25-year results after anterior cruciate ligament reconstruction with the use of a patellar tendon autograft

Line Lindanger

Thesis for the degree of Philosophiae Doctor (PhD)
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3. Abbreviations

ACL	Anterior Cruciate Ligament
ACLR	Anterior Cruciate Ligament Reconstruction
ACL-RSI	Anterior Cruciate Ligament - Return to Sport after Injury Scale
ADL	Acitivity of Daily Living
ALRI	Antero-Lateral Rotatory Instability
AM	Anteromedial
BMI	Body Mass Index
BPTB	Bone-Patellar Tendon-Bone
FRD	Flexion Rotation Drawer
ICRS	International Cartilage Repair Society
IKDC	International Knee Documentation Committee
JSN	Joint Space Narrowing
K-L	Kellgren-Lawrence
KOOS	Knee Injury and Osteoarthritis Outcome Score
LAD	Ligament Augmentation Device
LET	Lateral Extra-articular Tenodesis
LFC	Lateral Femoral Condyle
MFC	Medial Femoral Condyle
MPCI	Minimal Perceptible Clinical Improvement
MRI	Magnetic Resonans Imaging
NKLR	Norwegian Knee Ligament Registry
OA	Osteoarthritis
PCL	Posterior Cruciate Ligament
PL	Posterolateral
PM	Posteromedial
PROMs	Patient Related Outcome Measures
PT	Popliteus tendon
REK	Regional Etisk Komité (Regional committee for medical and health research ethics)

ROM	Range of Motion
STS	Side-To-Side

4. Abstract

Background: Only a few studies of ACL reconstruction with >20 years of follow-up exists. It is still a pause in the literature concerning the patient's further sports participation and long-term subjective and objective outcome after surgery.

Purpose: To report return to sports rate, the length of the sports career and the risk of reinjury after ACL reconstruction in pivoting sports athletes. Furthermore, to evaluate subjective and objective outcome and assess risk factors of knee OA at median 25 years after ACL reconstruction with a bone-patellar tendon-bone autograft.

Methods: Unilateral ACL reconstructions performed at "Kysthospitalet i Hagevik" from 1987 to 1994 were included. A prospective evaluation with clinical testing and questionnaires (PROMSs) were included at the 3, 6, 12 and 24-month follow-up. The median 25-year follow-up also included an evaluation of radiographs.

Results: Paper I: Although 83% of patients returned to pivoting sports after early ACLR, only 53% returned to preinjury level. The pooled reinjury rate after return to preinjury level of sports was 41% (30% contralateral injuries and 11%, revision surgery).

Paper II: Five *slightly loose* grafts (28%) and 6 *tight grafts* (5%) were classified as failures after 2 years (P = .002). Thirty percent of patients with *slightly loose* grafts and 6% with *tight* grafts had undergone revision (P = .004) by follow-up (25 years, range, 22-30 years).

Paper III: Sixty percent (141/235) of patients had radiographic osteoarthritis (OA) in the involved knee and 18% (40/227) in the contralateral knee at the long-term follow-up (P<0.001). Medial (OR 1.88 (95% CI, 1.03-3.43)) and lateral (OR 1.96 (95% CI 1.05-3.67)) meniscus surgery were independently associated with OA development.

Conclusions: The subjective and objective outcomes after ACL reconstruction are generally good 25 years after surgery. However, an ACL reconstruction does not

necessarily enable a return to preinjury sports participation. Return to sports also come with a prize as athletes returning to pivoting sports are facing a worryingly high risk of contralateral ACL injuries. Moreover, despite undergoing ACL surgery, a high incidence of OA development was seen 25 years after surgery in the current thesis.

Implications: Rupture of the ACL is a severe injury, and an ACL reconstruction does not necessarily reestablish the patients prior knee function and long-term knee health. Therefore, it is important to focus on preventive strategies to reduce ACL injuries. When an ACL injury has happened, patients should be informed about the surgical aspects, the return to sport rates, the risk of reinjuries and long-term outcome so as to be able to make informed decisions about their ACL treatment and further sports participation.

5. List of Publications

I Return to Play and Long-term Participation in Pivoting Sports After Anterior Cruciate Ligament Reconstruction

II Effect of Early Residual Laxity After Anterior Cruciate Ligament Reconstruction on Long-term Laxity, Graft Failure, Return to Sports, and Subjective Outcome at 25 Years

III Predictors of Osteoarthritis Development Median 25 Years After Anterior Cruciate Ligament Reconstruction Using Patellar Tendon Autograft

6. Introduction

6.1 ANTERIOR CRUCIATE LIGAMENT (ACL) ANATOMY

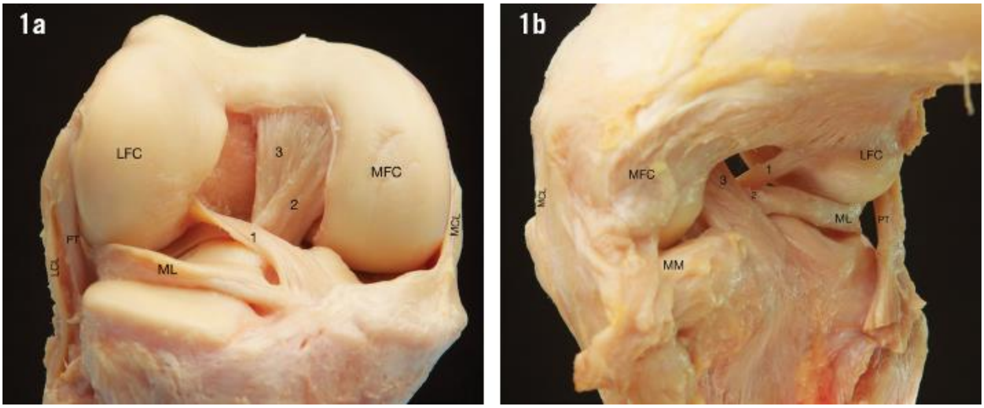

Figure 1a and b: 1=ACL, 2= anterior menisco-femoral ligament, 3=PCL.
LFC (lateral femoral condyle), MFC (medial femoral condyle), ML (lateral meniscus), MM (medial meniscus), MCL (medial collateral ligament), LCL (lateral collateral ligament), PT (popliteus tendon). *(Reprinted with permission from Robert Smigielski).*

The earliest known description of the ACL dates back to around 3000 BC when the anatomy was described in the famous Smith Papyrus (1600 BC).[1] The term ”ligamenta genu cruciata” was first mentioned by the Greek physician Claudius Galen of Pergamon (129 – 216 CE) who lived and served under the Roman Empire.[2] The first comprehensive textbook of anatomy ”De Humani Corporis Fabrica Libris Septum” (1543), by Andreas Vesalius, presented the first formal anatomic study of the ACL. However, a quantum leap of knowledge about the ACL size, shape and functional anatomy have been seen during the last 50 years. To illustrate this, a search on “ACL” on PubMed today lists > 30000 publications, with numbers increasing each day.

Microanatomy

The microstructure of the anterior cruciate ligament resembles other connective tissues, and is composed of multiple collagen fascicles, surrounded by a paratenon.[3]

Each fascicle consists of sub fasciculi, and, together with cells and matrix (collagen, glycosaminoglycans, glyco-conjugates and elastic components) they make up the ACL tissue.[3,4]

The nerve innervation of the ACL comes from the posterior articular branches of the tibial nerve.[5] Although most of the nerve fibers have a vasomotor function, mechanoreceptors essential for proprioception, and afferent signaling of knee postural changes have been observed.[5] A phenomenon called ”ACL reflex” is when the afferent nerve fibers activates muscles around the knee, and serve as an important response in normal muscle activation and knee function.[6] Loss of this reflex due to an ACL injury can induce muscle weakness, especially during activation of the hamstrings- and quadriceps femoris muscles.[6,7]

The vascularization of the ACL comes from the middle genicular artery, a branch of the popliteal artery, that crosses the posterior capsule and provide branches to the ACL that encloses and penetrate the ligament.[8] The vascularization is better in the proximal part of the ACL than distally, which might play a role in the healing potential of the ACL.[9]

Macroanatomy

The ACL is a band-like structure originating proximally at the posteromedial surface of the lateral femoral condyle and running distally towards the medial and anterior area of the tibial plateau. The ACL has an intra-articular length of approximately 22-41mm (mean 32 mm).[10] The cross-sectional shape varies with the flexion angle and the cross-sectional area increases from the femoral to the tibial attachment site.[11]

The structural appearance of the ACL is controversial and under ongoing debate. In the literature, the ACL is often described as divided into two distinct bundles; the anteromedial (AM) bundle and the posterolateral (PL) bundle based on its area of insertion onto the tibia.[12,13] The tibial insertion has been described as having an oval shape, and the AM bundle to insert anteromedially in relation to the medial tibia spine. The PL bundle insertion is described as posterolateral in the ACL footprint, closely related to the lateral tibial spine, and in front of the posterior root of the lateral meniscus.[14–17] At the tibial insertion indirect fibers fans out, preventing the ACL to impinge against the roof of the intercondylar notch during extension. The femoral insertion lies posteriorly on the medial wall of the lateral condyle, and the lateral intercondylar ridge (resident´s ridge) mark the anterior and superior extent of the femoral border in knee flexion. The lateral bifurcate ridge has been described to separate the attachments of the AM bundle originating from the anterior and proximal part (high and deep in the notch when the knee is flexed at 90 degrees), and PM bundle originating from the posterior and distal part of the footprint (shallow and low when the knee is flexed at 90 degrees).[10,18] The bony landmarks, together with the remnants of the torn ACL, are highly important structures to visualize for the surgeon when deciding on graft tunnel placements.

Recently, the anatomical view of the ACL as a two-bundle structure, has been challenged.[19,20] Anatomical studies have found the ACL to be a ”ribbon-like structure”.[20,21] A direct oval femoral insertion has been described, with accessory indirect fan-like extension fibers directed towards the posterior femoral cartilage border.[22] The ACL mid-substance is seen as flat and the direct tibial insertion as C-shaped. In a study by Siebold et al et al.,[19] the center of the C is seen as the bony insertion of the anterior root of the lateral meniscus, whilst the formerly denoted and “central” or “PL inserting” fibers of the ACL were not found. Moreover, in the “ribbon-shape” view, the formerly described two-bundle structure of the ACL was not found, but it was suggested that the twisting of the flat ribbon-like ACL during the flexion/extension movement could give a visual ”double-bundle effect”.[19,20]

Figure 1 and 2: Ribbonlike anatomy of the ACL *(Reprinted with permission from Robert Smigielski)*

6.2 ACL BIOMECHANICS AND TUNNEL PLACEMENT

The ACL is vital for the stability of the knee joint because of its role as the primary restraint to anterior translation of the tibia as well as a secondary restraint to internal tibial rotation.[23–25] It is also a minor secondary restraint to external rotation and valgus angulation.[26]

In the traditional view of the ACL as a two-bundle structure, the AM and PM bundle contributes differently to the restraint of tibial translation throughout the flexion-extension movement.[27] The AM bundle tightens and the PL bundle loosens when the knee is moving towards flexion, and the PL bundle tightens invariably towards extension.[10,28] It could therefore be argued that their different contributions to knee function could constitute a rationale for reconstructing both of these bundles.

Initially, by observing that the anterior ACL fibers remained tight throughout knee flexion led to a belief that these fibers were the most important. Further, by placing the graft isometrically, it would not be subjected to cyclical length changes throughout knee range of motion that could cause graft deformation or failure.[29] However, later it was demonstrated that isometry relies on normal kinematics and the loads imposed by the knee. Moreover, Zavras et al.[30] found the existence of an isometric zone only close to the posterior end of Blumensaats line (extreme anteroproximal corner of the natural femoral attachment) under a range of loading conditions. Therefore, an isometrically placed graft is considered non-anatomical, giving a femoral tunnel placed high and deep in the femoral notch during knee flexion.

Kawaguchi et al.[31] performed a biomechanical study where the fibers of the femoral attachment was cut sequentially. They found that 66-80% of the resistance to tibial anterior translation arose from the dense fibers in the central-proximal area of the femoral footprint, corresponding to the AM bundle. Findings were inconclusive in terms of which fibers were more important in resisting internal rotation. This central-proximal area also matches the anteroproximal isometric point or transition line of the femoral footprint.[30] Although this femoral graft tunnel placement mimic how the natural ACL resists tibial displacements, earlier findings clearly have stated that tunnel placement high in the notch is associated with a greater prevalence of rotational pivot-shift laxity.[32,33] A biomechanical study by Kato et al.[34] supports this notion, reporting that anatomic ACL reconstructions (distal and posterior to the isometric point) better restores knee kinematics when compared to non-anatomic reconstructions.

The biomechanical properties of the tibial attachment have also been studied. Lord et al.[35] have reported that the peripheral AM fibers were the most important for restraining tibial anterior translation and internal rotation and matched the C-shaped AM attachment of the dense collagen fibers of the ACL. However, a very anteriorly tibial graft tunnel placement is a well-known risk factor for graft impingement that needs to be accounted for in surgical reconstructions.[36]

Biomechanical findings and the limitations of the isometric graft placement, especially in controlling the tibial rotation, led to a shift towards a more anatomic tunnel placement technique. The double bundle description was the rationale for developing the anatomic double-bundle ACL reconstruction, normally performed as a procedure with 2 grafts and separate double tunnels in each of the tibia and femur, that was supported by superior results from biomechanical findings.[37] However, the double-bundle procedure did not show clinically superiority over an anatomic single-bundle technique.[38] Kondo et al.[32] found that superior rotational restraint was achieved if the femoral tunnel was drilled in a more laterally placed mid-bundle position when performing single-bundle reconstruction as compared to a non-anatomical single-bundle tunnel placement high in the notch, but similar results were seen for the single mid-bundle reconstruction and the double-bundle procedure.[32] The technically easier single-bundle procedure therefore gradually became the preferred anatomic reconstructive procedure.

The Pivot shift phenomenon is associated with ACL rupture, but in recent years there has been a renewed interest in the anterolateral structures of the knee and its role in controlling excessive tibial internal rotation.[39] Studies have found that additional injury to the anterolateral structures might be involved for the pivot-shift to appear in ACL deficient knees, and indicate a more severe knee injury.[40] Several biomechanical studies have examined the stabilizing role of different extraarticular structures, and found them to be important contributors in restraining internal rotation.[41–43]

6.3 EPIDEMIOLOGY

During the resent years the establishment of several nation-wide ACL registries have provided us with more extensive knowledge of the natural path of an ACL injury. However, mostly these registries hold information on the surgically treated ACL injuries, and less is known about non-surgically treated or untreated ACL patients. The Norwegian Knee Ligament Register (NKLR)[44] reported an incidence rate of 36 ACL surgeries per 100,000 inhabitants in Norway in 2019. The total number of ACL injuries per year is more difficult to extract as non-operatively managed patients have not been included in the registry. It is however, estimated that around 4000 ACL injuries occur yearly in Norway.[45]

According to the NKLR[44] the mean age at surgery in 2020 was 28 years, but a high incidence rate of new ACL reconstructions was seen in the age group < 20 years. In the youngest population (10-19 years) women dominate, while the incidence rate was highest among men aged 20-50 years. Soccer (38%), team handball (12%) and alpine skiing (14%) were the most common primary sports performed at the time of injury. There was no difference in the rate of ACL surgery between male and female team handball -and soccer players.

The primary ACL graft choice varies throughout the world. According to a recent worldwide survey from the ACL Study Group the most common primary graft choices were hamstring tendon autograft (53%) and bone-patella tendon-bone autograft (BPTB) (36%). A single-bundle technique was used in 90% of cases with hamstring autograft, and only 10% was performed as a double-bundle technique. Less than 10% of reconstructions were performed with a quadriceps autograft.[46] In Norway the use of patellar tendon autograft is increasing. It accounted for 77% of all ACL reconstructions in 2020, whereas hamstrings tendon autograft accounted for 23%. The use of quadriceps tendon autografts has decreased during the last years, probably due to the reported higher failure rate in the danish ACL registry.[47]

6.4 INJURY MECHANISM

Several mechanisms of injury have been found to cause an ACL tear. Various sports and activities have also different mechanisms of injury. It is common to categorize ACL injuries as either non-contact injuries or contact injuries. Contact injuries occurs if there is a direct contact or collision to the knee. Non-contact injuries are the most common and occurs when an excessive loading is applied on the ACL, e.g. in a cutting maneuver or by landing on one leg.[48] This injury mechanism is typically seen in pivoting sports such as handball and soccer when the knee moves towards extension with a valgus collapse combined with a rotational force applied on the tibia.[49,50] In alpine skiing the injury mechanism has been described as a slip-catch situation where the outer ski catches the snow at the inside, which forces the knee into internal rotation and valgus.[51]

6.5 RISK FACTORS FOR ACL INJURY

Female sex significantly increases the risk of sustaining a non-contact ACL injury. In a study of team handball players by Myklebust et al.,[52] a 5-fold higher risk of suffering an ACL injury was seen among women compared to their male counterparts. Likewise, the rate of ACL injury is higher for female athletes in both soccer and basketball.[53] This sex-related difference is not clearly understood, and a range of explanations have been proposed.[54] Non-modifiable differences in the bony anatomy, with a wider pelvis and shorter femur in women, gives a higher Q-angle, that in turn could predispose for ACL rupture. Convincing evidence is, however, lacking.[55,56] Females also have a decreased width of the intercondylar notch, which has been debated as an individual risk factor for ACL injury, although evidence is still unclear.[57] Increased posterior tibial slope is also found to be a risk factor for ACL injuries, although the differences between sexes are undetermined.[58] Generalized joint laxity and recurvatum is also responsible for increased ACL injury risk among both males and females. [59] Another risk factor is the women's menstrual cycle. Estrogen and relaxin fluctuate throughout the menstrual cycle and might affect the strength and flexibility of soft tissue. [60,61] It has been suggested that the risk of sustaining an ACL rupture increases in the preovulatory phase,[62] but these effects remain unclear,[63] and the role of contraceptive pills in regulating the estrogen cycle so as to prevent ACL injury, is highly controversial.[64,65]

Further, differences between males and females in relative muscle strength and biomechanical properties appear to be important risk factors for sustaining an ACL injury.[54] Weakness in the hamstrings muscle or in external hip rotation, muscle imbalance between the hamstrings and quadriceps muscle, as well as imbalance within the quadriceps muscle that can lead to increased valgus angulation during landing or redirection, are important risk factors - also when present in males.[66,67] Further, several extrinsic factors such as sports participation, type of shoes, shoe-surface interaction, knee bracing and weather conditions can influence on the risk of ACL injury.[68]

6.6 DIAGNOSTIC TOOLS

Patient history:

The patient's description of the injury mechanism, onset of effusion and knee function and stability following the injury normally rises the suspicion towards an ACL injury. "Giving way" episodes during sports participation or only in activity of daily living might be described.[69]

Clinical examination:

A thorough knee laxity testing is essential when diagnosing ACL injuries. The most commonly used tests for knee laxity include the Lachman test, the pivot-shift test and the anterior drawer test.[69,70] However, there is a large variability in the diagnostic accuracy of the clinical testing versus MRI or knee arthroscopy.[71] The examiners level of experience, timing of the examination (effusion, pain), the examiners hand size, the size of the patients thigh, associated injuries to the knee and muscular guarding are all factors that can contribute to the variability in sensitivity and specificity seen in the literature.[72,73] The sensitivity decreases when patients are awake as compared to in anesthesia, which reinforces the effect of muscular guarding during Lachman and pivot-shift examination.[71]
A meta-analysis by Benjaminse et al.[73] reported a pooled sensitivity of 85% and a pooled specificity of 94% for the Lachman test, a 24% sensitivity and 98% specificity for the pivot- shift test, and a 55% sensitivity and 92% specificity for the anterior drawer test. The reported sensitivity of the pivot-shift test was better (79%) in a more recent review analysis by LeBlanc et al.[71] - and the Lachman test and the Pivot-shift test is today considered as the most relevant clinical tests.

Radiographic evaluation:

Today MRI, together with a clinical examination, is the gold standard for diagnosing ACL injuries. During the last decades the MRI has become better available and today almost every patient in Norway have had an MRI scan of the injured knee prior to ACL surgery. The MRI provide 2-dimensional visualization of the cruciate ligaments and related structures, and thereby aid the evaluation of ligament integrity. Classic bone-bruise patterns on the lateral femoral condyle and at the posterolateral tibia plateau is described to be seen in up to 80% of ACL tears,[74] and will further enhance the diagnostic accuracy.[75] Moreover, the status of the menisci, cartilage, soft tissue, and collateral ligaments can be evaluated in the preparation for surgical procedures.

Before MRI came in regular use, diagnostic arthroscopy was frequently used to verify the ACL rupture if the diagnosis was uncertain. By looking directly into the knee joint, the surgeon would have a direct view of the intercondylar notch and could visualize the anterior cruciate ligaments, evaluate ligament integrity by using a hook, and at the same time perform a knee laxity testing under anesthesia. Although this procedure would verify the diagnosis, it came with both economic and time-consuming disadvantages as well as adding an extra surgical procedure in many cases. Therefore, MRI gradually took over as the leading diagnostic tool. A review analysis by Phelan et al.[76] compared results of MRI to the gold standard arthroscopic procedure and the reported sensitivity and specificity rate for detecting an ACL injury was high, 87% and 93% respectively.

6.7 SURGICAL VS NON-SURGICAL CONSIDERATIONS

ACL injuries can be treated surgically or non-surgically by active rehabilitation.[77] Persistent knee instability during daily living or bothersome episodes of instability during sports activity often lead to a surgical reconstruction. Patients who intend to return to pivoting sports or have physically demanding occupations are also often advised to undergo ACL reconstruction.[78,79] Associated knee injuries, age, sports participation, and activity level are important factors when discussing the two treatment options. An 8–12-week rehabilitation period is normally recommended for all patients before surgery is performed. If the non-operative rehabilitation does not lead to a satisfactory result, a surgical reconstruction, or in some cases an ACL orthosis, is considered.[78]

6.8 THE HISTORICAL EVOLUTION OF ACL SURGERY

Throughout the 20th century patients sustaining an ACL injury have been offered countless different procedures all aiming to restore knee stability.[80] Intraarticular ACL reconstruction was first performed by utilizing an iliotibial band graft harvested from the ipsilateral knee, retaining its upper attachment in the femur and threaded through a femoral and tibia tunnel. This reconstructive technique was first described by Hey Groves in 1917, although anecdotal reports of reconstructions earlier than this exists.[81,82] Further, semitendinosus grafts and medial patella tendon autografts with various fixation methods were introduced during the 20-30`s. Treatment of acute ACL injuries by repair was introduced by Palmer[83] in 1938 and popularized several times during the years to come.[84–87] These procedures were eventually, more or less, abandoned due to disappointing mid -and long-term outcome.[85,88]

In 1963, Jones reported the first method for ACL reconstruction with the use of a bone-block from the patella. He harvested the central third of the patellar tendon, but the graft remained attached distally at the tibia insertion. This led to a short graft, positioned in the femur just behind the front of the intercondylar notch, far from its anatomical site.[89] To give more graft length, a tibial tunnel was added, and Franke was, in 1969, probably the first who described a free patellar tendon graft with bone blocks at both tibial and patellar ends, known as the bone-patellar tendon-bone (BPTB) graft.[90]

Gradually, intraarticular ACL reconstructions using free autografts became the gold standard. Techniques developed in different parts of the world during the 1970´-1990´s, and a commonly used technique was introduced by Clancy et al.[91] in 1982. He used the flat patellar tendon graft with bone-blocks in both ends through an open medial parapatellar approach. Graft tunnels were drilled more anatomically, anteromedially in the tibial footprint and posteriorly in the femoral footprint. Focus was on creating isometry of the graft, which resulted in femoral graft tunnels often centered higher and deeper in the notch (in knee flexion) than the natural attachment area.

Lateral extraarticular tenodesis

During the 1960´-1980`s, the use of isolated lateral extraarticular reconstructions gained popularity due to the recognition of the importance of the pivot-shift sign.[92] However, variable results were reported,[93,94] and gradually they lost their appeal much due to the introduction of free patellar tendon grafts, and because of biomechanical concerns. There was a risk of over-constraint of the lateral compartment that were thought to lead to secondary degenerative changes.[95] In Norway, an alternative lateral extraarticular reconstruction was introduced by Pål Benum in 1982 utilizing the lateral third of the patellar ligament and the adjacent part of the patella as an extraarticular transplant to the lateral femoral condyle.[96] However, this procedure also came to an end due to disappointing biomechanical[97] and clinical results.[98]

Today, extraarticular tenodesis, in combination with an ACL reconstruction, has been popularized yet again, and is now a part of the orthopedic surgeons 'toolbox", along with a more individualized treatment strategy. A recent meta-analysis found that adding a lateral augmentation to an ACL reconstruction improved rotatory stability and reduced the risk of graft rupture.[99] Recent results from the STABILITY-study indicate that a combined approach (intraarticular ACL reconstruction with an adjunct tenodesis) can reduce the risk of graft failure when applied to a population of young patients with a substantial preoperative knee laxity aiming to return to pivoting sports.[100]

Allografts

Inferior clinical results of the extraarticular procedures led to the renewed interest in intraarticular techniques using auto –or allografts, and these procedures gained popularity throughout the 1980`s and 1990´s. Graft site morbidity was a concern among surgeons, and this matter could easily be overcome by using allografts. Although reports presented promising results, concerns regarding the sterilization method (irradiation) and its effect on the biomechanical properties of the graft,[101] as well as the fear of transmission of infectious diseases led to a fall in its popularity. Today their usage is still controversial, as failure rates have been found to be higher than for autografts.[102] In Norway allografts are rarely used for primary ACL reconstruction, but more frequently in multi-ligament reconstructions or revision surgery.[44]

Synthetic grafts

Synthetic grafts also gained popularity in the 1980´s, as a primary graft or augmentation of a tendon graft. Dacron®, Teflon® and Gore-Tex® were among the primary graft materials in the market. Results from the use of these devices were poor as compared to tendon grafts.[103,104]

Another popularized graft was a polypropylene diamond-braided ligament augmentation device (LAD) developed by Kennedy.[105] This device was sutured to the autograft and fixed to the lateral femoral condyle in an "over-the-top position" with sutures. Later, the Kennedy-LAD was also used together with a free BPTB autograft.[91,106] Its role was to "off-load" the graft, facilitating a safer and faster healing response. In practice this led to a more liberal rehabilitation and a stop in the use of demobilizing casts. Although acceptable results were seen after reconstruction with the use of the LAD, it was not superior to free BPTB autografts.[106,107] Further, when the interference screw was introduced for better and easier graft fixation,[108] the interest for synthetic grafts nearly came to an end.

Arthroscopically assisted ACL reconstruction

The evolution of endoscopic procedures to the knee joint started with Professor Takagi in 1918, when he used a small cystoscope to view the anterior of a cadaver knee. Later it was popularized, first as a diagnostic tool and then for treatment of different types of intraarticular injuries.[109] Gradually, during the 1980´s the arthroscopic procedure for ACL reconstruction replaced the open procedures.[110] In spite of the theoretic and cosmetic advantages of avoiding a medial arthrotomy, most studies did not find any difference in outcome when comparing it to an arthroscopic procedure, neither at short-term[111] nor at long-term follow-up.[112]

Initially, a two-incision technique was in use; the femoral tunnel was drilled outside-in by using a skin incision over the lateral femoral condyle. The tibia tunnel and graft harvest were made via a skin incision over the proximal tibia. The one-incision technique came as result of the development of specific offset aimers to guide the placement of the femoral tunnel, with the need for only one skin incision distally. The femoral tunnel could then be drilled through the tibia tunnel (transtibial approach) or from an accessory anteromedial (AM) portal. Due to a less invasive procedure, the morbidity of the one-incision technique was thought to be lower, although studies comparing the two techniques mostly have failed to prove this.[113,114] The transtibial one-incision technique provided a relatively quick and easy reconstructive procedure and was increasingly popular throughout the 1990s´. The resulting isometric, but non-anatomic femoral tunnel positions were high in the roof of the intercondylar notch compared to the native femoral insertion. Such placement is associated with a greater prevalence of rotational pivot-shift laxity.[33] Also, there was a concern over the anterior positioning of the tibia tunnel that could cause impingement of the ACL graft against the roof of the femoral notch and lead to graft failure.[36]A notchplasty was therefore an important step in the procedure. To further overcome the challenging impingement problem, a 70-degree tibial "anti-impingement" guide was designed. This guide used the roof of the femoral intercondylar notch as reference for tibial tunnel placement.[115] However, the resulting tibial tunnel placement could lead to a posterior femoral tunnel placement, producing a vertical graft and increasing the risk of residual rotational instability.[116,117]

A more "anatomic" reconstruction soon developed, and included the double-bundle technique, with the use of two separate femoral and tibial tunnels,[118] and single-bundle procedures (i.e.., central femoral and tibial tunnel placement). Studies comparing the transtibial procedure to an ”anatomic” procedure found knee kinematics closer to the native ACL for the latter technique.[32,119] In a systematic review by Lewis et al.,[120] however, high stability rates, subjectively high patient satisfaction, and low revision rates for the transtibial procedure were seen. The danish ACL registry also reported a higher risk for revision surgery after converting to the AM portal technique and suggested that a certain learning curve after introducing a new surgical method could be the explanation.[121] Another possible explanation could be the more vertical graft inclination seen when the transtibial technique is used, that is known to give lower in situ graft forces and could theoretically reduce the risk of ACL graft rerupture.[122]

Today ACL femoral tunnel placement through an accessory anteromedial portal, using bony landmarks and ACL-remnants as aids, is by many seen as a ”gold-standard”.[123] Tunnel placement and other aspect of ACL-reconstruction is, however, still under debate. The native ACL is not exactly reproducible, and by using ACL grafts to mimic the native ACL, one has to make some compromises in terms of graft placement strategies and isometry. Placement of the femoral tunnel has proven to be of special importance as malpositioned femoral tunnels is a frequent cause of failure.[124] A compromise between a central anatomic tunnel and an isometric tunnel, corresponding to the AM attachment area, have been proposed as the best tunnel placement strategy, based on the current biomechanical evidence.[34] During surgery this position translates into a lower and shallower femoral tunnel, as compared to the so called “isometric point”.

The positioning of the femoral tunnel may be aided by the use of an ACL ruler, or by use of fluoroscopy applying the grid method of Bernard et al.[125] By using an average femoral attachment derived from anatomical studies, the extrapolated weighted average position for the center of the femoral tunnel attachment was found to be located at 28% along the anteroposterior direction of the Blumensaats line and at 35% down the high-low direction of the intercondylar notch.[126]

6.9 REHABILITATION AND CLEARANCE TO SPORT PARTICIPATION

The phase of rehabilitation starts immediately after the ACL reconstruction and is highly important for optimizing clinical results and potential return to sports. Rehabilitation protocols have evolved over the years,[127] initially it was recommended immobilization in a cast and the use of crutches until 8-12 weeks post-surgery. In 1990 Shelbourne and Nitz[128] published a protocol advocating a more liberal and accelerated rehabilitation, that, with some modifications, laid the ground for the todays practice.

Nowadays, strategies for the rehabilitation after ACL surgery focuses on immediate motion and weightbearing, full passive extension and early neuromuscular training. However, there is a general lack of standardization in ACL-rehabilitation programs[129], and also an ongoing debate on criteria used to clear patients for return to sports and activities.[130,131] Although the physical rehabilitation and readiness has traditionally dominated the decision to recommence sports participation, emerging evidence of the importance of psychological readiness and fear responses has led to a broader focus in the phase of rehabilitation.[132,133] Scoring systems such as The Anterior Cruciate Ligament–Return to Sport after Injury (ACL-RSI) scale may aid the evaluation of patients' psychological readiness for return to sports.[134,135] By adding the scale, return to sports predictions may improve.[136] The timing of return to sports was for decades a time-based decision, mostly varying between 6-12 months post-surgery. Today a more individualized clearance for return to sports is recommended, using objective and criteria-based return to sports programs.[131] The process of rehabilitation is normally divided into phases, including specific clinical and functional milestones that are required to be met before progression to the next phases. As such, return to sports should not be understood as an isolated decision at the end of the rehabilitation process, but as a dynamic continuum.[131]

6.10 OUTCOME AFTER ACL RECONSTRUCTION

Return to sports and ACL reinjury

Because ACL injury is more common in a young and athletic population, the main goal for many ACL injured patients is to return to their primary sports after finishing rehabilitation. Athletes participating in pivoting sports (e.g., team handball, soccer, basketball) are especially at risk of ACL injury -and their return to sports requires a careful and thorough rehabilitation before recommencing sports participation.[131]

Return to sport is commonly used as one of several outcome measures that help map the success of the treatment.[137,138] In a review analysis by Ardern et al.[139], including various sports, 65% of patients returned to their preinjury level, and only 55% returned to competitive sports. Lai et al.[140] reviewed elite athletes only, participating in various sports, and presented an overall 83% return to preinjury sports rate after surgery. However, by conducting studies that are comparing various sports, activity levels and return to sports definitions, it is difficult to draw reliable conclusions.[141] The Panther Symposium ACL Injury Return to Sport Consensus Group, aimed to overcome these obstacles, by providing a clear definition of return to sports, defined as "achieving the pre-injury level of sports participation as defined by the same type, frequency, intensity and quality of performance as before injury".[131]

Reinjury of the ACL in the ipsilateral or contralateral knee is a feared endpoint after ACL reconstruction that is important to report in clinical studies. In a systematic review reporting 10-year results after ACL surgery in 2682 knees, 8% of patients had suffered a graft failure and 13% a contralateral ACL injury.[142] In a further long-term evaluation, Sanders et al.[143] estimated a graft survival rate of 91% in a population cohort analysis. Moreover, female sex[144] and young athletes returning to high-level sports have been found to have an increased risk of graft rupture and contralateral ACL injury.[145–147] In a recent 10-year follow-up study of 1661 soccer players from the Swedish National Knee Ligament Registry, players who returned to soccer had a significantly higher risk of sustaining an additional ACL injury than those who did not.

Of the players who returned to play soccer, 10% had suffered a graft failure and 21% a contralateral ACL injury.[148]

ACL injuries, and worse – reinjuries, have the capacity of severely reduce knee function and increase the odds of OA development over a lifespan. Whether return to sports affect this risk is unclear as most studies are limited to short-term follow-up, and less is known about the long-term consequences of returning to sports after surgery.

Radiographic osteoarthritis

A history of knee injury has been reported to give a four-fold increased risk of knee OA compared to uninjured patients.[149] More specifically, patients suffering an ACL injury are at high risk of developing secondary ipsilateral osteoarthritis during their lifetime.[150–152] Compared to an uninjured population, ACL injured patients have a sevenfold increased risk of developing OA[153] or undergoing knee replacement surgery.[154]

Unaddressed pathologic knee laxity also increases the risk of concomitant injuries to the cartilage, subchondral bone, and menisci, all recognized as predisposing factors for OA.[155,156] In particular, injury to the menisci at the time of ACL rupture, or later, is linked to later degenerative changes in the knee.[157]

ACL reconstruction has been shown to reduce the incidence of meniscal injuries and further surgery. However, an ACL reconstruction does not seem to reduce the incidence of post-traumatic OA, although conflicting results have been presented between studies comparing non-operative treatment with operative treatment.[158,159]

Moreover, reports on the long-term (>25 years) incidence of OA after ACL surgery are limited and calls for more high-quality studies. Long-term studies have reported rates of OA development that ranges from 20-80%.[160–166] These studies are limited by a variability in follow-up length, number of included patients and use of different OA classification systems.

Patient Reported Outcome Measures (PROMs)

To give a comprehensive assessment of the patients´ perceived and self-experienced outcome after ACL-surgery, validated Patient Related Outcome Measures (PROM) are useful tools. The Knee injury and Osteoarthritis Outcome Score (KOOS) and the International Knee Documentation Committee (IKDC) questionnaire are the most commonly used PROM's across clinical reports. When reporting the KOOS score of 698 patients, Ingelsrud et al.[167] found that two-thirds had an acceptable result 1-2 years after ACL surgery. Ten percent perceived the treatment to have failed (moderate to severe KOOS score). Better subjective score was seen in a systematic review reporting the IKDC score at minimum 2 years; 74% were graded as having a normal (IKDC A) or nearly normal (IKDC B) knee function.[120] In a recent systematic review, the maximal subjective improvement after ACL surgery was reported to be established at 1 year postoperatively, with little improvement beyond this time point for both scoring systems.[168] Shelbourne et al.[164] and Pernin et al.[169] have both published IKDC subjective scores > 20 years after surgery, both reporting a mean score of 75, with a decreasing score as the degree of OA increased. Similarly, Risberg et al.[163] reported KOOS score up to 20 years after surgery. A deterioration in symptoms and function between 15 and 20 years were found, but the mean changes were reported to be of questionable clinical importance.

The Lysholm score is still in use an outcome measure after ACL reconstruction, often complemented by the Tegner activity scale.[170] A systematic review of > 2600 ACL reconstructions by Magnussen et al., [142] with a minimum 10-year follow-up after ACL reconstruction, reported a mean Lysholm score of 92 and a mean Tegner score of 5.

6.11 WHY IS THIS THESIS NEEDED?

ACL injuries typically occur in the young and athletic population where many patients undergo ACL surgery to enable return to sports or recreational activities. Although the short-term outcome after ACL injury and reconstruction is thoroughly investigated, less is known about the long-term consequences of resuming sports activities after ACL surgery. There is only a few studies with > 20 years of follow-up of a cohort size comparable to the current thesis.[160–166]

It is especially important to increase the knowledge concerning reinjuries to the ipsilateral or contralateral knee, long-term subjective knee function and OA development after resuming physically demanding sports. There is still a pause in the literature concerning the expected level of physical activity after surgery and the patients' prospects of a long and successful sports career. By increasing the body of knowledge on long-term outcome after ACL reconstruction and the important risk factors that predispose for a less favorable result, physicians and therapists will be able to give more comprehensive advice on treatment strategies and assist athletes in forming realistic expectations after ACL surgery.

Although surgical techniques have evolved over the last decades, the surgical method and population investigated in the current thesis is comparable to today's practice – and results will therefore have a transfer value. The long-term consequences of additional meniscus injuries or surgery to the menisci, together with an ACL injury is still highly important. Evaluation 25 years after surgery might add further knowledge about of the influence of meniscus injuries on ACL injured knees. Hamstring tendon autografts have become many surgeons graft of choice, but in Norway the BPTB autograft (as was also used in the current cohort) has regained popularity. It is now dominant in primary ACL reconstructions. The tunnel placement techniques in the current thesis are different from the todays strategies, but graft tunnel placement is still under debate and this thesis may add to the body of knowledge on the long-term outcome. Moreover, a more liberal postoperative rehabilitation protocol was introduced in this period, which was still more restrictive, but comparable to today's physical rehabilitation.

This thesis aims to further increase our understanding of the course of an ACL injury, and to improve the base of knowledge physicians can rely on when guiding patients towards the best possible long-term outcome. In order to so, the proposed aims of the current thesis are presented in the next section.

7. Aims of thesis

The overall objective of this thesis was to investigate the long-term (median 25 years) clinical outcome after ACL reconstruction with a BPTB autograft.

The specific aims of the thesis were:

- To determine the rate of return to sports and the long-term sports participation in athletes participating in pivoting sports. (Paper I).
- To examine the long-term consequences of return to pivoting sports in terms of contralateral ACL injuries, revision surgery and knee replacement surgery (Paper I).
- To investigate how early residual knee laxity after ACL reconstruction affects the incidence of graft failure, the rate of return to pivoting sports, and long-term objective and subjective outcome (Paper II).
- To report the radiographic OA development rate and the objective and subjective outcome median 25 years after ACL reconstruction (Paper III)
- To determine any potential risk factors for radiographic OA development at long-term follow-up (Paper III).

8. Methods

8.1 STUDY DESIGN

Prospective data of all ACL surgery performed at the Coastal Hospital of Hagevik was from 1985 registered in a quality database for future use. Data from the preoperative evaluation, from surgery, and follow-up after 3, 6, 12 and 24 months were registered. Further, information on the cause of injury, preinjury – and postoperative sports participation, data on any new injury or surgery to either knee, as well as patient related outcome measures (PROMs) were also obtained. A subgroup of this prospective cohort was also included in a radiographic follow-up 10 years after surgery.

For the purpose of this study, only primary ACL reconstructions performed by use of a BPTB autograft from the ipsilateral knee during the period between 1987 and 1994 were included. The basis for this selection of patients was to keep a most uniform population in terms of surgical procedure, rehabilitation, and follow-up evaluation. A total of 404 ACL reconstructions fulfilled these criteria and was eligible for the study. Eligible patients first received a study invitation by post including login information to secure an online response to the questionnaires. Non-responders received a phone call or SMS with a reminder after 2 weeks. All patients were then offered a 25-year follow-up evaluation including a physical examination and radiographs. Patient evaluations were performed at Haraldsplass Deaconess Hospital in Bergen, Stavanger University Hospital, Haugesund Hospital and Lovisenberg Deaconess Hospital in Oslo. A few participants living in the northern part of Norway were examined by orthopedic colleagues at their local hospital. The main investigations were performed by the PhD-candidate Line Lindanger, assisted by Torbjørn Strand, MD, and/or Anders Odd Mølster, MD, PhD. Radiographs were evaluated by two independent radiologists.

8.2 PATIENT INCLUSION AND EXCLUSION

Exclusion criteria were contralateral ACL injury at the time of index surgery, concomitant PCL injuries or collateral ligament injuries requiring surgery. Study I and II included only patients participating in team handball, basketball, or soccer as their primary sports before injury (n=234). In study III all eligible patients were included (n=338).

Study I stratified patients into 2 groups depending on the time between injury and surgery: early ACLR (<24 months) and late ACLR (≥24 months) (n=217).
Study II included KT-1000 results 6 months after surgery (n=151).
Study III included all patients who attended a 25-year postoperative clinical and radiographic follow-up. (n=235)

8.3 OUTCOME EVALUATION

Patient related outcome measures (PROMs)

Return-to-sport-questionnaire: A questionnaire on sports participation was used routinely after surgery. For the purpose of the long-term follow-up evaluation, it was modified to be better suited for describing long-term sports participation and physical activity. Such a questionnaire was initially introduced to give a more accurate description of the type of sports, the degree and level of sports participation before and after surgery than already existing questionnaires could offer. Patients were classified into 4 levels of sports participation based on self-reported preinjury and postoperative levels: (1) elite, (2) highly competitive, (3) lower competitive, and (4) recreational. Overall successful return to sports was defined as participation in any sports for a minimum of 12 months after surgery. Return to competitive sports was defined as return to level 1, 2 or 3 after surgery, and return to preinjury level was defined as return to the same level of participation as before injury. Return to pivoting sports included team handball, soccer, and basketball. The duration of sports participation after surgery, causes of non-return, any new injuries to the same or contralateral knee, ACL revision surgery or knee replacement surgery were also inquired in the questionnaire.

Lysholm score was first described in 1982[171], and then modified in 1985 to also include evaluation of meniscal injuries [172] At first the scale was physician-administered, also including objective results, but it was early converted to a patient-administered form, as was also the practice in the current study. The score consists of 8 items that is summarized on a point scale of 0 to 100, were 100 is the best score. Limp, support, and locking are worth a potential of 23 points; pain and instability, 25 points each; swelling and stair-climbing, 10 points each; and squatting, 5 points. A frequent used outcome classification is “excellent” for 95 to 100 points; “good” for 84 to 94 points, “fair” for 65 to 83 points, or “poor” for less than 65 points. The Lysholm score was used throughout the current study period and included at the 25-year follow-up.

Tegner Activity Scale was published in 1985 as a complimentary scaling system where work and sports activity are graded numerically from 0 to 10, where 0 represents sick leave because of knee problems, whereas a score of 10 corresponds to participation in national or international elite competitive soccer, football, or rugby.[172] The Tegner Activity Scale was in use throughout the current study period and also included in the 25-year follow-up evaluation.

Knee Injury and Osteoarthritis Score (KOOS) is a self-administered questionnaire developed in the 1990s as an instrument to assess the patient experience of knee function and associated problems.[173] The form is widely in use for research and clinical purposes and is intended to be used to monitor disease course for knee injuries that can result in post-traumatic osteoarthritis (OA); i.e., ACL injury or meniscus injury. KOOS holds five subscales: Pain; other Symptoms; Activities of Daily Living; Sport and Recreation function; and knee-related Quality of Life. Each subscale is scored separately from 0 to 100 (no knee problems). It has been suggested that 8 to 10 points may represent the minimal perceptible clinical improvement (MPCI) of the KOOS[174], but these values are under debate.[175] The KOOS questionnaire was not available at time of inclusion into the current prospective cohort, but the scoring system was included at the 25-year follow-up.

Clinical evaluation

Evaluation of knee laxity, range of motion, patellofemoral joint symptoms, hydrops, and meniscus tests were performed at; the preoperative evaluation; the postoperative evaluation after 3, 6, 12 and 24 months; and at the 25-year evaluation. The early evaluations were performed by the knee surgeon (Torbjørn Strand) or one of his colleagues. At the long-term follow-up, the clinical evaluation was made by the PhD candidate assisted by one or two experienced knee surgeons. Two out of these three examiners were not formerly involved in patient care. In situations where the classification was unclear, cases were discussed and agreed upon by consensus.

Range of motion was recorded as absolute values for each knee, and the side-to-side difference (STS) between knees was graded according to the IKDC-classification system.[176] Normal knee extension should be < 3° of the noninvolved knee. Normal knee flexion should be < 6° of the involved knee.

Evaluation of knee laxity included KT-1000 (MEDmetric, CA, USA) arthrometer measures, Lachman- and pivot shift evaluation.

The KT-1000 arthrometer offers an objective evaluation of anterior translation by strapping the KT-1000 to the leg, pulling the tibia anteriorly, and quantifying the amount of movement in millimeters.[177] In the current study measurements were performed in 20-25 degrees of knee flexion and measured as the anterior tibial displacement found when applying a maximal manual force. The maximum manual difference (in mm) between knees was used for analysis. A side-to-side (STS) difference was graded according to the IKDC classification as follows; Normal: <3mm; Nearly normal: 3-5mm; Abnormal: 6-10 mm; Severely abnormal: >10mm.[176] In study II a tight graft (IKDC grade A) was defined as <3 mm STS difference between the injured and normal knee, a slightly loose graft (IKDC grade B) as a STS difference of 3-5 mm, and a loose graft (IKDC grade C or IKDC grade D) as >5mm STS difference at the 6-months postoperative follow-up. The KT-1000 arthrometer measurements at the 6-months follow-up was chosen because patients would at this time be in the midst of rehabilitation, but still restricted in their sports participation.

The Lachman test also assess anterior translation of the tibia relative to the femur.[70] It is performed with the patient lying in a supine position with the knee in about 20 degrees of flexion. One hand is placed behind the tibia with the other hand on the patient´s thigh. The tibia is then pulled anteriorly. This translational movement of the tibia was graded according to the IKDC classification by using the uninjured knee as reference.[176] Endpoints were classified as firm, soft or inconclusive. The Lachman test is superior to the anterior drawer test in detecting increased anterior translation and is therefore the recommended test used in clinical practice.[73,178]

Pivot-shift test evaluates the anterolateral rotational instability of the knee. An anterior subluxation of the lateral tibial plateau on the femoral condyle occurs as the knee approaches extension, and a spontaneous reduction of this subluxation occur during flexion of the knee. Several different techniques for eliciting this combined dynamic movement have been described, and there is no consensus on a ”gold standard” on how to perform the test.[179,180] In the current evaluation, a variant of the flexion-rotation-drawer (FRD) test described by Noyes was used,[181] and the execution resembles the description of the pivot-shift test.[69,179] The Slocum test was also in use when the results of the primary method was inconclusive.[182] The anterolateral rotational instability (ALRI) was graded as; 0 (negative), 1+ (glide), 2+ (clunk) or 3+ (gross) and used the uninjured knee as reference.[176] The term “guarding” was used if muscular tension prevented accurate classification. Using the pivot-shift test as a tool to evaluate knee laxity after ACL injury has proven to be predictable and correlates well with functional outcome. [183,184]

Graft failure

In study I only failure resulting in a revision ACL surgery was reported. In study II, however, graft failure was defined as ACL revision surgery during the follow-up period or >5mm STS difference measured by KT-1000 arthrometer or pivot-shift test ≥2+ at the 24-month follow-up. In study III an abnormal residual knee laxity was defined as KT-1000 > 5 mm or Lachman test ≥ 2+ or Pivot Shift test ≥ 2+ at the 1-year follow-up. The incidence of revision surgery during the 25-year follow-up was also reported.

Radiographic evaluation

At the long-term follow-up all included patients were offered a radiographic evaluation free of charge. A Synaflexer frame (Synarc Inc, San Francisco, CA, USA) was used for standardization of the bilateral weightbearing radiographs. Radiographs were taken in 45° of knee flexion in the frame, with a 15° craniocaudal x-ray beam for a posteroanterior view of the TF joint. Further, a lateral view of both knees in maximum extension was included.

Radiographs were evaluated according to the Kellgren-Lawrence classification (K-L).[185] Five levels were used to denote the radiological changes; Grade 0: no radiographic features of OA are present; Grade 1: doubtful joint space narrowing (JSN) and possible osteophytic lipping; Grade 2: definite osteophytes and possible JSN; Grade 3: moderate multiple osteophytes, definite JSN, some sclerosis and possible bony end deformity; Grade 4: large osteophytes, marked JSN, severe sclerosis and definite bony end deformity. Radiographic OA was defined as K-L ≥ Grade 2.[185,186]

The radiographs were evaluated by one experienced musculoskeletal radiologist at two different time-points with at least a 6-week interval between evaluations. Interrater reliability was established with a second radiologist who evaluated 30 radiographs (60 knees) blinded from the prior radiographic evaluation.

8.4 SURGICAL TECHNIQUE AND REHABILITATION

All surgeries in the current study period were performed or supervised by two experienced knee surgeons (mainly T.S). The ACL reconstruction performed during this period reflected that time´s current recommendations in surgical technique, graft choice, tunnel placement and graft fixation techniques.[91] The so-called Clancy plasty[91] was introduced 3 years prior to inclusion into the current study, and hence represents a well-established procedure during the study period. All ACL reconstructions in this thesis was performed with a bone–patellar tendon–bone autograft harvested from the central third of the patella tendon in the ipsilateral knee. During the first years (1987-1991), the surgery was performed as a mini-open technique[187] before the transtibial procedure was introduced. (1991-1994).[188] Independent of surgical approach, an arthroscopic evaluation was initially performed to verify the ACL injury and to treat any concomitant intraarticular pathology.

Most ruptures of both the medial and lateral meniscus were treated with a partial resection or left untreated if only a minor injury was found. Bucket handle injuries and unstable meniscocapsular tears in the vascularized zone were treated with meniscal repair if possible, and mostly performed as an open procedure.[189,190] The term ”ramp lesion” was not in use among the surgeons of that time, but posteromedial meniscocapsular ruptures were normally repaired, although an arthroscopic evaluation with probing of the posteromedial recess was not routinely performed.[191] Also, posterolateral root tears were rarely observed (and repaired).

The mini-open technique

Initially, the mini-open technique was performed ‘‘through the defect’’ of the central-third of the patellar tendon, with only a limited exposure of the knee joint.[187] Surgeons of the current cohort found that the transligamentous approach reduced postoperative pain compared to the medial arthrotomy.[192] The femoral tunnels were created by outside-in drilling using a femur guide in 90° knee flexion. Tunnel placement was guided by the remnants of the torn ACL and bony landmarks. The tibia tunnel was positioned anteriorly and medially whereas the femur tunnel was placed in a posterior and superior position relative to the femoral anatomical center.[91] A moderate notchplasty was done in every case. If an extended notchplasty was later needed, an arthroscopically assisted procedure was performed by using a burr or chisel.

A Kennedy-LAD was routinely in use as part of the ACL reconstruction from 1986 to 1988. The device was intended to load-share with the graft in an early phase before gradually transferring the load over to the autograft.[105,106] This polypropylene band (2x8mm) was sutured to the graft in 90° of knee flexion before harvesting the bone blocks. The graft and LAD were then fixed with staples to both the femur and tibia condyle.[106] The Kennedy-LAD was dynamized 6 months after the initial ACL surgery by removing the staples in the lateral femur. The use of the Kennedy-LAD came to an end when the metal interference screw was introduced (Kurosaka) in 1988, which was screwed into bone from the outside.[193]

Isometry of the graft was always evaluated before tibial fixation, leading to a graft fixation in nearly full extension in most cases.

The transtibial technique

The arthroscopic procedure gradually became the main approach for the ACL reconstructions during the study period. An offset aimer was used to guide the femoral tunnel placement, and the femoral tunnel was drilled through the tibial tunnel, allowing for only minor adjustments of the femoral tunnel placement. The femoral tunnel was usually reamed at 70-90° of knee flexion.[188] The tibia tunnel was placed in a central position in the tibial footprint, and the femoral tunnel normally ended up in a proximal and posterior position dependent of the tibial tunnel placement and the knee flexion angle. A moderate notchplasty was performed in every case. The graft was tested for isometry throughout the flexion movement and normally fixed in nearly full extension. Metal interference screws were used for graft fixation in both femur and tibia.[194]

Postoperative rehabilitation

Following surgery, a structured rehabilitation program was guided by physiotherapists for six months, initially assisted by an inhouse physical therapist and at local institutes after discharge. From 1987 to 1991 all patients used a postoperative DonJoy® orthosis that initially allowed patients full range of motion without weight bearing, but with restriction on the last 20° of knee extension during weight bearing until 6 weeks postoperative. From 1991 the rehabilitation was based on a protocol published by Shelbourne and Nitz.[128] In this program there was no restriction in range of motion, but patients were recommended partial weightbearing and the use a DonJoy® orthosis for the first 6 weeks. Normally the physical rehabilitation continued until patients were ready for return to sports. The rehabilitation included sports specific training, group sessions and functional tests. Return to competitive sports participation was usually permitted after 9 to 12 months, and patients were recommended to use the DonJoy® orthosis during the initial period of sports participation after surgery.

8.5 STATISTICS

Data analyses were performed by using the Statistical Package for the Social Sciences version 24/25 (IBM Inc, Chicago, Illinois). An a priori p-value of <0.05 was chosen to denote statistical significance. Normality of data was assessed visually and tested by using the Shapiro-Wilk test. Categorical variables were presented as numbers or percentages. Continuous variables were presented as median and range when nonnormally distributed or as mean and standard deviation for normally distributed variables. The Pearson chi-square test was used for between- group comparisons of various parameters. The Fisher exact test was used for group comparisons when appropriate. Non-parametric tests were conducted for exploring potential differences in a variety of continuous variables with a nonnormal distribution.

Paper I: Descriptive statistics were calculated for early and late ACLRs.

Paper II: Descriptive statistics were calculated for the 2 groups, *tight* grafts, and *slightly* loose grafts. A two-tailed paired T-test was used to compare repeated data from the same patient. An independent samples T-test was used to compare means between tight grafts and slightly loose grafts.

Paper III: Logistic regression with odds ratio analyses was used to assess the relative contribution of selected variables on a dichotomous outcome (presence of radiographic OA (K-L ≥2) 25 years after surgery). Multivariate analysis was performed to evaluate which factors (sex, age at surgery, time between injury and surgery, medial meniscus surgery, lateral meniscus surgery, the use of an additional Kennedy-LAD, or return to preinjury sports) were significant for predicting the presence of radiographic OA 25 years after surgery. The measure of agreement in the radiographic classification (inter-rater and intra-rater reliability) was calculated by using the Cohens weighted kappa statistics, which also takes into the account the degree of disagreement between two ratings. The minimum number of knee ratings needed for the Kappa statistics was calculated using the formula $N \geq 2K^2$, which led to an inclusion of 60 knees (30 radiographs) for this evaluation.[195]

8.6 ETHICS

A study protocol for the current research project was submitted, and the Regional Ethical Committee (REK VEST) approved the study design, collection, and storage of the data before any contact with the patients were made (REK ID 2016 00571). Data storage on a local research server at Helse-Bergen was approved by the Chief Safety Representative. All eligible patients were invited to participate in all parts of the study, and they could withdraw from any part at any time point if they wanted to. A written consent was obtained from all study participants. All investigations were performed free of charge for the patients (funded by the study financing). Potential travel expenses were not covered by the study, but effort was made to guide those who wanted to apply for a refund of travel expenses to a public refund program (Pasientreiser). If the clinical examination revealed knee problems that needed further investigation or treatment, patients were offered further follow-up as appropriate. Pregnant patients or women who were unsure on whether they could be pregnant, were either excluded from the radiographic evaluation or offered a later appointment.

9. Summary of Papers

9.1 PAPER I

Return to Play and Long-term Participation in Pivoting Sports After Anterior Cruciate Ligament Reconstruction

Background: The primary goal for most athletes who undergo ACLR is to return to preinjury sports participation after surgery. Is this goal achievable? And what are the potential downsides of returning to pivoting sports?

Aims: To examine the level and rate of return to sports after ACLR, the duration of sports careers and the long-term consequences of return to pivoting sports.

Methods: All ACLRs between 1987 and 1994 in patients participating in team handball, basketball or soccer prior to injury were included from a quality data database (n=234). A questionnaire focusing on return to pivoting sports, duration of sports participation, new ACL injuries, revision surgery or knee replacement surgery was used in a long-term evaluation (median, 25 years; range: 22-30). Patients were stratified into two groups depending on the time between injury and surgery; early (<24 months); late (≥24 months). To evaluate the effect of age differences, the population was divided into 3 groups: < 18 years, 18-25 years, and > 25 years at the time of surgery. The response rate on the questionnaire was 93% (N=217).

Results:

Patient data: The primary sports distribution was soccer (59%), team handball (36%) and basketball (5%). Ninety-four percent of ACL injuries occurred during primary sports participation. Median time between injury and ACLR was 15 months (range, 0-267 months). The surgical approach was a mini-open technique in 171 patients (79%) and an arthroscopic procedure in 46 patients (21%).

Return to sports and career length: 83% of pivoting sports athletes returned to pivoting sports, but only 53% returned to their preinjury level after early ACLR. Although the return-to-sports rates were similar between males and females, males experienced longer sports careers (median, 10 years; range 1-23 years) than females did (median, 4 years; range 1-25 years) ($P<0.001$).

Age groups: Female athletes who returned to sports were younger at the time of surgery than their male counterparts: 20 years versus 24 years. ($P<0.001$) No differences were seen between age groups in their return to sports rate, but longest sports participation after surgery was seen in the age group > 25 years (median, 10 years; range 2-24 years).

Reinjuries: 28% of athletes who returned to pivoting sports after early ACLR suffered a contralateral ACL injury versus only 4% of athletes who did not return ($P=0.017$). The pooled reinjury rate in patients who returned to their preinjury level of pivoting sports after ACLR was 41% (11% revision surgery and 30% contralateral injury). The incidence of a contralateral ACL injury after return to pivoting sports was 32% among females and 23% among males. ($P>0.05$). The incidence of revision surgery after returning to sports was 12% among females versus 7% among males ($P>0.05$).

Reasons for changing or ending a sports career: Overall, 52% of female and 45% of male athletes responded that changing their level of sports participation after return to sports was not related to knee function. Females more frequently than males reported fear of reinjury as the main reason (17% vs 1%).

Late ACLR: Athletes with a late ACLR was less likely to return to sports and had a lower incidence of contralateral ACL injuries. However, a higher incidence of knee replacement surgery was seen in patients who underwent ACLR ≥24 months after injury than in patients reconstructed within 24 months after injury (9% versus 3%, $P=0.049$).

Conclusion: Return to preinjury pivoting sports participation after ACLR is not achievable for all athletes, and by returning to pivoting sports, athletes are facing a high risk of subsequent ACL injuries.

9.2 PAPER II

Effect of Early Residual Laxity After Anterior Cruciate Ligament Reconstruction on Long-term Laxity, Graft Failure, Return to Sports, and Subjective Outcome at 25 Years

Background: A slight residual knee laxity may be found at follow-up evaluation after ACLR. What is the clinical consequence of this finding in a long-term perspective?

Aims: To evaluate whether a 3-5 mm increase in anterior translation 6 months after ACLR affect the return to sports rate, graft failure and long-term outcome.

Methods: Team handball, basketball and soccer players undergoing ACLR between 1987 and 1994 and attending a 6-month follow-up evaluation including KT-1000 arthrometer measures were included (n=151). A *tight graft* was defined as <3 mm side-to-side (STS) difference between knees (n=129), a *slightly loose* graft as 3 to 5 mm (n=20) and a *loose* graft as >5 mm (n=2). Graft failure was defined as; ACL revision surgery or >5 mm STS difference between knees or anterolateral rotational instability of 2+ or 3+ at the 2-year follow-up. A 25-year evaluation included a clinical evaluation and questionnaires.

Results:
Patient data: Sixty-six percent (n=98) of patients had a meniscus injury at the time of, or prior to surgery. Meniscal repair was performed in 10 patients, while the remaining patients either were treated with a meniscal resection (n=70) or left untreated (n=18). No significant difference in the frequency of meniscal injuries or surgery was seen between the two groups. The mean KT-1000 arthrometer STS difference before surgery was significantly higher in *slightly loose* grafts than in *tight* grafts (10.0 vs 8.7mm, P=0.04).

Return to sports and career length: Seventy-four percent of athletes with *tight* grafts and 70% of athletes with *slightly loose* grafts returned to pivoting sports overall.

Fourty eight percent of athletes with *tight* grafts and 40% of *slightly loose* grafts returned at preinjury level. Although return to sports were similar between athletes with *tight* and *slightly loose* grafts, the median duration of their sports participation was longer in patients with *tight* grafts: 6 years, range, 1-25 years) vs 2 years (range, 1-15 years) (P=0.01).

Failure of the ACLR: The overall rate of revision surgery was 9.4%. Thirty percent (n=6) of patients with *slightly loose* grafts and 6% (n=8) of those with *tight* grafts had undergone ACL revision surgery (P= 0.004) at the 25-year follow-up. Of patients with a *slightly loose* graft 28% (n=5) were classified as failures after 2 years, versus 5% (n=6) with *tight* grafts (P= 0.002). At the long-term follow up the anterior translation was still increased in *slightly loose* grafts as compared to *tight* grafts (P<0.05).

PROM data: 94% of patients with *tight* grafts had a Lysholm score ≥84 after 24 months and 58% after 25 years, as opposed to 78% and 33% among patients with *slightly loose* grafts. (P=0.02 and P=0.048, respectively).

Conclusion: A *slightly loose* graft 6 months after ACLR increase the risk of later ACL revision surgery or graft failure. Further, it could reduce the length of an athletes ‘sports career, cause permanent increased anterior knee laxity, and lead to inferior Lysholm score.

9.3 PAPER III

Predictors of Osteoarthritis Development Median 25 Years After Anterior Cruciate Ligament Reconstruction Using Patellar Tendon Autograft

Background: ACL injury is a well-known risk factor for OA development. However, only a few studies have reported the incidence rate of OA development > 20 years after ACLR. These reports display a wide range in outcomes.

Aims: To report on radiographic OA development and to assess risk factors of knee OA in a population of physically active patients 25 years after ACLR.

Methods: ACLRs between 1987 and 1994 were included (n=235) in the study. Results from clinical testing and questionnaires at the 3-month, 12-month and median 25-year follow-up are presented. A radiographic evaluation was also included at the 25-year follow-up. Radiographic OA was defined as Kellgren-Lawrence ≥ Grade 2. Possible predictors of OA development included age; sex; time from injury to surgery; use of a Kennedy ligament augmentation device (LAD); any concomitant meniscus surgery; and return to preinjury sports after surgery.

Results: Patients: Median time between injury and ACLR was 14 months (range, 0-267). After median 25 years, 20% had experienced a contralateral ACL injury and 9% had undergone ACL revision surgery. A Kennedy LAD was used in 11% of cases, and the surgical approach was by mini arthrotomy in 77% of patients. Medial meniscus surgery was performed in 49% of patients and lateral meniscus surgery in 32% of patients. At the 25-year follow-up, 68% of patients who had undergone surgery to either of the menisci had developed OA, versus 44% in the group who had no previous meniscus surgery (P<0.001).

OA development: Radiographic OA was found in 60% (141/235) of involved knees and in 18% (40/227) contralateral knees at the long-term follow-up (P<0.001).

Clinical evaluation: Extension deficit at the 3-months follow-up did not increase the odds of having an extension deficit at the long-term follow-up. However, having an extension deficit at the long-term follow-up increased the odds of having OA by 2.2 (P=0.01). Fifteen patients (12%) had a residual knee laxity at the 1-year follow-up, and the odds of also having this residual knee laxity at the long-term follow up was 5.6. Having a residual knee laxity at the long-term follow-up was associated with less development of OA (OR0.43) (P=0.019).

Predictors of OA development: Higher age at surgery, male sex, increasing time between injury and surgery, an additional Kennedy-LAD, and medial and lateral meniscus surgery were significant predictors of OA in the univariate analysis. Return to preinjury level of sports was associated with less OA development. Only medial and lateral meniscus surgery were independently associated with OA development in the multivariate model. The adjusted odds ratio was 1.88 for medial meniscus surgery and 1.96 for lateral meniscus surgery (P=0.035).

Return to sports: 75% of patients participated in pivoting sports prior to injury, and of these, 76% returned to their pivoting sport (135/177) Overall, 178 patients (76%) returned to any kind of sports, and 115 patients (49%) returned at their preinjury level.

PROM data: Patients who had developed radiographic signs of OA had significantly lower KOOS scores and Lysholm scores than those with no significant OA at the long-term follow up.

Conclusion: Twenty-five years after ACL reconstruction, 60% of patients had developed OA in the involved knee, and these patients reported significantly lower subjective outcomes. Medial and lateral meniscus surgery were independent predictors of OA development at the long-term follow-up.

10. Discussion

ACL injuries continue to occur in the young and athletic population. Patients therefore seek information on the expected short and long-term outcome after such an injury. This thesis provides information on 25-year outcome after ACL reconstruction in a representative cohort of patients in terms of age, sex, and sports participation. The inherent problem with long-term studies is that changing treatment protocols might yield results that sometimes does not hold validity for current practices. The current thesis has evaluated the long-term outcome in a cohort of patients presenting with an ACL injury at a time when both the surgical procedure and the post-operative rehabilitation were less evolved than they are perceived to be today. The general physician was perhaps less aware of ACL injuries, the diagnosis was less known, and the time until diagnosis was often longer than of what is currently seen. The current cohort have, however, been carefully selected to best represent the current situation, and to give a relevant picture of the knee function patients can expect 25 years after of surgery. The inherent limitations to this study will be further discussed.

10.1 METHODOLOGICAL CONSIDERATIONS

Study design

The strength of the current thesis is the median 25-year follow-up period of surgically treated ACL ruptures. Most outcome studies after ACL reconstruction are limited to a short (1-2 years) or medium (up to 10 years) follow-up period. By investigating the effect of return to sports, the length of a sports career, subjective knee function, objective knee laxity and the risk of OA development in surgically treated patients, the current thesis can achieve a comprehensive view of long-term knee health. The current evaluation includes a prospective patient cohort - a study design that is well suited to control exposures, confounders, and endpoints. Although the prospective data were the main source, an additional questionnaire on return to sports and long-term sports participation was also included at the long-term follow-up. This questionnaire relied partially on retrospective data and can therefore be subject to recall bias. In Paper I, to ensure the validity of these data, the reported rates of return to pivoting sports were validated against Tegner Activity Scale data collected at the 1-and 2-year follow-up. Further, the questionnaire was developed for the purpose of this study, to better report on return to sports rate and long-term sports participation, but it is not validated for use. Aiming to study return to sports and sports participation, a uniform group of only pivoting sports athletes (participating in team handball, soccer, or basketball prior to injury) were included in Paper I and Paper II. The current thesis reports sports participation in highly knee demanding (pivoting) sports, and results might therefore not be transferable to other types of sports.

A strength of the current thesis is the relatively good follow-up rate of the patient cohort. Loss to-follow-up is inevitable in a long-term follow-up study,[196] and efforts were made to reach out to as many as possible. By offering individual follow-up sessions and clinical examination at several locations across the country, the clinical follow-up evaluation included 70 % of the eligible patients.

The use of three different clinical examiners blinded from earlier findings, two of them not formerly involved in patient treatment, also added to the reliability of the results by reducing the risk of examiners bias.

The grading of knee laxity was discussed and agreed upon in each case by consensus. However, to further increase the reliability of the clinical data, interrater and intrarater reliability for the examinations should have been established. Unfortunately, this data was not registered during the evaluation, and is rarely seen in other clinical reports.

The radiographic long-term evaluation of OA development in Paper III was performed by one experienced musculoskeletal radiologist at two different time-points and interrater reliability was established with a second radiologist after evaluating 30 radiographs (60 knees). For the radiographic evaluation, the K-L classification of OA was chosen based on being a well-known and reliable classification system widely in use in long-term studies.[163,166,197] It was the most familiar classification-system for the radiologists´ in the current study and was considered the most versatile classification system when comparing OA development rates to that of other relevant studies. There is, however, a disagreement in the literature over the exact definition and grading of OA according to the original K-L classification system,[186] which is important to bear in mind when comparing results across studies. The current thesis used K-L≥2 as the cutoff for the presence or absence of OA,[186] but a division of K-L grade 2 into K-L2/ost (definite osteophyte only) and K-L2 (definite osteophyte and possible joint space narrowing) with K-L2 as the cutoff for the presence OA is also in use.[163,198]

A limitation in the current thesis is the lack of a control group of patients with a conservatively treated ACL injury. Therefore, the current study is not able to evaluate whether an ACL reconstruction reduce the incidence of long-term OA development or affect long-term subjective outcome as compared to a non-surgical treatment.

Long-term studies often exclude patients who have had a partial meniscus resection or chondral damage at the time of the ACLR, or have suffered a contralateral ACL injury, graft failure or undergone knee replacement surgery during follow-up.[164,197,199] The exclusions are made because these events might affect the radiographic, objective, and subjective evaluation. However, such a practice will yield more favorable results than what is seen in clinical practice. The clinical contribution, and generalizability, to the field of ACL surgery is then limited, as results would be highly affected by selection bias and not reflect the true clinical outcome after ACL surgery. Therefore, by also including those who didn't follow the most favorable path after surgery, the current thesis has evaluated patients from an intention-to-treat perspective.

Because this is a retrospective long-term evaluation of prospective data from a database, no power calculation exists, and the post hoc power analyses will always have low power when evaluating non-significant effects. Especially the numbers of revisions presented in Paper I are small, and these results should therefore be red with caution. The current thesis might also be limited by the relatively small group of slightly loose grafts in Paper II. Therefore, results should be read with this in mind as type II error could occur - meaning that the null hypothesis could be falsely accepted. In Paper III the best fitted, and simplest multiple logistic regression model was chosen. This model was also compared to computer assisted stepwise analyses. Likelihood ratio test was used to evaluate the importance of each variable in the model. The independent variables included in the final regression model was predefined based on clinical experience and recognized knowledge, together with an evaluation of P-values (< 0.1).[200]

Outcome evaluation

To determine the clinical efficacy and effectiveness of the ACL surgery, applying a rigorous outcome assessment is essential. A multitudinous approach, as suggested by the ACL consensus group, is reflected in the current thesis, including outcome measures that are reliable, valid, responsive, and comparable over time.[201]

Instrumented quantitative assessments of anteroposterior knee laxity (KT-1000 arthrometer) has proven to be among the most reliable measurements,[177,202,203] although results are prone to be examiner dependent.[204] The laxity assessment in the current thesis included a side-to-side comparison with the contralateral knee, and a contralateral ACL injury during follow-up led to exclusion from the KT-1000 arthrometer evaluation in Paper II and III. The dichotomization of the results of the KT-1000 arthrometer measurements into *tight* and *slightly loose* grafts in Paper II might be a simplification of the knee laxity results. Nevertheless, it represents the clinical implication of finding a postoperative knee laxity that neither corresponds to a failure, nor a successful result. The assessment of rotational laxity was performed by using the pivot-shift test, with its inherent limitations due to a large variability in execution techniques.[179,205] For standardization across examiners, instrumented objective measures have been found to improve the accuracy of the test.[206] Such objective measuring tools were not available when examining the current patient cohort, but a standardized method for executing the pivot-shift test by 3 different examiners contributes to the accuracy of the test in the current thesis.[69,179] Although most of pivot-shift testing techniques are executed in similar ways, it is important to keep this variability in mind when comparing rotational laxity results across studies and examiners.[72]

Failure of the ACL reconstruction do not have a clear definition in the literature.[207] It was defined as ACL revision surgery, >5mm STS difference measured by KT-1000, or Pivot Shift test ≥2+ in Paper II. In Paper I, failure was only defined as revision surgery, as this paper was based only on the Long-term Sports Participation Questionnaire at the long-term follow-up. Also, in Paper III only revision ACL surgery was reported. The latter definition is verifiable and clear but will probably underestimate the true failure rate. It is important to bear in mind that the inconsistency in the reporting of graft failure in the literature makes the comparison across studies uncertain. Moreover, there are many reasons for failure of the ACL graft, often classified as traumatic (e.g., reinjury), technical (eg, surgical errors) or patient related (e.g., generalized hyperlaxity, compliance, muscular strength). The currents thesis has not aimed to distinguish between the different reasons for failure as this is an area of uncertainty.

The patients` perspective of treatment outcome is evaluated with the use of PROMs that gives a comprehensive view of knee symptoms and function. The PROMs used in the current thesis was chosen based on of the purpose of the study and relied on the available PROMs at the time of inclusion. Due to concern over responder burden, the thesis is limited to the use of Lysholm and Tegner score, KOOS, and the Return-to-Sports and Sports participation Questionnaire developed for the purpose of this thesis.

KOOS is one of the most used PROMs and was developed to detect OA development after knee injury,[173] and hence considered ideal for the current thesis investigating OA-development at long-term follow-up. However, KOOS has been criticized for having a ceiling effect, which means that items are too easy for ACL injured patients relative to other patients. Also, it lacks a specific item for evaluating knee instability. Nevertheless, KOOS has displayed adequate content validity and reliable values in ACL injured patients and was in sum considered the best suited PROM in the current long-term evaluation.[208]

Lysholm score was used during the study period and was included at the long-term follow-up to allow for comparison of results over time. The Lysholm score has been in wide use since its introduction, and has been found to be a reliable outcome measure after ACL reconstruction.[209] A recent reevaluation of the Lysholm score and Tegner Activity Scale found acceptable overall floor and ceiling effects for both scoring systems.[170] However, Lysholm score has also been criticized for not being sensitive enough to detect changes and for creating a ceiling effect when ACL injured patients are followed over time.[210,211] Therefore, the addition of KOOS score at the long-term evaluation was seen as crucial to better reflect patients-centered function .

Another disadvantage of the Lysholm score is the influence of physical activity; if the patient reduces his or her physical activity, a higher score could result. To give a more realistic representation of knee function, the Tegner Activity Scale was therefore added. After 25 years in use, this test-battery has demonstrated acceptable psychometric parameters and responsiveness.[170] However, the Tegner Activity Score has some limitations of concern to the current studies. The pivoting sports evaluated (team handball, basketball and soccer) are not classified at the same level. Although team handball at elite level clearly is a highly knee demanding sport, it only counts for level 7 in the Tegner Activity Scale as opposed to level 10 for soccer players at elite level.

To give a more comprehensive evaluation of the patient's sports participation, a Return-to-Sports and Sports Participation Questionnaire was developed. Sports participation was classified into elite level, a high competitive level, a low competitive level and a recreational level, giving a more precise reporting than in previous studies.[139,212] Although controversies still remains in defining return to sports and a successful outcome, the current recommendation defines a successful return to sports as achieving the pre-injury level of sports participation, as it is presented in the current studies.[131] Although return to preinjury level is reached, it does not necessarily correspond to the preinjury performance or level of satisfaction.[213] The consensus statement from the Panther Symposium ACL Injury Return to Sport Consensus Group, therefore stated that the same quality of performance as before injury should be reached if the return is to be defined as a success.[131] However, such data would be highly subjective and hard to define. Considering these objections, and with a lack of prospective performance data, such an assessment was not included in the current thesis.

Another limitation of the current thesis is the lack of functional testing of the knee. Test batteries involving hop tests and isokinetic strength testing could have given a more comprehensive understanding of the knee function at the long-term follow-up.[214]

A limitation to the current evaluation of long-term knee OA development is the poor reporting of cartilage status of the knees at surgery. Unfortunately, the data were partially missing and of poor quality as no classification system for cartilage status existed when the current patient cohort underwent primary surgery. Classification systems, such as ICRS, was only later widely known and in more common use.[215] Another limitation to the current evaluation is the lack of reports of body mass index at follow-up. BMI is known to relate to development of OA and may therefore have affected results.[216] Finally, donor site complications (such as numbness, localized tenderness or tendinitis) were not prospectively registered. Patella fractures and patellar tendon ruptures are more severe complications that were registered. However, none of the patients in the current cohort suffered such a severe complication.

10.2 RESULTS

Return to sports and long-term sports participation

The treatment for most athletes who wants to return to sports after an ACL injury, is a surgical reconstruction.[79] However, as the current thesis illustrates, an ACLR does not necessarily enable a return to sports participation at the former level.

In paper I, although 83% of athletes returned to pivoting sports and 71% returned to a competitive level, only 53% returned at their preinjury level. In paper III, including all sports, only 49% returned at their preinjury level. The return to sport rates in the current thesis does not differ significantly from the results of a systematic review, reporting a 81% return to sports, 65% return to preinjury level and 55% return to competitive sports.[139] These results are probably lower than the previously communicated return to sports rate, as the rate differs depending on the population investigated (e.g., elite athletes versus recreational athletes) and the return to sports definition (e.g., preinjury versus overall return to sports).[137,138,140,217,218]

Elite level athletes were found to have a higher return to preinjury sports rate of 73% in paper I, but somewhat lower than the 83% preinjury return rate seen in a systematic review among elite level athletes.[140] The better return to sports rate among elite athletes might be explained by their physical capacity or superior athletic skills, psychological responses[132] or internal motivation. Elite level athletes are also normally provided with professional surroundings, dedicated therapists, and dedicated hours of daily rehabilitation. External factors such as financial benefits, expectations from the teams, coaches or media might also affect the return to sports decision.

Return to less than preinjury level has multitudinous causes, and is possibly related to surgical factors, rehabilitation, achieved knee stability and psychological factors, as well as to changes in the patients' goals and motivation throughout the course of treatment. Fear of reinjury and psychological responses have received increased attention during the recent years and are now recognized as important obstacles for a successful return to sports.[132,133,136] As the awareness raises, and more effort is placed on also addressing these aspects, one could hope that fear responses become less of a problem in the future. On the other hand, one could also argue that fear responses are appropriate, as return to preinjury sports comes with a high risk of reinjuries.

Even if a return to preinjury sports is achieved, there is no guarantee for a long and successful sports career, and few attempts have been made to evaluate sports career length after ACL surgery. The studies in the current thesis were well suited for investigating sports career length as the patients were followed in a "life-time" perspective. In Paper I, although the return to sports rate was similar between males and females, male athletes had significantly longer sports careers than females (10 years versus 4 years). The finding of similar return to sports between males and females differs from the systematic review by Ardern et al.[139] where male sex increased the odds of returning to preinjury level. Younger age did also increase the odds of returning to pivoting sports in the review analysis. In Paper I of the current thesis, however, all patients <18 years at the time of surgery were females while 74% of the oldest age group were males. It is therefore difficult to interpretate these results, as age and sex needs to be viewed as confounding factors affecting outcome. The reason for differing career length between males and females is uncertain as empirical data is lacking. Physical differences, pregnancy, differing social commitments or a higher proportion of females in educational institutions might be a part of the explanation. Also, in Paper I, females who made a successful return to sports but subsequently stopped participating or participated at a lower level, more often reported fear of reinjury as the primary reason for the change in sports participation than their male counterparts. Males were more likely to report the ACL injury as the primary cause for lowering their level of sports participation.

Having a slight residual knee laxity also affected the length of the sports career. In Paper II, patients with *tight* grafts returned to preinjury level of sports at similar rates as those classified as having a *slightly loose* graft, but those with *tight* grafts had significantly longer sports careers (6 years) than those with *slightly loose* grafts (2 years). The similar return to preinjury sports indicates that the slight residual anterior translation found in some patients after surgery, did not lead to a knee instability that affected the return to sports decision. However, patients with slightly loose grafts more often reported knee-related causes for giving up or lowering the level of sports participation over time, than patients with tight grafts. The higher incidence of graft failure seen for this group contributes to the shorter sports career, but recurrent symptoms of instability is probably also a main reason.

Finally, return to sports did not increase the incidence of OA at the long-term follow-up. On the contrary, patients who returned to their preinjury level of sports displayed lower odds of OA development. The result is in line with Oiestad et al.[219] who investigated the association between return to sports and the risk of developing OA 15 years after ACLR. Patients who returned to pivoting sports had lower odds of long-term knee OA and better self-reported ADL function compared to those who did not return to sports. Possible explanations to the counterintuitive finding of lower odds of OA in those who returned to their preinjury level of sports could be that athletes who aim for a return to sports after surgery may be more motivated during the phase of rehabilitation. This could lead to a better restoration of knee stability and function after surgery, and thereby further improve the long-term outcome. However, the knee related causes for not returning to sports after surgery is potential biases to this finding, as patients with concomitant injuries (e.g., meniscus or cartilage injuries) might be less likely to return to sports after surgery, and at the same time have an increased risk of OA development. Nevertheless, it seems like patients that can return to sports could do so without increasing their odds of developing OA 25 years after of surgery.

Subsequent knee injuries

In the current cohort, including all patients, 20% of the participants had sustained a contralateral ACL injury and 9% had undergone ipsilateral ACL revision surgery during the 25-year follow-up (Paper III). The overall occurrence of ACL revision surgery seen in the current patient population is therefore comparable to other long-term studies.[196,220] Sanders et al.[143] have reported an estimated graft survival rate of 91% at 25-year follow-up, and a systematic review by Magnussen et al.[142] including > 2600 reconstructions have reported a graft tear risk of 8 % (3% -11%) and a 13% (1%-23%) risk of suffering a contralateral injury within 10 years after surgery. A recent 10-year follow-up study of 244 patients reported a more than doubled risk of contralateral ACL reconstruction compared with ipsilateral ACL revision surgery, and a peak incidence of 40% ipsilateral or contralateral secondary injuries in young and active populations.[221]

When evaluating ACL reinjury risk, it is important to be aware of the background risk for sustaining an ACL injury in the population investigated. The risk of suffering an ACL injury during an athletes` sports career is high, especially among young female athletes.[222–224] Female soccer and basketball players have been found to have 3 times greater incidence of ACL injuries than their male counterparts, and a year-round injury rate as high as 5%.[225] Agel et al.[226] have reported a statistically significant increase in the average annual number of injuries in basketball for both males and females. Further, females continue to sustain ACL injuries at higher rates than males in the comparable sports of soccer and basketball.

Although high incidence rates have been seen in these studies, Paterno et al.[227] found a nearly 6 times greater incidence rate for a second ACL injury within 24 months after ACLR in patients who returned to pivoting sports, as compared to healthy controls participating in pivoting sports. Similarly, in a recent study by Fältström et al.[228] female soccer players that returned to sports had a > 2-fold higher risk of a new ACL injury than players who did not return, and a 4 fold higher risk than controls within 5-10 years after primary unilateral ACLR.

It is also important to be aware of the different approaches for reporting repeat ACL injury, as numbers would be expected to differ depending on the population investigated and whether return to sports are reached prior to the reporting of reinjuries. Moreover, contralateral ACL injuries often occur later than reruptures or ACL revision surgery, and a higher frequency of contralateral ACL injuries are reported as the follow-up time increases, which proves that long-term evaluation is important in the risk assessment after ACLR.[148] In the current thesis, the pooled reinjury rate among pivoting sports athletes who returned to preinjury level was as high as 41% (Paper I). Contralateral ACL injuries constituted 30%, and graft reruptures 11%. Comparable to the current result, Paterno et al.[227] found a pooled reinjury rate of 30% for athletes within 24 months of return to sports (21% contralateral injury and 9.0% graft rerupture). Moreover, in a 3-18-year follow-up on Australian football players, the pooled reinjury rate was 30% and as high as 50% among athletes aged < 21 years at the time of the first ACL injury.[229]

Young age,[146] female sex, [144,227] and return to high-level sports[145,227] have previously been reported to increase the risk of suffering contralateral ACL injuries. A 5-year follow-up study by Salmon et al.[145] including 612 patients, a return to level 1 or 2 sports was found to increase the risk of contralateral ACL injury a 10-fold as compared to participation at lower sports level. In line with these results, return to pivoting sports was found to be a significant risk factor for experiencing a contralateral ACL injury at median 6 years after the primary ACLR (30%) (Paper I). However, the incidence of contralateral ACL injury was similar in males and females, (32% versus 23%, P>0.05) in the current thesis.

Surprisingly, return to pivoting sports was not associated with increased risk of graft failure or revision surgery in the current patient cohort (Paper I and II). A slightly higher rate of revision surgery was seen in the non-return group (Paper I) but is suspected to be due to early recurrence of instability, before the recommended point of return to sports. Moreover, patient numbers are small for these calculations, and results should be read with that in mind.

The implication of having a slight sagittal laxity (3-5 mm STS difference) after surgery was investigated in Paper II. Studies investigating the effect of residual knee laxity on the risk of graft failure or revision surgery are scarce, and mostly limited to short-term follow-up.[230,231] A long-term evaluation by Goodwillie et al.[232] after mean 16 years, compared tight (<3mm) grafts and loose (>5mm) grafts as measured by KT-1000, and found that 2 tight grafts (4%) and none (0%) loose grafts had undergone ACL revision surgery. In contrast, our study found that slightly loose grafts at 6 months after ACLR did significantly increase the incidence of graft failure and ACL revision surgery in the current (Paper II). Five slightly loose grafts (28%) and 6 tight grafts (5%) were classified as failures after 2 years, and 30% of slightly loose grafts and 6% of tight grafts had undergone ACL revision surgery by the time of the long-term follow-up.

Subjective outcome

The long-term subjective outcomes (PROMs) after ACL reconstruction in the current cohort were generally good as most patients were likely to have a well-functioning knee after 25 years. Although ACLR is typically performed in an athletic population, patient activity levels have been reported to decline significantly with time from surgery.[233] In the current thesis the median Tegner was 4 points at the 25-year follow-up. This pattern is expected in response to older age and physiological body changes – and with typical lifestyle changes seen when patients are in their 20-30`s.

The KOOS and Lysholm score was found to be significantly lower among those who had developed OA than in those who had not. In Paper III the suggested 8-10 points of minimal clinical difference between the two groups was reached for all subscales of the KOOS except for the ADL subscale. Further, a 10-point difference between groups was seen for the Lysholm score. These results are in line with other long-term studies; reporting progressively lower subjective scores as the level of OA increases.[160,164,169] However, the direct relationship between long-term radiographic and symptomatic OA is unclear[196], and it is not sufficiently answered in the current thesis, although measures of knee pain are reported according to KOOS-pain subscale.

In Paper II a good or excellent result at the long-term follow-up (Lysholm score ≥84) was more often reported in patients with *tight* grafts (58%) as opposed to patients with *slightly loose* grafts (33%) at the 6 months evaluation. The KOOS score was lower for all subscales, but the difference was only statistically significant in ADL. Few similar studies have been performed, but a study by Sundemo et al.[234] investigated the relationship between early laxity results and long-term subjective outcome. In that study an association between the Pivot Shift and Lachman testing was found, but not for the KT-1000 arthrometer measurements. The study applied mean STS difference, and not dichotomized values, which could perhaps explain the somewhat divergent finding, although another study by Goodwille et al.,[232] using KT-1000 arthrometer, also concluded with no difference in subjective outcome between *tight* (<3mm STS difference) and *loose* grafts (>5mm STS difference) 16 years after ACLR.

OA development

The main finding in Paper III of the current thesis was the 60% (K-L≥2) OA development rate in the involved knee compared to a 18% OA development rate in the contralateral knee median 25 years after ACL surgery (P<0.001). Put into context, although regions and populations investigated varies, a meta-analysis of population-based observational studies found a pooled global prevalence of knee OA of 16% in individuals aged 15 and over and 23 % in individuals aged 40 and over.[235] Knee injuries, and especially ACL injuries are well-known risk factors for post-traumatic OA development.[150–152]

Unfortunately, although there is still limited high-quality evidence, an ACLR does not seem to reduce the risk of OA development.[236,237] Only a few evaluations of OA development >20 years after ACLR have been performed, and there is a vide variation in the reported rates of OA development (20%-80%).[160–166] When comparing the incidence rate between studies it is also important to bear in mind that different exclusion criteria are applied across clinical reports. Some studies have excluded patients with a surgically treated meniscus injury or chondral damage at the time of the ACL reconstruction, thereby reducing the incidence of post-traumatic OA in these studies compared to the studies that also includes the high-risk patients.[165,197,199]

OA incidence rates from the current thesis correspond to that of other studies using the K-L classification after minimum 20 years to follow-up, ranging from 42%-80%.[163,166,197] Although 60% of the patients of the current cohort had developed signs of OA, only 36% had developed severe OA ((K-L ≥3) or undergone knee replacement surgery) in the involved knee. By use of the IKDC classification, Shelbourne et al.[164] reported OA rates in > 400 knees at minimum 20 years of follow-up. In that study 29% had an IKDC radiographic rating of abnormal or severely abnormal and 65% had an IKDC rating of less than normal. Assuming that a K-L classification of ≥2 is similar, but not identical, to the IKDC classification of less than normal, the OA development rate in the current thesis seems to be in accordance with Shelbourne et al.

In Paper I a higher incidence of knee replacement surgery was seen in the group of patients that underwent ACL reconstruction ≥24 months after injury (9%) compared to the group of early (<24 months) reconstructions. Similarly, in Paper III, the time between injury and surgery was longer among patients that had developed OA at the long-term follow-up than in those who had not, (17 months versus 11 months, P=0.01). Although meniscal tear was the only variable independently associated with OA development in the adjusted regression model, time until surgery plays a role in the outcome after ACL injury. Long time between injury and surgery puts the secondary restraints – such as menisci - at risk of injury, and by that increases the risk of OA development.[155] It is, however, still uncertain whether the time between injury and surgery directly affect the incidence of OA.[157]

Having intact menisci have proven to be important in preventing OA development.[157,164] In Paper III we found that the time until surgery significantly influenced on the rate of medial meniscus surgery. Further, medial, or lateral meniscus surgery during the follow-up period significantly increased the odds of having developed OA at the long-term follow-up. It is therefore appropriate to assume that as more meniscus injuries are repaired, the rates of OA development might improve in future long-term studies.

Knee laxity

At the 25-year evaluation most patients were likely to have a stable and well-functioning knee. Low levels of abnormal knee laxity were seen, although the incidence was doubled as compared to the 1-year results (Paper III). According to the KT-1000 arthrometer measurements, 88 % had a normal or nearly normal knee at long-term follow-up. Results are in line with a recent systematic review of long-term studies by Everhart et al.[196], where 82% of knees were assigned a normal or nearly normal overall IKDC grading.

The preoperative knee laxity was evaluated in Paper II. There was an association between a severe preoperative knee laxity and having a slightly loose graft 6 months post-operative. As shown by Nicholas et al.,[238] these findings suggests that normalizing knee laxity in patients with a high grade of preoperative static laxity can be challenging.

The incidence of residual knee laxity after ACLR was reported in Paper II and III. Early residual knee laxity was found to increase the risk of ACL revisions. However, it did not significantly affect the OA development rate, as also reported by Shelbourne et al.[164] On the contrary, in the current cohort it seems like a residual knee laxity could sometimes be considered as favorable at the long-term follow-up. A loss of range of motion due to OA development might affect knee laxity, imposing a more stable knee over time, and thereby resulting in a decrease in the antero-posterior translation and antero-lateral rotation movement during clinical testing. Moreover, very tight ACLRs could be at risk of loss of motion over time and therefore develop OA due to over constraint of the knee joint.[207]

Finally, a range of different predictors of increased knee laxity in relation to the ACL injury have been suggested, but the data in the current thesis is insufficient for evaluating the multitudinous causes of post-operative knee instability.

10.3 GENERAL CONSIDERATIONS

The surgical procedure and rehabilitation that the patients evaluated in the current thesis underwent, is not identical to current practice. Results from this thesis might therefore not be directly transferable to the patients undergoing surgery today.

Graft tunnel placement techniques and its implication on residual knee laxity has been in focus over the last decade. Current tunnel placement practices are considered to be better suited in controlling the pivot shift phenomenon and more ”anatomic” than at the time when the participants of the current thesis underwent ACL surgery.[32,239]

Meniscal repair is indisputably important in restoring knee stability in ACL injured knees.[240,241] The patients of the current cohort were treated with meniscal repair if possible.[189,190] The term ”ramp lesion” was, to our knowledge, not in regular use during the 1980-1990´s, but the description fits well with the few sutured posteromedial meniscocapsular ruptures seen in our study. However, an arthroscopic evaluation with probing of the posteromedial recess[191] was not routinely performed, and the current thesis can therefore not rule out the possibility of overlooked ramp lesions. At that time, posterolateral root tears were rarely observed (and repaired) – in the current cohort none were reported. Further, current data from the Norwegian Knee Ligament Registry (dating back to 2004) show that concomitant partial meniscus resection has decreased from 80% to 30% over 15 years – whilst concomitant repair has increased from 5% to 55% in the same period.[44]

In recent years there has also been a renewed interest in the anterolateral structures of the knee[39] and some surgeons consider additional procedures to increase the likelihood of a successful ACLR in selected patients. Such additional lateral extra-articular (LET) procedures were rarely used at the time when the current patient cohort underwent surgery, due to reports of an increased risk of OA development from overconstraint of the knee.[93,242] Recent biomechanical studies have highlighted the anterolateral complex function as a secondary stabilizer to anterolateral rotatory laxity (ALRI) in ACL injured knees - leading to a revisiting of the lateral extra-articular procedures (LET).[43] These procedures might decrease ACLR failure rate, but there is a need for more clinical studies to shed light on long-term consequences of applying these modern procedures.[99,100,243,244] The increased focus on how both intra- and extraarticular structures may play a role, highlights how restoring knee stability after an ACL injury is a complex procedure that need a thorough and individualized approach.

Ongoing efforts to improve outcomes after ACL injury has led to an increasing interest in ACL repair and ACL augmentation procedures, particularly in combination with direct suture of the ACL.[245–247] The open ACL repair techniques were, however, more or less abandoned during the 1980`s due to disappointing clinical results. In recent years a variety of different ACL repair techniques have been introduced,[248,249] but only in small case series with short follow-up time, displaying mixed results.[250,251] However, historically a range of different tear types were treated with primary repair, but it is now suggested that only proximal tears should be treated by repair, as there is better vascularity at the proximal end of the ligament.[9] Nevertheless, high quality studies comparing the outcomes to ACL reconstruction with sufficient follow-up are needed before widespread use of ACL repair procedures.

Moreover, a recent study of suture ligament augmentation has provided disappointing (and high) failure rates compared to conventional ACL reconstruction in adolescent patients.[252] Augmentation devices were also in use together with an ACL reconstruction during the 1970-1980s. Although acceptable results were seen after reconstruction with the use of a Kennedy-LAD, they were never superior to free BPTB autografts.[106,107] Elveos et al.[162] evaluated ACLRs using a BPTB autograft with and without the Kennedy LAD at 25 years with no significant difference in outcomes (including the development of OA) between the two groups. In Paper III of the current thesis, an additional Kennedy LAD was used in 11% of patients. The development of OA was not statistically higher than in patients without this augmentation, but in the univariate analysis, the odds of developing OA after 25 years was 2.28 if the Kennedy LAD was added (P=0.075). This trend towards a less favorable result supports the earlier recommendations to avoid the use of reinforcement with this synthetic band.[107]

Surgery due to an extension deficit was performed in 9% of the study participants 6 months after ACLR (Paper III). Such extension deficits reflect on the past practice of a more anterior tibia tunnel placement than is seen today. Further, this might also reflect the more conservative rehabilitation and restriction in range of motion during the first 6 weeks after surgery. Although prior studies have found that an early loss of knee extension increased the risk of OA development,[253,254] the current thesis found no significant association between having a knee extension deficit at the 3-months follow-up and having developed OA at the long-term follow-up. Moreover, an early extension deficit was normally resolved by performing a notch plasty, and it did not increase the odds of having an extension deficit at the long-term follow-up. The knee extension deficit seen at the long-term follow-up was associated with OA, probably caused by the degenerative changes to the knee joint seen during the OA development.

Although the rehabilitation protocol restricted knee extension to only 20° during weight bearing in the earliest inclusion period of the current patient cohort , a more liberal rehabilitation program was introduced by Shelbourne and Nitz[128] in 1991 to overcome, among others, the problem with knee extension deficit. Unfortunately, the exact timing of the change in the rehabilitation regime is unclear and could not be controlled for in the current work. However, it should be noticed that the current cohort stayed at the hospital for several days after surgery, closely followed by both inhouse surgeons and physiotherapists. The rehabilitation program was well established and included several months of follow-up with close contact and multiple follow-up consultations with the surgeons and physiotherapist, thereby securing patients a very robust rehabilitation program.

11. Clinical implications and future perspective

By following a cohort of patients from their primary injury until median 25 years after surgery, the current thesis has contributed with new pieces to the puzzle of the ACL injury. Although a non-operative treatment is a reasonable option for many patients, ACL reconstruction is still the preferred treatment among athletes who wants to return to sports participation. The current thesis provides current and future patients with information on their expected long-term outcome after ACL reconstruction. According to the results of this thesis, patients have a high risk of ACL reinjuries and development of post-traumatic OA, but the overall long-term clinical and subjective results are still likely to be satisfactory.

The current thesis has shown that an ACLR facilitate return to sports, but it is not a guarantee for a successful return to preinjury level of activity. Although return to sports was the main indication for undergoing ACL surgery, only half of the patients of the current cohort did so. Pain or knee related problems added to the decision, but fear of reinjury and changes in goals and motivation throughout the course of rehabilitation were important factors in the decision to not return to preinjury sports participation. Athletes should therefore be informed about the statistical risk of not returning so as to create realistic expectations.

Results suggests that return to sports as the primary or only indication for ACLR is probably not appropriate, and there is increasing evidence towards a more individualized approach to both the decision on whether to reconstruct the ACL or not, and to the process of rehabilitation.[255] The surgical decision should probably include both an evaluation of the severity of the preoperative knee laxity and the subjective experience of knee stability, as well as inclusion of psychological[133] and social factors that could affect the return to sports decision during the course of rehabilitation.

Counselling patients to undergo surgery or not is often difficult and relies on the physician's experience and clinical judgement along with patient related factors. Return to preinjury level of sports is not always the goal, but patients might expect to have a life including work or other activities that can challenge the knee. Moreover, sports are a social arena, and plays a significant part in many patients' life and identity.

A surgical reconstruction could therefore also be viewed as important for psycho-social well-being.

Given the high risk of contralateral ACL injuries seen in the current evaluation, return to preinjury sports should probably not be recommended for all patients. The identification of high-risk patients is a difficult task, as a multifactorial etiology lays behind the course of an ACL injury. Further examination of known risk factors and intervention towards modifiable risk factors,[256] and an increased attention on prevention towards the contralateral knee is important to help reduce the future ACL reinjury rates.[257,258]

Before patients are cleared for return to sports participation after surgery it is recommended that they undergo an evaluation of knee laxity. A slight residual knee laxity can sometimes be seen at such evaluations. The current thesis investigated the clinical implication of this finding. The increased risk of later graft revisions or failures displayed in the results suggest that finding a residual knee laxity should affect further rehabilitation and recommendation for sports participation - and in some cases lead to a reevaluation of the surgical treatment or consideration of additional procedures. The reasons for early residual knee laxity might be many, and evaluating risk factors was not an aim of the current thesis. The literature is also inconclusive, which should inspire future research on this area.

Although patients in the current thesis underwent ACL reconstruction, a high proportion had developed knee OA at the 25-year follow-up. Moreover, the most important risk factor for developing OA was meniscus resections. Results from the current thesis therefore indicates, again, that ACL injury reduction strategies is highly important in an athletic population, and an increased attention towards injury prevention programs could potentially lower the incidence of post-traumatic OA in the future.[259] Further identification of modifiable risk factors (such as neuromuscular control) is crucial as part of preventive strategies and intervention programs aiming to reduce the incidence of ACL tears.[260,261]

However, although interventions are made, a high incidence of new ACL injuries are still seen.[44] Given that ACL injuries will continue to occur calls for more knowledge on how to best handle patients with ACL -and additional injuries.

Evaluation of the long-term outcome after meniscus repair or additional lateral extra-articular tenodesis (LET) might shed more light into the importance of the surgical evolvement seen in recent years.

In the late 1980s and early 1990s, when the current patient cohort underwent surgery, there could be a delay in the diagnosis and treatment of ACL ruptures that might have affected the long-term incidence of OA. The expression ”early reconstruction” in the current thesis, was used when the ACLR was performed within 2 years after injury which is far from what would be called an early reconstruction today (within weeks to a few months). Although the current thesis suggests that an ACL reconstruction should be performed within a reasonable time, there is still a need for further studies investigating the optimal timing of surgery and its long-term outcome. A recent systematic review analysis by Ferguson et al.[262] found no clear evidence to determine superiority of acute/early or delayed reconstruction of a ruptured anterior cruciate ligament. Furthermore, data from the Swedish national Register found a 2-3 fold increased rate of repeat ACL surgery or contralateral ACLR in primary ACLRs performed < 3 month after injury as compared to > 1 year, and the data supports a cautious attitude towards very early reconstructions.[263] Moreover, ACL reconstruction might be an unnecessary procedure in some athletes. At least a thorough subjective evaluation of knee stability should be performed before a surgical decision is made, which often involves > 3 months of rehabilitation.

The evolvement in the ACL treatment strategies seen today will hopefully lower the rate of ACL reinjuries and OA development in the future. Nevertheless, the reported mid-term results of modern procedures still reports disappointingly high risks of further ACL injuries and OA development among athletes.[228,237] This thesis should therefore inspire further long-term evaluations after surgery with comparison to a non-surgically treated group. The latter is needed to isolate the true effect of surgery.

Finally, as this thesis highlights; it is important to be aware of the work of the former pioneering surgeons and researchers. A revisitation of former procedures has been seen in the recent years. Although resent research seems to unveil new technical skills and possible benefits for future ACL-injured patients, we must not forget our history.

12. Conclusion

- ACLR does not necessarily enable a return to preinjury sports participation. Although > 80% of pivoting sports athletes returned to sports after ACLR, only 53% returned at their preinjury level.

- Return to pivoting sports rates were similar between males and females, but males had significantly longer sports career than their female counterparts (10 years versus 4 years)

- Return to sports come with a prize; by returning to pivoting sports, athletes are facing a worryingly high risk of contralateral ACL injuries (28-30%).

- Only a *slightly loose* knee at the postoperative follow-up matters. Having a *slight* residual knee laxity 6 months after ACLR increased the risk of later ACL revision surgery and/or graft failure.

- A slight residual knee laxity after ACLR also reduced the length of the athlete's sports career, caused permanent increased anterior laxity, and led to an inferior Lysholm score.

- There is a high incidence of OA development after ACL injury, despite undergoing ACL reconstruction. At median 25 years after ACL surgery, 60% of patients had developed OA in the involved knee and only 18% in the contralateral knee.

- The status of the menisci in the ACL injured knee is the most important predictor of OA development at the long-term follow-up after ACL reconstruction.

- The subjective scores are affected by the development of OA. Patients report progressively lower subjective scores as the level of OA increases.

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14. Papers I-III

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III

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