTUELLE OPERASJON (ett kryss)
 (Hvis ingen kryss, gå direkte til ANDRE PROSEDYRER.)

Rekonstruksjon av korsbånd Revisjonsrekonstruksjon

ÅRSAK TIL REVISJONSREKONSTRUKSJON (ev. flere kryss)

Infeksjon Graftsvikt
 Fiksasjonssvikt Nytt traume
 Ubehandlete andre ligamentskader
 Annet.....

ANDRE PROSEDYRER (ev. flere kryss)

Meniskoperasjon Osteosyntese
 Synovektomi Bruskoperasjon
 Mobilisering i narkose Artroskopisk debridement
 Fjerning av implantat Operasjon pga infeksjon
 Benreseksjon (Notch plastikk) Bentransplantasjon
 Osteotomi Artrodese
 Annet.....

GRAFTVALG (se forklaring på baksiden)

	ACL	PCL	MCL	LCL	PLC
<input type="checkbox"/> BPTB					
<input type="checkbox"/> ST – dobbel					
<input type="checkbox"/> ST – kvadrupel					
<input type="checkbox"/> STGR – dobbel					
<input type="checkbox"/> Double bundle- teknikk					
<input type="checkbox"/> BQT					
<input type="checkbox"/> BQT-A					
<input type="checkbox"/> BPTB-A					
<input type="checkbox"/> BACH-A					
<input type="checkbox"/> Direkte sutur					
<input type="checkbox"/> Syntetisk graft					
<input type="checkbox"/> Annet.....					

FIKSASJON
 Sett klistrelapp på merket felt på baksiden av skjemaet
 Skill mellom femur og tibia

AKTUELL BEHANDLING AV MENISKLESJON

	Reseksjon	Sutur	Syntetisk fiksasjon*	Menisk-tranapl.	Trepanering	Ingen
Medial	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lateral	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

* Sett klistrelapp på merket felt på baksiden

BRUSKLESJON (ev. flere kryss. Husk å fylle ut arealet)
 Er skaden: ny gammel vet ikke

	Omfang		Sannsynlig årsak** (1-5)	Behandlingskode*** (1-9)
	Areal (cm ²)	ICRS Grade* (1-4)		
Patella MF	<input type="checkbox"/>	<input type="checkbox"/>		
Patella LF	<input type="checkbox"/>	<input type="checkbox"/>		
Trochlea fem.	<input type="checkbox"/>	<input type="checkbox"/>		
Med. fem. cond.	<input type="checkbox"/>	<input type="checkbox"/>		
Med. tib. plat.	<input type="checkbox"/>	<input type="checkbox"/>		
Lat. fem. cond.	<input type="checkbox"/>	<input type="checkbox"/>		
Lat. tib. plat.	<input type="checkbox"/>	<input type="checkbox"/>		

***ICRS Grade:** 1 Nearly normal; Superficial lesions, soft indentation and/or superficial fissures and cracks; 2 Abnormal: Lesions extending down to <50% of cartilage depth; 3 Severely abnormal: Cartilage defects extending down >50% of cartilage depth as well as down to calcified layer; 4 Severely abnormal: Osteochondral injuries, lesions extending just through the subchondral boneplate or deeper defects down into trabecular bone.

****Sannsynlige årsaker:** 1 Traume; 2 CM: chondromalacia patellae; 3 OCD: osteochondritis dissecans; 4 OA: primær artrose; 5 Annet: Spesifiser årsak i aktuelle rubrikk.

*****Behandlingskoder:** 1 Debridement; 2 Mikrofraktur; 3 Mosakk; 4 Biopsi til dyrking; 5 Celletransplantasjon; 6 Celletransplantasjon med matrix; 7 Periosttransplantasjon; 8 Ingen behandling; 9 Annet: Spesifiser behandling i aktuelle rubrikk.

DAGKIRURGISK OPERASJON Nei Ja

PEROPERATIVE KOMPLIKASJONER Nei Ja, hvilke(n).....

OPERASJONSTID (hud til hud).....min.

SYSTEMISK ANTIBIOTIKAPROFLAKSE

Nei Ja, hvilken (A).....
 Dose (A).....Totalt antall doser.....Varighet.....timer
 Ev. i kombinasjon med (B).....
 Dose (B).....Totalt antall doser.....Varighet.....timer

TROMBOSEPROFLAKSE

Nei Ja, hvilken type.....
 Dosering opr.dag.....Første dose gitt preopr Nei Ja
 Senere dosering.....Antatt varighet.....døgn
 Ev. i kombinasjon med.....
 Dosering.....Antatt varighet.....døgn
 Annet, spesifiser.....

NSAIDs

Nei Ja, hvilken type.....

Legge:.....
 Legen som har fylt ut skjemaet (navnet registreres ikke i databasen).

RETTLEDNING

- Registreringen gjelder ALLE fremre og bakre korsbåndoperasjoner.
- Registreringen gjelder ALLE kneoperasjoner på pasienter som tidligere er korsbåndoperert.
- Ett skjema fylles ut for hvert kne som blir operert.
- Aktuelle ruter markeres med kryss. Stiplet linje fylles ut der dette er aktuelt.
- Pasienten skal på eget skjema gi samtykke til registrering.

KOMMENTARER TIL DE ENKELTE PUNKTENE**FORKORTELSER SOM ER BRUKT PÅ SKJEMAET**

- ACL: Fremre korsbånd
- PCL: Bakre korsbånd
- MCL: Mediale kollateralligament
- LCL: Laterale kollateralligament
- PLC: Popliteus kompleks/bicepsene kompleks
- BPTB; Patellarsene autograft
- AM: Anteromediale bunt av ACL
- PL: Posterolaterale bunt av ACL

SKADEDATO

Skriv inn skadedatoen så eksakt som mulig.
Ved ny skade av tidligere operert korsbånd, skriv inn den nye skadedatoen.

FIKSASJON

Angi hvilken fiksasjonstype som er brukt ved å feste klistrelapp på baksiden.
Husk å skille mellom femur og tibia for graffiksasjon, og mellom medial og lateral side for meniskfiksasjon.

PEROPERATIVE KOMPLIKASJONER

Ved en ruptur/kontaminering av høstet graft e.l. skal det opprinnelige graftet anføres her.
Andre peroperative komplikasjoner skal også fylles inn her.

**SYSTEMISK ANTIBIOTIKA**

Her føres det på hvilket antibiotikum som er blitt benyttet i forbindelse med operasjonen. Det anføres dose, antall doser og profylaksens varighet. F.eks. Medikament 1: Keflin 2g x 4, med varighet 12 timer.

TROMBOSEPROFYLAKSE

Type, dose og antatt varighet av profylaksen skal angis separat for operasjonsdagen og senere.

Kopi beholdes i pasientjournalen, originalen sendes til Nasjonalt Korsbåndregister.

Kontaktpersoner vedrørende registreringsskjema er

Professor Lars Engebretsen, Ortopedisk avdeling, Oslo Universitetssykehus
e-post: lars.engebretsen@medisin.uio.no
Lege Håvard Visnes, Haukeland universitetssjukehus
e-post: haavard.visnes@helse-bergen.no
Sekretær i Nasjonalt Korsbåndregister, Ortopedisk avd., Helse Bergen
Kate Vadheim, tlf.: 55 97 64 54 e-post: korsband@helse-bergen.no
Internett: <http://nrlweb.helse.net/>



GRAFTFIKSASJON		MENISKFIKSASJON	
FEMUR	TIBIA	MEDIAL	LATERAL

15. Papers I-III

I

II

Graft fixation influences revision risk after ACL reconstruction with hamstring tendon autografts

A study of 38,666 patients from the Scandinavian knee ligament registries 2004–2011

Andreas PERSSON^{1,2}, Tone GIFSTAD^{3,4}, Martin LIND⁵, Lars ENGBRETSSEN^{6,7,8}, Knut FJELDSGAARD¹, Jon Olav DROGSET^{3,4}, Magnus FORSSBLAD⁹, Birgitte ESPEHAUG¹⁰, Asle B KJELLENSEN¹, and Jonas M FEVANG¹

¹ Department of Orthopaedic Surgery, Haukeland University Hospital, Bergen, Norway; ² University of Bergen, Faculty of Medicine and Dentistry, Department of Clinical Medicine, Bergen, Norway; ³ Department of Orthopaedic Surgery, Trondheim University Hospital, Trondheim, Norway; ⁴ Norwegian University of Science and Technology, Trondheim, Norway; ⁵ Department of Orthopaedics, Aarhus University Hospital, Aarhus, Denmark; ⁶ Department of Orthopaedic Surgery, Oslo University Hospital, Oslo, Norway; ⁷ Faculty of Medicine, University of Oslo, Oslo, Norway; ⁸ Oslo Sports Trauma Center, Norwegian School of Sport Sciences, Oslo, Norway; ⁹ Stockholm Sports Trauma Research Center, Karolinska Institutet, Stockholm, Sweden; ¹⁰ Centre for Evidence-Based Practice, Bergen University College, Bergen, Norway

Correspondence: Andreas.persson@helse-bergen.no

Submitted 2017-04-06. Accepted 2017-10-23.

Background and purpose — A large number of fixation methods of hamstring tendon autograft (HT) are available for anterior cruciate ligament reconstruction (ACLR). Some studies report an association between fixation method and the risk of revision ACLR. We compared the risk of revision of various femoral and tibial fixation methods used for HT in Scandinavia 2004–2011.

Materials and methods — A register-based study of 38,666 patients undergoing primary ACLRs with HT, with 1,042 revision ACLRs. The overall median follow-up time was 2.8 (0–8) years. Fixation devices used in a small number of patients were grouped according to design and the point of fixation.

Results — The most common fixation methods were Endobutton (36%) and Rigidfix (31%) in the femur; and interference screw (48%) and Intrafix (34%) in the tibia. In a multivariable Cox regression model, the femoral fixations Rigidfix and Transfix had a lower risk of revision (HR 0.7 [95% CI 0.6–0.8] and 0.7 [CI 0.6–0.9] respectively) compared with Endobutton. In the tibia the retro interference screw had a higher risk of revision (HR 1.9 [CI 1.3–2.9]) compared with an interference screw.

Interpretation — The choice of graft fixation influences the risk of revision after primary ACLR with hamstring tendon autograft. ■

The most commonly used grafts in Scandinavia for anterior cruciate ligament reconstruction (ACLR) are hamstring tendon autografts (HT) or patellar tendon autografts (Granan et al. 2009). There are multiple devices available on the

market for fixation of the graft. Most devices have been evaluated mechanically tested with acceptable results (Ahmad et al. 2004, Milano et al. 2006, Aga et al. 2013). Numerous clinical studies have found similar objective or subjective outcomes comparing different fixation techniques (Laxdal et al. 2006, Rose et al. 2006, Moiala et al. 2008, Myers et al. 2008, Harilainen and Sandelin 2009, Drogset et al. 2011, Frosch et al. 2012, Gifstad et al. 2014). Hence, there is no definite recommendation for the best fixation technique and the surgeon's choice of fixation is likely to be influenced by personal experience, local traditions, and possibly marketing from the industry.

A recent study (Persson et al. 2015) from the Norwegian Knee Ligament Registry (NKLR) identified combinations of fixations for HT with increased risk of revision at 2 years. In addition, a higher risk of revision when using cortical buttons compared with transfemoral or intratunnel fixations in the femur was observed. These findings call into question the increasing use of cortical buttons for HT fixation (Ahlden et al. 2012). In addition, Andernord et al. (2014) found a reduced risk of early revision when a metal interference screw was used to fixate semitendinosus grafts in the tibia.

This study further investigates the risk of revision for the most common fixation techniques and devices in HT reconstructions during the period 2004–2011, using a combined dataset from all 3 Scandinavian ACL registries (the NKLR, the Swedish National Anterior Cruciate Ligament Registry, and the Danish Knee Ligament Reconstruction Register).

Materials and methods

Data sources

The Scandinavian knee ligament registries were established in 2004–2005 and are similar in design (Granán et al. 2008, Ahlden et al. 2012, Rahr-Wagner and Lind 2016). Patient-specific data (sex, age, previous surgery/injuries to index or contralateral knee), surgical details (graft choice, fixation choice, potential treatment of other ligament injuries or meniscal/cartilage injuries) and intraoperative findings (meniscal and cartilage injuries and signs of arthrosis) are reported at the time of surgery. Patients are followed prospectively with revision ACLR, subsequent surgery to the index knee, and patient-reported outcome (Knee Injury and Osteoarthritis Outcome Score at 1, 2, 5, and 10 years follow-up) as endpoints. The report rates to the registries are similar, from 86% to $\geq 90\%$ (Ytterstad et al. 2012, Rahr-Wagner et al. 2013a, www.aclregister.nu 2014).

This study includes all 38,666 patients registered from the start of the Scandinavian registries up to December 31, 2011, with a primary ACLR with an HT. The following data were considered in the study: date of primary and potential revision reconstruction, patient age and sex, fixation of the graft in femur and tibia, activity at primary injury, location (right/left knee), meniscal injury or treatment (yes/no), cartilage injury (yes/no), medial collateral injury (yes/no), and other concomitant injuries (fractures, nerve injuries, and vascular injuries). Patients with concomitant ligament injuries treated surgically were not included.

Exposure

We analyzed the revision rate and risk dependent on what tibial and femoral fixation device was used in the primary ACLR. The fixation device in the femur and tibia was either registered by the catalogue number of each device by using the unique bar-code sticker delivered by the manufacturer, or reported manually by the surgeon with either the registered trademark name of the device or a description of the fixation design, such as interference screw. Devices used in fewer than 500 patients were grouped according to their design and point of graft fixation. The femoral devices in the dataset were grouped as: cortical fixation (Endobutton [Smith & Nephew] or other), transfemoral fixation (Rigidfix [DePuy Mitek], Transfix [Arthrex] or other), interference screw, or other/unknown. The tibial devices in the dataset were grouped as: cortical fixation, interference screw, Intrafix (DePuy Mitek), retro interference screw, Rigidfix (DePuy Mitek), or other/unknown.

Statistics

Statistical analyses were performed using SPSS Statistics software version 22 (SPSS Inc, IBM Corp, Armonk, NY, USA). All tests were 2-sided with a 0.05 significance level.

Unadjusted cumulative implant revision curves were established using Kaplan–Meier estimates and crude 2- and 5-year revision percentages are reported. Unadjusted and adjusted hazard ratios (HR) with 95% confidence intervals (CI) were

estimated in Cox regression analyses. The multivariable analyses were stratified for country. The assumption of proportional hazards of the Cox regression model was evaluated with log–log plot and was found suitable. All survival analyses were performed with revision as the endpoint. No data were received on death or emigration. Patients were at risk and followed until revision or end of study.

Confounding factors

Patient age (5-year categories) at the time of the primary reconstruction, sex, meniscal injury to 1 or both menisci (yes/no), cartilage injury (yes/no), and activity at primary injury (pivoting activity [soccer, team handball, alpine activities]/other activities) were considered as possible confounding factors as these are potential risk factors for revision and may also influence the choice of fixation method. Further, none of the factors were considered as possible mediating variables. Additional analyses showed that meniscal injury and cartilage injury was not associated with, and thus did not inform, the fixation method. They were therefore not entered into the multivariable Cox regression analysis. Additional adjustment was made for corresponding fixation in the tibia when analyzing femoral fixations and for corresponding fixation in the femur when analyzing tibial fixations.

Ethics, funding, and potential conflicts of interest

Informed consent has been signed by all the participants in the NKLR, and the NKLR is approved by the Norwegian Data Inspectorate. No written consent is necessary in Denmark and Sweden for national healthcare registries. The study was funded by a grant from the Norwegian Orthopedic association.

LE has received course honoraria from Smith & Nephew, a fellowship grant from Arthrex to his institution, royalties for making of tools from Arthrex, and travel/accommodation expenses covered or reimbursed by Smith & Nephew for Multiligament course in Vail.

Results

The mean age at surgery was 28 years, and 57% were men. The median time from initial injury to the time of primary ACLR was 8 months (range 0–45 years). The most commonly used fixations in the femur were the Endobutton and Rigidfix, used in 14,106 and 12,041 patients respectively. The most commonly used tibial fixations were interference screw and Intrafix, used in 18,640 and 13,014 patients respectively. The median overall follow-up time was 2.8 (1.8–4.3) years (Table 1). The most commonly used combinations of fixations (femoral x tibial) were Rigidfix x Intrafix and Endobutton x Interference screw, used in 8,023 and 8,006 patients respectively (Table 2).

The use of femoral fixation with Endobutton increased during the entire study period while the usage of Rigidfix decreased after a peak in 2007 (Figure 1). The use of tibial

Table 1. Patients' characteristics and baseline epidemiology. Values are percentages unless otherwise specified

Femoral fixation	Cortical fixation		Transfemoral fixation			Interference screw	Other/unknown
	Endobutton	Other	Rigidfix	Transfix	Other		
n	14,106	4,352	12,041	3,652	520	3,453	542
Age, mean (SD) ^{a,b}	27 (10)	28 (11)	29 (10)	28 (10)	28 (10)	28 (10)	28 (11)
Pivoting activity ^c	66	66	66	66	72	67	64
Male	56	58	57	59	57	59	54
MCL injury	2.5	2.1	1.9	3.2	3.7	1.2	3.3
Menisc injury	41	44	38	42	42	43	40
Cartilage injury	21	21	20	29	28	20	23
Other injury	0.4	0.5	0.7	0.5	1.3	0.3	0.4
Follow-up, mean (SD) ^b	2.2 (1.8)	2.5 (1.7)	3.7 (1.8)	3.9 (1.8)	5.4 (2.0)	3.0 (1.8)	2.9 (2.1)

Tibial fixation	Cortical fixation	Interference screw	Retro interference screw		Other/unknown	
			Intrafix	Rigidfix		
n	4,814	18,640	13,014	508	867	823
Age, mean (SD) ^{a,b}	27 (11)	28 (10)	29 (11)	27 (10)	27 (10)	27 (11)
Pivoting activity ^c	65	66	67	63	59	66
Male	55	58	58	58	54	57
MCL injury	3.4	2.3	1.6	0.8	3.6	5.1
Meniscal injury	43	43	37	46	37	45
Cartilage injury	19	24	18	30	25	29
Other injury	0.5	0.4	0.8	1.0	0.2	0.9
Follow-up, mean (SD) ^b	3.2 (2.0)	2.7 (1.9)	3.3 (1.9)	3.3 (1.8)	4.1 (1.7)	2.8 (2.3)

^a At time of surgery.
^b Years.
^c At primary injury (soccer, team handball, alpine activities).

Table 2. Combinations of fixations used in more than 500 patients

Fixations (femoral x tibial)	n
Endobutton x interference screw	8,006
Endobutton x intrafix	3,154
Endobutton x cortical fixation	2,541
Other cortical x interference screw	1,856
Other cortical x cortical fixation	1,483
Other cortical x Intrafix	948
Rigidfix x Intrafix	8,023
Rigidfix x interference screw	2,661
Rigidfix x Rigidfix	825
Transfix x interference screw	3,123
Interference screw x interference screw	2,859
Other combinations (used in less than 500 patients)	3,187
Total	38,666

fixation with interference screw increased after 2006 while the use of Intrafix decreased after a peak in 2006 (Figure 2).

Revision rate during the first postoperative year was low (Figures 3 and 4).

The 5-year revision rate according to femoral fixation was 5.0% (CI 4.4–5.7) for Endobutton, 3.4% (CI 3.0–3.8) for Rigidfix, and 3.5% (CI 2.8–4.1) for Transfix. For tibial fixation the 5-year revision rate was 4.2% (CI 3.7–4.6) for interference screw, 4.0% (CI 3.0–3.8) for Intrafix, and 2.5% (CI 1.4–3.7) for Rigidfix (Figures 3, 4 and Table 3).

In the multivariable analysis, the HR for revision was 0.7

Femoral fixation methods (%)

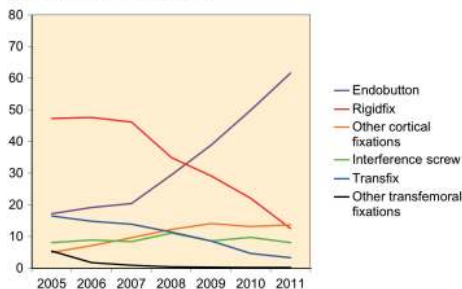


Figure 1. Femoral fixation in Scandinavia 2005–2011.

Tibial fixation methods (%)

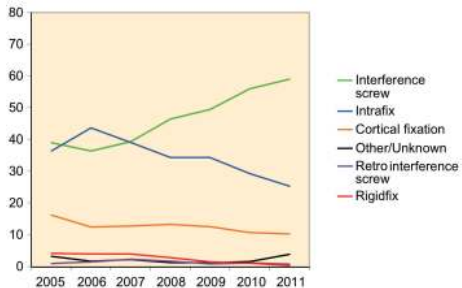


Figure 2. Tibial fixation in Scandinavia 2005–2011.

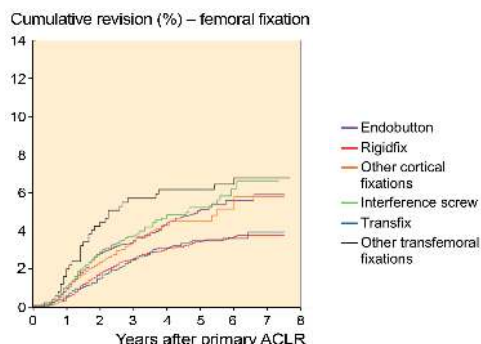


Figure 3. Cumulative revision curve for femoral fixations.

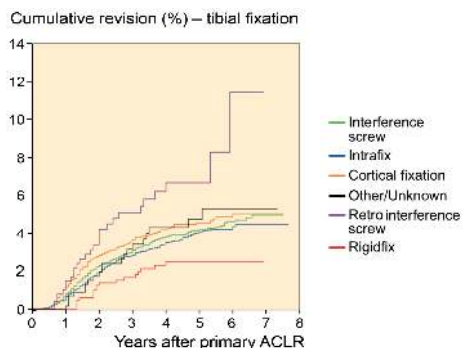


Figure 4. Cumulative revision curve for tibial fixations.

Table 3. Crude revision rates for patients within the examined groups of fixations at 2 and 5 years

Fixation point and group	n (revisions)	Revision rate (CI) % 2 years	Revision rate (CI) % 5 years
Femoral fixation ^a			
Cortical fixation			
Endobutton	14,106 (342)	2.7 (2.4–3.1)	5.0 (4.4–5.7)
Other	4,352 (115)	2.2 (1.7–2.7)	4.5 (3.6–5.4)
Transfemoral fixation			
Rigidfix	12,041 (316)	1.7 (1.4–1.9)	3.4 (3.0–3.8)
Transfix	3,652 (100)	1.5 (1.1–1.9)	3.5 (2.8–4.1)
Other	520 (32)	4.2 (2.5–6.0)	6.1 (4.0–8.3)
Interference screw			
Other/unknown	3,453 (119)	2.7 (2.1–3.3)	5.2 (4.2–6.2)
Tibial fixation ^b			
Cortical fixation			
Endobutton	4,814 (159)	2.8 (2.3–3.3)	4.6 (3.8–5.3)
Other	18,640 (462)	2.2 (2.0–2.5)	4.2 (3.7–4.6)
Interference screw			
Intrafix	13,014 (355)	1.9 (1.6–2.1)	4.0 (3.6–4.5)
Retro interference screw	508 (27)	3.4 (1.7–5.1)	6.7 (4.1–9.3)
Rigidfix	867 (18)	1.3 (0.4–2.0)	2.5 (1.4–3.7)
Other/unknown	823 (21)	1.8 (0.6–2.9)	4.7 (2.7–6.8)

Log-rank test for difference in overall revision between groups:

^a p-value < 0.001

^b p-value = 0.001

Table 4. Results (hazard ratios – HR) from the Cox regression models with revision as endpoint

Fixation point and group	HR (CI)	Adjusted HR (CI) ^a
Femoral fixation		
Cortical fixation		
Endobutton	Ref.	Ref.
Other	0.9 (0.8–1.2)	0.8 (0.7–1.1)
Transfemoral fixation		
Rigidfix	0.7 (0.6–0.8)	0.7 (0.6–0.8)
Transfix	0.7 (0.5–0.8)	0.7 (0.6–0.9)
Other	1.2 (0.9–1.8)	1.1 (0.7–1.6)
Interference screw		
Other/unknown	1.1 (0.9–1.3)	1.1 (0.9–1.4)
Other/unknown	1.1 (0.7–1.7)	1.1 (0.7–1.9)
Tibial fixation		
Cortical fixation		
Endobutton	1.1 (1.0–1.4)	1.1 (0.9–1.4)
Interference screw		
Other	Ref.	Ref.
Intrafix	0.9 (0.8–1.1)	1.0 (0.9–1.2)
Retro interference screw	1.8 (1.2–2.6)	1.9 (1.3–2.9)
Rigidfix	0.6 (0.3–0.9)	0.9 (0.5–1.4)
Other/ unknown	1.1 (0.7–1.6)	1.0 (0.6–1.5)

^a Adjusted analysis model stratified for country (Sweden, Denmark, Norway) and adjusted for gender, age at surgery (5-year categories), activity at primary injury, and corresponding fixation in tibia or femur.

for the Rigidfix (CI 0.6–0.8) and Transfix (CI 0.6–0.9) groups compared with the Endobutton group and 1.9 (CI 1.3–2.9) for the group with the tibial fixation retro interference screw compared with the interference screw group (Table 4).

Discussion

In this large multiregistry-based study from the Scandinavian countries, the main finding was that the HR for revision was reduced by 30% when using transfemoral fixation with Rigidfix or Transfix compared with cortical fixation with Endobutton, independent of the tibial fixation used. The hamstring tendon autograft was fixed with the cortical fixation Endobut-

ton in one-third of the patients, with increasing use during the last years of the study period.

These results are in line with the recent findings of increased risk of revision within 2 years for cortical fixation compared with transfemoral fixation from the NCLR (Persson et al 2015). One can question the clinical relevance of a minor difference in revision risk. However, when clinical outcome after revision ACLR may be worse than after primary ACLR (Battaglia et al. 2007, Grassi et al. 2016), we believe the differences are of interest.

Previously, a variety of outcomes have been studied in clinical studies comparing different fixation devices and techniques (Drogset et al. 2005, Rose et al. 2006, Capuano et al. 2008, Moiala et al. 2008) with similar outcomes in the examined

groups. However, there are a few clinical, biomechanical, and anatomical studies that have reported differences between different graft fixations in the femur. A recent meta-analysis by Browning et al. (2017) included 41 clinical level 1–4 studies comparing clinical outcome for patients treated with an ACLR with 4-strand hamstring autograft using either suspensory or aperture fixation. They found better arthrometric stability and fewer graft ruptures using suspensory compared with aperture fixation at a minimum of 2-year follow-up; however, they included graft fixation in the femur with cross-pins in the suspensory group. In a clinical trial of double-bundle ACLR, Ibrahim et al. (2015) found that 4 out of 32 patients with ACL grafts that were fixed in the femur with cortical fixation had > 5 mm of postoperatively instrumented knee laxity compared with 0 out of 34 patients with transfemoral fixation at a mean follow-up of 2.5 years. They found no difference between the 2 groups in the Lachman and pivot-shift test. Frosch et al. (2012) compared, in a prospective non-randomized study, femoral fixation with bioabsorbable interference screws in 31 cases and bioabsorbable Rigidfix in 28 cases. They found similar subjective results but less side-to-side anterior translation as measured with a KT-1000 arthrometer in the cases with femoral fixation using Rigidfix.

Biomechanical studies most frequently investigate graft-fixation complex stiffness, pull-out strength, or graft-fixation complex lengthening after cyclic loading. Laxity of the graft-fixation complex and graft-tunnel motion might disturb the biologic incorporation of the graft in the bone tunnel (Hoher et al. 1998), leading to a weaker reconstruction. In a cadaver model measuring graft-fixation complex stiffness in double-looped semitendinosus grafts, To et al. (1999) found the stiffness of the graft and fixation complex to be dependent on the fixation method rather than the graft, with decreased stiffness when using a suture loop and a cortical button. Höher et al. (1998) found up to 3 mm of graft-tunnel motion when using a titanium button and polyester tape to fix quadruple hamstring grafts within the femoral bone tunnel. To further investigate the histological insertion point or the graft itself there is a need for more studies where samples are collected from revision ACLRs.

There has been a debate as to whether the surgical technique for femoral tunnel drilling affects the clinical outcome. Both Rigidfix and Transfix are likely to mainly have been fixed through a transtibial technique (TT) for drilling the femoral tunnel. TT has been shown to have a lower risk of revision compared with the anteromedial (AM) technique in a previous register study (Rahr-Wagner et al. 2013b). The authors argued that it could be due to the increased load on an anatomic reconstructed graft, due to potential problems with a shorter femoral tunnel or as a result of the surgeon's learning curve when the new AM technique was introduced. However, they did not adjust for graft fixation in their analysis. Liu et al. (2015) found, in a systematic review, superior results for the AM technique based on physical examination, and it is possible that the

mentioned difference in revision risk could be due to an unknown confounder, such as the graft fixation.

A change from transfemoral devices to cortical fixation has previously been reported from the Swedish ACL registry, probably as a result of the focus on anatomic ACL reconstruction using the AM technique (Ahlden et al. 2012). This tendency is also clear in our study.

Among the investigated tibial fixation devices the retro interference screw was the only device with a statistically significantly higher risk of revision compared with the interference screw. The retro interference screw (available in titanium or degradable poly-L-lactic acid [PLLA]) is placed retrogradely into the tibial bone tunnel from inside the joint. Although poor results have been reported in a previous biomechanical study (Scannell et al. 2015), and the possible risk of failure when using PLLA screws (Drogset et al. 2005, Persson et al. 2015) could explain the increased revision risk for the retro interference screw found in this study, we interpret the results with caution due to the small sample size. Further, we did not have data defining the material of the included retro interference screws and thus may not know whether this could have contributed to the inferior results.

A limited number of register studies have been conducted on the current topic. Andernord et al. (2014) found a statistically significant lower incidence of revision surgery when a metal interference screw was used in semitendinosus tendon autograft reconstructions compared with a bioabsorbable interference screw, AO screw, metal interference screw + staple, or Intrafix registered in the Swedish National Anterior Cruciate Ligament Registry 2005–2011. This was, however, not found in the group with a combined semitendinosus and gracilis graft, which was used in four-fifths of the patients, in line with our results.

Strengths and weaknesses

The most important strength in this study is the large sample size of the groups investigated. A randomized controlled trial is difficult to conduct with enough statistical power to investigate a rare endpoint such as revision ACLR (Naylor and Guyatt 1996). A sample size calculation shows that 1,000 patients are needed in each group to detect a statistically significant difference in 2-year revision rates of 2.4% and 4.7%, equivalent to a hazard rate ratio of 2 (with a 2-sided 0.05 level and power of 80%). In general, prospective registry-based cohort studies are considered to be hypothesis-generating and not proving causality. However, in modern observational studies where potential biases are considered, estimates of treatment effects may be similar to those found in randomized controlled trials (Benson and Hartz 2000). Therefore, we believe our study to have a good methodology to investigate the risk of failure for different surgical techniques, such as choice of fixation method for the graft.

The baseline data of the Norwegian registry have been shown to be congruent with other registries (Maletis et al.

2011, Granan et al. 2012). Accordingly, we believe the results to be applicable not only to the countries where the study was conducted, but to a general orthopedic community.

We acknowledge the existing weaknesses of this study. For the smallest patient groups our results might be influenced by hospital-dependent revision rates. Experienced surgeons at large-volume clinics might be more prone to revise patients, and could have a different fixation choice for the primary ACLR than surgeons in low-volume clinics. These surgeons could also attract more high-level athletes with a higher risk of re-injury. We have no complete data on the surgeons' experience, the postoperative rehabilitation protocol, graft size, activity level of the patient, if TT or AM technique was used for femoral drilling, or if the hamstring tendons are semitendinosus grafts or a combination of semitendinosus and gracilis, which are factors that potentially could influence the risk of revision.

The use of revision surgery as the endpoint is a robust outcome measure, but it does not include patients with subjective or objective graft failures that have not undergone revision surgery. Although the number of graft failures is probably greater than the number of patients reaching our endpoint, we believe the observed differences are valid. In addition, we have no reason to believe that patients in certain fixation groups would be more prone to seek clinical attention and be considered for revision surgery. We do not have the data on why the patients were revised, which could potentially differ between fixation groups.

We have no data on death or emigration, which potentially could bias our results as a competing risk to revision. With a mean age of 28 years in the population, occurrence of death in the follow-up is likely to be low. We do not believe that occurrence of emigration would differ between the groups. Further, we do not have data on possible bilateral observations included. Even though the occurrence is probably not different amongst the groups investigated, this might have biased our results.

Summary

Although that the cause of revision ACLR is often multifactorial, the results from this study suggest that there could be substantial differences in revision risk dependent on what fixation method is used in hamstring autograft ACL reconstructions. The results illustrate the need for continuous multiregister cooperation with fixation devices registered by catalogue number to allow for early detection of possible implant failures.

All authors contributed to the planning of the project, interpreting results, draft revision, and approval of the manuscript. AP, TG, and BE did the statistical analysis.

The authors would like to thank all colleagues for reporting primary ACLRs and revisions to the registries. Special thanks are extended to the staff of the registries for data processing and quality assurance.

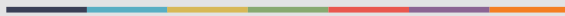
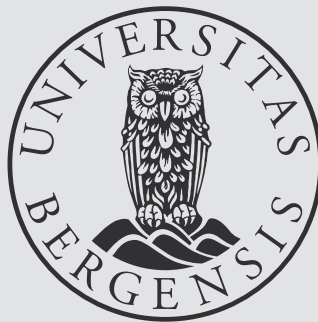
Acta thanks Brian Devitt and Jos van Raaij for help with peer review of this study.

- Agar C, Rasmussen M T, Smith S D, Jansson K S, LaPrade R F, Engebretsen L, Wijdicks C A. Biomechanical comparison of interference screws and combination screw and sheath devices for soft tissue anterior cruciate ligament reconstruction on the tibial side. *Am J Sports Med* 2013; 41 (4): 841–48.
- Ahlden M, Samuelsson K, Sernert N, Forssblad M, Karlsson J, Kartus J. The Swedish National Anterior Cruciate Ligament Register: A report on baseline variables and outcomes of surgery for almost 18,000 patients. *Am J Sports Med* 2012; 40 (10): 2230–35.
- Ahmad C S, Gardner T R, Groh M, Arnouk J, Levine W N. Mechanical properties of soft tissue femoral fixation devices for anterior cruciate ligament reconstruction. *Am J Sports Med* 2004; 32 (3): 635–40.
- Andernord D, Björnsson H, Petzold M, Eriksson B I, Forssblad M, Karlsson J, Samuelsson K. Surgical predictors of early revision surgery after anterior cruciate ligament reconstruction: Results from the Swedish National Knee Ligament Register on 13,102 patients. *Am J Sports Med* 2014; 42 (7): 1574–82.
- Battaglia M J 2nd, Cordasco F A, Hannafin J A, Rodeo S A, O'Brien S J, Altchek D W, Cavanaugh J, Wickiewicz T L, Warren R F. Results of revision anterior cruciate ligament surgery. *Am J Sports Med* 2007; 35 (12): 2057–66.
- Benson K, Hartz A J. A comparison of observational studies and randomized, controlled trials. *N Engl J Med* 2000; 342 (25): 1878–86.
- Browning W M 3rd, Kluczynski M A, Curatolo C, Marzo J M. Suspensory versus aperture fixation of a quadrupled hamstring tendon autograft in anterior cruciate ligament reconstruction: A meta-analysis. *Am J Sports Med* 2017; 45 (10): 2418–27.
- Capuano L, Hardy P, Longo U G, Denaro V, Maffulli N. No difference in clinical results between femoral transfixation and bio-interference screw fixation in hamstring tendon ACL reconstruction: A preliminary study. *Knee* 2008; 15 (3): 174–79.
- Drogset J O, Grontvedt T, Tegnander A. Endoscopic reconstruction of the anterior cruciate ligament using bone-patellar tendon-bone grafts fixed with bioabsorbable or metal interference screws: A prospective randomized study of the clinical outcome. *Am J Sports Med* 2005; 33 (8): 1160–65.
- Drogset J O, Straume L G, Björkmo I, Myhr G. A prospective randomized study of ACL-reconstructions using bone-patellar tendon-bone grafts fixed with bioabsorbable or metal interference screws. *Knee Surg Sports Traumatol Arthrosc* 2011; 19 (5): 753–59.
- Frosch S, Rittsteg A, Balcarek P, Walde T A, Schuttrumpf J P, Wachowski M M, Stürmer K M, Frosch K H. Bioabsorbable interference screw versus bioabsorbable cross pins: Influence of femoral graft fixation on the clinical outcome after ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2012; 20 (11): 2251–56.
- Gifstad T, Drogset J O, Grontvedt T, Hørtemo G S. Femoral fixation of hamstring tendon grafts in ACL reconstructions: The 2-year follow-up results of a prospective randomized controlled study. *Knee Surg Sports Traumatol Arthrosc* 2014; 22 (9): 2153–62.
- Granan L P, Bahr R, Steindal K, Furnes O, Engebretsen L. Development of a national cruciate ligament surgery registry: The Norwegian National Knee Ligament Registry. *Am J Sports Med* 2008; 36 (2): 308–15.
- Granan L P, Forssblad M, Lind M, Engebretsen L. The Scandinavian ACL registries 2004–2007: Baseline epidemiology. *Acta Orthop* 2009; 80 (5): 563–7.
- Granan L P, Inacio M C, Maletis G B, Funahashi T T, Engebretsen L. Intraoperative findings and procedures in culturally and geographically different patient and surgeon populations: An anterior cruciate ligament reconstruction registry comparison between Norway and the USA. *Acta Orthop* 2012; 83 (6): 577–82.
- Grassi A, Ardern C L, Marcheggiani Muccioli G M, Neri M P, Marcacci M, Zaffagnini S. Does revision ACL reconstruction measure up to primary surgery? A meta-analysis comparing patient-reported and clinician-reported outcomes, and radiographic results. *Br J Sports Med* 2016; 50 (12): 716–24.

- Harilainen A, Sandelin J. A prospective comparison of 3 hamstring ACL fixation devices—Rigidfix, BioScrew, and Intrafix—randomized into 4 groups with 2 years of follow-up. *Am J Sports Med* 2009; 37 (4): 699-706.
- Hoher J, Moller H D, Fu F H. Bone tunnel enlargement after anterior cruciate ligament reconstruction: Fact or fiction? *Knee Surg Sports Traumatol Arthrosc* 1998; 6 (4): 231-40.
- Ibrahim S A, Abdul Ghafar S, Marwan Y, Mahgoub A M, Al Misfer A, Farouk H, Wagdy M, Alheran H, Khirait S. Intra-tunnel versus extra-tunnel autologous hamstring double-bundle graft for anterior cruciate ligament reconstruction: A comparison of 2 femoral fixation procedures. *Am J Sports Med* 2015; 43 (1): 161-8.
- Laxdal G, Kartus J, Eriksson B I, Faxen E, Sernert N, Karlsson J. Biodegradable and metallic interference screws in anterior cruciate ligament reconstruction surgery using hamstring tendon grafts: Prospective randomized study of radiographic results and clinical outcome. *Am J Sports Med* 2006; 34 (10): 1574-80.
- Liu A, Sun M, Ma C, Chen Y, Xue X, Guo P, Shi Z, Yan S. Clinical outcomes of transtibial versus anteromedial drilling techniques to prepare the femoral tunnel during anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2015; [Epub ahead of print]
- Maletis G B, Granan L P, Inacio M C, Funahashi T T, Engebretsen L. Comparison of community-based ACL reconstruction registries in the US and Norway. *J Bone Joint Surg Am* 2011; 93 (Suppl 3): 31-6.
- Milano G, Mulas P D, Ziranu F, Piras S, Manunta A, Fabbriani C. Comparison between different femoral fixation devices for ACL reconstruction with doubled hamstring tendon graft: A biomechanical analysis. *Arthroscopy* 2006; 22 (6): 660-8.
- Moisala A S, Jarvela T, Paakkala A, Paakkala T, Kannus P, Jarvinen M. Comparison of the bioabsorbable and metal screw fixation after ACL reconstruction with a hamstring autograft in MRI and clinical outcome: A prospective randomized study. *Knee Surg Sports Traumatol Arthrosc* 2008; 16 (12): 1080-6.
- Myers P, Logan M, Stokes A, Boyd K, Watts M. Bioabsorbable versus titanium interference screws with hamstring autograft in anterior cruciate ligament reconstruction: A prospective randomized trial with 2-year follow-up. *Arthroscopy* 2008; 24 (7): 817-23.
- Naylor C D, Guyatt G H. Users' guides to the medical literature, X: How to use an article reporting variations in the outcomes of health services. The Evidence-Based Medicine Working Group. *JAMA* 1996; 275 (7): 554-8.
- Persson A, Kjellsen A B, Fjeldsgaard K, Engebretsen L, Espehaug B, Fevang J M. Registry data highlight increased revision rates for endobutton/biosure HA in ACL reconstruction with hamstring tendon autograft: A nationwide cohort study from the Norwegian Knee Ligament Registry, 2004–2013. *Am J Sports Med* 2015; 43 (9): 2182-8.
- Rahr-Wagner L, Lind M. The Danish Knee Ligament Reconstruction Registry. *Clin Epidemiol* 2016; 8: 531-5.
- Rahr-Wagner L, Thillemann T M, Lind M C, Pedersen A B. Validation of 14,500 operated knees registered in the Danish Knee Ligament Reconstruction Register: Registration completeness and validity of key variables. *Clin Epidemiol* 2013a; 5: 219-28.
- Rahr-Wagner L, Thillemann T M, Pedersen A B, Lind M C. Increased risk of revision after anteromedial compared with transtibial drilling of the femoral tunnel during primary anterior cruciate ligament reconstruction: Results from the Danish Knee Ligament Reconstruction Register. *Arthroscopy* 2013b; 29 (1): 98-105.
- Rose T, Hepp P, Venus J, Stockmar C, Josten C, Lill H. Prospective randomized clinical comparison of femoral transfixation versus bioscrew fixation in hamstring tendon ACL reconstruction: A preliminary report. *Knee Surg Sports Traumatol Arthrosc* 2006; 14 (8): 730-8.
- Scannell B P, Loeffler B J, Hoenig M, Peindl R D, D'Alessandro D F, Connor P M, Fleischli J E. Biomechanical comparison of hamstring tendon fixation devices for anterior cruciate ligament reconstruction, Part 2: Four tibial devices. *Am J Orthop* 2015; 44 (2): 82-5.
- To J T, Howell S M, Hull M L. Contributions of femoral fixation methods to the stiffness of anterior cruciate ligament replacements at implantation. *Arthroscopy* 1999; 15 (4): 379-87.
- www.acregister.nu. Swedish ACL Register. Annual Report 2014.
- Ytterstad K, Granan L P, Ytterstad B, Steindal K, Fjeldsgaard K A, Furnes O, Engebretsen L. Registration rate in the Norwegian Cruciate Ligament Register: Large-volume hospitals perform better. *Acta Orthop* 2012; 83 (2): 174-8.



Graphic design: Communication Division, UiB / Print: Skipes Kommunikasjon AS



uib.no

ISBN: 9788230866771 (print)
9788230866689 (PDF)