The impact of implant design and severity of knee osteoarthritis on clinical outcome after total knee arthroplasty

PhD Thesis

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Abbreviations

ACL	Anterior cruciate ligament
AS	Anterior-stabilized
ASA	American Society of Anaesthesiologists
BMI	Body Mass Index
BMP	Bitmap
CR	Cruciate-retaining
EQ-5D-3L	Three-level Euro-Qol five-dimension index
EQ-5D-5L	Five-level Euro-Qol five-dimension index
EQ-VAS	EQ-5D visual analogue scale
KL	Kellgren and Lawrence
KOOS	Knee injury and Osteoarthritis Outcome Score
LCL	Lateral collateral ligament
NAR	Norwegian arthroplasty register
MCID	Minimally Clinically Important Difference
MCL	Medial collateral ligament
MIC	Minimal Important Change
OA	Osteoarthritis
OKS	Oxford Knee Score
PCL	Posterior cruciate ligament
PROM	Patient reported outcome measures
PS	Posterior-stabilized
RCT	Randomized control trial
ROM	Range of motion
RSA	Radio Stereometric Analysis
TKA	Total Knee Arthroplasty

Thesis Summary

Background

It is estimated that around 10% of adults over 60 experience symptomatic knee osteoarthritis (OA). OA is estimated to affect approximately 4% of the world's population, with prevalence increasing with age. Total knee arthroplasty (TKA) is a widely used surgery that has radically improved the quality of life of millions of people suffering from symptomatic knee OA during the last few decades. However, several clinical studies have revealed that only 75-89% of patients are satisfied with their outcomes after TKA. These reports indicate that TKA is not reaching its goals of reducing pain and restoring function in many patients. The reasons for patient dissatisfaction are varied.

Aims

Study I aimed to evaluate the association between the radiographic degree of OA and the improvement in patients' health state measured one year after TKA. We investigated the in vivo kinematics of three different TKA implant designs during a step-up movement in study II. Finally, in study III, we compared patient reported outcome measures (PROMs) two years after surgery between three TKA implant designs.

Materials and methods

Study I used data from a prospective cohort of OA patients treated with TKA at Lovisenberg Diaconal Hospital from 2012 to 2014. Two independent investigators reviewed all the preoperative radiographs of each patient. They graded the OA changes based on Kellgren and Lawrence (KL) classification. The health state index, a score based on the five EQ-5D-3L dimensions, was used to measure patients' health state. We used multiple linear regression to analyze the association between KL grade and improvement in patients' health state. Study I included 156 patients. We used dynamic radiostereometric analysis (RSA) in study II and compared the kinematics of different knee prosthesis designs during a step-up movement. Study II included 39 patients.

We designed and conducted a randomized controlled trial (RCT) in study III. We compared patients with three implant designs and followed them for two years. The

primary outcome measure was the composite score of the Knee injury and Outcome score ($KOOS_5$). Study III included 216 patients.

Results

In study I, we found that patients categorized with KL grade 4 OA had significantly more improved health at 12-month follow-up than those with KL grades 2 and 3 OA. In study II, we found that the cruciate retaining (CR) and anterior stabilized (AS) implant designs showed a similar kinematic pattern during a step-up motion. However, this pattern differed significantly from the posterior stabilized (PS) implant design.

In study III, we found no significant difference between the three implant designs in the composite $KOOS_5$ score at two-year follow-up.

Conclusions

Our research discovered that people with advanced radiographic OA experienced more significant improvement in their health state after undergoing TKA. Also, we noticed that patients satisfied with their TKA only had a kinematic pattern similar to a natural knee when using the PS implant design. Even though there were differences in constraints and design, all three implant designs produced comparable clinical results.

Sammendrag på norsk (Thesis summary in Norwegian)

Bakgrunn

Kneleddsartrose er en vanlig tilstand, hvor prevalensen øker med alderen. En totalprotese i kne er en mye brukt operasjon som radikalt har forbedret livskvaliteten til millioner av mennesker som lider av symptomatisk kneleddsartrose i løpet av de siste tiårene. Flere kliniske studier har imidlertid avdekket at kun 75-89 % av pasientene er fornøyde med resultatene etter kneproteseoperasjon. Disse rapportene indikerer at TKA ikke når sine mål om å redusere smerte og gjenopprette funksjon hos mange pasienter. Det er flere årsaker til misnøye hos pasientene.

Hensikt

Studie I hadde som mål å studere sammenhengen mellom graden av røntgenologisk artrose og forbedringen i pasientenes helsetilstand målt ett år etter kneprotese. Vi undersøkte i studie II in vivo bevegelsen til tre forskjellige kneprotesedesign ved en step-up-bevegelse. Til slutt, i studie III, sammenlignet vi pasientrapporterte utfallsmål (PROM) to år etter operasjonen mellom tre kneprotesedesign.

Material og metode

I studie I brukte vi data fra en prospektiv kohort av artrosepasienter som ble operert ved Lovisenberg diakonale sykehus fra 2012 til 2014. To forskere gjennomgikk alle de preoperative røntgenbildene av pasientene. De graderte artroseforandringene basert på Kellgren og Lawrence (KL) klassifisering. Helsetilstandsindeksen, en poengsum basert på de 5 EQ-5D-3L dimensjonene, ble brukt for å måle den helserelaterte livskvaliteten. Vi brukte multippel lineær regresjon for å analysere sammenhengen mellom KL-grad og forbedring i helsetilstanden. Studie I inkluderte 156 pasienter.

Vi brukte dynamisk radiostereometrisk analyse (RSA) i studie II og sammenlignet kinematikken til forskjellige kneprotesedesign ved en step-up-bevegelse. Studie II inkluderte 39 pasienter.

I studie III designet vi og gjennomførte en randomisert kontrollert studie (RCT). Vi sammenlignet pasienter med tre implantatdesign og fulgte dem i to år. Det primære utfallsmålet var «Knee injury and Osteoarthritis Outcome Score» ($KOOS_5$). Studie III inkluderte 216 pasienter.

Resultater

I studie I fant vi at pasienter kategorisert med KL grad 4 artrose hadde betydelig mer forbedring i helse enn de med KL grad 2 og 3.

I studie II fant vi at to av implantatdesignene (CR og AS) viste likt kinematisk mønster ved en step-up-bevegelse. Dette mønstret skilte seg imidlertid seg fra det tredje (PS) implantatdesignet.

I studie III fant vi ingen signifikant forskjell mellom de tre implantatdesignene i den sammensatte $KOOS_5$-skåren.

Konklusjoner

Studie I viste at det å ha alvorlig artrose på røntgen var assosiert med større bedring i helsetilstanden etter en kneprotese.

Studie II viste at selv om alle inkluderte pasienter var fornøyde med sin kneprotese, så var det en forskjell i kinematikken. Imidlertid var det bare PS-implantatet som hadde et kinematisk mønster som lignet på et naturlig kne.

Studie III viste at de kliniske resultatene var like mellom de tre ulike implantat-designene.

Articles in the thesis

The thesis consists of the following studies:

1. More Severe Radiographic Osteoarthritis Is Associated With Increased Improvement in Patients' Health State Following a Total Knee Arthroplasty
   Rehman Y, Lindberg MF, Arnljot K, Gay CL, Lerdal A, Aamodt A.
   J Arthroplasty. 2020 Nov;35(11):3131-3137. doi: 10.1016/j.arth.2020.06.025. Epub 2020 Jun 17.

2. Comparison of the in-vivo kinematics of three different knee prosthesis designs during a step-up movement
   Rehman Y, Koster LA, Röhrl SM, Aamodt A. Clin Biomech (Bristol, Avon). 2022 Dec; 100:105824. doi: 10.1016/j.clinbiomech.2022.105824. Epub 2022 Nov 17.

3. No difference in patient-reported outcomes with cruciate-retaining, anterior-stabilized and posterior-stabilized total knee arthroplasty designs.
   A three-armed, blinded, randomized study with 2-year follow-up
   Rehman Y, Korsvold AM, Lerdal A, Aamodt A.
   The article has been accepted for publication (The Bone & Joint journal).

Background

Anatomy of the knee

The human knee joint is a complex synovial joint made up of articular cartilage, subchondral bone, and a joint capsule. It is the largest joint in the body and involves four bones (femur, tibia, fibula and patella) and two joints: the tibiofemoral and patellofemoral.[1] The tibiofemoral joint connects the tibial plateau (the top part of the tibia) and the distal femur, while the patellofemoral joint connects the posterior of the patella to the anterior aspect of the distal femur. There is also the proximal tibiofibular joint, which connects the inferior lateral tibial condyle to the head of the fibula, but this joint is irrelevant in TKA.

The knee joint is responsible for weight-bearing between the tibia and femur. Its primary purpose is to support activities like running, walking, and standing by maintaining balance. It also helps transfer both internal forces created by muscle tension near the joint and external forces from the impact of the foot on the ground. Most of the loading on the knee during activity is due to muscle tension compressing the joint surfaces together. For example, when standing up from a sofa, the force on the tibiofemoral joint can be more than three times the person's body weight.[2]
The knee joint is covered with hyaline cartilage on all articulating surfaces. This cartilage has an ultra-low coefficient of friction, which, combined with synovial fluid that lubricates the joint, enables smooth sliding and rolling of the surfaces over one another. The primary muscles responsible for knee flexion are the hamstring muscles, which include the biceps femoris, semitendinosus and semimembranosus. Other muscles involved in knee flexion are the sartorius, gracilis, gastrocnemius, plantaris, popliteus and the short head of the biceps femoris. The only muscle responsible for knee extension is the quadriceps femoris. The patella is embedded in the quadriceps tendon, improving muscle efficiency and protecting the front of the knee from trauma.
The articular surface of the femur is made up of two rounded prominences that are eccentrically curved, meaning they are more curved at the back than at the front. The tibial condyles, on the other hand, are relatively flat. The medial tibial condyle is concave, whereas the lateral condyle is almost flat (Figure 1).

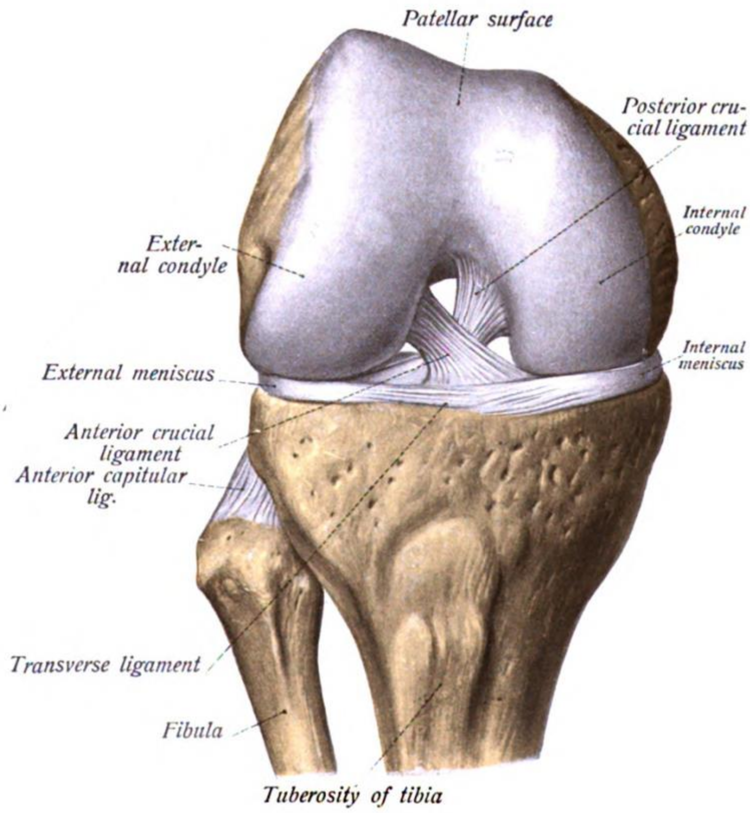


Figure 1. Knee joint in flexion. "Sobotta 1909 fig.220 - knee joint in flexion - English Labels" at AnatomyTOOL.org by Johannes Sobotta is in the Public Domain.

Two C-shaped, fibrocartilaginous structures partially compensate for the incongruity in the tibiofemoral joint: the medial and lateral meniscus[1] (Figure 2). The menisci act as cushions and ensure an even distribution of the load in the joint. Both menisci deform and move with the femoral condyle during flexion and extension. The lateral meniscus moves more than the medial. While the lateral meniscus is mobile and follows the translations of the lateral femoral condyle, the medial meniscus is connected to the medial collateral ligament and is, therefore, more fixed.[3]

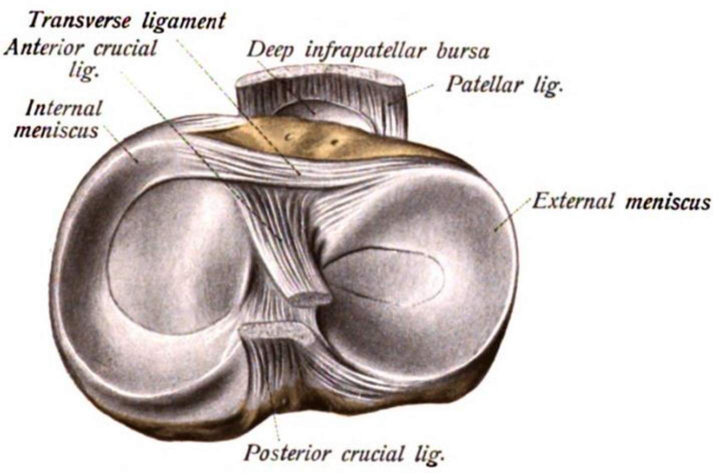


Figure 2. Menisci and origin of the crucial ligaments. "Sobotta 1909 fig.221 - menisci and origin of the crucial ligaments - English Labels" at AnatomyTOOL.org by Johannes Sobotta is in the Public Domain.

Other important anatomical structures of the knee joint are the anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), medial collateral ligament (MCL) and lateral collateral ligament (LCL). The articular surfaces are held in place by these strong ligaments. The LCL is attached to the lateral epicondyle of the femur proximally and to the fibular head distally. The LCL acts primarily against varus stress but also against the internal rotation of the tibia.[1]

The MCL consists of a superficial and a deep part. The superficial part of the MCL attaches to the femur posterior and proximal to the medial epicondyle and has two attachment points on the tibia, with a mean distance of 49.2 mm between them. It has an elongated attachment directly to the bone (mean 61.2 mm from the joint line). The proximal tibial attachment (mean 12.2 mm from the joint line) is partially to surrounding soft tissue and partially to the meniscotibial part of the deep MCL.

The deep MCL is considered a part of the joint capsule. The MCL's deep part is small and consists of two portions. A short, meniscotibial part attaches slightly distal to the joint line on the tibia (average 3.2 mm), and a meniscofemoral part, which is longer and attaches somewhat distally to the superficial MCL's attachment to the femur (mean 15.7 mm from the joint line on the femur).

The long superficial part of the MCL plays a crucial role in TKA as it is the primary restriction against the valgus in the knee at 15-90° flexion. It is also the primary limitation against the outward rotation of the tibia. MCL deficiency in a TKA patient can increase the risk of prosthesis failure.
The weaker and smaller deep part of the MCL primarily stabilizes the medial meniscus to the femur and tibia and contributes to valgus stability.
Together with the ACL, the MCL complex is essential in preventing the tibia from moving forward in relation to the femur. The posteromedial capsule is an important secondary restraint in limiting outward rotation and valgus instability when the knee is fully extended.

The ACL consists of two separate bundles of fibers that attach on the tibia anterolaterally to the anterior tibial spine; the fibers wind on themselves and run obliquely to attach to an area on the medial aspect of the lateral femoral condyle in the intercondylar notch (Figure 3). The ACL is essential for preventing the anterior translation of the tibia. Most TKA designs, however, require the removal of the ACL.

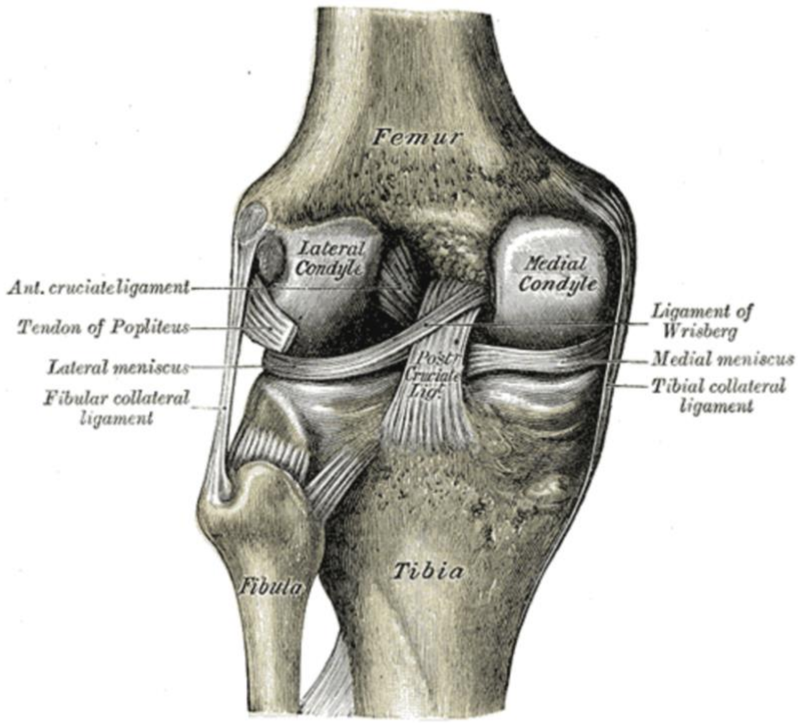


Figure 3. Left knee joint from behind, showing interior ligaments, by Bartleby.com edition of Gray's Anatomy of the Human Body, licensed under CC BY 2.0.

Posterior Cruciate Ligament

The PCL is a vertically oriented ligament that is stronger and twice as thick as the typical ACL (Figures 1 and 3). The PCL originates on the posterolateral aspect of the medial femoral condyle within the intercondylar notch.[4] The tibial attachment of the knee ligament is located at the back of the plateau, approximately 1 cm below the joint line. The average length and width of the PCL are 38 mm and 13 mm, respectively, while the ACL measures 38 mm in length and 11 mm in width. Therefore, the PCL is generally regarded as the strongest ligament in the knee. The PCL consists of two bundles, the anterolateral bundle, which comprises about 65% of the PCL, and the posteromedial bundle, which comprises 35%. The anterior bundle is tight in flexion and lax in extension. The posterior bundle is tight in extension and lax in flexion. A gradually changing pattern of fiber tension goes from anterior to posterior as the knee is extended.

An accessory meniscofemoral ligament is present in 70% of knees. The anterior meniscofemoral ligament, also known as the "ligament of Humphrey," is located in front of the PCL. It originates from the back of the lateral meniscus and attaches to the PCL. The posterior meniscofemoral ligament, also known as the "ligament of Wrisberg," starts from the back of the lateral meniscus and is closely connected to the PCL.[4] The PCL and medial meniscus are not connected. The PCL is important for keeping the knee stable and preventing the tibia from moving too far backwards. Studies on cadavers have shown that the PCL is responsible for about 95% of the force that keeps the tibia from moving too far back, both when the knee is bent at a 90-degree angle and at a 30-degree angle. The PCL is an essential secondary stabilizer to varus-valgus stress during knee extension and may retain this important role following TKA.

The PCL is a crucial structure that behaves differently depending on whether the knee is in varus or valgus. In varus knees, the PCL is contracted, while in valgus knees, it is stretched. Tightness in the PCL can lead to increased backwards sliding of the femur during flexion, known as rollback. To prevent this, surgeons have three options for managing the PCL during TKA. One option is to retain the ligament, preserving the knee's anatomy and function. This approach can enhance stability, improve knee flexion, and increase the mechanical advantage of the quadriceps muscle. Additionally, preserving the ligament can help prevent unpredictable loading patterns that could impact the cemented implant and cement bone interfaces.[5] Some authors also believe that the ligament retains its proprioceptive properties and should therefore be preserved during knee replacement, although this has yet to be confirmed biomechanically.[5]

The second option is to excise the ligament to facilitate the correction of any fixed deformities. This allows more accurate and reliable soft tissue balancing, resulting in improved fixation of the components. Studies show that PCL is degenerative in most arthritic knees.[6] The PCL's function can be replaced with a prosthesis design that restricts the posterior translation of the tibia.

The third option is to release the PCL and still use a knee prosthesis design that does not substitute for the ligament. Some authors believe that this offers a compromise between preservation and excision.[7] In addition, releasing a tight ligament may reduce excessive forces on the patellofemoral joint and thereby reduce postoperative pain and improve knee flexion.

Osteoarthritis of the knee

Osteoarthritis (OA) of the knee is a common joint disease, and its prevalence rises with age. About 10% of adults older than 60 years suffer from symptomatic OA.[8] OA affects approximately 4% of the world's population, and the knee is the most frequently affected joint.[9] OA of the knee is a slowly progressive, degenerative process in one or more of the three compartments of the knee joint. Pain after loading, joint stiffness and reduced function are the main symptoms of OA. Other symptoms can include a limited range of motion, joint instability, swelling, a grinding sensation (crepitus), muscle weakness, and psychological distress related to pain. Many patients have reported that taking breaks and resting can help relieve knee pain.

OA affects the entire joint, including the hyaline cartilage, subchondral bone, ligaments, capsule, synovial membrane, and periarticular muscles.[10] Additionally, it is

important to note that OA is an active condition caused by an imbalance between joint tissue repair and destruction rather than a passive degenerative disease.[11]
In the past, knee OA was described as a "wear and tear" condition in which the articular cartilage broke down and osteophytes were formed. The breakdown and loss of cartilage were thought to be the source of knee pain. However, a few facts have challenged that perspective. First, hyaline cartilage is avascular and aneural,[12] so the cartilage itself is not a pain generator.[13] Second, studies that link the amount of joint degeneration seen on X-rays to patients' pain levels offer inconsistent results.[14] Some patients demonstrate severe degenerative changes and little to no pain, while others have less degeneration and severe pain. There is no clear linear association between the amount of degeneration and pain level.[15] In recent decades, inflammation, not just degenerative changes, has been recognized more and more as an origin of pain in knee OA, and increased attention has been given to considering OA as a condition that affects the whole joint.[16] The cartilage gradually erodes, because the collagen matrix in the cartilage becomes less organized due to the uncontrolled production of matrix-degrading enzymes. As a result, the cartilage becomes depleted with proteoglycans and increasingly filled with water, which makes it less capable of absorbing forces. At the same time, chondrocytes proliferate and hypertrophy, which increases the metabolic activity of the chondrocytes and accelerates degenerative changes. Just beneath the cartilage, calcification, hardening, and cysts form in the subchondral bone. Furthermore, at the edges of the joint, abnormal bone growth creates osteophytes or bone spurs.

In OA, the synovium acquires more inflammatory markers and cells. In addition, fragments of bone or cartilage may become embedded in the synovium, which can exacerbate the synovium's inflammation and lead to synovitis. Over time, thickening and possible fibrosis of the synovium can occur. Finally, these structural and chemical changes may also affect the nerves that innervate the joint and become more easily sensitized. The current understanding is that a combination of peripheral and central neural mechanisms drives OA pain.

Kellgren and Lawrence classification

Knee OA is diagnosed based on the patient's history and clinical examination and confirmed by radiographs, which remain the gold standard. Anteroposterior, mediolateral, knee flexion (Rosenberg) and skyline views are recommended for diagnostic purposes. Typical X-ray findings include (Figure 4):

- Loss of cartilage
- Joint space narrowing
- Subchondral sclerosis; hardening of the bone beneath the joint surface
- Osteophyte formation; small bony growths around the edges of the joint
- Bony cyst formation
- Bony erosion

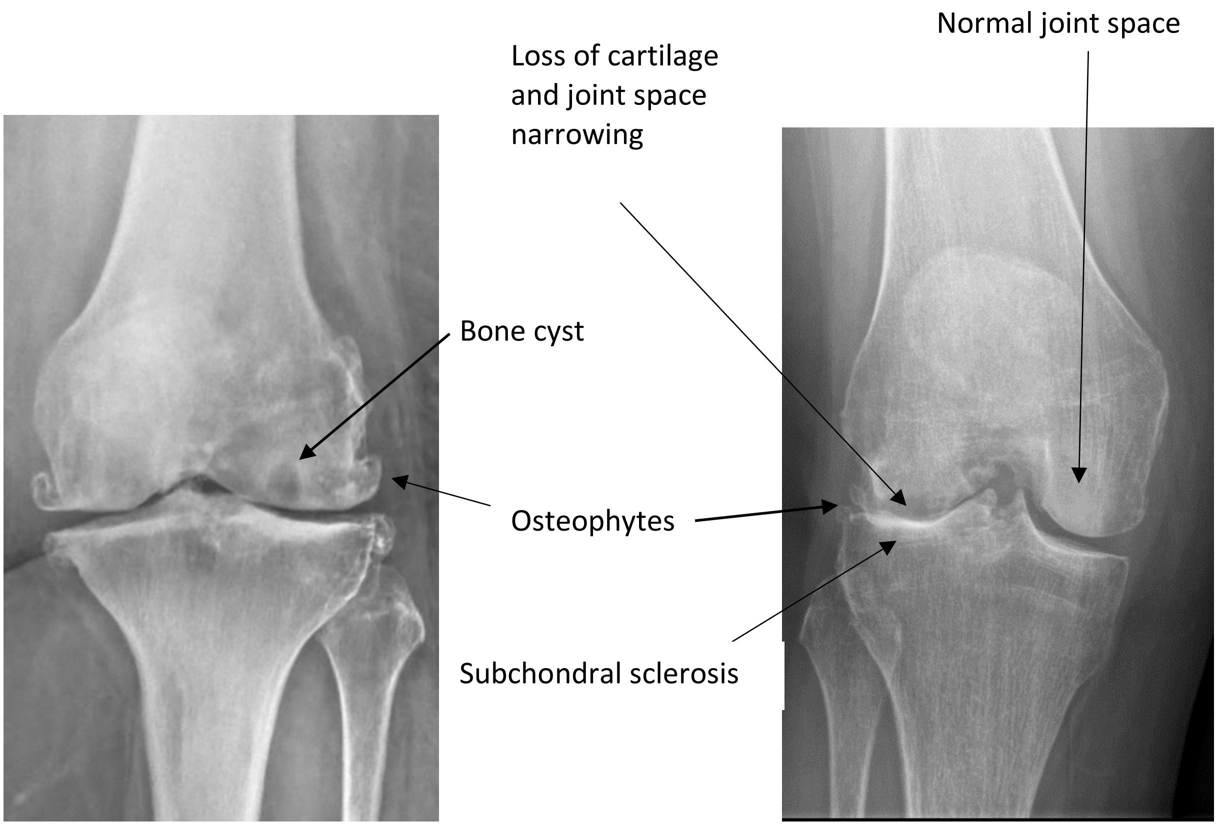


Figure 4. Radiographs showing changes related to osteoarthritis.

The subchondral bone reaction and especially osteophytosis, usually appears earlier than joint space narrowing. However, joint space narrowing is more significant and sensitive to change. There is a poor correlation between clinical symptoms and radiographical changes.

Radiographs are frequently used to determine the severity of knee OA. The most recognized method is the five-grade radiological classification system for OA published by Kellgren and Lawrence (KL) in 1957.[17] Today, this system is still the most widely used radiological system for the classification of OA. The diagnosis of knee osteoarthritis is most often made in grades 2-4.[17] The joint changes are graded from 0-4 as follows:

- Grade 0: no OA with a definite absence of x-ray changes due to OA.
- Grade 1: doubtful OA with doubtful joint space narrowing and possible osteophytic lipping.
- Grade 2: minimal OA with definite osteophytes and possible joint space narrowing.
- Grade 3: moderate OA with moderate multiple osteophytes, definite narrowing of joint space and some sclerosis and possible deformity of bone ends.
- Grade 4: severe OA with large osteophytes, marked narrowing of joint space, severe sclerosis, and definite deformity of bone ends.

Despite the widespread use of the KL classification, it has been criticized for the fact that grade 3 contains all degrees of joint space narrowing regardless of the extent and does not consider the Rosenberg view. Several different modifications have been suggested in the literature.[18] The Ahlbäck grading system is another well-suited system for grading knee OA.[19]

Total knee arthroplasty

Treating knee OA with TKA is an established and reliable method. Dr Themistocles Gluck, a German physician and surgeon, performed one of the first known knee replacements in the 1890s. He invented endoprostheses from ivory, and in 1890 in Berlin, a tuberculous knee joint of a 17-year-old woman was replaced by a hinged ivory prosthesis. These early implants had high failure rates due to fixation problems, infections and material defects.[20] However, this was a success due to the lack of other treatment options. The modern TKA, "total condylar knee", was presented by Insall et al. in 1972.[21] This was a semi-constrained prosthesis with the femoral component made of metal and the tibial component of polyethylene. Since then, there have been many changes. There are variations in both production methods and the materials used. In addition, various attempts have been made to design implants that are more anatomical in shape and maintain normal kinematics after TKA to improve the patient's clinical outcomes.

TKA designs aim to provide stability, normal kinematics and longevity. The modern TKA implant (Figure 5) is a total condylar knee with a stemmed tibial component, and there are many different manufacturers and over 100 brands of implants. There are also differences in the geometry, metal, under-surface texture, implant coatings, and the keel or stem can have different shapes. TKA implants are usually made of 3 or 4 parts, called prosthesis components, made of metal (titanium or cobalt-chrome) and polyethylene. The femoral component, made of metal, curves around the distal end of the femur. The tibial component consists of either a metal platform with a plastic component fixed on the top or a plastic component alone. The tibial metal platform usually has a keel or stem to enhance fixation. A patellar component is also available. Patellar components are mostly made of polyethylene material alone (Figure 9).

Figure 5. Legion total knee prosthesis, front and side views. With approval from Johan Dahlstrøm, Smith & Nephew

Total knee arthroplasty designs

Primary TKA designs can be subdivided according to modularity, fixation, bearing or constraint. Most orthopaedic surgeons in Norway use modular implants with polyethylene inserts and metal alloy femoral and tibial components.[22] The insert is attached to the tibial component through a locking mechanism. Thus, the articulation is between the femoral component and the polyethylene insert.

There are generally three types of fixations in use today. Most commonly, all the prosthetic components are fixated with the use of polymethyl methacrylate cement. In uncemented TKA, the fixation relies on the primary mechanical stability of the components and secondary bony ingrowth to the undersurface of the prosthesis. In hybrid fixation, usually, the tibial component is cemented, and the femoral component is uncemented. The surface of the uncemented components facing bone is supposed to stimulate bony ingrowth, which can be achieved by making the under-surface rough by blasting or coating with a highly porous material or a bio-active substrate.

The most used metals in knee prostheses are titanium in the tibial tray and cobalt-chrome in the femoral component. The Norwegian joint registry found that the lowest cumulative revision rate for cruciate retaining (CR) implants is achieved through a hybrid fixation with cemented tibial and uncemented femoral components. The second-lowest revision rate is achieved through cemented fixation of both components. The lowest cumulative revision rate for PS implants is achieved through cemented fixation.[22]

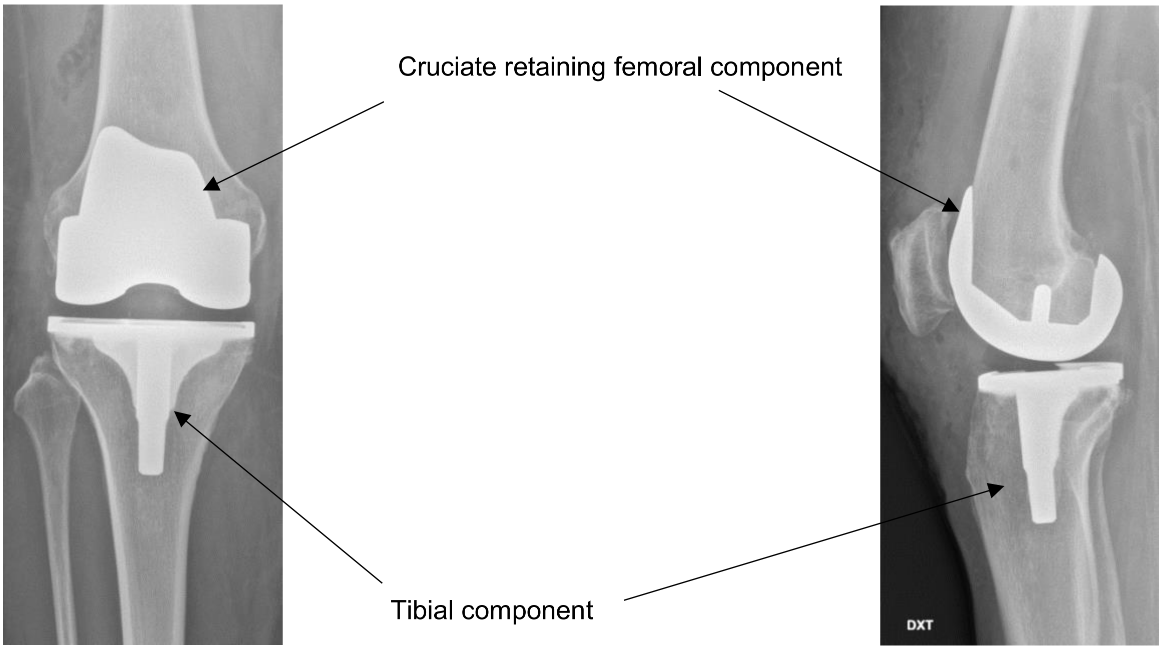
Fixed-bearing and mobile-bearing are two types of bearing designs for TKA, the former is most common in contemporary TKA designs. In fixed bearings, the polyethylene insert is firmly attached to the metal tibial component and the femoral component rolls on this cushioned surface. With a mobile-bearing TKA, the polyethylene insert will move with the femur throughout the flexion and extension and thus moves on the top surface of the tibial tray. Potential advantages are improved patella tracking, reduced wear, and minimalization of cutting forces. Mobile bearings are known for a higher revision rate due to soft tissue entrapment, dislocation and loosening.[23]

TKA models also differ in terms of the types of constraints of the arthroplasty. The constraint is defined as the prosthesis's ability to provide varus-valgus and flexion-extension stability in the face of ligamentous laxity or bone loss. Fully constrained or hinged implants are the most rigid, while cruciate-retaining implants are the least constrained.

Regarding constraint, there are several different TKA designs on the market, but those currently being used the most are cruciate-retaining (CR), which preserves the PCL, posterior-stabilized (PS), and anterior-stabilized (AS), the latter two being PCL-sacrificing designs. There is still an ongoing debate regarding the retention or sacrifice of the PCL, and, if removed, how it should be replaced.

CR TKA is a minimally constrained design that depends on an intact PCL to provide stability in flexion. CR design (Figures 6 and 7) is the design used the most in Europe and Australia. Proponents of PCL retention claim that a CR TKA maintains femoral rollback, prevents flexion-extension gap mismatch and improves knee flexion as well as extensor efficiency.[24-26] Further advantages with the CR design are that it avoids tibial post-cam impingement/dislocation and wear that may occur in PS knees,[27,28] and less bone in the distal femur needs to be cut than in a PS knee. Disadvantage is that an insufficient or ruptured PCL may lead to secondary flexion instability and subluxation.[29]

Figure 6. Legion cruciate retaining prosthesis; femur and tibial component with cruciate-retaining insert. With approval from Johan Dahlstrøm, Smith & Nephew



Anteroposterior x-ray | Mediolateral x-ray

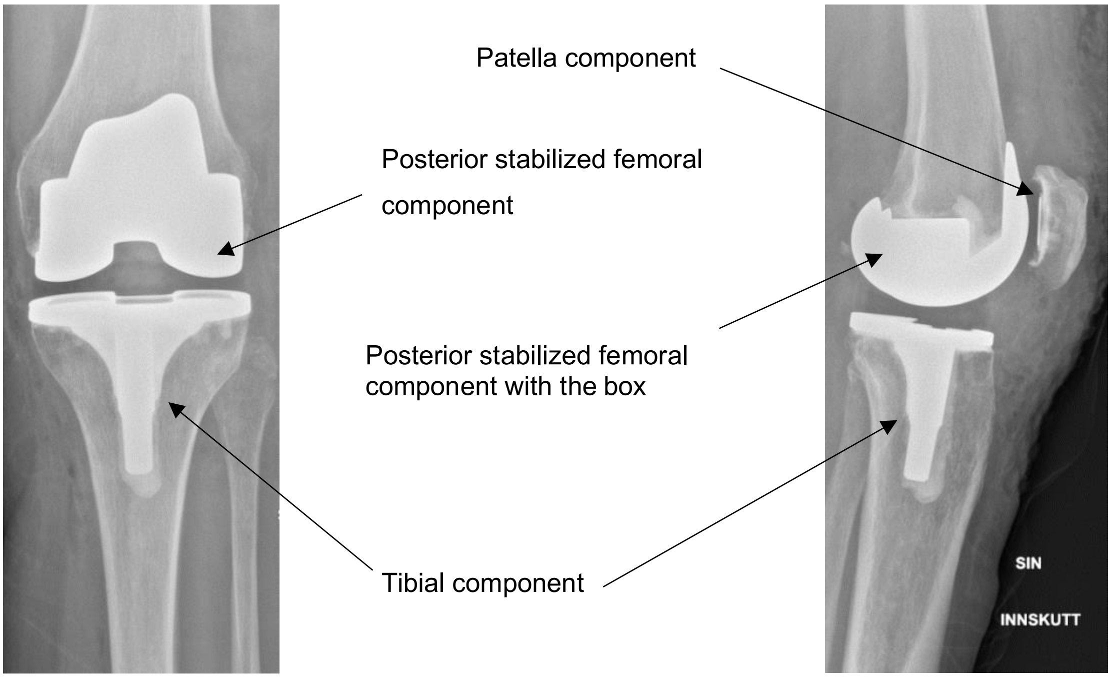
Figure 7. Radiographs of a cruciate retaining total knee prosthesis

PS TKA is a slightly more constrained prosthesis that requires a sacrifice of the PCL. The femoral component contains a cam that engages the tibial polyethylene post during flexion and forces the femur backwards, resembling the native knee femoral rollback.[30] The cam and post mechanism does not provide valgus or varus constraints. Resection of the PCL increases the flexion gap in relation to the extension gap; however, the gaps should be equal to avoid flexion-extension mismatch.[26] Proponents of PCL sacrifice claim that release of the PCL allows for improved correction in knees with severe deformities, improves the range of motion, and avoids the instability that may occur because of postoperative PCL failure.[29] Furthermore, the PCL is histologically abnormal in arthritic knees;[31] therefore, some surgeons pre-emptively choose to sacrifice the PCL and use a PS design. PS implants are the most common primary TKA in the USA.

On a mediolateral radiograph, a PS implant will show the outline of the box in the femoral component (Figures 8 and 9).

Figure 8. Legion posterior stabilized prosthesis; femoral component, tibial component, and posterior-stabilized insert with the post. With approval from Johan Dahlstrøm, Smith & Nephew

According to research, there are benefits and drawbacks to a PS TKA procedure. On one hand, it may be easier to intraoperatively balance a knee prosthesis without an intact PCL. Further, it may increase the range of motion (ROM) and provide better surgical access.[5,32,33] Potential complications with a PS TKA to be aware of are cam jump, tibial post polyethylene wear, post-breakage, and patellar "clunk" syndrome.[27,28] These issues can occur if the cam rotates over the post and dislocates the joint, if scar tissue gets caught in the box as the knee extends, or if there is a loose flexion gap or hyperextension.



Anteroposterior x-ray

Mediolateral x-ray

Figure 9. Radiographs of a posterior stabilized total knee prosthesis with patella component

When performing primary TKA, PCL substitution has traditionally used a cam-post restraint mechanism. While this method has been successful, it has also been associated with certain complications as outlined above. Clinical evidence suggests that the PCL also can be replaced with either an ultra-congruent or an anterior stabilized (AS) tibial insert.[34] The function of the PCL can be replaced by a PS- or an AS TKA. The AS implant differs from the standard CR implant in that it has an increased anterior lip, deeper trough, and more conforming articular surface, providing greater anteroposterior stability (Figure 10).

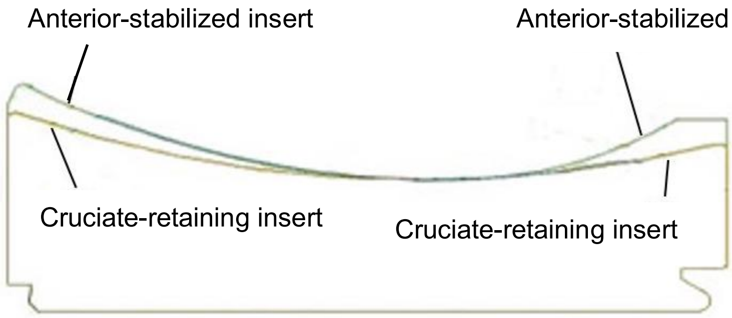


Figure 10. Schematic drawings of anterior-stabilized and cruciate-retaining inserts

The AS design has been reported to have several advantages, such as making it easy to replace a missing or non-functional PCL, preserving femoral bone, and avoid cam-post impingement.[34] Critics have, however, highlighted that the AS design may not fully replicate the natural kinematics and stability of the knee.[30]
Some clinical studies have reported no difference in functional or radiographic outcomes between AS and PS inserts after TKA.[35,36] On the other hand, some studies have concluded that AS designs lead to notably less femoral rollback and less anteroposterior stability compared to PS inserts.

Dynamic Radio Stereometric Analysis (RSA)

A knee joint's movement is complex. The knee joint involves the rolling and gliding motion of the femoral condyles and the rotation of the tibia.[37] Much effort has been put into developing knee implants that can replicate the natural movement of a healthy knee joint. While several implant designs have been developed to address different variables, most are based on theoretical considerations regarding knee kinematics. Therefore, more research is needed to understand better the actual kinematics involved.

Radiostereometric analysis (RSA), a static evaluation, is an accurate technique for measuring the 3D positioning of an object in space using X-rays.[38] As an example, RSA has been used to evaluate in vivo translation and rotation of implants relative to the bone in three dimensions. The method has a high degree of precision and accuracy and is a valuable tool in clinical research. Studies have indicated that implants that exceed a certain migration threshold within the first 1-2 years are more likely to experience aseptic loosening at a later stage.[39]

Dynamic RSA is an improved version of RSA that utilizes uniplanar fluoroscopy recording (15 frames/s) to accurately measure the 3D movements of knee prosthesis components in real time during physical activity.[40] Thus, dynamic RSA makes it possible to accurately assess the replaced knee's kinematics during active motions.

A disadvantage of conventional RSA is that one must attach markers (tantalum beads) to the implants. This drawback is resolved with model-based RSA. Model-based RSA is a method whereby a 3D model of the implant is used for matching with the actual images and the assessment of the position and movements of the implant relative to the surrounding bone.

Figure 11. Adora flat-panel fluoroscopy setup

Figure 12. Stairs used at the fluoroscopy lab

Figure 13. A patient performing a step-up movement while being monitored by fluoroscopy

Patient-Related Outcome Measures (PROMs)

In the past, the success of a TKA was mainly measured by implant survival, complications and other objective observations, which are essential from a surgical point of view. Nonetheless, patients and surgeons may have varying views on whether the TKA was successful. Therefore, to assess patient satisfaction and health status, PROMs play an important role. PROMs can be either generic or tailored to a specific condition, with more in-depth questions for a comprehensive analysis of patient outcomes. Over time, there has been a shift in focus from a disease-center approach to a patient-centered one, with PROMs becoming increasingly popular. Patients' subjective outcome measures, such as their own experiences of symptoms, function, and quality of life after TKA, are considered more important than objective measures. PROMs involve patients completing questionnaires designed to capture their self-evaluations, providing valuable "real world" data on how TKA impacts their daily lives. By comparing PROMs before and after surgery, we can assess the patient's health gain or loss (i.e., improvement or deterioration).

PROMs are valuable for evaluating the effectiveness of TKA from the patient's perspective. Since patients are the only ones who can report their own experiences, PROMs offer unique insights into the treatment's effects. Several outcome measures are formally validated and take a short time to complete. Various outcome scores are available for knee disorders, including the Knee injury and Osteoarthritis Outcome score (KOOS), Oxford Knee Score (OKS), and EuroQol instruments (i.e. EQ5D-5L).

Knowledge gaps

When treating patients with a functional PCL, surgeons tend to choose a particular design based on their personal preference and level of training rather than scientific evidence supporting the clinical outcomes of each design. The AS design has displayed promising results as a substitute for PCL over the last two decades.[35,41] However, there are limited published reports on this design compared to the CR or PS designs.

A few studies have compared PROMS or objective measures of knee function for CR, AS, and PS designs.[42,43] However, these studies had small sample sizes, varying outcome measures, poor randomization, retrospective designs, or compared designs from different prosthesis brands. Likewise, previous in vivo studies have analysed kinematics in different TKA implant designs.[44-46] However, none have investigated the same manufacturer's CR, PS, and AS designs in a prospective randomized clinical trial.

Several studies suggest that less severe OA is linked to worse long-term outcomes for pain and function following a TKA.[47,48] These studies typically used a cross-sectional or retrospective design, and the radiographic classification was usually performed by only one rater or did not report the number of raters. Additionally, most studies do not report intra-rater reliability.

To address these knowledge gaps, there is a need for prospective randomized controlled trials (RCTs) that use modern and rigorous methods, employing the same primary TKA system in their designs.

Aims of the thesis

This thesis aimed to increase knowledge on the treatment of knee OA and identify the best implant design option for patients needing a knee replacement.
The specific aims of the three studies were:

Study I
To document the preoperative radiographic severity of knee OA in patients undergoing TKA and evaluate the association between the degree of preoperative radiographic OA and improvement in patient health states one year after TKA.

Study II
To compare the kinematics of a cruciate-retaining, an anterior-stabilized and a posterior-stabilized knee prosthesis during a step-up motion using dynamic radiostereometric analysis.

Study III
To compare clinical and functional results two years after TKA between patients with a cruciate-retaining, an anterior-stabilized and a posterior-stabilized knee prosthesis design.

Materials and methods

Study design

All studies were single-center studies undertaken at Lovisenberg Diaconal Hospital. Study I was an observational study, part of a prospective cohort study. In this study, we explored how the severity of OA evident in preoperative radiographs relates to the changes in health state outcomes reported by patients after knee replacement.

Study II was a randomized study including a subset of the patients in study III. We used model-based dynamic RSA to compare the in vivo kinematics of CR, AS, and PS designs of the same primary TKA system during a step-up movement.
Study III was a prospectively randomized controlled trial (RCT) with equal allocation to three groups. As a template for our study design, we used the CONSORT 2010 statement guidelines. The patients and the physiotherapists responsible for the follow-ups were blinded as to the TKA design. Unfortunately, it was not possible to blind the surgeons. In this study, we compared the patient-reported and functional outcomes of CR, AS and PS TKA designs.

Patients

All patients recruited to the studies were referred from outpatient clinics and general practitioners. The patients received written information about the study prior to inclusion, and after signing the informed consent, the patients completed the baseline questionnaires.

In study I, we enrolled patients with OA who were 18 years or older and undergoing primary TKA. They needed to be able to read and comprehend Norwegian, complete questionnaires, and have knee radiographs taken within six months prior to the surgery. Mental and physical measures were also registered. Of 245 patients invited to participate in the study, 33 declined, and six cancelled their surgery. The study enrolled 206 consenting patients, but two were later excluded due to postoperative disorientation, and one patient passed away. Furthermore, 47 patients had some missing data, which resulted in their exclusion. One hundred fifty-six patients (77%)

had complete data. They were included in the analysis of the relationship between OA grade and clinical outcome. Patients were enrolled between October 2012 and September 2014.

In study III, 1011 patients eligible for the study were asked to participate. The inclusion criteria were: primary OA, varus or valgus deformity ≤15º, intact PCL, age 45-77 years, BMI < 35 kg/m^2 and ASA classification I or II. Exclusion criteria were prior knee ligament surgery, previous osteotomy, flexion < 90°, flexion contracture > 10°, place of residence > 2 hours' drive from the hospital, peripheral neuropathy, malignancy, rheumatic disease or inability to speak Norwegian. These criteria were chosen based on clinical experience and similar studies.[49,50] Enrollment of the patients was conducted from March 2017 to January 2020.

795 patients were excluded for not meeting the study criteria (Figure 14). A total of 216 patients were included in the study and assigned randomly into three groups, each comprising 72 patients. The study could have been more widely applicable if the criteria for selecting participants were less strict. However, this could have also reduced the internal validity of the study's results. The flow chart below summarises the patients who were included and excluded.

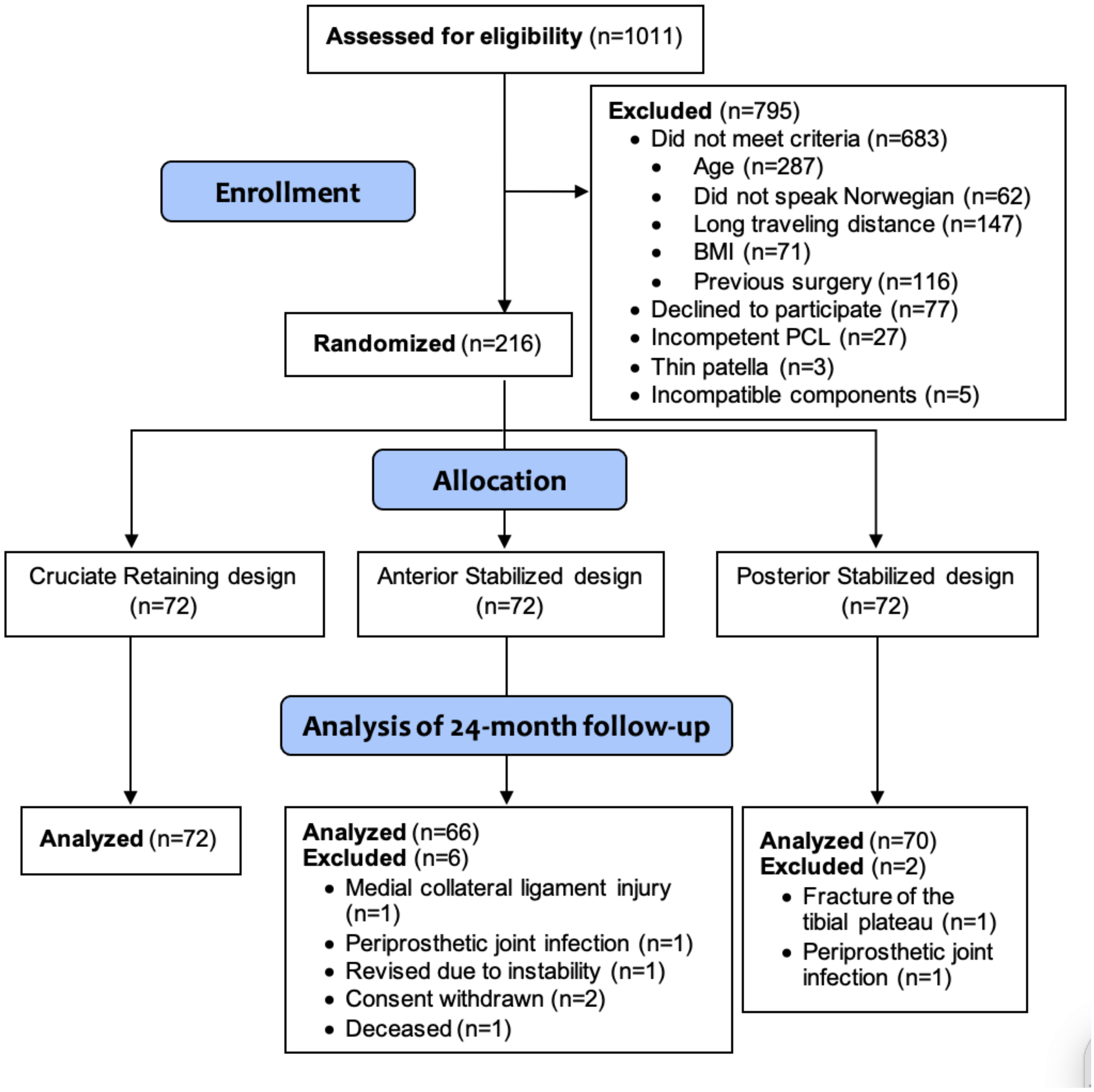


Figure 14. CONSORT flow diagram depicting participant flow throughout the clinical trial, from eligibility assessment through enrolment, intervention, and completion of follow-up.

The patients included in study II were a subgroup of those included in study III. There were 39 patients in this subgroup, with 13 having each implant design. All of them expressed satisfaction with their knees following the operation.

The selection process was rigorous, requiring patients to meet certain criteria, such as being free of knee pain post-operation, scoring above 80 on the KOOS subscales for Pain, Symptoms, ADL, and QOL, scoring above 60 on the KOOS Sport/Rec subscale, and demonstrating the ability to perform the necessary step-up movement for the fluoroscopic procedure 12 months after the surgery.

Surgical intervention

Surgical protocol for study I

This section pertains specifically to patients involved in study I. The surgical technique for these patients differs slightly from the methods used in studies II and III. All patients in study I underwent TKA using spinal anaesthesia and a standard technique. This involved making a medial parapatellar arthrotomy in the knee and starting with the femur, using a mechanical alignment technique. A 5° valgus cut angle was used to cut the distal femur with the aid of an intramedullary guide. The proximal tibia was cut while protecting the PCL using a Y-shaped retractor. All patients received the same implant type, a posterior cruciate-retaining fixed modular-bearing (Profix TKA, Smith & Nephew), without patella resurfacing. A tourniquet was used during surgery, and drains were placed and removed on the first day after surgery. Patients could bear full weight on their affected leg from the first day after surgery and received physiotherapy after the operation.

Surgical protocol for studies II and III

All patients were operated on under spinal anaesthesia. A standardized surgical technique was used, with medial parapatellar arthrotomy, femur first and mechanical alignment technique. An intramedullary guide was utilized to cut the distal femur at a 5° valgus cut angle. We carefully protected the PCL using a Y-shaped PCL-retractor and by impacting an osteotome vertically into the tibia anterior to the footprint to preserve a bony island around the PCL. After tibial plateau resection, the integrity of the PCL was evaluated visually and by palpation. The PCL was assessed again during knee ligament balancing, with trial components in place and deemed intact by a negative posterior drawer test and the tibiofemoral contact point at the middle of the tibial bearing. Then, the patient was randomly assigned to one of the three Legion TKA designs (CR, AS or PS) (Smith & Nephew, Inc, Memphis, TN, USA). The tibial baseplate was identical in all three designs, and the shape of the tibial insert was the only difference between the CR and AS designs. The PS insert was equipped with a post on the posterior intercondylar surface that engages against a cam in the PS box of the femoral component.

Randomization was computer-generated with a variable block size of three. A nurse opened the envelope with the patient’s group assignment when the PCL was deemed intact during surgery. After randomization, we resected the PCL in the AS and PS groups. The patella was resurfaced in all patients with a Genesis (Smith & Nephew, Inc, Memphis, TN, USA) inset biconvex patellar button. The femoral component was uncemented in the CR and AS groups. The patellar- and tibial components were cemented using Palacos R+G cement (Heraeus, Hanau, Germany). In the PS group, all components were cemented. We did not use wound drains or a tourniquet.

We intravenously administered first-generation Cephalosporin (2 g x 4) as antibiotic prophylaxis. Patients allergic to Penicillin got Clindamycin (600 mg x 3). All patients received intravenous Tranexamic acid (10 mg/kg) twice. A local infiltration analgesia mixture (Naropin, Ketorolac and Epinephrine) was injected during surgery.
Low molecular weight heparin (LMWH) was given for two weeks postoperatively as prophylaxis against thrombosis. Patients on regular Aspirin (Albyl-E 75 mg) continued taking aspirin and were not given LMWH. All patients were treated postoperatively using the same standardized analgesia and mobilization protocol. The patients were mobilized on the day of surgery and received physiotherapy from a therapist blinded to the prosthesis design.

Outcome measures

Knee injury and Osteoarthritis Outcome Score (KOOS)

The KOOS is a patient-completed questionnaire designed to assess the symptoms and function of individuals with knee injuries and OA in the short and long term. It takes around 15 minutes to complete. The KOOS asks about symptoms experienced in the past week and includes 42 questions that assess how knee problems affect daily activities. Each question is weighted equally and is scored between 0 and 4, with higher scores indicating better outcomes. The KOOS questionnaire has five subscales: pain, symptoms, daily activities, sports and recreation, and quality of life. Scores are converted to a scale of 0-100, with 0 indicating severe knee problems and 100 indicating no problems. The KOOS has been validated for TKA and is valid, reliable, and responsive.[51] It has been recommended that an improvement of at least 8-10 points is necessary to achieve a clinically meaningful difference. A Norwegian translation of the Swedish version of KOOS is approved as the official Norwegian version. The validation process for this translation is described at www.koos.nu. The KOOS was chosen as the primary outcome for study III.

EQ-5D and EQ VAS

The widely used EuroQol-5 (EQ-5D-3L and EQ-5D-5L) is a general health measure not specific to the knee joint.[52,53] It is simple to use, valid, responsive to change, and reliable for group comparisons.[54] The EQ-5D has five items that assess different dimensions of health status and one self-rated health item that assesses the respondent's perception of his/her overall health on a visual analogue scale. Each dimension in the EQ-5D-3L has three levels; in the EQ-5D-5L, each dimension has five levels. The scale ranges from 0 (worst imaginable health state) to 100 (best imaginable health state).

A health state index score can be calculated from the five dimensions using the European VAS-based value set.[55] The health state index score goes from -0.59 to 1, where lower scores indicate a reduced quality of life. The minimal clinically important difference for the health state index score is 0.074 (95% confidence interval -0.011 to 0.140).[56]
Study I used EQ-5D-3L as the primary outcome, while study III utilized EQ-5D-5L and EQ VAS as secondary outcomes.

Oxford Knee Score (OKS)

The OKS is a brief patient-completed questionnaire for patients undergoing TKA.[57] The OKS questionnaire is a short survey that patients undergoing TKA can fill out to evaluate their knee-related health status and the benefits of treatment. It takes 5-10 minutes to complete. It includes 12 questions covering pain severity, mobility, limping, stairs, standing after sitting, kneeling, giving way, sleep, personal hygiene, housework, shopping, and transport. Each question has five response options with scores ranging from 0-4, with 0 being the worst and 4 being the best. The total score

ranges from 0-48, with 48 being the most favorable outcome. The OKS questionnaire has been validated in Swedish,[58] and a Norwegian version has been translated from the Swedish version. The minimum clinically important difference (MCID) value for the OKS is between 3-5 points.[57]
The OKS was used as a secondary outcome in study III.

Dynamic Radio Stereometric Analysis (RSA)

Dynamic RSA is a highly accurate and precise method for measuring translations and rotations of TKA implants.[59] Patients perform active movements under fluoroscopic surveillance. We used an Adora DRFI flat-panel fluoroscopy system (15 frames/s) to assess the translation at least 12 months after TKA. The parameter of interest was the anterior-posterior displacement of the contact points, defined as the shortest distance between the tibial metal baseplate and the medial and lateral condyle of the femur. Before data acquisition, the patients received instructions and performed the task several times to gain comfort with the setup. Built-in laser guidance helped with correct patient positioning and ensured a standardized setup. The recordings are obtained in DICOM format, and each frame must be separated into high-quality bitmap (BMP) grayscale images. Model-based RSA software was used to analyze the data (RSAcore, Leiden, The Netherlands). We obtained three-dimensional (3D) computer-aided design (CAD) models of the Legion knee prosthesis (tibial and femoral component) from the manufacturer (Smith & Nephew, USA). The CAD models were superimposed on their respective projections in the two-dimensional (2D) fluoroscopy images.[60] 3D in vivo kinematics were extracted from the 2D images.[61]

Data were analyzed from above 90° of flexion to full extension. The contact point positions were estimated for the medial and lateral femoral condyles with respect to the tibial plateau based on the minimum joint space width from the fluoroscopy data.[62] Using these contact points, we estimated the internal and external femoral rotation during the step-up movement.
Dynamic RSA was used in study II as a primary outcome.

Kellgren and Lawrence (KL) classification

The KL system is a standard method for categorising the severity of OA using five grades (described on page 18). Before surgery, all patients underwent routine weight-bearing anterior-posterior (AP) knee radiographs. The radiographs were taken with a standardised knee protocol, and all the radiographs were taken at the same radiology lab. One experienced radiologist and one orthopaedic surgeon, blinded to the clinical data, independently evaluated the OA severity of each radiograph. KL classification was used based on the original description.[17] Two reviewers (one experienced radiologist and one orthopaedic surgeon) graded cases; if their grades differed, a third experienced reviewer made the final decision on the KL grade. The observers were not involved in patient treatment or follow-up. The reviewers re-examined the images at least one week after the initial reading, with their previous ratings hidden. The second reading scores were compared and combined for further statistical analysis. The inter-observer and intra-observer reliability were calculated between the two reviewers and two readings from reviewer one.
In all three studies, KL was utilized to determine the severity of OA. In Study I, we analyzed the association between KL grade and the enhancement of health state scores.

Range of motion assessment

Two blinded physiotherapists performed a ROM assessment preoperatively, at 6 weeks, 3 months and annually for 2 years postoperatively. The ROM was measured using a long-arm goniometer. The patient was supine with a pad under their ankle to measure the passive extension. Next, the patient sat on the treatment bench for active and passive flexion and active extension. Legwear was removed before measuring the ROM. Landmarks such as the greater trochanter, lateral epicondyle, and lateral malleolus were used to measure the angle to the nearest degree. Although we did not calculate inter-observer reliability between the two physiotherapists, it is essential to note that the physiotherapists did examine several patients together and agreed on the method before starting the study. Furthermore, several studies have shown the accuracy of this method.[63] Patients who could not

achieve a flexion greater than 90° within six weeks after TKA were scheduled for manipulation under anaesthesia.
ROM was used as a predictor for outcome in study II and as a secondary outcome in study III.

Radiographs

Radiographs were obtained no more than three months before surgery and then two days, three months, one year, and two years after surgery.
The anteroposterior radiographs taken preoperatively were used for the KL assessment.

Other recorded parameters

During each interaction with the patient, any issues such as infection, lung embolism, deep venous thrombosis, fractures, and other complaints were consistently documented.
As part of the follow-up process, patients were asked to rate their satisfaction with their TKA on a scale of 1 to 5, with one being very dissatisfied and five being very satisfied. During the two-year follow-up visit, patients were asked whether they would be willing to undergo the same operation again, with a yes or no response. This data was used as a secondary outcome in study III.

Statistics

Study I

We used SPSS for Windows, version 24.0 (IBM Corp Armonk, NY, USA) for all analyses in study I. The sample size was not calculated for this study. We used descriptive statistics to describe patient characteristics and OA severity. Continuous data were provided as means with standard deviations, and categorical data as numbers and percentages. Change in patient-reported outcomes from before surgery to 1 year postoperatively was assessed using paired-sample t-tests. Intra-rater and inter-rater reliability were determined using kappa statistics for categorical data.[64]

Crude associations between KL grade and change in patient-reported outcomes were assessed using Pearson correlation coefficients, and adjusted associations were evaluated using multivariable regression analysis, controlling for relevant covariates, including patient age, sex, number of comorbidities, body mass index, prior ipsilateral knee surgery, prior hip or contralateral knee arthroplasty, and preoperative rating of the patient's worst level of pain experienced in the past 24 hours. The variables were obtained through a review of medical records. *P* values <.05 were considered statistically significant.

Study II

We used SPSS for Windows, version 28.0 (IBM Corp. Armonk, NY, USA) for all study II analyses. The sample size was calculated based on a phantom study from our clinic showing a standard deviation (SD) of 0.37 mm for zero motion in the antero-posterior plane. A mean group difference of 1 mm translation or more was determined to be clinically significant. With statistical power of 80% and a significance level of 0.05, the required total sample size was estimated to be 27 patients. Allowing for dropouts, we included 13 patients in each of the three groups, for a total of 39.

We used descriptive statistics to summarize sample characteristics. Normality was assessed with the Kolmogorov-Smirnov test. In addition, Mann-Whitney U, Kruskal-Wallis, independent-sample *t*-tests, ANOVA and Pearson's chi-squared test were used as appropriate to compare groups. All analyses were two-sided and statistical significance was defined as $p < 0.05$.

Study III

For analyses in study III, we used SPSS for Windows, version 28.0 (IBM Corp. Armonk, NY, USA). The sample size was calculated based on the minimal important change (MIC) of 10 points and the standard deviation for the $KOOS_5$, which is an average score for the five KOOS subscale scores.[65,66] Therefore, with statistical power of 80% and a significance level of 0.05, the required total sample size to detect a difference in the $KOOS_5$ of at least 10 points between the study groups was estimated to be 180. To account for dropouts, our target for enrolment was 216 patients (72 per group). A per-protocol analysis was performed, including only patients who completed the 2-year follow-up.

Descriptive statistics were provided as frequencies or means with standard deviations, and group comparisons were performed for the following outcomes: KOOS, OKS, EQ-5D-5L, EQ-VAS, ROM, satisfaction, KL grade and the question "willingness to undergo the same operation again". Data were checked for normality using the Kolmogorov Smirnov test. In addition, we used independent-sample t-tests, Mann-Whitney and Kruskal Wallis tests to assess group differences, and the Kruskal Wallis test was also used to assess skewed variables. P values <.05 were considered statistically significant.

RCTs have long been assumed to be the gold standard of clinical research. They are almost at the top of the evidence-based medicine pyramid, only surpassed by systematic reviews and meta-analyses.[67] In RCTs, patients with a given condition, for instance, knee OA, are recruited into the study and randomly divided into two or more interventional groups receiving different treatments. We usually compare a new treatment with a well-documented treatment. For example, we can compare a new implant design with an established implant. By randomizing, we minimize the effect of possible confounders and create groups that are as similar as possible, making the intervention the main difference between them.[68] It is possible to blind participants, care providers and those assessing outcomes to reduce bias.[69] This is often challenging within surgical specialties. Block randomization is also possible, for instance, to ensure an equal gender distribution and that surgeons operate on an equal number of patients in each group.

Block randomization of three in our study was performed with help from a statistician and a randomization software program. All patients were given a study number, which they kept throughout the trial and was used to determine their randomization assignment. In study III, randomization was done during surgery. The envelope was opened when the PCL was thoroughly examined and found to be intact and functional.

Results

Main results of study I

In study I, we investigated the association between the degree of preoperative radiographic OA and improvement in patient health state one year after TKA. One hundred fifty-six patients (77%) had sufficiently complete data and were included in the analysis. We did not find any significant differences in the preoperative characteristics (i.e., age, sex, and health state) between patients in the different KL groups. We found substantial intra-rater and inter-rater agreement of KL grades. The two reviewers disagreed on 10 cases (6%). In most cases, this difference was between KL grades 3 and 4 (9 cases). 98% of the patients had KL grade 3 (74%), and KL grade 4 (24%) changes.

Our main finding was that preoperative KL grade 3 and 4 was associated with greater improvement in the health state index score, as measured by the change in the score from before to 1 year after TKA ($r = 0.172$, $p = .033$). Conversely, patients with KL grade 2 had no clinically meaningful improvement in their health state index score.

Main results of study II

In study II, we investigated the kinematics of three different TKA designs during a step-up motion using dynamic RSA. All three patient groups had similar demographic characteristics and preoperative KOOS subscales, as well as KOOS subscales one year after TKA. All the included patients in this study were satisfied with their knees and had good knee function. The RSA analysis revealed no significant differences between the CR and AS groups in how the medial and lateral contact points translated during step-up. However, the PS group's medial and lateral contact points showed a different pattern than CR and AS. In both the CR and AS groups, the medial contact points moved posteriorly throughout the movement; hence a paradoxical translation compared with a healthy, unoperated knee. However, in the PS group, both the medial and lateral contact points moved anteriorly. All three groups showed similar contact point positions from 40° to full extension. However, the PS group's lateral contact points translated the most.

Main results of study III

In study III, we compared the clinical and functional results of three different TKA implant designs. We included two hundred sixteen patients, and two hundred eight completed the two-year follow-up. The groups had similar baseline characteristics except for BMI, which was significantly higher in the PS group. The mean operative time was significantly longer for the PS group compared to the CR- and AS groups. We found no statistical significance between the three groups for the primary endpoint at two years ($KOOS_5$), nor did we find any significant group differences on the secondary outcomes (individual KOOS subscales, OKS, EQ-5D-index, EQ-VAS and knee extension). However, the mean knee flexion angle was significantly better in the PS group compared to the CR and AS groups (129° vs 122°, $p<0.001$). Mean flexion in the CR and AS groups was the same ($p=0.5$). More than 90% of the patients were satisfied with their knees, and most were willing to go through the surgery again. We had a low complication rate in the study. A total of nine patients needed mobilization under anaesthesia, two patients suffered prosthetic joint infection, one in the AS group was re-operated for instability and one was treated for a lung embolism.

Discussion of main findings

TKA is an effective procedure that reduces pain, restores knee function, and enhances the quality of life in patients with advanced OA.[70] About 10% of adults older than 60 years suffer from symptomatic OA. According to the Norwegian arthroplasty register (NAR), over 20,000 patients per year receive surgery to insert or replace artificial joints due to joint disease. Between 2013 and 2021, there has been a significant rise in primary knee replacements in Norway, steadily increasing from 5,041 to 7,478 knees per year. During the COVID-19 pandemic, fewer prosthetic surgeries were conducted, resulting in an 8.7% decrease in primary knee replacements in 2020. However, in 2021, there were more knee replacements than ever, with 7,478 primary knee replacements performed, setting a new national record.[22] It is anticipated that as the population continues to age, the demand for TKA will persistently rise.[22] Even with a conservative estimate, the United States, which presently holds the highest rate of knee arthroplasty worldwide, is expected to experience a staggering 143% increase in TKAs by 2050.[71]

Although the success rate of TKA procedures has improved and their frequency is on the rise, it is crucial to acknowledge that a considerable number of patients still encounter significant pain and dissatisfaction after surgery. Several studies[72,73] and our empirical findings[74] indicate that approximately 20 % of TKA patients continue to experience moderate to severe pain during activity and report disappointment with their surgical outcome. Identifying a single or combination of factors contributing to poor clinical outcomes is essential to improving patient care and postoperative functionality. Patients developing chronic pain or being dissatisfied after TKA are characterized by a combination of physical and psychological health factors such as multiple painful sites,[75] a lower degree of OA on preoperative radiographs,[76] female gender, younger age,[77] previous knee surgery,[78] higher preoperative pain intensity[79] and catastrophic thinking.[75] Some factors are also related to the surgeon or the surgery, such as implant design,[34,80,81] knee kinematics,[82] use of navigation,[83] and the PCL's fate.[84] The literature on risk factors implies that to improve outcomes in TKA, the risk factors need to be addressed and/or optimized. Olsen et al.[76] found that higher BMI is linked to poorer physical function, and more severe OA is related to improved physical function 12 months after TKA. According to Olsen et al.,[76] it is advisable to consider these factors while developing predictive models to identify patients at risk of experiencing poor function after TKA.

In study I, we examined the impact of the preoperative degree of OA on patients' health states following TKA. Our main finding was that patients who had OA with KL grades of 3 or 4 on preoperative radiographs experienced a significant improvement in their health state. However, those with KL grade 4 improved significantly more than those with KL grade 3. In addition, patients with KL grade 2 changes did not experience any improvements in their health state.

Our study I findings are consistent with the current literature[85,86] that OA severity is recognized as an essential factor in modifying satisfaction in TKA patients. The severity of the preoperative radiographic joint damage is inversely related to the probability of a good outcome. This could have significant implications for surgical decision-making. Surgeons should be particularly cautious of operating on patients with modest X-ray changes.

We used the KL classification to describe the preoperative degree of OA. However, the literature is inconsistent about whether KL grade is the best tool to evaluate OA.[87,88] Our study's KL grading demonstrated substantial intra-rater and inter-rater agreement, suggesting that KL grading is a reliable tool for assessing the radiographic severity of OA. Study I has several strengths that make it a valuable contribution to the existing literature. The advantages are the prospective design, large sample size, and two experienced independent raters.

In study II, using dynamic RSA, we compared three prosthesis designs to map whether they had similar in vivo kinematics during a step-up movement from deep flexion to full extension. Our paper is the first to investigate the kinematics of three implant designs from the same manufacturer in a prospective randomized clinical trial. We found that CR and AS designs had similar contact kinematics, and their kinematics differed from the PS design. Further, we found that the contact kinematics of the PS design resembled a native knee.

TKA aims to ensure stability, durability, and natural movement of the knee while replicating its normal function.[89] There are several types of knee implant designs on the market. The kinematics of a CR design is assumed to be closer to the natural knee than PCL-substituting designs since the PCL is retained in the CR design. Several fluoroscopic studies have indicated that natural knee kinematics are challenging to reproduce after TKA.[90,91] All patients in our study were satisfied with their knees and had a good range of motion. However, our data showed that patients in the AS and CR groups had contact point kinematics different from a natural knee during step-up, while the PS group showed kinematics more like a native knee. Iwamoto et al.[92] also compared in vivo kinematics but did not find significant differences between a CR and an AS implant design. However, unlike our study, they investigated a step-down movement. Other studies have shown contact point translation patterns for the CR design comparable to our results.[93,94] The screw-home mechanism, found in native knees, was present in all three designs, compatible with other studies.[93,95]

The contact point translation pattern for the three designs mainly differed from deep flexion to 40°, but with further knee extension, the kinematics were essentially the same. During extension up to 40°, the knees with a CR or AS design displayed a paradoxical posterior translation of the femoral condyles, in contrast to the physiological anterior translation observed in the PS knees. The contact point translational pattern of the PS design results from the cam-and-post mechanism: the cam engages the post at around 40° of flexion.[96] The mechanism drives the femorotibial contact points posteriorly during further knee flexion, preventing anterior sliding of the contact points. Our results agree with other studies that imply that the cam-and-post mechanism engages between 40° and 100° of flexion.[97,98]

Although patients were satisfied with their knees and experienced no restrictions in their knee function, we found striking differences in the kinematics of the three TKA designs. Our results are, however, not generalizable to other TKA designs since other implant brands, even those of the same kind, can show different knee kinematics.[90] Study II provided valuable insight into the in vivo kinematics of different TKA designs during a step-up activity.

In study III, we compared the clinical results of three different knee prosthesis designs after two years. Of particular interest was to explore whether an AS insert was clinically as effective as a PS design in substituting for the PCL. The main finding was that although there were differences in the implant designs, the patients reported no differences across the groups of TKA design, and over 90% were pleased with their knees. The only difference was significantly better flexion in the PS group compared to the CR and AS groups. However, the clinical significance of this finding is limited. The findings in paper III are comparable with other RCTs comparing similar TKA designs.[5,35,99]

Several improvements have been made in TKA implant designs to improve patient outcomes. However, Carr et al.[89] noted in 2012 that the number of available implants had increased significantly but with little or no evidence of improved effectiveness. Hamilton et al.[100] compared an older TKA design with a newer TKA design and found significant differences in change in the OKS between the groups.

There is a debate about the role and management of the PCL as efforts are made to improve the procedure and clinical outcomes. As a result, we utilized three implant designs from the same manufacturer, all commonly used in current practice. The AS implant design is an invention for PCL substitution with good results in a few published reports compared with the literature on CR and PS designs.[5,35,101] A few studies have compared the CR, AS and PS designs.[42,43] The studies conducted had limitations such as small sample sizes, inconsistent outcome measures, inadequate randomization, retrospective design, or comparison of different brands of prostheses. The strength of study III is that it is a large and prospective study in which there were almost no losses to follow-up or missing data.

All three implant designs are possible choices for primary TKA in osteoarthritic knees, but specific indications, such as the quality of the PCL, may necessitate a certain type or design of the implant to be used.

Methodological considerations

Study design

This thesis is based on one prospective observational study (study I) and one RCT (studies II and III). A subset of patients from study III was included in study II.
Study I is an epidemiological study that did not include interventions or experiments and is part of a prospective longitudinal study where a sample of similar individuals (i.e., OA patients scheduled for TKA) was followed for 12 months. This study design is considered appropriate to answer the research question in study I.

Studies II and III were designed as a prospective RCT with equal allocation to three parallel groups. An RCT is the best study design for comparing treatment modalities (Level I evidence).[102] As a template for our study, we followed the Consolidated Standards of Reporting Trials (CONSORT) statement.[69] In RCTs, the random assignment is made to prevent bias due to non-comparability between groups caused by differences in other factors, such as age, gender, and BMI. Because the interventions are applied through random assignment, detecting causality is possible. The outcomes for the different intervention groups can be compared statistically, and conclusions can be drawn with a relatively high degree of certainty if the observed differences are statistically significant.[69] A blinded RCT is preferable to ensure the validity of the findings. Our study blinded the patients and the examining physiotherapists to the implant design throughout the follow-up period. It was not possible to blind the surgeons.
Based on these considerations, we concluded that an RCT would be the best tool to examine the causal relationship between the type of TKA design and clinical outcome. Our analyses in studies II and III were, therefore, RCT-based.

There are several potential biases in RCTs based on performance, selection, detection or attrition.[103] We took several measures to reduce potential biases. Most importantly, the study was blinded. Eleven orthopaedic surgeons, certified by the board and specializing in joint replacement surgeries, conducted the surgeries. Due to the nature of the surgical study, it was not feasible to blind the surgeons. In addition, the patients were randomized by block randomization with variable block sizes to prevent selection bias.

PROMS

PROMs directly report the patient's health status without needing interpretation by healthcare professionals or study staff. In recent years, the health authorities have encouraged using PROM in clinical studies and the National quality registers. The systematic collection of PROMs is essential for quality improvement, research, and innovation.

PROMs provide the opportunity to capture vital patient aspects, such as quality of life, level of functioning, coping and symptom mapping. PROMs can be divided into two groups: generic and disease-specific. There are good reasons to use both generic and disease-specific PROMs. Generic PROMs are designed to provide information about the patient's general health and can be used by all patient groups. In contrast, disease-specific PROMs are designed to be relevant to a narrow patient group and illuminate problems this group experiences.

There is no PROM without weaknesses; a PROM that works well in one patient population can perform poorly in another. Therefore, it is essential to choose PROMs wisely to avoid both the "ceiling effect" (one can no longer measure improvement since the patient already has the best possible score) and the "floor effect" (one can no longer measure decline since the patient already has the worst possible score). Less than 15% of patients in a population should have the best or worst PROM score. For this thesis, we chose PROMs used in earlier studies to facilitate comparisons between our findings and those of other studies. Further, we chose validated PROMs, such as the KOOS, EQ-5D-5L and OKS, to strengthen our study’s methodological rigor. Validated PROMs are designed to provide robust and meaningful measurements. Even though there are ceiling- and floor effects in most PROMs, the KOOS is among the best PROMs to evaluate outcomes in OA patients.[104]

A statistically significant difference in a PROM does not necessarily indicate that the difference is clinically relevant. The minimal clinically important change (MIC) is defined as the smallest change score required for the effect to be clinically meaningful.[105] The MIC in PROMs helps interpret the results. However, studies show that no MIC exists for all conditions for a PROM.[106] An instrument's MIC can be affected by factors like the patient group, intervention, and follow-up time. Due to this, there may be different ranges of MICs for the same instrument. Ongoing research is working towards establishing various MICs for the KOOS in different contexts. However, until then, it is generally accepted that a MIC of 8-10 is appropriate for the KOOS.[66] Hence, we selected a MIC of 10 for our study.

Statistics

When planning an RCT, estimating the number of patients to include is crucial. This involves determining the clinically relevant difference between the groups that would be significant to detect, setting the desired probability of detecting this difference (test strength or "power", which is often set at 80% or 90%), and then calculating the required number of patients to be included based on these parameters. For study III, we utilized the standard deviation (SD) from a prior study conducted at our department. [83] We aimed to identify any disparity between the treatment groups, assuming the difference was 10 points or above. Consequently, we needed three groups, each consisting of 60 patients, to have an 80% chance of detecting such a difference. An insufficient number of patients is the most common cause of type II error.[102] We anticipated possible dropouts and therefore included a total of 216 patients.

It is important to note that thirty-nine patients from study III were included in study II. We conducted a power analysis to determine the required number of study patients to ensure accurate results. Our clinic's phantom study revealed that no motion in the antero-posterior plane had a standard deviation of 0.37 mm. A mean difference of 1 mm translation was deemed clinically significant. Based on these factors, we determined that each group would require nine patients, with an estimated standard deviation of 0.37, a 5% type 1 error rate, and 80% power. We included 13 patients per group to account for potential dropouts, consistent with other kinematic studies.

Radiological definition of knee OA

Radiographs are the mainstay of diagnosing and monitoring the progression of tibiofemoral OA. Several classifications are in use to grade radiological OA. All the classification systems are based on the grading of weight-bearing anteroposterior radiographs. Wright et al.[107] graded radiographic findings using six commonly used classification systems. They found that none of the radiographic classification systems had excellent inter-rater reliability but had moderate or good reliability for classifying tibiofemoral OA. KL classification is a widely accepted grading system for defining radiological OA and has been used the most as a research tool in studies of OA. Schiphof et al.[108] documented the existence of five different KL versions. Although the differences seem small, the impact of these variabilities remains unclear. For instance, the number of cases classified as having OA may differ between the versions. According to Schiphof et al.,[108] the different versions impact the classification of OA. However, all versions have strengths and weaknesses. The different ways of classifying knee OA emphasize, to varying degrees, osteophytes or reduced joint space,[17,109] which can affect the threshold value for knee OA. Those assessed as having knee OA in one study might have been excluded from another study because different markers are used to assess the severity of knee OA.

Whether a connection between increased pain and increasing severity of knee OA is discovered in studies depends on which method has been used to assess the severity of knee OA. This could explain why studies that examined the association between radiographic knee osteoarthritis and pain, symptoms and function found different results. Therefore, there is a need for more consensus regarding the descriptions and interpretations of the KL classification criteria.

All studies included preoperative weight-bearing anterior-posterior radiographs of the patients. The radiographs were evaluated based on the original description of the KL classification criteria.[17] The KL classification was initially described using anterior-posterior knee radiographs, and therefore, we used them in this thesis as well. However, Wright et al.[107] demonstrated that the Rosenberg view (45° posteroanterior flexion weight-bearing radiographs) had higher inter-rater reliability than anteroposterior radiographs. As a result, we will incorporate the Rosenberg view in our future research.

Preservation of the PCL

The PCL is a crucial and strong ligament in the knee. However, in primary TKA, there is still debate on whether to sacrifice or retain the PCL. Based on clinical evidence, sacrificing the PCL can lead to improved knee function if some PCL substitution is performed. The most commonly used primary TKA design in Norway is the PCL-retaining implant design (CR).[22] The design of CR TKA makes use of the natural PCL. Some surgeons believe in preserving the PCL whenever feasible and applying minimal constraint in the arthroplasty to achieve knee stability. However, according to the Norwegian Arthroplasty Register,[22] instability is the second most common reason for revision surgery. Instability can also be caused by a late rupture of the PCL.[110,111] A PCL injury significantly increases the flexion gap medially and laterally compared with the extension gap.[26] An assumption for CR TKA is an intact PCL. However, the PCL can be damaged entirely or partially during surgery if not adequately protected.[84,112] To retain the tibial attachment of the PCL as much as possible, both a Y-shaped retractor and an osteotome just anterior to the footprint of the insertion of the PCL should be used. Wood et al.[84] showed a risk reduction of 50% for PCL insufficiency in a cadaver study where the same measures to protect the PCL were employed as in study III. However, Wood et al. also showed that even though the PCL was protected with a bony island and a retractor, around 20% of the PCL attachment got damaged. Although protective measures are taken as outlined during the surgical procedure, determining the extent of damage to the PCL can still be a challenge. We consider it crucial to preserve the PCL during CR TKA and to date, no patients in the CR group have required revision due to anteroposterior instability.

External validity

The inclusion and exclusion criteria were strict and remained unchanged throughout the study III. The criteria were chosen to obtain as homogeneous a group as possible since we did not want the PCL to be compromised. Similar studies had the same criteria. The criteria can influence the findings' generalizability and need to be discussed. While studies typically exclude older patients, we had an upper age limit of 77 years for participation. The age of this sample ranged from 45-77 years. This wide range of age expanded the generalizability of our findings to older patients. In addition, the mean age of the total sample was close to that of patients undergoing primary TKA in Norway,[22] increasing our sample's generalizability. In our sample, around 60% were women. That is consistent with the gender distribution reported in the national arthroplasty register,[22] which suggests that the gender distribution of our sample is comparable to the population. Thus, we believe that our sample is representative of the typical TKA population in terms of age and gender. However, generalizations about non-Norwegian-speaking patients should be made with caution. Another aspect that may affect generalizability is that all patients in this study were enrolled at a single surgical clinic. There may be local differences between surgical clinics in Norway that pose a risk of bias, for example, socio-demographic differences between patients enrolled from specific geographical areas. High-volume clinics generally have better results than low-volume clinics regarding complications[113] and PROMS.[114] Including patients from only one area or a clinic with a low volume of TKAs may result in a biased sample. Geographic differences exist in Norway's socioeconomic status and health conditions.[115] To reduce the risk of bias, we allowed the inclusion of patients admitted from several regions of Norway to a high-volume surgical clinic which performs the largest number of TKA procedures in Norway. Therefore, we do not believe that bias due to inclusion from a single surgical clinic poses a significant risk of bias in this study. Loss to follow-up may distort the results and reduce generalizability. Only a few patients were lost to follow-up in study III.

Ethical considerations

TKA, the chosen trial intervention in all three studies in this thesis, is a safe and effective orthopaedic surgical intervention for treating knees with severe and symptomatic OA.[22] In addition, removing the intact and functioning PCL when using the AS and PS designs is an established procedure in knee replacement surgery.[50,116]

All the studies in this thesis adhered to the Helsinki declarations. Since study I was an observational study, it adhered to the STROBE checklist.[117] Papers II and III being RCT's and adhered to the CONSORT statement.[69] All three studies were preapproved by the Regional Ethical Committee of Western Norway with approval numbers as listed in table 1. All patients provided free and informed consent before inclusion in the studies and could withdraw at any time point without any consequences for the quality or level of treatment or follow-up. All patients were diagnosed and treated as part of regular clinical practice, in line with standardized quality measures, and at no additional costs. Personal information was de-identified, and participants were labelled with a number documented in a key table for referral and securely locked up at the study center. Only the principal investigator had access to this key table. All personal information and data were handled following appropriate guidelines and were stored anonymously. Each patient received a study ID. The randomization key and identity were stored separately.

Study	Institution	Type of approval	Reference no.	Clinical Trials
I	Regional Ethics Committee South East	Approval study I	2011/1755	Not registered
	Data protection officer	Approval study I		
II	Regional Ethics Committee South East	Approval study II	2016/1981	NCT03059927
III	Regional Ethics Committee South East	Approval study III Change study III	2016/1981	NCT03059927

Table 1. Different approvals

Competing interests

The authors of the three articles in this thesis did not exhibit any apparent competing interests, including financial ones.

The South-Eastern Norway Regional Health Authority provided financial support for 50% of the study's funding.

The surgeons who performed the operations did not declare any competing interests.

Conclusions

Knee OA is one of the most common reasons for disability, especially in older people. Non-operative treatment, including physical training, medication, and weight loss, is often sufficient, and no surgery is needed. If non-surgical treatment is unsuccessful, TKA can be considered. Study I showed a relationship between the severity of OA evident on preoperative radiographs and improvements in patients' health state index scores 12 months after primary TKA. Patients with severe radiographic OA experienced a more significant improvement in specific dimensions of the HRQoL questionnaire EQ-5D after surgery compared to those with mild or moderate OA. This discovery has important implications for selecting patients and determining the timing for TKA. Additionally, using KL classification to grade radiographs before surgery may help identify which patients are likely to benefit most from TKA.

Study II showed that, unlike the PS design, total knee arthroplasty (TKA) using a CR or an AS design does not fully restore natural joint kinematics when stepping up. The PS design mimics the anterio-posterior translations and rotations of the tibiofemoral contact points of a natural knee during a step-up motion.

According to Study III, patients who received different designs of the same primary TKA system (CR, AS, and PS) reported no significant difference in their outcomes after two years. More than 90% of patients in all three groups expressed satisfaction with their knees. The PS design resulted in slightly better flexion than the other designs, but this may not be important in a clinical context. All three designs are viable options for patients with uncomplicated OA knees.

Implications for future research

This thesis has several implications for future research. First, additional follow-up consultations beyond two years (i.e., after 5-15 years) may be necessary to obtain a more valid mid-to long-term comparison of different TKA designs. Second, around 8-10% of our patients reported no effect of the surgery. Therefore, it is imperative to concentrate on developing methods to recognize individuals who may not respond well to surgery beforehand. Furthermore, it is possible that some of our patients who received TKA may not have experienced significant benefits from the procedure. How to avoid operating on these patients and how to treat them should be an important topic for research. Fourth, it is essential to conduct further research on the latest implant designs available in the market to identify the most suitable ones for different patients.

Register-based RCTs may be considered for evaluating new implants' clinical effectiveness, as they reduce the costs and time needed for inclusion and conducting adequately-powered studies. Finally, all OA research will benefit from the development of a better and internationally valid classification system for knee OA.

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Paper I

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Primary Knee

More Severe Radiographic Osteoarthritis Is Associated With Increased Improvement in Patients' Health State Following a Total Knee Arthroplasty

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ABSTRACT

Background: To assess whether preoperative radiological severity of osteoarthritis (OA) is related to the level of improvement in patients' health state measured 1 year after total knee arthroplasty (TKA).
Methods: Radiographic severity of OA was graded using the Kellgren-Lawrence (KL) classification. Two independent observers were blinded to patients' outcome scores. Health-related quality of life was measured using EQ-5D-3L preoperatively and at 12-month follow-up. The 5 dimensions of the EQ-5D were converted into a health state index score. The association between KL grade and improvement in health state score was analyzed using multiple linear regression.
Results: Among 156 consecutive patients (68% females, mean age 69 years) who underwent primary TKA, 3 knees (2%) were classified as KL grade 2, 115 as KL grade 3 (74%), and 38 as KL grade 4 (24%). Follow-up rate was 77%. There was substantial intra-rater and inter-rater agreement (Cohen's kappa = 0.80 and 0.79). Most patients (64%) had clinically significant improvement in their health state score 1 year after TKA. However, after adjusting for relevant covariates, patients with severe OA (KL grade 4) were found to have significantly more improvement in their health state score than patients with mild or moderate OA (KL grade 2 or 3, respectively). Separate analysis of the 5 EQ-5D dimensions showed that the KL group differences were most evident in the "usual activities" and "pain/discomfort" dimensions.
Conclusion: Patients with severe OA have significantly more improvement in their usual activities and pain/discomfort 1 year after TKA than patients with less severe OA.

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Total knee arthroplasty (TKA) is generally considered a highly effective and successful procedure for relieving pain, restoring knee function, and improving health-related quality of life (HRQoL) in patients with knee osteoarthritis (OA) [1]. Despite the overall effectiveness of TKA, a subset of patients experience unsatisfactory results with respect to pain, function, and restoration of quality of life [2]. Lindberg et al [3] showed that 1 in 5 patients reported only temporary improvement in pain during walking in the first 3 months following TKA, followed by a distinct increase in pain, returning to preoperative levels 12 months after surgery. Several potential predictors of poor outcomes have been investigated [4], but the results so far are inconclusive and the reasons are likely to include both physical and psychosocial factors. Preoperative identification of patients at increased risk would be very helpful. Grade of radiographic OA may be a prognostic marker to determine the optimal timing of surgery. A consensus statement issued in 2015 [5] concluded that medial unicompartmental arthroplasty (UKA) should only be performed in cases showing severe OA with bone-on-bone contact on preoperative radiographs. No such recommendation exists for TKA. Niinimaki et al [6] and Pandit et al [7] examined pain and revision rates after UKA and found that patients with less than bone-on-bone contact radiographically were more likely to experience persistent pain and go on to subsequent conversion to TKA. It is unclear, however, whether a similar relationship applies to dissatisfaction after TKA. Polkowski et al [8] noted that among patients assessed for pain following TKA with acceptable postoperative radiographs, 50% had only mild or moderate preoperative radiographic disease before their TKA procedure. We identified several studies showing an association between less severe OA and poorer long-term results for pain and function after a TKA [8–13], but they had several weaknesses. Most of these studies used either a cross-sectional [10] or retrospective design [8,12,13]. Moreover, the radiographic classification was usually performed by only 1 rater [8,10,11] or did not report the number of raters [12], and most studies did not report intra-rater reliability [8,12,13]. Thus, to fill this gap of knowledge, there is need for a prospective study, using rigorous methods for classification of radiographic disease progression.

In this prospective study, we aimed to (1) describe the preoperative radiographic severity of knee OA in patients undergoing TKA and (2) evaluate the association between the degrees of preoperative radiographic OA and improvement in patient health states 1 year after TKA.

Methods

This longitudinal study is part of a prospective cohort study on pain, functioning, and quality of life in patients undergoing primary TKA. The original study was conducted between October 2012 and August 2013 and included 203 patients [14].

Patients and Procedures

At a hospital in Oslo, Norway, we recruited consecutive patients who were undergoing primary TKA due to OA, aged 18 years or older, able to read and understand Norwegian, mentally and physically capable of completing questionnaires, and had standardized radiographs of the knee taken within 6 months before surgery.

We collected baseline data prospectively and included radiographic assessment of OA severity, sociodemographic factors, knee functioning, pain intensity, prior trauma or surgery (meniscus and ligament surgery) to the knee, and health states. Clinical variables at baseline, including comorbidities, American Society of Anesthesiologists (ASA) classification score, and type of implant, were extracted from the medical records through chart review. We assessed knee functioning, pain intensity, and health states again 12 months after surgery.

Table 1
Kellgren and Lawrence Classification.

Grade	Description
0	No joint space narrowing or reactive changes
1	Doubtful joint space narrowing and possible osteophytic lipping
2	Definite osteophytes and possible joint space narrowing
3	Moderate osteophytes, definite joint space narrowing, sclerosis, and possible bony deformity
4	Large osteophytes, marked joint space narrowing, severe sclerosis, and definite bone end deformity

Radiographs and Grading of OA

Before surgery, all patients underwent routine weight-bearing, anteroposterior (AP) radiographs of the knee. All radiographs were taken with a standardized knee protocol at the same radiology lab. One experienced musculoskeletal radiologist and 1 orthopedic surgeon, who were blinded to the clinical data, independently evaluated the radiographs with regard to OA severity. This was conducted using the Kellgren-Lawrence (KL) classification based on the original description [15] (Table 1). If the 2 reviewers graded cases differently, a third experienced reviewer made the final decision on KL grade. Neither of the reviewers took part in the treatment or follow-up of the patients. At least 1 week apart from the first reading, the images were examined again while the reviewers were blinded to their previous ratings. The 2 reviewers compared their second reading and combined their scores to be used for further statistical analyses. We calculated inter-rater reliability between the 2 raters and intra-rater reliability between the 2 readings from 1 rater.

Measurements

HRQoL was measured preoperatively and at 12-month follow-up with the generic questionnaire EQ-5D-3L [16], which consists of 2 parts. The first part assesses health in 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each of which has 3 levels of response (no problems, some problems, extreme problems/unable to do). From these 5 dimensions, we calculated a health state index score using the European visual analog scale–based value set [17]. The health state index score is represented on a scale from −0.59 to 1, where lower scores indicate reduced quality of life. The minimal clinically important difference (MCID) for the health state index score is 0.074 (95% confidence interval, −0.011 to 0.140) [18]. The second part of the questionnaire measures the patients' self-rated health based on a visual analog scale score ranging from 0 (worst imaginable health) to 100 (best imaginable health). The EQ-5D-3L has been shown to be simple to use, valid, responsive to change, and reliable for group comparisons.

Clinical rating and functional assessment of the knee were done using the American Knee Society Score (KSS) [19]. Clinical rating comprises pain, stability, and range of motion (ROM), with deductions for flexion contractures, extension lag, and malalignment. A well-aligned knee with no pain, 125° of motion, and negligible AP or mediolateral instability obtains the maximum score of 100. Fifty points are allotted for pain, 25 for stability, and 25 for ROM. Walking distance and stair climbing are the main parameters in the function score and a maximum score of 100 is assigned to individuals who can walk unlimited distances and can climb upstairs

Table 2
Patient Characteristics (N = 156).

Characteristic	Statistics
Female, n (%)	106 (68%)
Age, mean (SD) [range]	69 (9) [45 to 90]
BMI, mean (SD) [range]	29.2 (4.6) [21.0 to 43.0]
ASA classification, n (%)	
1	17 (11%)
2	116 (74%)
3	23 (15%)
Comorbidities, mean (SD) [range]	1.2 (1.0) [0 to 5]
Prior ipsilateral knee surgery, n (%)	59 (38%)
Prior arthroplasty (hip or contralateral knee), n (%)[a]	45 (30%)
KL grade, mean (SD) [range]	3.2 (0.5) [2 to 4]
2	3 (2%)
3	115 (74%)
4	38 (24%)
KSS total score, mean (SD) [range][b]	108 (30) [32 to 179]
KL grade 2	135 (38) [112 to 179]
KL grade 3	111 (29) [32 to 176]
KL grade 4	96 (27) [47 to 170]
KSS knee score, mean (SD) [range]	46 (15) [12 to 84]
KL grade 2	58 (24) [37 to 84]
KL grade 3	46 (15) [12 to 77]
KL grade 4	43 (15) [20 to 84]
KSS function score, mean (SD) [range]	62 (19) [20 to 100]
KL grade 2	77 (17) [62 to 95]
KL grade 3	65 (19) [20 to 100]
KL grade 4	53 (15) [27 to 86]
KSS ROM and stability score, mean (SD) [range]	36 (8) [17 to 50]
KL grade 2	41 (9) [32 to 49]
KL grade 3	37 (8) [17 to 50]
KL grade 4	35 (8) [22 to 50]
KSS pain score, mean (SD) [range]	11 (11) [0 to 40]
KL grade 2	17 (16) [5 to 35]
KL grade 3	11 (10) [0 to 40]
KL grade 4	11 (12) [0 to 40]
Health state index score, mean (SD) [range]	
Preoperative	0.59 (0.17) [0.15 to 1.00]
1-y Postoperative[c]	0.75 (0.18) [0.27 to 1.00]
Change from preoperative to postoperative[c]	0.16 (0.19) [−0.39 to +0.73]
Self-rated health, mean (SD) [range]	
Preoperative	60.9 (19.7) [19 to 100]
1-y Postoperative	74.7 (16.0) [025 to 100]
Change from preoperative to postoperative	+13.8 (18.8) [−39 to +80]
Improved at least 10 points, n (%)	95 (61%)
IADL score, mean (SD) [range][d]	
Preoperative	7.4 (0.9) [3 to 8]
1-y Postoperative	7.6 (0.7) [5 to 8]
Change from preoperative to postoperative	0.2 (0.8) [−2.3 to +3.7]
Improved at least 1 point, n (%)	32 (23%)
Declined at least 1 point, n (%)	10 (7%)

SD, standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists; KL, Kellgren-Lawrence; KSS, Knee Society Score; ROM, range of motion; IADL, Lawton Instrumental Activities of Daily Living scale.
[a] N = 148 because 8 patients had missing data regarding prior arthroplasty.
[b] N = 148 because 8 patients were missing KSS.
[c] For health state index score, n = 156 at 1 y and for change scores.
[d] For IADL, n = 148 preoperative, n = 143 at 1 y, and n = 139 for change scores.

and downstairs normally. Deductions are made for use of a walking aid.

Pain and interference with functioning were measured using the Brief Pain Inventory (BPI) [20]. The BPI consists of 4 items that evaluate pain intensity rated on a numeric rating scale from 0 (no pain) to 10 (pain as bad as you can imagine); 7 items that evaluate pain interference with 7 domains of life (ie, general activity, mood, walking ability, normal work, relations to other people, sleep, and enjoyment of life) rated from 0 (no interference) to 10 (interferes completely); 1 item on pain relief; and a body map that evaluates pain locations. The validity and reliability of the Norwegian version of the BPI are well established [20].

Independence with activities of daily living (ADL) was measured using the Lawton Instrumental Activities of Daily Living (IADL) [21] scale. The instrument assesses 8 independent living skills (ie, using the phone, shopping, food preparation, housekeeping, laundering, mode of transportation, responsibility for own medication, and finances). The respondents rate their highest level of functioning for each skill. The total score ranges from 0 to 8, with higher scores indicating more independence.

Statistical Analyses

All analyses were conducted using SPSS software, version 24 (IBM Corp, Armonk, NY). We used descriptive statistics to describe patient characteristics and OA severity. Means and standard deviations were reported for continuous data, and numbers and percentages to describe categorical data. Change in patient-reported outcomes from before surgery to 1 year (11-13 months) postoperatively was assessed using paired sample *t*-tests. Intra-rater and inter-rater reliability were determined using kappa statistics for categorical data [22]. The kappa coefficient indicates the level of agreement beyond chance and ranges from 0 (indicating no agreement) to 1 (perfect agreement). A kappa of 0-0.2 is considered poor, 0.21-0.4 fair, 0.41-0.6 moderate, 0.61-0.8 substantial, and 0.81-1 almost perfect [23]. Crude associations between KL grade and change in patient-reported outcomes were assessed using Pearson correlation coefficients, and adjusted associations were evaluated using multivariable regression analysis, controlling for relevant covariates, including patient age, sex, number of comorbidities, body mass index, prior ipsilateral knee surgery, prior hip or contralateral knee arthroplasty, and preoperative rating of worst pain. *P* values <.05 were considered statistically significant. Standardized beta coefficients are reported for all factors in the model.

In addition to evaluating clinical predictors of change in the multidimensional health state index score following TKA, clinical predictors of change in patients' rating of their self-rated health and IADL scores were also evaluated.

Ethical Perspectives

The Regional Medical Research Ethics Committee of Health Southeast of Norway #2011/1755 approved the protocol for this study. Informed written consent was obtained from all participants. Only the research group had access to the data. All data were depersonalized before the statistical analysis.

Results

A total of 245 consecutive patients were invited to participate in the study, of which 33 declined to participate and 6 patients cancelled their surgery. A total of 206 consenting patients were enrolled in the study. Two patients were later excluded due to postoperative disorientation, 1 patient died, and 47 had incomplete data on several of the variables of interest, leaving a total of 156 (77%) who had sufficiently complete data to be included in analysis of the relationship between OA grade and clinical outcome. Patient characteristics are summarized in Table 2. No statistically significant differences in the preoperative characteristics (ie, age, sex, and health state) were found between patients who were lost to follow-up and those who were not. Most patients had no prior surgeries on the ipsilateral knee (62%). However, 32% had meniscus surgery, 2% had ligament surgery, 2% had medial high tibial osteotomy, and 2% had fracture fixation. A total of 45 patients (30%) had a prior hip or contralateral knee arthroplasty, of which only 11% also had prior ipsilateral knee surgery. In contrast, almost half (48.5%) of the 103 patients who had no prior knee or hip arthroplasty had prior

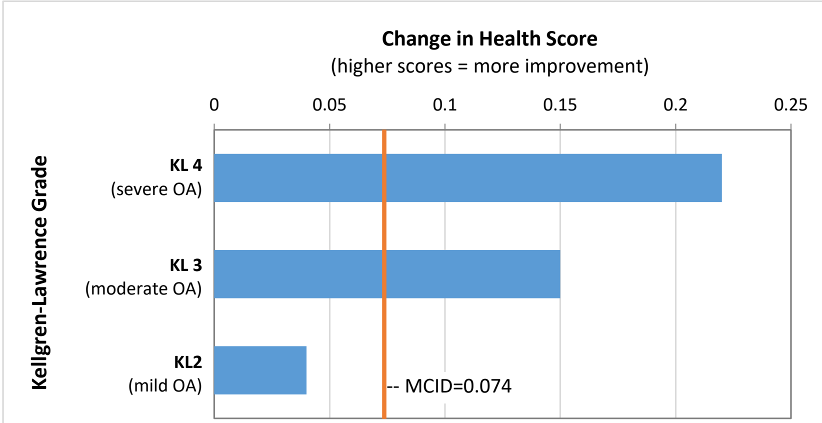

Fig. 1. Change in the health state index score by Kellgren-Lawrence (KL) grade. The red line represents the minimal clinically important difference (MCID) for the health state index score. N = 148. OA, osteoarthritis.

ipsilateral knee surgery, indicating these procedures were inversely associated ($P < .001$).

Intra-rater and inter-rater agreement of KL grades were both substantial, with kappa values of 0.80 and 0.79, respectively. The 2 reviewers disagreed on 10 cases (6%). In most cases, this difference was between KL grades 3 and 4 (9 cases). In total, most of the patients (74%) were classified as KL grade 3, with a significant minority (24%) classified as KL grade 4 and 3 patients (2%) classified as KL grade 2. Patients with KL grade 2 were all arthroscopically evaluated before TKA and found to have more extensive OA than seen on the radiographs. The 3 KL grades did not differ in terms of age, sex, body mass index, ASA classification, or number of comorbidities. However, as shown in Table 2, the KL grades did differ with respect to their preoperative KSS total scores ($P = .008$), mostly due to differences in their KSS function score ($P = .002$), with lower KL grades having better KSS. KSS knee scores, ROM, and stability scores and pain scores did not differ by KL grade.

Changes in HRQoL and ADL Dependence Over the 12 Months following Surgery

For the total sample, health state index score improved following TKA, with mean score increasing from 0.59 at the preoperative assessment to 0.75 one year after surgery ($P < .001$; Table 2). The average improvement in scores was 0.16, which exceeds the MCID of 0.074 for the health state index score. At the individual level, 64% of patients demonstrated an improvement that exceeded the MCID in the health state index scores, while the remaining 36% did not experience meaningful improvement. The EQ-5D dimensions showing the most significant improvements were "usual activities," "pain/discomfort," and "mobility" (all $P < .001$), with each of these dimensions showing an average of 16%-22% improvement in scores. There was a similar improvement in patients' self-rated health, with overall self-rated health increasing an average of 13.8 points from before surgery to 12 months after surgery ($P < .001$). At the individual level, 61% of patients rated their health at least 10 points higher (on a 0-100 scale) at 12 months than before surgery.

The improvement in overall IADL scores was more modest, but significant 1 year after surgery ($P = .001$). The largest improvements occurred in the areas of shopping and housekeeping: 67% of the 48 patients who reported some level of preoperative dependence with shopping and 59% of the 51 patients who reported preoperative dependence with housekeeping reported improved independence in these areas 12 months postoperatively.

Clinical Predictors of Improvement in Quality of Life Indicators

Higher preoperative KL grade was associated with greater improvement in the health state index score, as measured by change in the score from before to 1 year after TKA (r = 0.172, $P = .033$). As shown in Figure 1, the 3 patients with KL grade 2 had no clinically meaningful improvement in the health state index score (change = 0.04), while patients with either KL grade 3 or 4 showed improvement that was clinically meaningful (change in the health state index score of 0.15 and 0.22, respectively). Although patients with KL grade 4 had greater improvement than those with KL grade 3, this difference did not reach clinical or statistical significance in unadjusted analyses (mean difference = 0.067; $P = .067$). However, after adjustment for the relevant covariates of age, sex, comorbidities, body mass index, prior ipsilateral knee surgery, prior hip or contralateral knee arthroplasty, and preoperative pain level, patients with a KL grade of 4 were found to have significantly higher health state index score improvement 1 year after surgery than patients with KL grades of 2 or 3 (Table 3). Additional analyses indicated that KL grade was specifically associated with improvements in the EQ-5D dimensions of "Usual activities" and "Pain/discomfort," and not with the dimensions of "mobility," "self care," or "anxiety/depression" (Table 4).

Sensitivity analyses excluding the 3 patients with KL grade 2 were also conducted to determine the impact of these patients on the results. The association between KL grade and change in the health state index score attenuated only slightly (<4% change in beta), indicating that these 3 patients alone did not account for the observed association between higher KL grade and greater improvement in the health state index score 1 year after surgery. Similarly, the associations between KL grade and changes in the

Table 3
Predictors of Change in the Health State Index Score From Before to 12 Months After TKA (N = 148).

Independent Variables	Beta	*P* Value
Age	−0.080	.35
Female gender (reference is male)	0.115	.16
Number of comorbidities	0.116	.15
Body mass index	0.109	.21
Prior ipsilateral knee surgery	−0.078	.38
Prior arthroplasty (hip or contralateral knee)	0.194	.028
Preoperative worst pain rating	0.107	.20
KL grade = 4 (reference is KL < 4)	0.163	.040

TKA, total knee arthroplasty; KL, Kellgren-Lawrence.

Table 4
Regression Analyses Evaluating KL Grade as a Predictor of Improvement on Each of the 5 Different Dimensions of EQ-5D[a].

Dependent Variables: Change in the Following EQ-5D Dimensions	Beta for KL Grade = 4[b]	P Value
Mobility	0.067	.43
Self-care	−0.082	.32
Usual activities	0.181	.032
Pain/discomfort	0.236	.004
Anxiety/depression	−0.123	.14

KL, Kellgren-Lawrence.
[a] Each regression model included the same predictors as shown in Table 3.
[b] Reference is KL grade <4.

dimensions of “usual activities” and “pain/discomfort” remained significant ($P = .028$ and .006, respectively) when the 3 patients with KL grade 2 were excluded.

Given the association between KL grade and change in the “pain/discomfort” dimension of the EQ-5D, additional analyses were conducted to determine whether KL grade was associated with improvement in standard pain measures. However, KL grade was not associated with change in ratings of worst, average, or current pain.

Unlike KL grades, KSS was unrelated to quality of life improvements, as measured by change in the health state index score from before to 12 months after TKA. Also, neither the KL grade nor KSS was associated with changes in the patients’ self-rated health or their independence in ADL (data not shown).

Discussion

This prospective study, using rigorous state-of-the-art methods, has shown that patients with radiographic evidence of severe OA (ie, KL grade 4) have more substantial improvements in their health state index score following TKA, compared to patients with mild to moderate OA (KL grades 2 and 3). Despite the widespread and increasing use of TKA to reduce pain and improve both function and HRQoL, many patients fail to report improvement in HRQoL after surgery. While the reasons may be attributed to a variety of causes, our findings add to the body of knowledge on risk factors for nonimprovement after TKA. While both patient groups with severe and moderate OA obtained clinically meaningful improvement in their health state index score 1 year after TKA, the improvement was less substantial for patients with moderate OA. Patients with mild OA changes did not obtain any clinically meaningful improvement, but this result must be interpreted with caution because only 3 patients had knees classified as KL grade 2. Low-grade OA is a known risk factor for pain and dissatisfaction after TKA. However, prospective studies reviewing the relationship between preoperative radiographic features and outcome after TKA are limited. Pandit et al [7] described higher rates of postoperative pain and dissatisfaction requiring conversion to TKA in patients when UKA was performed in the absence of bone-on-bone OA (KL grade <4), whereas Tilbury et al [24] and Vina et al [25] did not find any statistically significant differences between the outcomes in patients with different grades of radiographic severity. In contrast, Valdes et al [10] and Dowsey et al [26] found significantly better improvement in physical functioning and patient satisfaction in patients with severe OA, and Keurentjes et al [11] showed that patients with less preoperative radiographic OA undergoing TKA were more likely to experience more pain after surgery. Dowsey et al [26] showed similar results. Comparisons with the literature are, however, hampered by the large diversity in study designs, analyses, and patient-reported outcome measurements (PROMs) being used. Several of the aforementioned studies have compared patients with KL grades 0-2 or 1-2 with 3-4. One may question whether KL grade 0 and 1 should be characterized as OA at all and whether surgery is the right option for these patients. According to Osteoarthritis Research Society International (OARSI) recommendations [27], the first-line treatment for patients with knee OA should be individualized and consist of education, land-based exercise, and weight reduction when relevant, combined with nonsteroid anti-inflammatory drugs. As these interventions represent a noninvasive option for patients with low-grade radiographic OA, they should be recommended to patients before considering surgery. Kellgren et al described in 1957 their classification system to grade the severity of OA [15], and the literature suggests a cutoff at KL grade 2 for the diagnosis of OA [28,29]. No radiographs were classified as grade 0 or 1 in our cohort.

Overall, our results are in accordance with several studies concluding that more severe radiographic OA preoperatively is associated with better outcomes. A recent study by Hoorntje et al [30] investigated the relationship between KL grade and a number of PROMs. In this study, patients with KL grades 3 and 4 as compared to KL grades 1 and 2 had significantly better scores in some but not all of the PROM subscores. The authors suggest that the reasons for these contradictory findings may be due to the use of a variety of PROMs and the use of generic PROMs not specific to OA. The main clinical outcome measure in our study was the EQ-5D-3L, which is a generic HRQoL instrument, and not a disease-specific outcome measure. However, EQ-5D is one of the most widely used instruments for measuring HRQoL, is tested in various population groups, including patients having total joint arthroplasty, and is therefore comparable across surgical groups. However, it has shown ceiling effects in population surveys and patient populations [31], thus limiting its usefulness as an outcome measure in total joint arthroplasty [32]. The newer version of the EQ-5D, the 5L version, shows improved responsiveness compared to the 3L system, and also good validity and reliability [33,34]. We will implement the newer version of the EQ-5D in future research.

We found a significant association between KL grade and change in the “pain/discomfort” dimension of the EQ-5D, which is a generic outcome measure. This association, however, was not present when we used a different pain measure (BPI). This discrepancy may be due to different levels of responsiveness for the 2 instruments. Intuitively, one would consider a generic instrument to be less responsive than a pain-specific instrument, but responsiveness may not be predetermined [35]. Instead, responsiveness seems to be a relative property of outcome instruments and depends on the condition and treatment under study. Furthermore, the pain terminology differs between the 2 instruments. While the BPI assesses the severity of pain, the EQ-5D also includes discomfort. Thus, it is possible that the 2 instruments assess slightly different concepts. Focus group interviews with OA patients revealed that patients with OA use several descriptors of pain, including ache, tenderness, and discomfort [36]. Thus, the pain/discomfort dimension of the EQ-5D might be more sensitive to subtle changes than the BPI.

Our study had a number of limitations. First, only 77% of the patients in the original sample had sufficiently complete data to be included in the multivariate analysis, although no significant differences were found between those who were included and those who were not in terms of age, sex, and health state. An attrition rate of 23% may introduce selection bias, loss of statistical power, and lower validity of the study; however, there are no generally accepted standards for follow-up rates in cohort studies. The fact that attrition in the present study appeared to occur at random reduces the significance of this potential bias. Second, we only included KL grading applied to the AP knee radiographs. We did this because KL classification was originally described using AP knee radiographs [15]. Information from plain radiographs is used to determine the presence of OA and to assess disease severity, and thus, plain radiographs play an important role when treatment options are selected. The position of the knee in the radiographs is important. Semi-flexed knees can give a different KL grading than straight legs. Rosenberg et al [37] suggest that using the Rosenberg view (45° AP flexion weight-bearing radiograph) results in higher inter-rater reliability and better correlation to arthroscopic evidence of OA than does using the AP radiograph. The authors argue that this may be because the Rosenberg radiograph provides better visualization of the femoral condyles in midflexion, a common site of articular surface degeneration. It remains unclear whether the current results might have differed if we had instead evaluated semi-flexed knee radiographs. Third, measures of postoperative stability and malalignment were not included in this study, and therefore, the impact of such factors on the study findings is unknown. Fourth, we used Lawton's IADL scale to measure the functional status of nondisabled patients, and clinical outcome scores may exhibit a ceiling effect when used in populations that are healthier and more active than the population the scoring system was intended to evaluate [38]. In our study, 85% of the patients were classified as having an ASA score of 1 or 2 and 60% of the patients had the maximum IADL score preoperatively and therefore had no possibility for improvement. In retrospect, using a different scoring system or implementing strategies known to reduce the ceiling effect might have yielded a more useful measure.

It has been mentioned in some studies that KL score should not be the preferred tool for assessing OA severity [9,39], as some studies question the classification's inter-rater and intra-rater reliability [29,40] and the use of differing descriptions of the grading system [29] makes it difficult to compare findings between studies. A study comparing 3 different X-ray scoring methods of knee OA concluded that joint space width evaluation on semi-flexed views might be the preferred method to evaluate the severity of knee OA [39]. They found higher inter-rater reliability for joint space width evaluation in comparison with KL and OARSI atlas (kappa 0.86 vs 0.56 and 0.48 for KL and OARSI, respectively). As there is no gold standard for diagnosing OA severity, we used the KL classification because it has been commonly used as a research tool in studies of OA.

This study has several strengths. The prospective design and relatively large sample size are major benefits. Two independent raters with extensive experience, who were blinded to patient data, rated the radiographs, which increases the reliability of the ratings. We also evaluated the intra-rater and inter-rater agreement of the KL grading and the gradings demonstrated substantial intra-rater and inter-rater agreement. Our findings indicate that KL grading is a reliable tool for assessing the radiographic severity of OA.

In conclusion, we have shown that there is a relationship between the severity of OA evident on preoperative X-rays and improvements in patients' health state index score after primary TKA. The patients in this study with severe radiographic OA had significantly more improvement in some dimensions of the HRQoL questionnaire EQ-5D after surgery than those with mild or moderate OA. This finding has important clinical implications for patient selection and optimal timing of TKA. Furthermore, radiographic grading of X-rays using KL classification might be a useful preoperative tool to help choose patients who would derive the most benefit of a TKA.

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Paper II

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Comparison of the in-vivo kinematics of three different knee prosthesis designs during a step-up movement

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ABSTRACT

Background: There is no consensus on the importance of the kinematics of the prosthetic joint for the clinical outcome after total knee arthroplasty. A 3-armed randomized controlled trial was done to determine and compare the in vivo kinematics of a posterior cruciate-retaining and two posterior cruciate-sacrificing (Anterior-Stabilized and Posterior-Stabilized) prosthetic designs from the same total knee arthroplasty system. Since the anterior-stabilized and posterior-stabilized designs are posterior cruciate ligament-sacrificing designs, we hypothesized they would have similar contact-point kinematics. Further, we hypothesized that the cruciate-retaining design would have contact-point kinematics different from the anterior-stabilized and the posterior-stabilized designs, but comparable to a native knee.

Methods: Thirty-nine patients with a well-functioning total knee arthroplasty one year postoperatively underwent kinematic analysis of a weight-bearing step-up movement under fluoroscopic recording. Model-based radiostereometric analysis was used to determine anteroposterior contact-point translations and rotations through the movement path to assess knee kinematics.

Findings: The cruciate-retaining and anterior-stabilized groups' medial and lateral contact-points displayed similar paradoxical posterior translations during step-up in the magnitude of 7 and 2 mm, respectively. In contrast, the posterior-stabilized group's contact-points translated anteriorly by 4 and 10 mm throughout the movement and were significantly more posterior than the cruciate-retaining and the anterior-stabilized groups from >100° to 40° of flexion. The femur rotated internally with all designs.

Interpretation: The cruciate-retaining and anterior-stabilized designs displayed similar contact-point translation patterns during a step-up movement. Only the posterior-stabilized design showed a pattern comparable to native knees. Conversion from a cruciate-retaining to an anterior-stabilized design because of posterior cruciate ligament insufficiency will not change knee kinematics.

1. Introduction

One of the unresolved topics in total knee arthroplasty (TKA) is the effectiveness of the prosthesis in reproducing physiological kinematics comparable to a healthy native knee (Arnout et al., 2015; Dennis et al., 2003a). Implant design is one factor that influences post-TKA kinematics. However, there is still no consensus on the relationship between joint kinematics and TKA outcomes (Arnout et al., 2015). Non-physiological kinematics might result in impaired knee function due to reduced range of motion (RoM), paradoxical sagittal femorotibial translation or loss of femoral axial rotation (Angerame et al., 2019; Dennis et al., 2003b). Abnormal kinematics may also lead to increased polyethylene wear (Bourdon et al., 2021). Five percent of new TKAs fail within ten years, and about half for biomechanical reasons (Khan et al., 2016).

Healthy knee kinematics are complex, with a combination of rolling and gliding motions of the femoral condyles and tibial rotation (Smith et al., 2003). The posterior cruciate ligament (PCL) contributes to knee kinematics by preventing posterior translation of the tibia, contributing to femoral rollback during flexion and the "screw-home" mechanism in extension. Various attempts have been made to design implants that maintain normal kinematics after TKA. The decision to retain or sacrifice

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the PCL during TKA remains a controversial issue. Advocates of PCL-retention argue that the PCL provides more natural knee kinematics, improves proprioception, and enhances stability (Broberg et al., 2020a; Chalidis et al., 2011). Those who favour sacrificing the PCL claim that it allows for better ligament balancing, a more straightforward surgical procedure, reduced tibiofemoral loads and more predictable kinematics (Broberg et al., 2020a). Clinical evidence suggests that if the PCL is sacrificed, knee function can be improved with PCL-substitution (Harato et al., 2008). There are two ways to substitute PCL function; either with a central polyethylene post on the tibial insert and a transverse cam on the femoral component in the posterior-stabilized (PS) TKA or with a more congruent tibial insert, anterior stabilized (AS), characterized by a higher anterior wall and deeper trough compared to the standard cruciate-retaining (CR) insert. Some clinical studies have reported no difference in functional or radiographic outcomes between AS and PS inserts after TKA (Scott, 2018; Sur et al., 2015). Others have concluded that AS designs result in significantly less posterior femoral rollback, less anteroposterior stability and inferior patient-reported outcomes than PS inserts (Fritzsche et al., 2018; Han and Kang, 2020). However, evidence regarding AS designs is lacking. This dynamic, radiostereometric study aimed to compare the joint kinematics of AS, CR and PS designs of the same knee replacement system in a step-up movement from deep flexion to full extension. We hypothesized that an AS design would not significantly alter the contact kinematics compared to a PS design. Further, we hypothesized that the CR design would have contact kinematics different from AS and PS designs but resemble a native knee. Although previous in vivo studies have reported on the kinematics in different TKA implant designs (Banks et al., 1997; Broberg et al., 2020a; Cardinale et al., 2020; Cates et al., 2008; Jang et al., 2019), to our knowledge, none has investigated CR, PS and AS designs from the same manufacturer in a prospective randomized clinical trial.

2. Methods

This study is part of a larger prospective, randomized clinical trial comparing clinical outcomes of CR, AS and PS options of the same primary TKA system. The original study was conducted between March 2017 and January 2020 and included 216 patients. Eligible patients to the main study had primary osteoarthritis, varus or valgus deformity ≦15°, intact PCL, age between 45 and 77 years, body mass index <35 kg/m^2 and American Society of Anesthesiologists score of I or II. Exclusion criteria were: 1) prior anterior cruciate ligament surgery, 2) impaired collateral ligaments, 3) flexion <90°, 4) flexion contracture >10°, 5) peripheral neuropathy, 6) malignancy, 7) patients who did not speak Norwegian, 8) rheumatic disease and 9) previous osteotomy.

We used the primary Legion TKA system (Smith & Nephew, USA), which offers CR, AS and PS options. The CR and AS options entail identical tibial and femoral components but different designs of the tibial insert. The AS insert is a sagitally-curved tibial insert with vertically prominent anterior and posterior lips intended to provide stability for an insufficient or resected PCL.

The PS design has a typical cam-and-post mechanism to replace the role of the PCL in preventing anterior translation of the femur, still allowing for femoral rollback.

All participants provided informed consent before surgery. All procedures were carried out under spinal anaesthesia without a tourniquet. We used, in all cases, a mechanical alignment and measured resection with a femur-first technique. A medial parapatellar arthrotomy was used, and the patella resurfaced in all cases. A bony island and PCL-retractor protected the PCL during surgery. After resection of the tibial plateau, the PCL's integrity was assessed visually, by palpation and with trial components in place using the posterior drawer test. Patients with an intact PCL were randomly allocated to one of the three implant designs (CR, AS or PS). Patients with a compromised PCL underwent a routine cruciate-substituting TKA outside the study protocol. The postoperative care and rehabilitation were identical for the three groups.

Two independent physiotherapists, blinded to the study design, measured the knee RoM using a goniometer 12 months postoperatively. Patients completed the Knee injury and Osteoarthritis Outcome Score (KOOS) preoperatively and 12 months postoperatively.

To be included in the present radiostereometric substudy, eligible patients had to report no knee pain, have KOOS subscores >80 on the Pain, Symptoms, ADL and QOL subscales and > 60 on the Sport/Rec subscale 12 months postoperatively, and be capable of the step-up movement needed for the fluoroscopic procedure. In vivo knee kinematics were assessed for 39 consecutive patients from the three randomized groups, 13 with each implant design.

The patients' preoperative x-rays and x-rays taken one year after TKA were examined for measurements of hip-knee-ankle angle (HKA), medial proximal tibial angle (MPTA), mechanical lateral distal femoral angle (mLDFA) and posterior tibial slope; these parameters were compared between the groups.

2.1. Fluoroscopy and kinematics

All 39 patients underwent kinematic evaluation a minimum of 12 months after TKA using an Adora DRFI flat-panel fluoroscopy system (15 frames/s). Before data acquisition, patients received thorough instructions and performed the step-up task 2–3 times to gain comfort with the setup. Evaluations were done without shoes, and balance railings ensured patient safety. Patients placed their non-operated foot on the ground, their operated knee 30 cm from the detector and their operated foot on a 50 cm high staircase. Standardized positioning was ensured with built-in laser guidance. Then, under fluoroscopic surveillance, patients put weight on their operated knee and stepped up.

Recordings were in DICOM format, and each frame was separated into high-quality BMP grayscale images. Model-based RSA software was used to analyze the data (RSA*core* Leiden, The Netherlands). Three-dimensional (3D) computer-aided design (CAD) models for the Legion knee prosthesis (tibial and femoral components) were obtained from the manufacturer (Smith & Nephew, USA). The CAD models were superimposed on their respective projections in the two-dimensional (2D) fluoroscopy images (Fregly et al., 2005); 3D in vivo kinematics were also extracted from the 2D images (Mahfouz et al., 2003).

Data were analyzed from flexion (> 90°) to full extension in 20° intervals. We calculated the contact point positions of the medial and lateral femoral condyles with respect to the tibial plateau based on the minimum joint space width from the fluoroscopy data (van Ijsseldijk et al., 2012). Using these contact points, we also calculated the internal and external femoral rotation during the movement.

A coordinate system on the tibial plateau was created using the center point of the tibial baseplate in the mediolateral (x-axis) / anteroposterior (z-axis) direction and on the upper surface of the tibial baseplate (y = 0). Contact point positions anterior to the center point were defined as positive and posterior contact point positions as negative. The main parameter of interest was the anterior-posterior displacement of the contact points, defined as the shortest distance between the tibial metal baseplate and the medial and lateral condyle of the femur.

2.1.1. Ethics

The Regional Ethics Committee (2016/1981) approved the study, and it is registered at ClinicalTrials.gov (NCT03059927).

2.1.2. Statistics

A power analysis determined the number of study patients needed. A phantom study from our clinic showed a standard deviation (SD) of 0.37 mm for zero motion in the z-plane. A clinically significant group difference was a mean difference of 1 mm translation. Therefore, nine patients were needed in each group with an estimated SD of 0.37, a type 1 error rate of 5%, and a power of 80%. Allowing for dropouts, we included 13 patients per group, similar to other kinematic studies (Cates et al., 2008; Klemt et al., 2022).

Descriptive statistics were used to summarize sample characteristics. Normality was assessed with the Kolmogorov-Smirnov test. Mann-Whitney U, Kruskal-Wallis, independent sample *t*-tests, ANOVA and Pearson's chi-squared test were used as appropriate to compare groups. All analyses were two-sided and statistical significance was defined as $p < 0.05$. Statistical analyses were performed using IBM SPSS software, version 28.0 (IBM Corp, Armonk, NY, USA).

3. Results

Patient demographics (Table 1) and KOOS subscores preoperatively and at one year did not differ significantly between the three groups (Fig. 1).

At 1-year follow-up, flexion was significantly better in the PS group than in the CR and AS groups (Table 2). A comparison of the HKA angle, MPTA, mLDFA and posterior tibial slope did not show any statistically significant difference between the groups (Table 2).

3.1. Locations of contact points

Medial and lateral contact point translation patterns were determined for each group during the step-up movement. Figs. 2 and 3 show that the medial and lateral contact point lines of the CR and AS groups overlap. We found no statistically significant differences between the CR and AS groups in how the contact points translated during step-up.

The medial contact points in the PS group (Fig. 2) exhibited more posterior contact than the CR and AS groups throughout early flexion at >100° ($P = 0.0003$), 80° ($P < 0.001$), 60° ($P < 0.001$) and 40° ($P < 0.001$). The PS, CR and AS groups showed similar contact points from <40° of flexion ($P = 0.7$) to full extension ($P = 0.2$). In both the CR and AS groups, the medial contact points moved posteriorly approximately 7 mm throughout the movement (Fig. 2); hence a paradoxical translation compared with a healthy, unoperated knee. In the PS group, the medial contact points moved anteriorly approximately 4 mm from >100° to 60°, but from 60° to full extension, there was just a slight anterior movement of the contact points.

The lateral contact points showed a similar trend (Fig. 3). The PS group had more posterior contact points than the CR and AS groups throughout early flexion at >100° ($P < 0.0003$), 80° ($P < 0.001$), 60° ($P < 0.001$) and 40° ($P = 0.045$). All three groups showed similar contact point positions from 40° ($P = 0.5$) to full extension ($P = 0.3$). In the PS group, the lateral contact point moved anteriorly around 10 mm from >100° to 40° of flexion and remained relatively constant from 40° to full extension, moving only slightly anteriorly. The lateral contact points of the CR and AS groups moved only slightly posteriorly, around 2 mm throughout the motion. The PS group's lateral contact points translated the most. However, the medial contact points moved in opposite directions: posteriorly for the CR and AS groups versus anteriorly for the PS group. As a result, the PS group's lateral contact points translated the most, while those of the CR and AS groups moved slightly (Figs. 2 and 3).

In full extension, the medial and lateral contact points of all three groups ended up at almost the same relative positions, approximately 5 mm posterior to the tibial plateau's center point.

Table 1
Baseline characteristics for the three implant groups.

	CR (n = 13)	AS (n = 13)	PS (n = 13)	P-value
Age, mean (SD)	68 (5)	69 (4)	67 (5)	0.5
Body mass index, mean (SD)	28 (4)	27 (3)	29 (4)	0.7
Male/Female distribution, n/n	9/4	6/7	8/5	
Operated right side	8	9	9	
Days from surgery to fluoroscopy exam, mean(SD)	504 (98)	504 (109)	485 (80)	0.8

CR, cruciate-retaining; AS, anterior-stabilized; PS, posterior-stabilized.

There was an internal femoral rotation (external tibial rotation) throughout the step-up motion, with no significant group differences (Fig. 4).

4. Discussion

This study compared the in vivo kinematics of CR, AS, and PS designs of the same primary TKA system during a step-up movement using model-based dynamic RSA. We examined two PCL-sacrificing designs (AS and PS) and one PCL-preserving design (CR). Our main finding was that the PS design showed different contact point translations than the CR and AS designs. PS TKA had significantly more posterior tibiofemoral contact position for both medial and lateral condyles than CR and AS TKA from >100° to 40°. The PS group experienced *anterior* translation of the contact points of both condyles, more *laterally* than medially, resulting in internal rotation of the femur with respect to the tibia. In contrast, the AS and CR groups experienced *posterior* translation of the contact points of both condyles, but *more medially* than laterally, thus also resulting in internal rotation of the femur. Despite the differences in contact point translations of the PS design compared to the CR and AS designs, due to the direction and differences in the magnitude of the medial and lateral contact point translations, the resulting femoral axial orientation was the same in all three designs. All three designs showed a progressive internal rotation of the femoral component relative to the tibia during extension. The screw-home mechanism, associated with normal knee function, was present in all three designs, consistent with several other studies (Belvedere et al., 2017; Okamoto et al., 2014). The translation pattern for the PS group, but not the AS or CR groups, resembles native knee kinematics (Komistek et al., 2003).

Iwamoto et al. (Iwamoto et al., 2021) compared in vivo kinematics of CR and AS designs and found no significant difference between them. Unlike us, they examined the patients during deep knee flexion and not a step-up movement. Other studies have shown contact point translation patterns for the CR design similar to our findings (Okamoto et al., 2014; Victor et al., 2005). Victor et al. (Victor et al., 2005) studied the Genesis II TKA (Smith&Nephew, USA) and found progressive anterior contact point translation during flexion for the CR design, but the displacement pattern for the PS differed.

A pre-condition for CR TKA is that the PCL is fully functioning. However, some studies have demonstrated that the PCL in osteoarthritic knees is histologically abnormal, questioning this assumption (Akisue et al., 2002; Arbuthnot et al., 2011). Our kinematic analysis showed that the AS design mimicked the CR design. A few studies compared the outcome of a PCL-retaining TKA in patients with and without a PCL (Dion et al., 2019; Misra et al., 2003). Misra et al. (Misra et al., 2003) conducted a prospective randomized controlled trial with five-year follow-up where they compared resection with retention of the PCL when using a standard PCL-retaining TKA. They found no significant group differences regarding pain relief, RoM, strength or stability. A recent study (Dion et al., 2019) of 677 CR TKAs (540 retained intact PCL, 24 partially recessed PCL at the femoral side, and 113 completely excised PCL) reported no significant difference in clinical outcomes among the three groups, although there was significant variability in TKA types within each group. Dennis et al. (Dennis et al., 2003a) showed that even different models of the same type of implant could have different knee kinematics. A CR insert from another manufacturer might differ in depth, the anterior lip's prominence, or the posterior lip's size/presence, which can alter kinematics.

Both the AS and PS designs sacrifice the PCL, but they address substitution differently. With the PS design, the PCL is resected off the femur and removed with some intercondylar bone, whereas with AS design the PCL is often recessed or excised off the tibia and might remain attached to the posterior capsule, which might impact the knee's stability. Our primary hypothesis was that AS and PS designs would have similar contact point translation since they are PCL-sacrificing designs. The AS design's mean medial and lateral contact point translation was

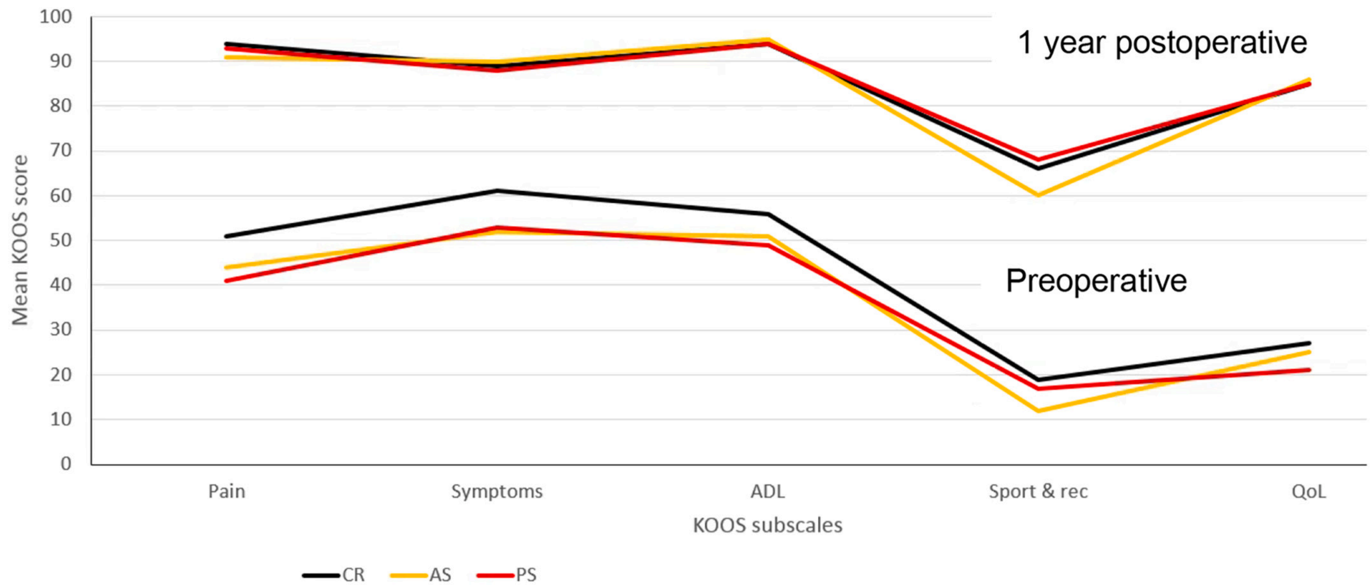

Fig. 1. KOOS profiles before and one year after TKA for the three implant designs.

Table 2
Pre- and postoperative knee alignment parameters and range of motion one year after total knee arthroplasty.

Parameters	CR	AS	PS	P-value
Flexion at one year, mean (°) (SD)	120 (7)	124 (4)	129 (7)	<0.05[a]
Extension at one year, mean (°) (SD)	-2 (3)	-2 (3)	-1 (2)	
HKA preoperative, mean (°) (SD)	5.9 (4.8)	5.0 (6.4)	6.8 (3.6)	0.7
HKA at one year, mean (°) (SD)	1.4 (1.8)	2.6 (2.1)	2.0 (1.8)	0.3
PTS[b] preoperative mean (°) (SD)	84.3 (6.3)	84.5 (3.6)	82.8 (4.8)	0.6
PTS[b] at one year, mean (°) (SD)	87.8 (3.9)	86.6 (2.3)	86.7 (2.7)	0.6
MPTA[c] preoperative, mean (°) (SD)	86.8 (2.9)	86.1 (2.1)	85.6 (2.9)	0.5
MPTA[c] at one year, mean (°) (SD)	87.7 (0.8)	87.3 (1.7)	87.2 (0.8)	0.5
mLDFA[d] preoperative, mean (°) (SD)	89.3 (2.5)	88.3 (3.4)	88.8 (2.2)	0.7
mLDFA[d] at one year, mean (°) (SD)	90.3 (2.3)	91.1 (2.1)	91.3 (1.7)	0.4

CR, cruciate-retaining; AS, anterior-stabilized; PS, posterior-stabilized; HKA, hip- knee- ankle angle; PTS, posterior tibial slope; MPTA, Medial proximal tibial angle; mLDFA, mechanical lateral distal femoral angle.

[a] Statistically significantly different from CR and AS ($p = 0.002$ and $p = 0.009$, respectively).

[b] Angle formed between the vertical line of the tibial anatomical axis and the tibial plateau tangent in the sagittal plane.

[c] Medial angle between the tangent to the tibial plateau and the mechanical axis of the tibia.

[d] Lateral angle between the distal femoral joint line and the mechanical axis of the femur.

significantly different from the PS group from 100° to approximately 40–50° of flexion. However, from 40-50° to full extension, the pattern was similar for the three designs. We believe the contact point pattern of the PS design is a result of the cam-and-post mechanism: the cam engages the post at around 40° of flexion (Banks et al., 1997), and drives

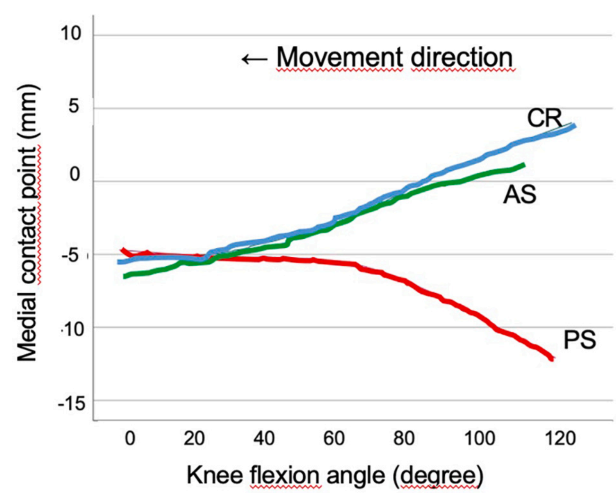

Fig. 2. Medial contact point motion plotted against knee flexion angles for the CR, AS and PS groups.

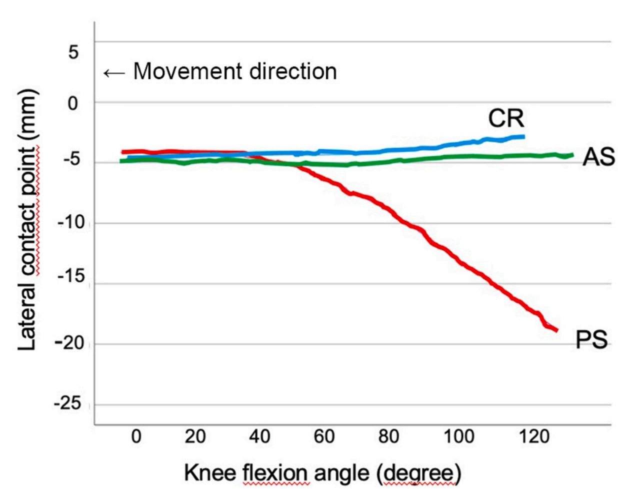

Fig. 3. Lateral contact point motion plotted against knee flexion angles for the CR, AS and PS groups.

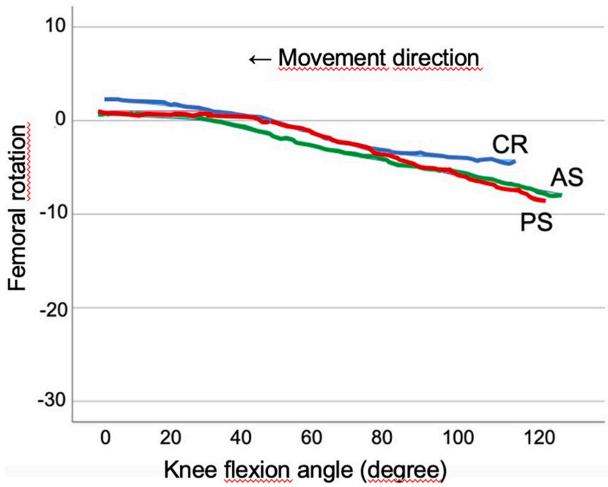

Fig. 4. Axial rotation of the femur with respect to the tibia for the CR, AS and PS groups. Negative and positive values correspond to external and internal rotation, respectively.

the femorotibial contact points posteriorly during further knee flexion, preventing anterior sliding of the contact points. This mechanism (femoral rollback) enables deeper flexion. Our results agree with other studies that suggest that the cam-and-post mechanism engages between 40° and 100° of flexion (Broberg et al., 2020b; Mihalko et al., 2016).

Multiple in vivo, weight-bearing, fluoroscopic analyses have indicated that natural knee kinematics are challenging to obtain after TKA (Dennis et al., 2001; Dennis et al., 2003a). In addition, combined kinematic abnormalities (decreased femoral rollback, paradoxical anterior femoral translation, reverse axial rotational patterns, and femoral condylar lift-off) typically are present (Dennis et al., 2001; Dennis et al., 2003a). All patients included in the present study were satisfied with their knees and had good RoM. However, our data showed that patients in the AS and CR groups had contact point kinematics different from a natural knee during step-up. In contrast, the PS group showed contact point translation and axial rotation that was more like a native knee. Moreover, we found significantly better RoM in the PS group compared to the AS and CR groups. This finding is consistent with several studies that report better RoM with PS design than CR or AS designs (Bercik et al., 2013; Hirsch et al., 1994; Li et al., 1995).

Several study limitations need to be considered. First, we analyzed only a step-up movement, as few studies have analyzed knee joint kinematics during such movement (Li et al., 2013; Okamoto et al., 2014). However, retrospectively, including a step-down movement would have yielded a more comprehensive kinematic investigation. Second, all patients had knee prostheses from the same manufacturer. Thus, the study findings may not be generalized to different TKA systems since other implant models, even of the same kind, can have different knee kinematics (Dennis et al., 2003a). However, limiting this study to one implant design nullified the influence of varying implant model designs on kinematics. More long-term follow-up studies of different implant models are required for more general conclusions. Third, we recruited well-performing patients to observe the impact of the prosthesis design, but this sample is not necessarily representative of the entire clinical population receiving these TKA designs.

Despite these limitations, our study provided valuable insight into the in vivo kinematics of three different TKA designs during weight-bearing step-up activity.

Study strengths were the precise kinematic measurements using a validated methodology, a standardized step-up movement and a consistent surgical technique.

5. Conclusion

TKA with either a CR or an AS design fails to restore physiological joint kinematics during step-up loading, in contrast to a PS design. The PS design provides a contact- point translation like the native knee during a step-up movement.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Paper III

No difference in patient-reported outcomes with cruciate-retaining, anterior-stabilized and posterior-stabilized total knee arthroplasty designs. A three-armed, blinded, randomized study with 2-year follow-up

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Keywords:	Total knee arthroplasty, Knee injury and Osteoarthritis Outcome Score, Prosthesis designs

Abstract

Aims: This study compared patient-reported outcomes of three total knee arthroplasty (TKA) designs from one manufacturer; one cruciate-retaining (CR), and two cruciate-sacrificing designs, anterior-stabilized (AS) and posterior-stabilized (PS).

Methods: Patients scheduled for primary TKA were included in a single-center, prospective, three-armed, blinded randomized trial (n=216, 72 per group). After intraoperative confirmation of posterior cruciate ligament (PCL) integrity, patients were randomly allocated to receive a CR, AS, or PS design from the same TKA system. Insertion of an AS or PS design prompted subsequent PCL resection. The primary outcome was the average score of all five subscales of the Knee injury and Osteoarthritis Outcome Score (KOOS) at two-year follow-up. Secondary outcomes included all KOOS subscales, Oxford Knee Score, EQ-5D, EQ-VAS, range of motion (ROM), and willingness to undergo the operation again. Patient satisfaction was also assessed.

Results: Patients reported similar levels of pain, function, satisfaction, and general health regardless of the prosthetic design they received. Mean maximal flexion (129°) was greater in the PS group than in the CR and AS groups (122°).

Conclusion: Despite differences in design and constraint, CR, AS, and PS designs from a single TKA system resulted in no differences in patient-reported outcomes at 2-year follow-up. PS patients had statistically better ROM, but the clinical significance of this finding may be limited.

Level of evidence: 1

Introduction

Total knee arthroplasty (TKA) is an effective procedure in patients with advanced osteoarthritis (OA).[1] However, some patients report dissatisfaction[2] after primary TKA, although historical data on the prevalence of patient dissatisfaction has recently been disputed.[3] Through efforts to improve the procedure and clinical outcomes, several TKA designs have been utilized. Currently, three TKA designs are commonly used; cruciate-retaining (CR), which preserves the posterior cruciate ligament (PCL), posterior-stabilized (PS), and anterior-stabilized (AS), the latter two being PCL-sacrificing designs. The decision of whether to keep or remove the PCL during primary TKA and how to replace it in case of removal is still uncertain.

The effect of resecting the PCL on knee biomechanics has not yet been fully clarified; however, supporters of retaining the PCL argue that keeping it intact maintains femoral rollback, prevents flexion-extension gap mismatch and improves knee flexion as well as extensor efficiency.[4,5] In contrast, current evidence suggests that retaining the PCL does not significantly improve joint proprioception after TKA,[6] and sacrificing the PCL in TKA achieves similar clinical outcomes compared to CR TKA.[7]

PCL substitution in primary TKA has traditionally relied on a cam-post restraint mechanism. Although this design has proven successful, complications like dislocation,[8] post breakage and wear have been reported.[9] Increasing the sagittal plane conformity of the tibial insert is an alternative to the PS design and can be obtained with an AS design or dished insert. The AS implant differs from the standard CR implant because the insert has an increased anterior lip, deeper trough and more conforming articular surface, providing increased anteroposterior stability. Reported advantages of the AS design include the simplicity of replacing an absent or non-functional PCL, preservation of femoral bone and elimination of cam-post impingement.[10] As part of our current study, we conducted a radiostereometric analysis highlighting how the AS design cannot fully restore normal knee kinematics.[11]

The AS design shows favorable results in a few published reports compared with existing CR or PS designs.[12,13] Some studies have compared the CR, AS and PS designs on patient-reported outcomes or objective measures of knee function.[14,15] However, these studies had either small numbers of patients, varying outcome measures, poor randomization, retrospective design or compared different prosthesis brands.

This study aimed to compare clinical results using the Knee injury and Osteoarthritis Outcome Score (KOOS) among patients receiving CR, AS or PS designs from the same primary TKA system. The primary hypothesis was that the KOOS would be equivalent between the three implant designs at 2-year follow-up. Secondly, there would be no differences in the knees' ROM.

Methods

We conducted a prospective, single-center, blinded, three-armed, randomized controlled trial (RCT) with two-year follow-up. Study design and implementation followed CONSORT statement guidelines. The patients and physiotherapists who conducted the follow-up assessments were blinded to the implant design throughout the study. The Regional Ethics Committee approved the study (2016/1981), and the protocol is registered in ClinicalTrials.gov (NCT03059927). All patients received written information and gave informed consent before surgery.

Patients

Patients were included from March 2017 to January 2020. Table 1 displays the inclusion and exclusion criteria. Of the 216 patients included in the study, 208 (96.3%) completed it, two withdrew consent, four were revised (2 infections, 1 instability, 1 tibia plateau fracture), one had a perioperative injury to the medial collateral ligament, and one died (Figure 1).

Surgical technique and Randomization
The surgeries were performed by a team of eleven board-certified orthopaedic surgeons who specialize in joint replacement surgery. All patients were operated on under spinal anaesthesia, and a consistent surgical technique was used, as described in table 2.

Patients were randomly allocated to one of the three Legion TKA designs (CR, AS or PS) (Smith & Nephew, Inc, Memphis, TN, USA). The tibial baseplate was identical in all three designs, and the shape of the tibial insert is the only difference between the CR and AS designs (Figure 2). The PS design relies on a post-cam mechanism to replace the role of the PCL. Randomization was computer-generated with a variable block size of three.

Baseline characteristics
Data on comorbidities, body mass index (BMI), American Society of Anesthesiologists (ASA) classification score, age at surgery, gender, smoking status, length of surgery and hospital stay were extracted from medical records (Table 3).

Clinical outcomes
Patients completed the KOOS,[16] Oxford Knee Score (OKS),[17] and two health-related quality of life measures (EQ-5D-5L and EQ-VAS)[18] were filled out by the patients independently preoperatively, and one and two years postoperatively. At one-year follow-up visit, patients were asked to describe their TKA on a 5- point Likert scale (1=very dissatisfied to 5=very satisfied). The primary outcome measure was the average score of the five KOOS subscales ($KOOS_5$)[19] 2 years after surgery. Secondary outcomes were the five individual KOOS subscales, OKS, EQ-5D-5L, EQ-VAS and ROM and patients' willingness to undergo the same operation again.

Clinical follow-up
Two physiotherapists performed clinical examinations preoperatively, at 6 weeks, 3 months and annually for 2 years postoperatively. For the ROM examination, a long-arm goniometer was used to measure the angle to the nearest degree using landmarks such as the trochanter, lateral epicondyle, and lateral malleolus. Patients were positioned supine with a pad under their ankles to measure passive extension and then seated on the treatment bench to measure flexion.

Plain weight-bearing radiographs (anterior-posterior (AP) and lateral views) and hip-knee-ankle radiographs were obtained no more than three months before surgery. AP- and lateral views were retaken 3 months after TKA and then yearly. OA was graded using the Kellgren-Lawrence (KL)[20] classification. Complications were registered at each patient contact.

Statistics
The minimal important change (MIC) of 10 points for the $KOOS_5$ and KOOS subscales was considered clinically relevant.[21,22] We calculated that a sample of 180 patients (60 per group) was needed to detect this MIC with 80% power using a two-sided test and 5% significance level.[23] To account for loss to follow-up, our target enrolment was 216 patients (72 per group). A per-protocol analysis was performed, including only patients who completed the 2-year follow-up.

Descriptive statistics included frequencies or means with ranges, and group comparisons were performed for the following outcomes: KOOS, OKS, EQ-5D-5L, EQ-VAS, ROM, satisfaction, KL grade and "willingness to undergo the same operation again". Data were checked for normality using the Kolmogorov Smirnov test. We used independent samples t-tests, Mann-Whitney and Kruskal Wallis test to assess group differences. P-values <0.05 were considered statistically significant; all tests were 2-sided. Data were analysed using SPSS v24.0 software (IBM Corp, Armonk, NY).

Results

The three groups had similar baseline characteristics regarding age, gender, and KL grade, although the PS group had higher BMI (Table 3). About half the patients were women (54%), and most (98%) were non-smokers. Mean operative times in the CR- and AS groups were 79 and 82 minutes, respectively, significantly shorter than the 92 minutes for the PS group (p<0.001). The average hospital stay was approximately three days in all three groups (p=0.88) (Table 3).

Clinical outcomes

The primary outcome ($KOOS_5$) was not significantly different between the three groups preoperatively, and we found no difference between the groups at 2 years (Table 4). In addition, there were no statistically significant differences in the KOOS subscales between baseline and the 2-year follow-up. Furthermore, there were no significant group differences on the KOOS subscales, OKS, EQ-5D-index and EQ-VAS at 2 years (Figure 3, Table 4). All three groups reported more than 90% satisfaction rates, and there were no disparities among them (Table 5). Additionally, 92% of the CR group, 75% of the AS group and 90% of the PS group were willing to undergo the same operation again. There was no group difference in mean postoperative knee extension angle (p>.99), although mean knee flexion angle was significantly better in the PS group compared to the CR and AS groups (129° vs 122°, p<0.001) (Table 6).

Complications

One patient in the CR group, four in the AS group and five in the PS group failed to achieve flexion greater than 90° by six weeks and required manipulation under anaesthesia. Further, in the AS group, one patient was treated for prosthetic joint infection (PJI), one was reoperated due to instability, and one had a perioperative injury to the MCL. In the PS group, one patient was reoperated for a PJI, and another was treated for a lung embolism. There were no significant group differences in complications.

Discussion

In this RCT, we compared the clinical outcomes of patients who underwent TKA using three different implant designs from the same primary total knee system. Of particular interest was to explore whether a more conforming tibial insert (AS) was clinically as effective as a post-cam design (PS) in replacing a deficient PCL. A panel of validated PROMs assessing various outcomes was administered. After two years, we observed no significant differences in any of the PROMs between patients randomly assigned to receive CR, AS, or PS TKA. We also found no significant group differences in KOOS change scores from baseline to the 2-year follow-up. All three implants performed well with good clinical and functional outcomes, and more than 90% of the patients were satisfied with their TKA. Our findings are similar to those reported in other studies showing no significant clinical differences between PCL-retaining and PCL-sacrificing designs.[12,24] However, previous trials had fewer participants than ours or mostly compared only two designs. Raja et al.[25] showed in a meta-analysis that AS TKA had similar functional outcomes to PS TKA but was associated with less femoral rollback and increased sagittal laxity. Few studies have compared more than two TKA designs, and they had small sample sizes, short-term follow-ups, insufficient statistical power, or significant dropout rates.[14,15]

Prosthesis survival is a common TKA outcome for comparing the performance of prosthesis brands or design subsets. In a registry study comparing the long-term survivorship of one manufacturer's CR, AS, and PS designs, Dalton et al.[15] found that AS and CR TKAs had comparable revision rates. However, the AS design resulted in a lower revision rate than the PS design. The authors proposed that this difference might be due to PS designs being selectively used in more complex TKA cases at higher risk of revision.

Our research findings indicate that the box cut and cementing of the femoral component required for PS cases resulted in longer operating times. This result is consistent with other studies.[12] Additionally, prior research has shown better flexion with a PS design. A meta-analysis of 1,114 patients revealed a significant difference in knee flexion in favour of the PS design.[26] In PS implants, the post-cam mechanism creates a posterior translation of the femur on the tibial plateau during flexion, increasing the rollback movement and, thus, the degree of flexion.[11] Studies have shown that greater ROM can improve functional scores.[27] However, many daily activities, such as climbing stairs, only require knee flexion of about 90°. Nevertheless, whether the flexion difference (7º) observed in our study is noticeable or clinically significant for patients remains uncertain. According to the study conducted by Hancock et al.,[28] using a long-arm goniometer requires a minimum difference of 10º between measurements to ensure a valid difference. Further, our flexion and extension data were passive, and the force applied by the physiotherapists varied. In contrast, Hancock et al.'s data were active and subject-controlled, which may make them more reliable. The long-arm goniometer, however, had high inter-rater and intra-rater reliabilities.

A prerequisite for CR TKA is a functioning PCL. In the case of a tight PCL, some surgeons suggest balancing in terms of partially releasing the ligament,[29] which may increase the risk of later insufficiency. We believe it is essential to maintain an intact PCL during CR TKA, and no patient in the CR group was revised because of anteroposterior instability. Wood et al.[30] showed a risk reduction of 50% for PCL insufficiency in a cadaver study where the same method to protect the PCL was employed as in the present study.

A cause of revision knee arthroplasty is late rupture of the PCL.[31] An isolated tibial insert exchange (ITIE) is an option in revising a sagittally unstable CR knee prosthesis. This alternative can be appealing as it reduces surgical complexity, preserves bone stock, and may accelerate rehabilitation compared to a complete prosthesis revision. In the absence of infection, ITIE has been undertaken in patients for various indications, such as polyethylene wear, instability, stiffness, and effusion.[32] A recent study by Tetreault et al.[32] showed that ITIE yielded lower ten-year survival when performed for instability than isolated insert wear. ITIE is the second most common TKA revision procedure, accounting for almost 20% of cases in the US[33], but only a few extensive studies have analyzed its outcome. Therefore, patient selection for this procedure should be carefully made for indications other than early PJI.

There are situations where a CR TKA is challenging to perform, and the surgeon should therefore be capable of converting to an AS or PS design. For example, PCL insufficiency, coronal malalignment and difficulty balancing often necessitate PCL resection.[34] Laskin[35] reported that CR TKA performed in patients with a coronal deformity of >15° was associated with an increased risk of revision and pain. In addition, conversion from a CR- to a PS design is reported to increase in patients with flexion contracture >20°.[34] Prior knee injuries or surgery may reduce the quality of the remaining ligaments,[34] so accurate soft tissue balancing would be easier with a sacrificed PCL in these patients.

TKA seeks to restore native knee kinematics, and knee implant designs evolve as our understanding of knee kinematics continues to develop. Intact cruciate ligaments are a prerequisite for normal knee kinematics, which change as soon as one or both cruciate ligaments are removed. A recent report from a subset of patients in the present study showed that CR and AS designs failed to restore physiological joint kinematics during a step-up movement, in contrast to the PS design in patients with a well-functioning TKA.[11] However, it is unresolved whether this has clinical significance.

The main strengths of our study were the prospective randomized controlled design, the large sample and high follow-up rate of 96% at two years. In addition, the inclusion and exclusion criteria were strict, and the surgical protocol for the initial preservation of the PCL was standardized. Also, patients and the physiotherapists performing the functional testing were blinded to the patients' TKA design.

Our trial had some limitations. Only a small proportion of patients met the rigorous eligibility standards, and we used a TKA design from a single manufacturer, which helped ensure we had a uniform and consistent group, but may limit the generalizability of our findings to the broader TKA population. The follow-up period was only two years, so the clinical results may not fully represent longer-term outcomes. Several surgeons performed the TKAs, so there may have been minor differences in surgical technique.
Our trial may be underpowered, as using MIC values to calculate sample size is not recommended,[36] despite the KOOS user guide indicating that it is feasible to do so. We did not conduct a post-operative radiographic assessment, so we cannot rule out the potential impact of differences in alignment on the study outcomes. Lastly, using a hybrid TKA in the AS and CR groups may introduce a bias and limit the generalizability of the results. However, the hybrid procedure has been the leading procedure at our hospital for several years and the Norwegian joint registry indicates better survival of hybrid TKAs than cemented ones.[37]

Conclusion

We have performed a blinded RCT comparing the CR, AS and PS designs of the same primary TKA system and found no difference in PROMs after two years. More than 90% of patients in all three groups reported being satisfied with their knees. The PS design performed better in terms of flexion compared to the other designs. Nonetheless, the difference may not be large enough to have clinical relevance. All three designs are viable options for primary TKA in uncomplicated OA knees.

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Table 1. Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
Primary osteoarthritis	Prior ligament surgery
Varus or valgus deformity ≤15º	Previous osteotomy
Intact posterior cruciate ligament	Flexion < 90°
Age 45-77 years	Flexion contracture > 10°
Body mass index < 35 kg/m^2	Live >2 hours away from the hospital
ASA classification I - III	Peripheral neuropathy
	Malignancy
	Not fluent in Norwegian
	Rheumatic disease

ASA: American Society of Anaesthesiologists

Table 2. Description of surgical technique

- All surgeries included a medial parapatellar arthrotomy, femur-first and mechanical alignment technique.
- The goal for coronal alignment was 5° valgus (anatomic axis) and 0° mechanical axis.
- The tibia cut was neutral to the mechanical axis in the coronal plane and with 3° of posterior slope using an intramedullary guide.
- The bone resection and the insert slope defined the composite posterior slope. CR and PS designs had a composite slope of 7°, while AS's slope was 6°.
- The PCL was carefully protected using a Y-shaped retractor and preserving a bony island around the PCL tibial footprint.[30]
- After tibial plateau resection, PCL integrity was evaluated visually and by palpation.
- The PCL was assessed again during knee ligament balancing and deemed intact by a negative posterior drawer test and the tibiofemoral contact point located at the middle of the tibial bearing.
- Following randomization, the PCL was resected in the AS and PS groups.
- The patella was resurfaced in all patients with a Genesis inset biconvex button (Smith & Nephew, Inc, Memphis, TN, USA).
- The femoral component was uncemented in the CR and AS groups, and the patellar- and tibial components were cemented using Palacos R+G cement (Heraeus, Hanau, Germany). In the PS group, all components were cemented.
- No wound drain nor tourniquet was used.
- First-generation cephalosporin (2 g x 4) was administered as antibiotic prophylaxis. Patients allergic to penicillin received clindamycin (600 mg x 3).
- All patients received intravenous tranexamic acid (10 mg/kg) twice.
- A local infiltration analgesia mixture (ropivacaine, ketorolac, and epinephrine) was injected during surgery.
- Low molecular weight heparin (LMWH) was given for two weeks postoperatively as prophylaxis against thrombosis.
- Patients on aspirin (75 mg daily) continued their medication and were not given LMWH.
- All patients were treated postoperatively using the same multimodal analgesia and mobilization protocols.
- Patients were mobilized on the day of surgery and received physiotherapy from a therapist blinded to the prosthesis design.

Table 3. Baseline characteristics and surgical parameters between the three groups

Measure	CR (n=72)	AS (n=72)	PS (n=72)	P-value
Age at surgery, mean (range)***	69 (56-77)	68 (53-77)	67 (47-77)	0.47
Female sex, n (%)	38 (53)	41 (57)	38 (53)	
BMI, mean (range)†	28 (19-35)	28 (19-35)	30 (22-35)	0.01
Kellgren-Lawrence grade 1-4				
mean (SD)***	3.3 (0.5)	3.4 (0.5)	3.2 (0.4)	0.08
Grade 1, n (%)	0	0	0	
Grade 2, n (%)	2 (3)	0	1 (2)	
Grade 3, n (%)	48 (67)	44 (61)	55 (76)	
Grade 4, n (%)	22 (30)	28 (39)	16 (22)	
Comorbidities				
Atrial fibrillation, n (%)	8 (11)	3 (4)	5 (7)	
Heart attack, n (%)	4 (6)	1 (1)	4 (6)	
Stroke, n (%)	6 (8)	2 (3)	2 (3)	
COPD, n (%)	3 (4)	2 (3)	3 (4)	
Diabetes type 2, n (%)	4 (6)	3 (4)	4 (6)	
Hypertension, n (%)	35 (49)	36 (50)	32 (44)	
Smokers, n (%)	1 (1)	0	3 (4)	
ASA, mean (SD)***	2.06 (0.37)	1.96 (0.52)	2.00 (0.44)	0.43
Operation time, minutes, mean (range)***	79 (60-112)	82 (62-146)	92 (67-147)	<0.001
LOS in days, mean (range)***	3.03 (1-7)	2.88 (1-5)	2.85 (1-6)	0.88
Length of follow-up, days, mean (range)***	756 (719-915)	749 (723-929)	764 (722-1182)	0.31

CR, cruciate retaining; AS, anterior stabilized; PS, posterior stabilized; BMI, Body Mass Index; SD, standard deviation; LOS, Length of Stay; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists

*** Kruskal Wallis test

† Mann-Whitney test

Table 4. Patient-reported outcome measures preoperatively and at two-year follow-up.

Measure	Preoperative				Follow-up (2 years)			
	CR (n=72)	AS (n=72)	PS (n=72)	P-value	CR (n=72)	AS (n=66)	PS (n=70)	P-value
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)		Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	
$KOOS_5$ **	39 (36, 42)	40 (37, 42)	36 (34, 39)	0.12	76 (72, 80)	76 (72, 80)	76 (72, 80)	0.96
KOOS Pain***	46 (42, 50)	46 (43, 49)	42 (38, 45)	0.16	84 (81, 88)	85 (81, 89)	84 (80, 88)	0.72
KOOS Symptoms***	55 (51, 59)	56 (53, 60)	51 (48, 55)	0.23	84 (80, 87)	83 (80, 87)	82 (79, 85)	0.72
KOOS ADL***	52 (48, 56)	54 (51, 58)	49 (46, 53)	0.18	84 (80, 88)	87 (84, 91)	85 (81,88)	0.37
KOOS Sport&Rec***	17 (14, 20)	17 (13, 20)	15 (12, 18)	0.72	52 (46, 58)	51 (45, 57)	53 (47, 59)	0.89
KOOS QoL***	26 (23, 30)	26 (23, 29)	23 (20, 26)	0.34	74 (69, 79)	75 (70, 80)	75 (70, 80)	0.83
Change from baseline								
KOOS Pain***					39 (34, 43)	39 (34, 44)	42 (38, 47)	0.43
KOOS Symptoms***					29 (24, 33)	27 (22, 32)	30 (26, 35)	0.57
KOOS ADL***					32 (28, 37)	33 (28, 38)	35 (30, 39)	0.63
KOOS Sport&Rec***					35 (28, 42)	34 (28, 40)	37 (31, 43)	0.74
KOOS QoL***					47 (42, 53)	48 (42, 55)	51 (46, 57)	0.52
Oxford Knee Score (0-48) **	24 (23, 26)	25 (24, 27)	23 (22, 25)	0.15	41 (39, 42)	41 (40, 43)	41 (39, 42)	0.56
EQ5D-5L-index***	0.59 (0.54,0.64)	0.64 (0.59,0.69)	0.62 (0.58,0.67)	0.21	0.87 (0.83,0.91)	0.90 (0.87,0.93)	0.91 (0.88,0.93)	0.49
EQ-VAS (0-100) ***	62 (57, 68)	67 (61, 72)	64 (59, 69)	0.39	70 (63, 77)	67 (60, 75)	62 (55, 69)	0.11
Patients not achieving MIC for KOOS, n (%)					3 (4)	8 (12)	3 (4)	

CR, Cruciate-Retaining; AS, Anterior Stabilized; PS, Posterior Stabilized; CI, confidence interval; KOOS, Knee injury and Osteoarthritis Outcome Score; $KOOS_5$, Average score of the five KOOS subscales; QoL; Quality of Life; ADL, Activities of Daily Living; EQ-5L-index, European Quality of Life 5 Dimensions 5 Level Version index score; EQ-VAS, Euro Qol-Visual Analog Scale; MIC, minimal important change

** Analysis of variance

*** Kruskal Wallis test

Table 5. Percentage of patients in the three groups who were moderately to very satisfied with their TKA at one-year follow-up (defined as a rating ≥3 on a 1-5 Likert scale.

	CR (n=72)	AS (n=69)	PS (n=70)	P-value
Percentage of satisfied patients***	99	91	99	0.91

TKA, total knee arthroplasty; CR, cruciate-retaining; AS, anterior-stabilized; PS, posterior-stabilized
*** Kruskal Wallis test

Table 6. Measurements of flexion and extension preoperative and two years after total knee arthroplasty for the three implant designs.

Range of motion measure	Preoperative			Follow-up (2 years)		
	CR (n=72)	AS (n=72)	PS (n=72)	CR (n=72)	AS (n=66)	PS (n=70)
	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)
Flexion in degrees†	126 (124, 128)	127 (124, 129)	125 (123, 127)	122 (121, 124)	122 (120, 124)	129 (127, 131)*
Extension in degrees†	-5 (-6, -4)	-5 (-6, -4)	-5 (-6, -4)	-1 (-1, -1)	-1 (-1, 0)	0 (-1, 0)

CR, cruciate-retaining; AS, anterior-stabilized; PS, posterior-stabilized; CI, confidence interval
*Significantly more flexion than cruciate-retaining and anterior-stabilized designs ($p < 0.001$ for both).
†Mann-Whitney test

Fig. 1. CONSORT flow diagram depicting participant flow throughout the clinical trial, from eligibility assessment through enrolment, intervention, and completion of follow-up.

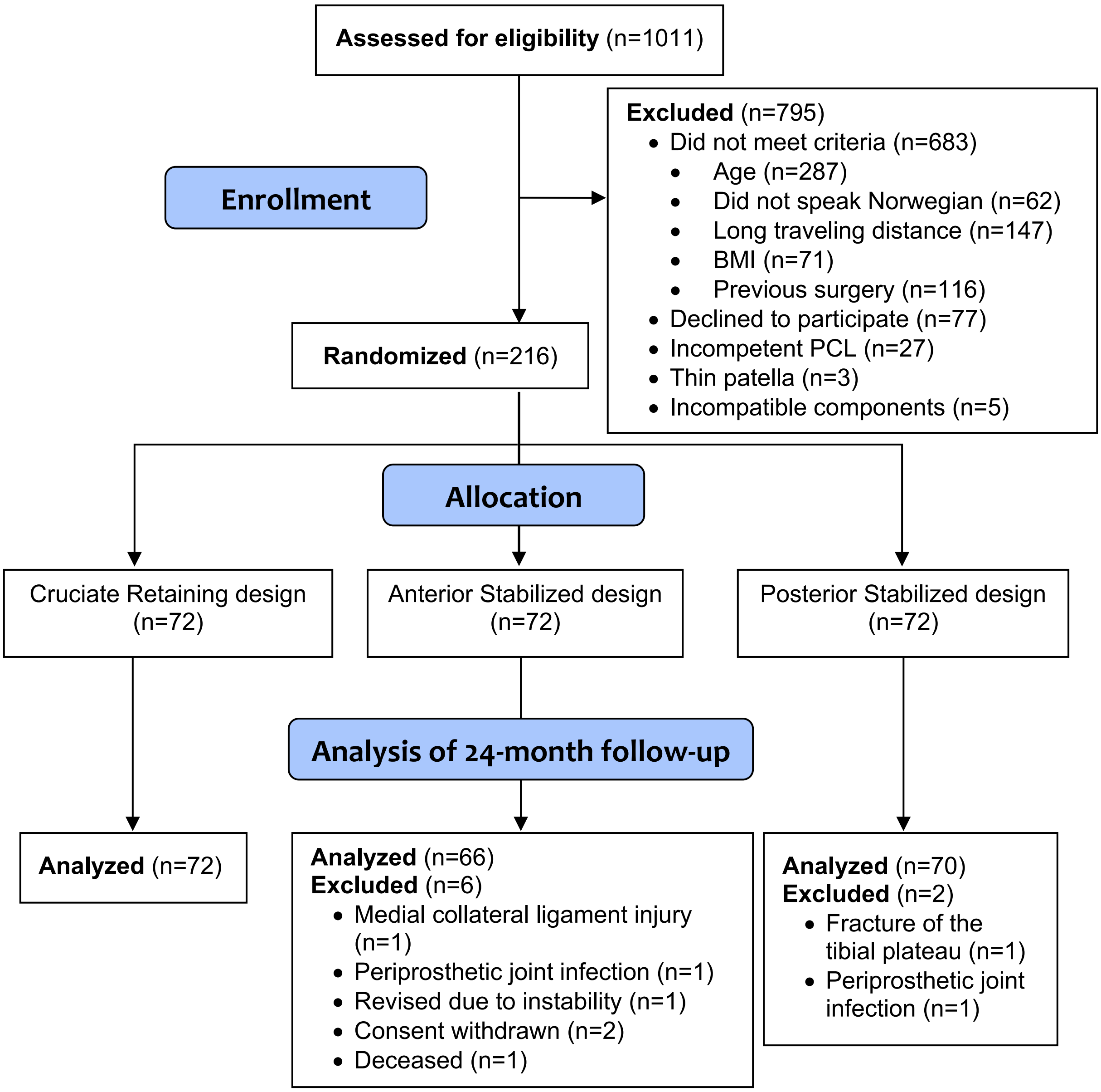
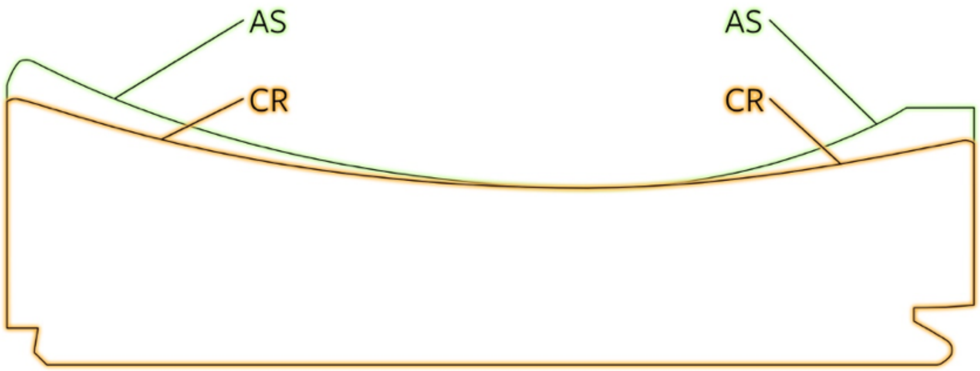
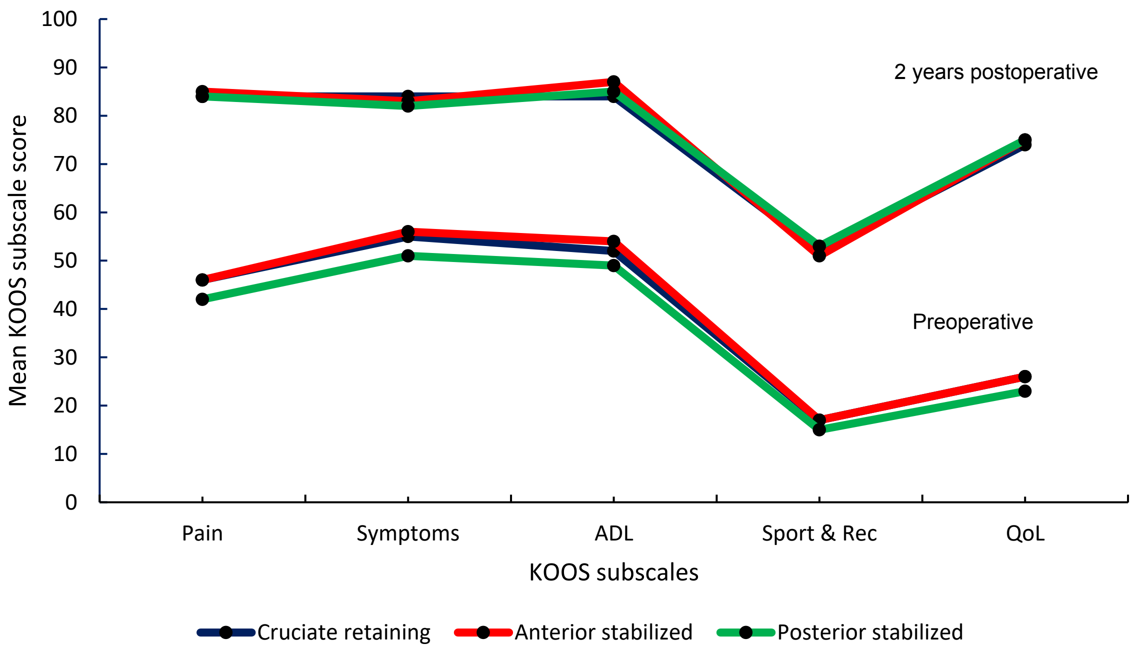


Fig. 2. Schematic drawing of the AS- and CR inserts



AS, anterior stabilized; CR, cruciate retaining

Fig. 3. KOOS profiles before and two years after TKA for all three designs. Mean KOOS subscale scores at the preoperative and two-year assessments after TKA



KOOS, Knee injury and Osteoarthritis Outcome Score; TKA, total knee arthroplasty; ADL, activities of daily living; QoL, quality of life