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UNIVERSITY OF TURKU

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To my godmother Merja

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ABSTRACT

Even though total knee arthroplasty has been a highly successful operation, as many as 20% of patients are somewhat dissatisfied with their prosthesis. In at least 25% of patients, the pattern of osteoarthritis is isolated medial, which could be treated with medial unicompartmental rather than total knee arthroplasty. Medial unicompartmental arthroplasty has been associated with a shorter hospital stay, faster recovery time, lower cost, subjective preference for a more normal-feeling knee, and reduced perioperative morbidity and mortality compared with total knee arthroplasty. However, its survival has been inferior to that of total knee arthroplasty in national registries.

The primary objective of this study was to evaluate the influence of the preoperative degree of knee osteoarthritis on the risk of reoperation; to determine the short-term survivorship of cementless mobile-bearing unicompartmental arthroplasty and to compare that of cemented mobile-bearing unicompartmental arthroplasty and total knee arthroplasty; to evaluate the clinical effectiveness of medial unicompartmental knee arthroplasty versus total knee arthroplasty in a randomized, controlled, assessor-blind comparison.

We found that in the preoperative weight-bearing radiographs, the degree of knee osteoarthritis should be severe, to diminish the revision rate. In the short term, use of a cementless unicompartmental device is associated with increased survivorship over the use of a cemented device and the functional outcome scores favored medial unicompartmental arthroplasty at 2 months and 1-year follow-up but the primary outcome were comparable for medial unicompartmental arthroplasty and total knee arthroplasty at 2 years.

The present study supports the use of medial unicompartmental arthroplasty in patients with anteromedial arthritis. The revision rate can be reduced by following the original indications and using cementless mobile-bearing components. Medial unicompartmental arthroplasty provides a comparable outcome for medial unicompartmental arthroplasty and total knee arthroplasty at 2 years and faster postoperative recovery than total knee arthroplasty. However, the overall survivorship of mobile-bearing unicompartmental knee arthroplasty is inferior to that of cemented total knee arthroplasty and must be taken into consideration.

KEYWORDS: unicompartmental knee arthroplasty, total knee arthroplasty, knee osteoarthritis

TURUN YLIOPISTO
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TIIVISTELMÄ

Vaikka kokotekonivelleikkaus on erittäin hyvä hoitomuoto, niin jopa 20 % potilaista on leikkauksen jälkeen osittain tyytymättömiä lopputulokseen. Vähintään 25 %:lla potilaista polven nivelrikko on rajoittunut polven sisäreunalle ja osatekonivel soveltuu näiden potilaiden hoitoon. Osatekonivelen etuina kokotekonivelleikkaukseen verrattuna ovat muun muassa lyhyempi sairaalahoitoaika, nopeampi toipuminen toimenpiteestä, edullisempi hoidon hinta, sekä pienempi leikkauksen jälkeinen sairastuvuus ja kuolleisuus. Lisäksi leikattu polvi voi myös tuntua enemmän omalta polvelta. Siitä huolimatta sen uusintaleikkausriski on ollut merkittävästi korkeampi kaikissa kansallisissa tekonivelrekistereissä.

Tämän tutkimuksen tavoitteena oli: 1) selvittää leikkausta edeltävän nivelrikon vaikeuden vaikutusta leikkauksen jälkeiseen uusintaleikkausriskiin. 2) Selvittää sementillisen ja sementittömän osatekonivelen uusintaleikkausriskiä lyhyellä aikavälillä verrattuna polven kokotekoniveleen. 3) Selvittää polven osatekonivelleikkauksen vaikuttavuutta verrattuna polven kokotekonivelleikkaukseen kontrolloidussa, kaksoissokkoutetussa vertailututkimuksessa.

Tutkimuksen johtopäätöksenä voidaan todeta, että polven nivelrikon aste seisten otetussa kuormitusröntgenkuvauksessa tulee olla pitkälle edennyt, jotta uusintaleikkausmäärä vähenee. Polven sementittömän osatekonivelen pysyvyys oli viiden vuoden seurannassa parempi kuin sementillisen ja polven osatekonivelleikkauksesta toipuminen tapahtui nopeammin verrattuna kokotekonivelleikkaukseen.

Tämän tutkimuksen perusteella polven osatekonivelen uusintaleikkausmääriä voidaan vähentää pitäytymällä alkuperäisissä indikaatioissa, välttämällä lievän nivelrikon hoitoa tekonivelleikkauksella ja käyttämällä sementitöntä osatekoniveltä. Polven osatekonivelleikkaus tuottaa potilaalle nopeamman toipumisen ja tulos kahden vuoden kohdalla on verrannollinen kokotekonivelleikkauksen tulokseen. Tämä tutkimus tukee polven osatekonivelen käyttöä polvinivelen sisäpuolen nivelrikon hoitona. On kuitenkin huomioitava, että polven osatekonivelen pysyvyys on sementöityä kokotekoniveltä huonompi.

AVAINSANAT: Polven osatekonivel, polven kokotekonivel, polven nivelrikko

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Abbreviations

AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry
ASA	American Society of Anesthesiologists classification
BMI	Body mass index
CI	Confidence interval
FAR	Finnish Arthroplasty Register
HTO	High tibial osteotomy
KL	Kellgren-Lawrence classification
KOOS	Knee injury and Osteoarthritis Outcome Score
KOOS4	Knee injury and Osteoarthritis Outcome Score, quality of life
KSS	Knee Society Score
NJR	National Joint Registry of England and Wales
NZJR	New-Zealand Joint Registry
OA	Osteoarthritis
OKS	Oxford Knee Score
PROM	Patient-reported outcome measure
RCT	Randomized controlled trial
ROM	Range of Motion
TKA	Total knee arthroplasty
UKA	Unicompartmental knee arthroplasty

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Knifsund J, Hatakka J, Keemu H, Mäkelä K, Koivisto M, Niinimäki T. Unicompartmental Knee Arthroplasties are Performed on the Patients with Radiologically Too Mild Osteoarthritis. *Scandinavian Journal of Surgery*. 2017 Dec;106(4):338–341.

II Knifsund J, Reito A, Haapakoski J, Niinimäki T, Eskelinen A, Leskinen J, Puhto AP, Kettunen J, Manninen M, Mäkelä KT. Short-term survival of cementless Oxford unicondylar knee arthroplasty based on the Finnish Arthroplasty Register. The Knee. 2019 Jun;26(3):768–773.

III Knifsund J, Niinimaki T, Nurmi H, Toom A, Keemu H, Laaksonen I, Seppänen M, Liukas A, Pamilo K, Vahlberg T, Äärimaa V, Mäkelä KT. Functional results of total-knee arthroplasty versus medial unicompartmental arthroplasty: two-year results of a randomised, assessor-blinded multicentre trial. *BMJ Open.* 2021 Jun 23;11(6):e046731

1 Introduction

Knee osteoarthritis (OA) is a common joint disease which may cause severe pain and lead to a reduced quality of life. The prevalence of symptomatic OA in people aged 60 years and above is 10% for men and 18% for women (Bedson et al., 2005). The incidence of knee osteoarthritis in people over 30 years and above is 6.1% for men and 8.0% for women in Finland (Arokoski, et al, 2007)Total knee arthroplasty (TKA) has for decades been the gold standard treatment for symptomatic and painful severe OA of the knee when conservative treatment is insufficient (Carr et al., 2012) (Skou et al., 2015). In 2014, over 680,000 primary TKAs were performed in the United States alone, and the number of arthroplasties is increasing especially among younger patients (Singh et al., 2019) (Leskinen et al., 2012). Even though TKA has been a highly successful operation, as many as 20% of patients are somewhat dissatisfied with their implant (Carr et al., 2012) (Bourne et al., 2010).

In at least 25% of patients, the pattern of knee OA is isolated medial, which could be treated with medial unicompartmental knee arthroplasty (UKA) instead of TKA (Ackroyd, 2003). It has been suggested that up to 48% of medial knee OAs are eligible for UKA (Willis-Owen et al., 2009). Isolated medial OA is typically anteromedial, the knee having functional cruciate ligaments and healthy lateral compartment cartilage. This can be confirmed with weight-bearing radiographs of the knee in 20 degrees of flexion combined with clinical examination (Goodfellow J, O'Connor J, 2006). Medial unicompartmental arthroplasty has been associated with a shorter hospital stay, faster recovery time, lower cost, subjective preference for a more normal-feeling knee, and reduced perioperative morbidity and mortality compared with TKA (Brown et al., 2012) (Lombardi et al., 2009) (Beard DJ et al. 2019).

Surgeon's low experience and low operative volume have been found to be associated with the UKA failure rate (Badawy et al., 2014) (Kim et al., 2014). The higher revision rate of UKA compared with TKA may also be associated with the severity of the preoperative OA. UKA is a tempting procedure for patients with a mild or moderate degree of OA, which has been found to be associated with increased risk of reoperation and dissatisfaction following knee arthroplasty compared with severe OA (Pandit et al., 2015) (Niinimäki et al., 2014). Degenerative changes of the knee (narrowing of the joint space, partial thickness, loss of cartilage, and degenerative meniscus rupture) are common findings in middle-aged and elderly people, even if the knee is asymptomatic. Therefore, in symptomatic patients, degenerative changes are not necessarily the cause of the pain.

Although several studies have reported good long-term results in single-center series for medial UKA, its survival has been inferior to that of TKA in national arthroplasty registries (Niinimäki et al., 2014) (AOANJRR, 2017) (NJR, 2016) (Costa et al., 2011) (Newman et al., 1998) (Newman et al., 2009) (Sun & Jia, 2012) (Kulshrestha et al., 2017). Therefore, whether patients should undergo UKA at all is still a matter of debate.

Cementation in UKA may be challenging, and cementation errors may lead to loosening, pain, and excess wear (Hooper et al., 2015). Cementless UKA was introduced to secure long-term fixation and consequently reduce the risk of revision, but experience with cementless fixation in UKA has been limited. Several recently published reports claim that cementless UKA has comparable clinical and radiological outcomes to those of cemented UKA or at least some advantages. (Hooper et al., 2015) (Kendrick et al., 2015) (Liddle et al., 2013) (Pandit et al., 2009) (Pandit et al., 2013). The most common cemented UKA design is the Oxford Partial Knee (Zimmer Biomet, UK) with a congruent mobile bearing to minimize wear (AOANJRR, 2017) (NJR, 2016). A cementless version of the Oxford UKA with a porous titanium and calcium hydroxyapatite coating was first implanted in June 2004 and came onto the market in 2008. It is currently the leading UKA brand in Finland (Hooper et al., 2015) (Finnish Arthroplasty Register, n.d.). According to the New Zealand Registry data, the implant survival of the cementless Oxford is higher than that of the cemented Oxford 3 (New Zealand Orthopedic Association Joint Registry, 2017). However, comparison of implant survivorship between cementless and cemented Oxford UKAs is not available in other major arthroplasty register yearbooks.

To our knowledge, there are five (six if counting both the 5- and 15-year results from the same trial by Newman et al.) previously published randomized studies comparing medial UKA with TKA (Beard DJ et al. 2019) (Costa et al., 2011) (Newman et al., 1998) (Newman et al., 2009) (Sun & Jia, 2012) (Kulshrestha et al., 2017). The largest of these is the TOPKAT study of 528 patients (Beard DJ et al. 2019), which reported a similar patient-reported outcome and lower cost at 5 years for medial UKA compared with TKA. However, like all other earlier randomized studies, the TOPKAT study was not assessor-blinded and patient expectations might have influenced the results. The use of selected patient-reported outcome measures (PROM) in these studies are also challenging because of the ceiling effect related to the use of all PROMs.

The primary objective of this thesis is to assess the indications, survival and clinical effectiveness of medial UKA versus TKA in patients with anteromedial OA of the knee in retrospective analysis, register-based analysis and finally a randomized, controlled, assessor-blind comparison.

2 Review of the Literature

2.1 Knee osteoarthritis

2.1.1 Epidemiology and pathophysiology

Knee OA is the most prevalent joint disease and source of disability in the United States (Murray et al., 2013) and other developed nations (Vos et al., 2012). The Global Burden of Disease Study 2010 reported that knee OA affects 3.6% of the global population across all ages (Vos et al., 2012). Framingham reported the prevalence of symptomatic knee OA to be 7% among men and 11% among women (Felson et al., 1987). The Johnston County cohort reported prevalence rates of 17% for symptomatic knee OA (Chen et al., 2007).

OA progresses with age but is an independent process. Substantial evidence indicates that knee OA is possibly caused by the breakdown of joint tissues from mechanical loading (Felson, 2013) combined with inflammation (Robinson et al., 2016), but the deeper underlying causes of its high prevalence is unclear. A combination of changes—including the capacity of joint tissues to adapt to biomechanical insults, biological changes such as cellular senescence, poorer adjustment to biomechanical challenges due to sarcopenia, an age-related condition characterized by loss of skeletal muscle mass and function, and increased bone turnover—are likely contributing factors (Johnson & Hunter, 2014).

Females are associated with a higher prevalence and severity of OA and are more often affected by hand, foot and knee OA than men (Srikanth et al., 2005). OA appears to be strongly genetically determined, with genetic factors accounting for up to 40% of knee OA (Spector & MacGregor, 2004).

Obesity is a global health challenge. A high body-mass index (BMI) is significantly associated with OA risk not only in the knee, but also in other joints. A 5-unit increase in BMI was associated with an 35% increased risk of knee OA (Jiang et al., 2012). Obesity is also associated with hand OA, conferring the possibility that obesity may also provide some metabolic and inflammatory systemic effects and that increased mechanical load is not the only factor to launch OA progression (Carman et al., 1994).

Sociodemographic factors, such as low education level and low household income, also seem to be associated with the risk of radiographic knee OA (Hong et al., 2020). However, occupation is not associated with radiographic knee OA after taking into account for age, gender, area of residence, education level, household income, and obesity. (Hong et al., 2020). Population-based surveys have shown that men and women in rural environments have roughly twice the prevalence of knee OA compared with their urban counterparts (Fransen et al., 2011). In elderly Japanese population-based cohorts, residents of mountainous areas have shown a greater risk of radiographic knee OA compared to urban residents, indicating the involvement of environmental factors such as nutrition or occupation (e.g., farming, forestry), which demand physical activity and repetitive use of the knee joints (Muraki et al., 2009).

Total meniscectomy is related to a higher risk of secondary knee OA. In a prospective longitudinal study by Jorgensen et al. of 147 athletes, radiographic deterioration started after the 4.5-year review in 49% of the patients and was more frequent after lateral than medial meniscectomy (Jorgensen et al., 1987). At highest risk are older patients, those with abnormal leg alignment, and those who have undergone lateral versus medial meniscectomy (Allen et al., 1984).

Knee injuries are also related to increased risk of secondary knee OA. The reported rates of OA after an anterior cruciate ligament (ACL) injury vary between 10% and 90% at 10–20 years after the ACL injury in different publications. Stating a mean OA rate is difficult because of the great variability of the reported results, but an overall long-term mean of more than 50% may be suggested (Lohmander et al., 2007).

Table 1. Risk factor for knee osteoarthritis. The level of evidence is graded from A to D, according to Finnish current care guideline. A represents best scientific research evidence. (Treatment of knee and hip osteoarthritis. Finnish Current Care Guideline, 2018)

Risk Factor	Level of Evidence
Female gender	A
Age	A
Obesity	A
Previous knee injury	A
Heavy sports	B
Heavy manual labour	B
Previous meniscectomy	C
Genetics	B
Varus- or valgus malalignement	B

OA can be diagnosed radiologically and clinically. Weight-bearing radiographs are often used as the standard for defining knee OA (Figure 1). Kellgren-Lawrence (KL) grading is one of the systems used for defining the severity and presence of OA (Kellgren and Lawrence, 1957). Severity is graded on a scale of 0–4 with >2 defining radiographic OA. For the knee it can only be used to define tibiofemoral, not patellofemoral, OA.

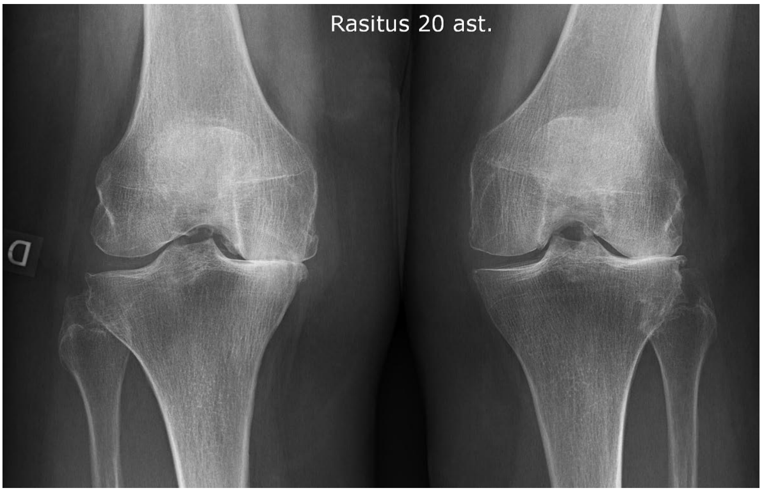


Figure 1. Radiograph showing OA of the knee.

2.1.2 Conservative treatment options

Physiotherapy exercise, patient education and weight loss for obese patients are first-line treatments recommended for knee OA (Skou & Roos, 2019). Existing studies include a number of exercise programs that are not detailed enough to be incorporated into clinical practice (Bartholdy et al., 2019). Comparing the programs grouped into the three subgroups of aerobic, resistance, and performance exercise show all three to have similar effects (Juhl et al., 2014). It does not mean that all patients should be offered the same exercise regimen; individualization could well increase the effects of treatment (Skou & Roos, 2019). Juhl et al. evaluated the impact of exercise type and dose in knee OA in a systematic review and meta-regression analysis of randomized controlled trials. 48 RCTs were included in the study. They concluded that optimal exercise programs for knee OA should have focus on improving aerobic capacity, quadriceps muscle strength, or lower extremity performance. Program should be supervised and carried out three times per week and such programs have similar effect regardless of patient characteristics (Juhl et al., 2014).

Passive treatments such as massage, neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, ultrasound, and laser cannot be recommended as part of the treatment, based on the absence of high-quality supportive evidence. Knee orthoses are one alternative for conservative treatment but cannot be recommended in the first-line conservative treatment protocol due to lack of good evidence (Bannuru et al., 2019).

Non-steroidal anti-inflammatory drugs (NSAIDs) are recommended for use as part of conservative treatment in knee OA patients with no comorbidities. According to the latest guidelines of the Osteoarthritis Research Society International (OARSI), paracetamol has little to no efficacy in individuals with OA and includes the possible risk of hepatotoxicity. Additionally, the Panel strongly recommends against the use of either oral or transdermal opioids in individuals with OA, largely in response to recent international concerns about the devastating potential for chemical dependency posed by opioid medications (Bannuru et al., 2019). Intra-articular corticosteroid may provide short term pain relief, whereas Intra-articular hyaluronic acid may have beneficial effects on pain at and beyond 12 weeks of treatment and a more favorable long-term safety profile than repeated intra-articular corticosteroids (Bannuru et al., 2019).

For weight loss interventions in patients who are overweight or obese, evidence is available for symptomatic knee osteoarthritis, with an effect size of 0.30 (SMD -0.30 CI -0.52 to -0.08) to the function but the effect to the pain was not significant (Hall et al., 2019). However, combination of dietary weight management and exercise yield better effects on pain and function than either diet or exercise alone (Hunter & Bierma-Zeinstra, 2019).

2.1.3 Operative treatment options

Total knee arthroplasty is the gold standard for treatment of symptomatic OA of the knee (Figure 2). In addition, UKA can be used to treat OA when it is confined to a single compartment (Ackroyd, 2003). There are several medial UKAs on the market, which fall into two groups: those with a fixed-bearing or those with a mobile-bearing device (Figure 3). Partial knee replacement can also be used for lateral or patellofemoral OA, which is not included in this study.

Medial UKA may have some advantages over TKA (e.g. faster recovery, reduced perioperative morbidity and mortality, subjective preference for a more normal-feeling knee, lower cost, and more rapid return to work and sport) (Beard et al., 2019)(Lombardi et al., 2009)(Brown et al., 2012).

Arthroscopic treatment, including debridement and/or meniscus resection of knee OA, is not effective. Thus, there is uncertainty around the current evidence and differences of opinion, especially within the orthopedic community, supporting or opposing the use of surgery in mild to moderate knee OA (Palmer et al., 2019). Patients with a history of meniscal tear and arthroscopic partial meniscectomy are at greater risk of knee arthroplasty than the general population. This risk for OA is threefold compared to the contralateral knee (Abram et al., 2019).

Valgus high tibial osteotomy (HTO) aims to shift the weight bearing of the knee medial compartment laterally and can be used to treat OA of the medial compartment. It is more appropriate for younger (probably under 40 to 50 years) patients who only wish to accept a slight reduction of physical activity (Spahn et al., 2013). However, TKA or UKA offer a better outcome for more severe OA (Broughton et al., 1986) (Stukenborg-Colsman et al., 2001). There is no high-quality evidence on the efficacy of HTO in older patients or in more severe OA.

Figure 2. Cruciate-retaining total knee implant.

Figure 3. Oxford unicompartmental knee implant.

2.1.4 History of knee artroplasty in brief

During the late 19th and early 20th centuries, interposition arthroplasty was introduced in which soft tissues were placed between the articular spaces. In 1860, Verneuil proposed interposition arthroplasty involving the insertion of soft tissue to reconstruct the joint surface (Song et al., 2013).

The concept of UKA for the treatment of medial knee OA dates back to the 1950s, when it was developed to prevent direct bone-on-bone apposition and provide satisfactory pain relief. The real pioneer of unicompartmental arthroplasty was Campbell, who in 1940 reported his preliminary results on the interposition of vitallium plates in the medial compartment of arthritic knees (Campbell, 1976).

Thereafter, McKeever in 1957 introduced his vitallium tibial prosthesis ("The Classic. Tibial Plateau Prosthesis. By Duncan C. McKeever, 1960.," 1985), followed in 1958 by MacIntosh's tibial plateau (MacIntosh, 1958). Modern UKA implants started with Marmor, who introduced modular unicompartmental arthroplasty in 1972 and in 1979 reported good results in 56 patients with a minimum of 4-year follow-up (Marmor, 1979).

In the 1970s and 1980s, several studies began to report unsuccessful results with UKA (Insall & Aglietti, 1980)(Laskin, 1978). A review of these articles suggests that inappropriate patient selection was a major contributory factor, since many of the Insall and Aglietti group had undergone prior patellectomy, and in Germany the prosthesis had frequently been used for bicompartmental disease and often in the presence of rheumatoid arthritis and joint instability. These papers were accompanied by later reports of mechanical failure of certain prostheses, such as the Brigham one due to thin polyethylene and possible edge contact, and the PCA Uni due to poor quality heat-treated polyethylene (Bruni et al., 2013). In part, these reasons for high revision rates are the same as those discussed in the 21st century (Kim et al., 2014).

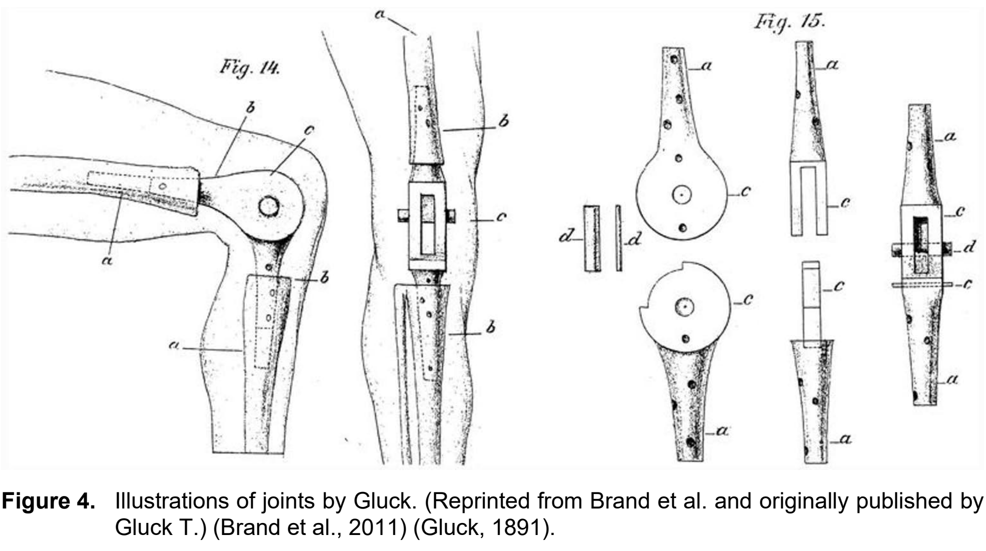


Figure 4. Illustrations of joints by Gluck. (Reprinted from Brand et al. and originally published by Gluck T.) (Brand et al., 2011) (Gluck, 1891).

The development of TKA began in 1890, when German surgeon Themistocles Gluck surgically implanted the first primitive hinge joints made of ivory (Figure 4) (Eynon-Lewis et al., 1992). He was most likely the first to implant an artificial joint. The history of today's condylar replacement started much later. Geomedic knee arthroplasty was introduced by Coventry et al. at the Mayo Clinic in 1972. The main limitation and problem of this design was rapid loosening. Freeman et al. at Imperial College Hospital (London) designed a femoral and tibial prosthesis, which also had problems with loosening. (Dall'Oca et al., 2017).

For TKA, the 1970s and 1980s were the turning point. At the same time as unicompartmental prostheses were failing in long-term follow-up, the first designs and concepts of TKA were gaining popularity. There were two main design theories: the functional design tried to reconstruct knee function while the anatomy was secondary; the anatomic design did the opposite, attempting to preserve knee anatomy rather than focusing on function (Robinson, 2005).

2.1.5 Epidemiology of arthroplasty

The prevalence of knee OA and arthroplasties has been rising for decades. In 2010, the incidence of TKAs in the total U.S. population was 1.52% and was higher among women and with increasing age. It has been estimated that in the US alone there are 4,700,000 individuals who have had TKA (Kremers et al., 2014). Even these numbers, however, probably underestimate the prevalence of symptomatic knee OA, as only part of the US population has access to these expensive procedures.

In Finland, in 1980 fewer than 500 knee arthroplasties were performed annually, compared to around 12,000 today (Figure 5) (Finnish Arthroplasty Register, n.d.). In the Scandinavian countries the total incidence of TKAs and UKAs rose in all countries from 1997 to 2012 at a similar rate. The total increase in arthroplasties in all countries mainly reflects a greater incidence of TKAs. The increase of incidence was highest in the age group 65 or younger (Niemeläinen et al. 2017).

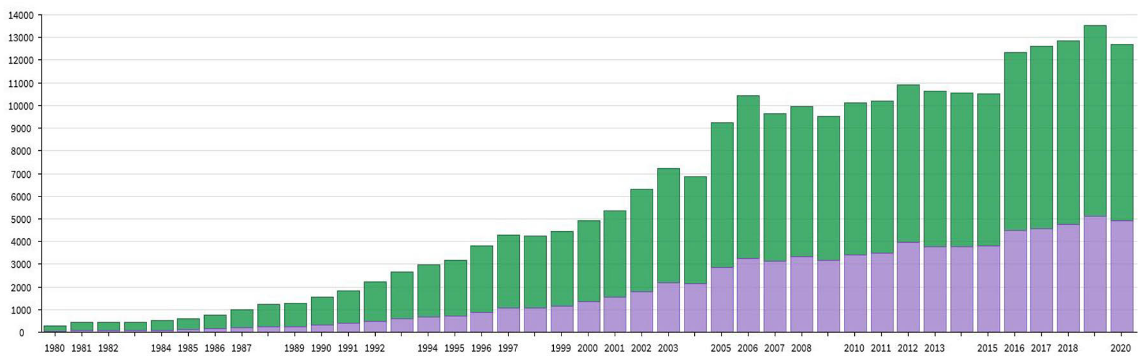


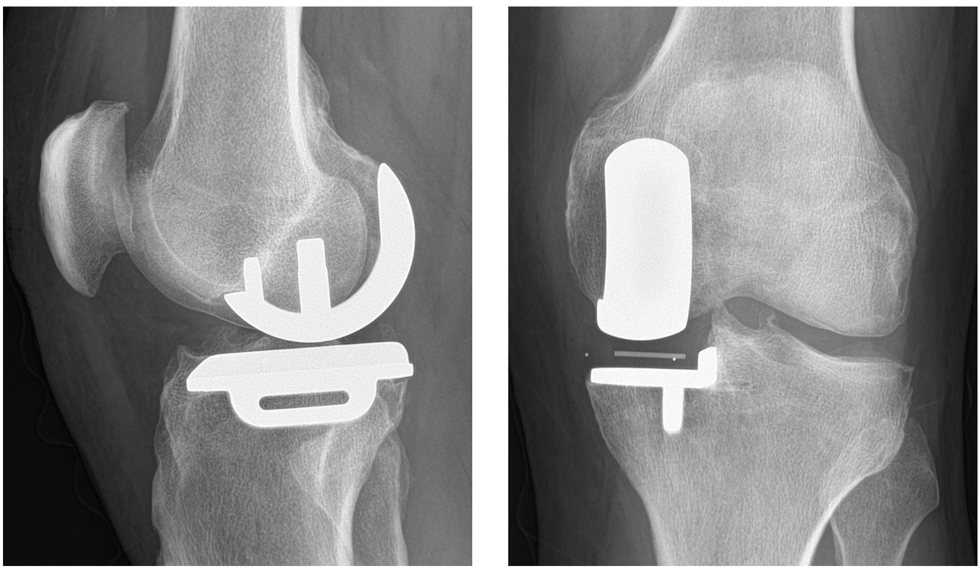
Figure 5. Number of all knee arthroplasties in the Finland, 1980–2020. Data taken from FAR. www.thl.fi/far/.

2.2 Medial unicompartmental knee arthroplasty

A UKA involves the medial side of the tibial and femoral surfaces of the knee being replaced (Figures 6 and 7). The patellar and trochlear surfaces are not replaced. The procedure is commonly performed through a minimally invasive skin incision. An intramedullary guide is used for femoral and an extramedullary guide for tibial alignment. Robotic assistance can also be used to align the femoral and tibial saw cuts and component positions. Components are either cemented in place or cementless. The bearing is either mobile or fixed depending on the UKA model.

The most commonly used UKA prosthesis in the United Kingdom and Finland is the Oxford Knee (Figure 6 and 7) (Biomet, Swindon, UK) (NJR, 2016) (Finnish Arthroplasty Register, n.d.). It has a congruent mobile bearing to minimize wear.

The standard and original method of fixation for UKA is cementation. Cemented UKAs are commonly performed using a minimally invasive technique; however, this is a challenging procedure since cementation errors may lead to loosening, pain, and excess wear (Hooper et al., 2015). Cementation of UKA may be especially problematic compared with TKA, because the medial tibial bone is often very sclerotic and suboptimal for cementing, compared to TKA where cemented fixation adheres also to the cancellous lateral tibial bone tissue, which enhances fixation.



Figures 6 and 7. Radiographs of Oxford unicompartmental knee arthroplasty.

2.2.1 Indications and contraindications for medial unicompartmental arthroplasty

Medial unicompartmental arthroplasty can be used as the treatment for knee OA isolated to a single compartment instead of TKA. Strict commitment to the indication and contraindication criteria is required to achieve good results and optimal survival. Other accepted criteria are correctable intra-articular varus deformity in the knee at 20 degrees of flexion, full-thickness cartilage preserved on the back of the medial tibial plateau and lateral compartment, no previous HTO, and fixed varus deformity of less than 15 degrees in the fully (as near as possible) extended knee. Pain is typically present during gait and relieved by sitting (Goodfellow J, O'Connor J, 2006).

Some of the contraindications are relative or unnecessary. Patellofemoral OA can be accepted if the patella is not in subluxation or deformed with bone loss or grooving. Age or obesity does not have an influence on survival, but morbid obesity (BMI over 40) may be considered to affect the survival of any arthroplasty (Berend et al., 2015) (Chaudhry et al., 2019). Pain location, age, weight, chondrocalcinosis and activity have not had any influence on outcomes of UKA (Berend et al., 2015) (Beard et al., 2007). UKA may also be used to treat spontaneous osteonecrosis of the knee, which is a rarer indication.

2.2.2 Results of medial unicompartmental knee arthroplasty

Both UKA and TKA have been used for decades as a treatment for knee OA (Zipple & Meyer-Ralfs, 1975)(Insall & Walker, 1976).Operative indications for these devices overlap but they are not similar. All knees suitable for UKA are suitable for TKA, but not the opposite. Some advantages of UKA over TKA have been reported, including faster recovery time, reduced perioperative morbidity and mortality, a subjective preference of feeling a more normal knee, lower cost, and improved return to work and sport (Lombardi et al., 2009)(Brown et al., 2012)(Beard DJ et al. 2019). In the observational study by Hunt et al. unicompartmental knee arthroplasty was associated with lower mortality than was total knee replacement (HR 0.32, 95% CI 0.19–0.54, $p<0.0005$). Several comorbidities were associated with increased mortality: myocardial infarction (HR 3.46, 95% CI 2.81–4.14, $p<0.0005$), cerebrovascular disease (3.35, 2.7–4.14, $p<0.0005$), moderate/severe liver disease (7.2, 3.93–13.21, $p<0.0005$), and renal disease (2.18, 1.76–2.69, $p<0.0005$). This study was included adjustments for age, sex and comorbidities (Hunt et al., 2014). On the other hand, national arthroplasty registers like the National Joint Registry of England and Wales (NJR), the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), the Swedish Knee Arthroplasty Register

(SKAR), and the Finnish Arthroplasty Register (FAR) consistently report around a threefold increase in crude cumulative revision rate at 8–10 years for UKA compared with TKA (Niinimäki et al., 2014) (NJR, 2016) (AOANJRR, n.d.) (The Swedish Knee Arthroplasty Register, 2012). However, survival as a measure of success of the operation has been subject to criticism. According to the NJR, knees which scored <20 points on the OKS, 89% of the TKRs and 37% of the UKRs, were subsequently not revised (Goodfellow et al., 2010). The higher revision rate of UKR might not be because its results are worse. It seems likely that the UKA is more often revised because it is easier to do.

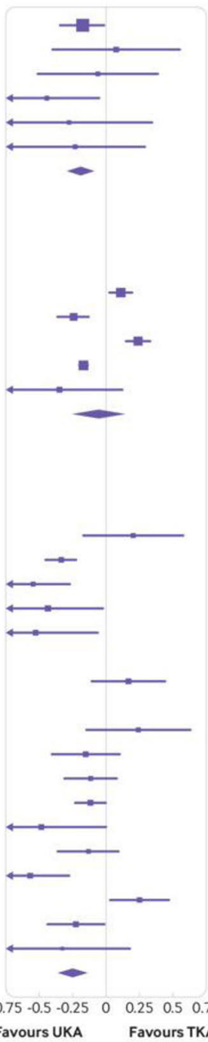
Few randomized controlled trials (RCTs) have been published about PROMs following TKA compared with UKA (Table 2). Newman et al. compared fixed-bearing UKA to TKA and reported a better range of movement (ROM) after UKA. Sun PF et al. compared mobile-bearing UKA with fixed-bearing TKA and did not find a significant difference in range of movement (ROM) or Knee Society score (KSS) postoperatively after a mean of 52 months follow-up, but the TKA group had significantly more prevalent postoperative deep vein thrombosis and greater post-operative blood loss. The TOPKAT trial compared UKA and TKA with a randomized, multicenter setup and concluded that UKA is cost-effective compared to TKA in a 5-year follow-up (Beard DJ et al. 2019).

Table 2. Randomized controlled studies comparing unicompartmental knee arthroplasty.

Author (year)	Number of patients	Number of knees included in final analysis (UKA/TKA)	Mean age	Mean BMI	Follow-up	No. of study sites	Assessment	Primary outcome
Newman J (1998)	94	91 (45/46)	70 (53-85)	n/a	5 years	1	RCT, FB/TKA	BKS
Newman (2009)	94	30 (13/17)	70 (53-85)	n/a	15 years	1	RCT, FB/TKA	BKS
Costa CR (2011)	34	68 (34/34)	73 (49-86)	n/a	5 years	1	RCT, FB/TKA	KSS
Sun PF (2012)	56	56 (28/28)	60 (55-67)	30	52 months	1	RCT, MB/TKA	KSS
Kulschetra (2017)	80	80 (40/40)	61 (SD 8.7)	28			RCT, FB/TKA	KOS-ADLS
Beard DJ (2019)	531	528 (264/264)	65 (SD 8.8)	31	5 years	27	RCT, MB/TKA	OKS

KSS=knee society score, BKS=Bristol knee score, OKS=Oxford knee score, KOS-ADLS= Knee Outcome Survey Activities of Daily Living Scale. FB = Fixed bearing, MB=Mobile bearing.

A systematic review and meta-analysis of patient relevant outcomes of UKA versus TKA concluded that both treatment alternatives are viable options, but UKA demonstrates slightly better results (Figure 8) (Wilson et al., 2019).



Study	UKA Mean	UKA SD	UKA Total	UKA Mean	UKA SD	UKA Total	Weight (%)	Standard mean difference IV random (95% CI)
Group 1							37.9	
Beard 2017 OKS	-36.9	9.9	264	-35.1	10.3	264	4.9	-0.18 (-0.35 to -0.01)
Costa 2011	-91.5	5.5	34	-91.97	5.46	34	5.3	0.08 (-0.40 to 0.55)
Kulshrestha 2017	-17.1	4.1	34	-16.8	5.5	40	7.2	-0.06 (-0.65 to 0.40)
Newman 1998	-91.1	9.6	50	-86.7	10.07	52	2.8	-0.44 (-0.84 to -0.05)
Newman 2009	-92.0	13.5	21	-87.5	18.9	19	4.0	-0.27 (-0.89 to 0.35)
Sun 2011	-80.6	9.0	28	-78.9	4.56	28	100.0	-0.23 (-0.76 to 0.29)
Subtotal			431			437		-0.19 (-0.32 to -0.05)
Total (95% CI)								
Test for heterogeneity: τ^2=0.00; χ^2=3.23, df=5, P=0.67; I^2=0%								
Test for overall effect: Z=2.37, P=0.006								
Group 2							14.2	
Baker 2012	-34.0	13.9	23 393	-35.5	12.9	505	13.7	0.11 (0.02 to 0.20)
Burn 2016	-39.2	12.7	567	-35.9	14.5	566	14.0	-0.24 (-0.36 to -0.13)
Ko 2011	-19.6	5.9	527	-21.0	5.9	1716	14.7	0.24 (0.14 to 0.34)
Liddle 2015	-37.7	6.1	3519	-36.1	10.5	10 557	6.3	-0.17 (-0.21 to -0.13)
Manzotti 2007	-80.6	4.9	34	-78.9	4.6	34	100.0	-0.35 (-0.83 to 0.13)
Subtotal			28 761			24 653		-0.05 (-0.25 to 0.15)
Total (95% CI)								
Test for heterogeneity: τ^2=0.04; χ^2=125.52, df=7, P<0.001; I^2=94%								
Test for overall effect: Z=2.03, P=0.04								
Group 3							4.5	
Amin 2006	-82.0	10.0	54	-84.0	10.0	54	7.1	0.02 (-0.18 to 0.58)
Craik 2015	-37.8	8.9	334	-35.5	6.7	4495	5.5	-0.33 (-0.45 to -0.22)
Fabre Aubrespry 2018	-88.2	8.9	101	-82.3	12.5	101	4.2	-0.54 (-0.85 to -0.02)
Fisher 2010	-96.0	6.0	41	-92.0	11.0	50	3.7	-0.44 (-0.85 to -0.02)
Horikawa 2015 JKSC*	-83.6	9.2	28	-78.3	10.4	50		-0.53 (-1.00 to -0.05)
Howell 2015	-87.0	0.0	110	-85.0	0.0	142	4.9	Not estimable
Kim 2017 WOMAC	-10.2	5.3	100	-11.2	6.6	100		0.17 (-0.11 to 0.44)
Lim 2014	-88.0	0.0	602	-87.0	0.0	602	3.7	Not Estimable
Liu 2010	-27.5	2.5	48	-28.1	2.4	52	5.1	0.24 (-0.15 to 0.64)
Lombardi 2009 KSS†	-92.0	12.0	115	-90.0	13.5	115	5.7	-0.15 (-0.41 to 0.11)
Lum 2016	-90.3	15.5	201	-88.6	14.2	189	6.4	-0.11 (-0.321 to 0.08)
Lyons 2012 WOMAC	-74.0	21.1	279	-71.4	21.7	5606	3.0	-0.12 (-0.24 to 0.00)
Mathews 2013 OKS	-29.1	13.4	34	-19.9	23.1	34	5.4	-0.48 (-0.96 to 0.00)
Siman 2017	-85.4	11.0	120	-84.0	10.6	188	4.7	-0.13 (-0.36 to 0.10)
Van der List 2016	-89.7	13.6	163	-81.2	18.0	63	5.5	-0.57 (-0.86 to -0.27)
Walton 2006	-22.2	9.0	183	-24.5	9.7	142	5.5	0.25 (0.03 to 0.47)
Xie 2009	-86.4	14.7	102	-83.4	13.5	431	2.9	-0.22 (-0.43 to -0.00)
Xu JP 2013	-87.0	3.0	30	-86.0	3.0	30	100.0	-0.33 (-0.84 to 0.18)
Subtotal			2043			11 842		-0.19 (-0.31 to -0.06)
Total (95% CI)								
Test for heterogeneity: τ^2=0.04; χ^2=59.82, df=15, P<0.001; I^2=75%								
Test for overall effect: Z=2.93, P=0.003								

* Knee specific, † Primary outcome

Figure 8. From Wilson et al. (Wilson et al., 2019). Forest plot comparing combined pain and function measured using knee-specific patient reported outcome measures after unicompartmental (UKA) versus total knee arthroplasty (TKA). IV=inverse variance weighting; OKS=Oxford knee score; JKSC=Japanese knee osteoarthritis score; WOMAC=Western Ontario McMaster Universities osteoarthritis index; KSS=Knee Society Score; JOA=Japanese Orthopaedic Association score. Group 1 included five RCT studies and two subsequent reports, Group 2 included publications from seven national joint registries and five multicentre database studies. Group 3 included 36 cohort studies. The standardized mean difference (**SMD**) measure of effect is used when studies report efficacy in terms of a continuous measurement. An SMD of zero means that the new treatment and the placebo have equivalent effects. For example in comparison of NSAIDs to plasepo for pain in osteoarthritis, the SMD is -030; 95%CI -0.40 to -0.20 (Zeng et al., 2018).

The most common reason for revision of UKA according to the NJR is aseptic loosening, accounting for up to 48% of all revisions (NJR, 2016). Other reasons for revision are malalignment, prosthesis fracture, instability, infection, fracture, patella complication and other reasons (35%) (T. Niinimäki et al., 2014). A RCT of 62 knees comparing cemented and cementless Oxford UKA demonstrated a greatly reduced incidence of tibial radiolucencies with similar functional outcomes at 1 year (Beard et al., 2007) (Pandit et al., 2013). The cementless Oxford UKA is a relatively new device, implanted for the first time in 2004. It was relaunched on the market in 2008 in the United Kingdom and in 2009 in Finland (Hooper et al., 2015)(Finnish Arthroplasty Register, n.d.). It was developed to address problems related to cement fixation, and has been demonstrated in a randomized study to have similar clinical outcomes with fewer radiolucencies than observed with the cemented device (Pandit et al., 2013). The New-Zealand Joint Registry (NZJR) data show a revision rate of 1.37/100 component years for cemented Oxford phase 3 UKA and 0.72/100 component years for cementless Oxford phase 3 UKA. The uncemented Oxford UKA has a significantly lower revision rate than the overall mean of 1.27 /100 observer component years. On the other hand, cementless UKA shows lower survivorship compared with cemented TKA in FAR data (Finnish Arthroplasty Register, n.d.).

2.3 Total knee arthroplasty

Total knee arthroplasty is the most common surgical treatment for end stage knee OA, over 90% of all knee arthroplasties in the United Kingdom being TKAs. The number of arthroplasties continues to grow especially among younger patients (Figure 9) (National Joint Registry 15th, 2018) (Finnish Arthroplasty Register, n.d.).

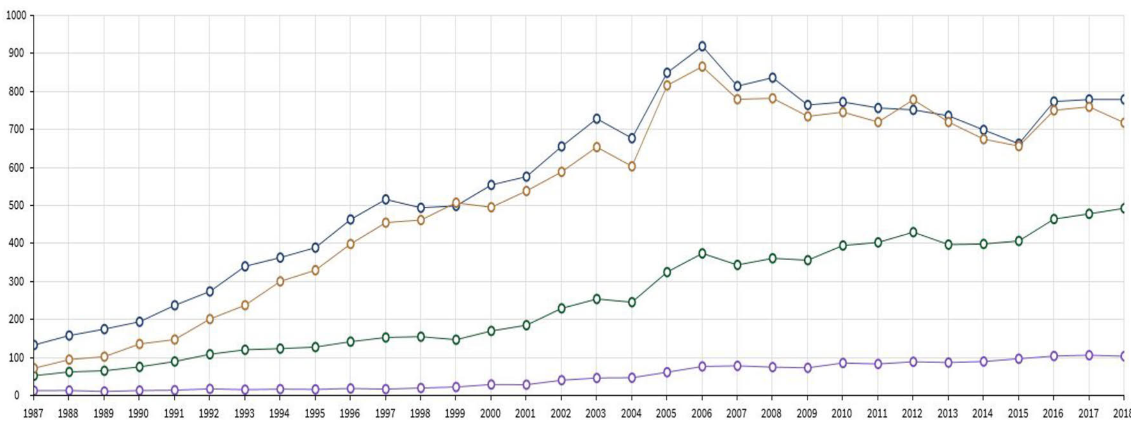


Figure 9. Number of annual knee arthroplasties per 100,000 inhabitants over the age of 40, ● under the age of 55, ● 55–64, ● 65–74, ● over 75. Data and figure from FAR (Finnish Arthroplasty Register, n.d.).

A TKA involves all tibial and femoral surfaces of the knee being replaced (Figure 10 and 11). The patellar surface is optional and is replaced if needed. The procedure is commonly performed through a standard medial parapatellar skin incision, which provides easy access to the knee joint. Also other approaches can be used. An intramedullary or extramedullary guide, navigation or robotic assistance is used for alignment of femoral and tibia saw cuts and component positions. Most commonly the components are cemented into position, but also cementless components can be used.

The preliminary aim of TKA is to eliminate the pain and ideally to restore normal knee kinematics. However, none of the current TKA designs are able to replicate normal knee kinematics (Blaha, 2004). The most commonly used components and instrumentations of TKA can be divided into four categories. The most commonly used are the cruciate-retaining (CR) and posterior stabilized (PS) models. CR is practically knee "surfacing" arthroplasty, where all other ligaments than the ACL are spared. The stability is based on the patient's own ligaments and the shape of the bearing. In the PS design, the cruciate ligaments are removed and the bearing of the implant substitutes for the posterior cruciate ligament (PCL). The more rarely used semi-constrained or hinge prosthesis are used mainly for revision surgery or for knees with severe deformity, instability or bone loss.

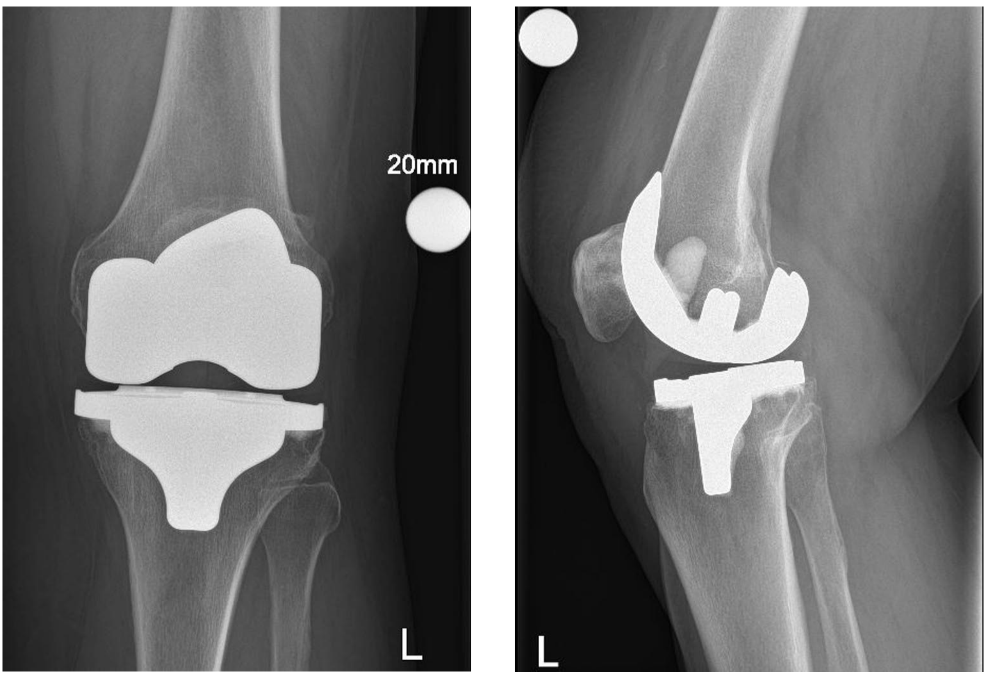


Figure 10 and 11. Radiographs of total knee arthroplasty in a 59-year-old woman 2 years after surgery.

2.3.1 Results of total knee arthroplasty

The RCT showed that TKA followed by nonsurgical treatment is more efficacious than nonsurgical treatment alone in providing pain relief and improving function and quality of life after 12 months in patients with knee OA who are eligible for TKA (Skou et al., 2015). Skou et al. reported a significantly greater improvement in the KOOS and quality of life (KOOS4) score for TKA than in the nonsurgical-treatment group, with a crude mean difference of 16.5 and an adjusted mean difference of 15.8. The number needed to treat TKA for a 15% improvement from baseline to 12 months in KOOS4 was 5.7 in the intention-to-treat analysis (Skou et al., 2015).

The pooled registry data show that 82.3% of TKAs last 25 years (Evans et al., 2019). In the registries, typical 10-year revision rates stay at <5%, which is excellent survival (NJR, 2016). The specific implants and bearing surfaces have shown to be an independent factor affecting survivorship, and this data is quickly and easily accessed from national registries.

Despite TKA being a highly successful operation in terms of revision rate, as many as 20% of patients are somewhat dissatisfied with their implant (Carr et al., 2012) (Bourne et al., 2010). Revision rate is also not the best measure of the success of surgical treatment, because only the worst cases end up in revision. Also, revision has been criticized as not being an objective measurement of the overall success of an implant (Goodfellow et al., 2010). Because revision surgery is a smaller procedure for medial unicompartmental than for total knee arthroplasty, the revision threshold between these implant types may vary.

One of the challenges related to TKA is arthrofibrosis, the pathologic stiffening of a joint caused by an exaggerated inflammatory response. Proliferation of metaplastic fibroblasts and excessive deposition of extracellular matrix (ECM) proteins lead to the development of thick, noncompliant, fibrous scar tissue (Skutek et al., 2004) (Abdul et al., 2015). For patients undergoing TKA, arthrofibrosis is estimated to be responsible for 28% of 90-day hospital readmissions and 10% of revision surgeries within the first 5 years (Schroer et al., 2013). However, infection is the predominant mechanism of failure of TKA, followed by aseptic loosening, instability, polyethylene wear, arthrofibrosis, and malalignment (Finnish Arthroplasty Register, n.d.) (AOANJRR, n.d.). These six mechanisms of failure represent almost 90% of all failures (Schroer et al., 2013).

3 Aims of the study

1. To evaluate the influence of the preoperative degree of OA on the risk of reoperation following UKA with retrospective single-center analysis.
2. To determine the short-term survivorship of cementless mobile bearing UKA using data from FAR and compare that of cemented mobile-bearing UKA and TKA.
3. To assess the clinical effectiveness of medial UKA versus TKA in patients with anteromedial OA of the knee in a randomized, controlled, assessor-blinded comparison.

4 Materials and Methods

4.1 Patients

In study I, data were collected from the patient records of Turku University hospital. A total of 294 cemented Oxford phase III UKAs were performed in 241 patients, of whom 37% (108/294) were male, with symptomatic OA between 2001 and 2012. The mean age of the patients was 67 years (range 37–88). The mean follow-up time was 8.7 years (range 1.9–13.5). The data included age, gender, date of primary UKA, follow-up time, preoperative medial and lateral (M/L) joint space widths, preoperative KL grading, and date of revision if any.

The study II data were collected from FAR (Table 3). The Finnish Arthroplasty Register has collected information on joint replacements since 1980. Hospitals are obliged to provide all information essential for maintenance of the register to the Finnish National Institute for Health and Welfare. Dates of death are obtained from Statistics Finland. The data capture of FAR is high compared to the Hospital Discharge Register. Since May 19th, 2014, all knee data have been recorded electronically based on bar-code readings. FAR data for the years 2005–2017 is currently based on product codes (ref-codes) instead of the old model codes. The precision of identifying devices has increased remarkably, allowing us to assess separately cementless and cemented Oxford devices.

Table 3. Demographic data for study II. Cementless Oxford, cemented Oxford 3, and cemented TKA reference group.

Demographic	Cementless Oxford	Cemented Oxford 3	Cemented TKA
N	1,076	2,279	65,563
Follow-up (years)			
Mean	2.7	7.4	4.9
Min	0.05	0.05	0.003
Max	7.8	11.7	11.7
Median	2.1	7.9	4.5
Males (%)	44.1	39.1	34.7
Age, mean (SD)	61.5 (9.3)	62.1 (9.6)	68.4 (9.3)
Implanting period	2008–2015	2005–2014	2005–2015
No. of hospitals	20	46	64

TKA=total knee arthroplasty. SD=standard deviation.

The study III design is a parallel (1:1) multicenter, assessor-blind and randomized superiority trial of knee arthroplasty patients to assess the efficacy of medial UKA. In all, 143 patients were enrolled between 9th December 2015 and 28th May 2018 and operated on by four orthopedic surgeons in three central hospitals: Turku University hospital, Oulu University hospital and Central Finland hospital (Figure 12). All patients had anteromedial bone-to-bone knee OA with a functionally intact ACL. Only patients with isolated anteromedial OA who met the original indications for medial unicompartmental arthroplasty with the Oxford knee were considered for the trial (Berend et al., 2015) (Goodfellow J, O'Connor J, 2006).

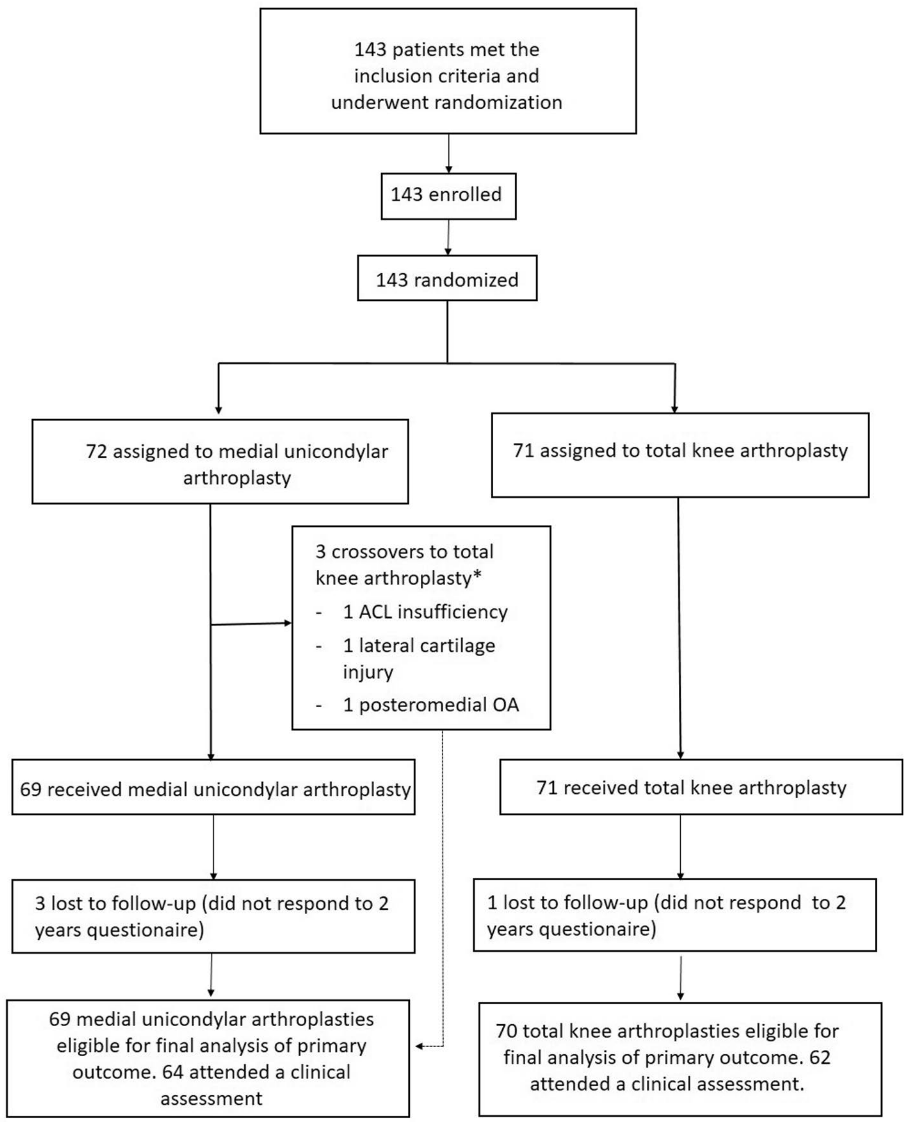
Inclusion criteria

- Symptomatic medial knee osteoarthrosis with exposed bone on both femur and tibia (bone-on-bone osteoarthritis in weight-bearing radiographs)
- Age between 45 and 79 years
- Failed conservative treatment of knee osteoarthritis (physiotherapist-supervised exercise therapy and pain medication)
- Mechanical axis from 5 to 15 degrees varus
- Functionally intact anterior cruciate ligament at clinical examination
- Full-thickness lateral cartilage present
- Correctable intra-articular varus deformity in the knee on 20 degrees flexion

Exclusion criteria

- Rheumatoid arthritis or other inflammatory disorders
- Osteonecrosis
- Osteochondritis dissecans
- Symptomatic hip or spinal pathology (registered in medical history or suspected in a clinical examination)
- Previous knee surgery other than diagnostic arthroscopy or medial meniscectomy
- Previous infectious knee arthritis
- Significant osteoarthritis of the lateral facet of the patella, patellar subluxation or concave patella
- Previous ligament injury and instability (crucial or collateral ligaments)

- Range of knee movement within 15–100 degrees (flexion deformity >15 degrees or flexion range <100 degrees)
- Patient is planned to undergo simultaneous bilateral knee arthroplasty
- American Society of Anesthesiologists (ASA) classification 4 or above.



* Included in final analysis according to intention-to-treat principles

Figure 12. Flow chart.

4.2 Methods

4.2.1 Study I

All operations with surgical code NGB10 (partial knee arthroplasty) were identified from the hospital operation register (Opera, GE Healthcare) and inspected manually. All partial knee arthroplasties other than medial unicompartmental where excluded. Patient data were collected from hospital patient records, including the parameters age, gender, date of primary UKA, follow-up time and date of revision if any.

4.2.1.1 Radiological assessment

Each patient had preoperative radiographs taken with the patient standing upright in front of the film cassette with the knee in full extension or 20 degrees of flexion. The medial and lateral joint space widths were measured on the radiographs in the middle of the respective compartments. The M/L joint space ratio was calculated as described in a previous study (Niinimäki et al., 2011). The radiological measurements were carried out by two senior orthopedic surgeons. In addition to these measurements, the preoperative degree of OA was assessed using the KL scale (Kellgren and Lawrence 1957).

4.2.1.2 Statistics

Continuous variables were described by means and standard deviations, and categorical variables were described using frequencies and percentages. The associations between reoperation and potential risk factors (gender, preoperative medial joint space width, preoperative M/L ratio, and KL grade) were analyzed using logistic regression. The results were expressed by odds ratios (OR) and 95% confidence intervals (95% CI). Reoperation was defined as any operation performed on the UKA knee after the primary operation. P values of less than 0.05 were considered statistically significant. Statistical analysis was carried out using SAS for Windows, Version 9.3 (SAS Institute Inc., Cary, NC, USA).

4.2.2 Study II

For this study, data were obtained on 1,076 cementless Oxford UKAs, 2,279 cemented Oxford 3 UKAs, and 65,563 cemented TKAs treated for primary OA in Finland in 2005–2015. All data were from the FAR database. The TKA reference group consisted of the three most common prosthesis brands in Finland, the Triathlon CR (Stryker, Mahwah, NJ), Nexgen flex CR (Zimmer Biomet, Warsaw, IN) and PFC

Sigma CR (DePuy, Warsaw, IN). Crude implant survival of the cementless Oxford, cemented Oxford 3, and cemented TKA in the control group was assessed by suitable statistical methods and is described later in the text.

4.2.2.1 Statistics

Crude implant survival of the cementless Oxford, cemented Oxford 3, and cemented TKA in the control group was assessed using Kaplan-Meier analysis. The Cox regression model was used to assess the differences in revision rates of the devices and to adjust for any confounding factors. Revisions were linked to the primary operation through personal identification numbers. The survival endpoint was defined as revision when either any of the components or the entire implant was removed or exchanged. The first revision for any reason served as an endpoint. Kaplan-Meier survival data were used to construct the crude survival probabilities of the implants with the 95% CI. Patients who died during the follow-up period (until December 31, 2015) were not included. The factors studied with the Cox model were the age groups of <55 years and ≧55 years and gender.

The proportional hazards assumption of the Cox models was checked by inspecting the Kaplan-Maier graphs. It was found that the survival rates of the Oxford implants intersected at approximately 18 months of follow-up. For the Cox analyses comparing the cementless Oxford, cemented Oxford 3, and cemented TKA reference group, we divided the total follow-up time into two periods of 0–18 months and >18 months, because the proportional hazards assumption was not fulfilled for the total follow-up. For the shorter follow-up, all knees with a follow-up of >18 months were excluded. For the longer time period, knees with a follow-up of <18 months were excluded from the analyses.

The inclusion of bilateral cases in a survival analysis violates the basic assumption that all cases are independent. However, reports have shown that the effect of including bilateral cases in studies of hip and knee joint prosthesis survival, as done in our study, is negligible (Lie et al., 2004). The Wald test was used to test the estimated hazard ratios. The differences between the groups were considered to be statistically significant if the p-values were less than 0.05 in a 2-tailed test.

4.2.3 Study III

4.2.3.1 Trial design

The study design is a parallel (1:1) multicenter, accessor-blind and randomized superiority trial of knee arthroplasty patients to assess the clinical effectiveness of medial UKA over TKA. The patients were enrolled and operated on by four orthopedic surgeons in three central hospitals. The surgeons were not involved in the follow-up to ensure blinding.

4.2.3.2 Power analysis and randomization

The necessary sample size was calculated to detect potential between-group differences in patient-reported outcome measures on the OKS and KOOS. The trial was powered to detect a 5-point difference in the OKS (SD 10 points) and 10-point difference in the KOOS (SD 20) (Beard et al., 2015; Murray et al., 2007; Roos & Toksvig-Larsen, 2003) with 80% power at 5% significance level. An 10% dropout was assumed. Based the power analysis, 140 patients (70 in each group) were needed for the trial.

Randomization was performed in a 1:1 ratio with a block size of four (known only by the statistician). The randomization sequence involved stratification according to age (45–60 years or 61–79 years), gender, and preoperative OKS (0–17, 18–27 or 28–48). If a patient was confirmed to be eligible for the trial, an envelope containing the study-group assignment (medial unicompartmental or total knee arthroplasty) was opened 2 to 24 hours before the operation. The assignment was not revealed to the patient or personnel outside of the operation room. The study participants excluded after randomization were included in the final analysis according to intention-to-treat (ITT) principles.

4.2.3.3 Blinding

To ensure blinding, only the operating orthopedic surgeon and the staff in the operating room were aware of the group assignment, and they did not participate in further treatment or clinical follow-up of the patient. Skin incision of all study patients was performed to the midline and was equally long in both study groups. Postoperative and follow-up radiographs were stored with a personalized study number and assessed by the surgeon responsible for the surgery. None of the radiographs or surgery reports were linked to the patient's personal identification number after surgery. To ensure blinding, the postoperative clinical examination was performed by an orthopedic surgeon who had not participated in the surgery and did not see the radiographs.

The study nurse worked in the three study hospitals. After recruitment of the patient, the surgeon called the study nurse (who was not involved with clinical work or patients preoperatively), who opened the randomization envelopes and informed the surgeon of the type of operation. The operations were performed in arthroplasty theaters and time slots, which allowed us to use any arthroplasty implant needed (including knees and hips, primary and revision). All the implants used in study were in routine use in the study hospitals, including implants and several surgical instruments on the shelves, ready for use at short notice. After the operation, the second surgeon, who was blinded to the type of operation, took care of postoperative treatment and follow-up visits in collaboration with the blinded nurses and physiotherapist.

4.2.3.4 Study treatments

The study implant for TKA was a Triathlon CR. The operation was performed through a standard medial parapatellar incision described precisely in the study protocol and final publication. The components were cemented in place and the patella was not resurfaced.

The study implant for UKA was a cementless Oxford phase 3 mobile-bearing implant. The procedures were performed with microplasty instrumentation. To ensure blinding, a midline skin incision was performed similarly in both groups. After skin incision, the knee joint and fascia were opened with a standard Oxford minimally invasive incision (*Oxford Surgical Technique*, n.d.). If the anterior cruciate ligament was not intact, or if there was remarkable OA of the lateral compartment, the procedure was changed to TKA (included in the final analysis according to ITT principles). Intraoperative local infiltration analgesia was used for postoperative pain management for all operated knees.

Our primary outcomes were the between-group differences in OKS and KOOS 1–5 at 2 year after surgery. The OKS has 12 items and a score range from 0 to 48, a higher score indicating less severe symptoms. The KOOS consists of five subscales: pain, function in daily living, function in sport and recreation, and knee-related quality of life. The OKS and KOOS have been previously validated for knee OA patients and knee arthroplasty and are responsive to change following knee arthroplasty (David J. Beard et al., 2015; Roos & Toksvig-Larsen, 2003). Outcome scores were collected preoperatively and at 2 and 12 months postoperatively. The mean differences between the study groups were measured. Secondary outcomes included complications and revision rates according to Clavien-Dindo (Clavien et al., 1992)(Clavien et al., 2009), a change in the 15D score between groups, the knee society score (KSS) (Scuderi et al., 2012)(Sintonen, 2001), and radiographic findings including signs of potential failure such as component loosening and periprosthetic fracture.

Clavien-Dindo is a classification of complications based on the type of therapy needed to correct the complication. Grade I complications are any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside. Within grade II complications requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included. Grade III complications are those requiring surgical, endoscopic or radiological intervention. Grade IIIa intervention not under general anesthesia and grade IIIb intervention under general anesthesia. Grade IV complications are life-threatening complications (including CNS complications) requiring IC/ICU-management. Grade V complication is death. The KSS is subdivided into a knee score that rates the stability, movement, alignment and stairs, contractures of the knee joint itself, and a functional score that rates the patient's ability to walk and climb. The maximum score is 200 and minimum 0; higher scores indicate better function of the knee.

4.2.4 Statistical analysis

In study I, continuous variables were described by means and standard deviations, and categorical variables were described using frequencies and percentages. The associations between reoperation and potential risk factors (gender, preoperative medial joint space width, preoperative M/L ratio, and KL grade) were analyzed using logistic regression. The results were expressed with ORs and 95% CIs. Reoperation was defined as any operation performed on the UKA knee after the primary operation. P values of less than 0.05 were considered statistically significant. Statistical analysis was carried out using SAS for Windows, Version 9.3 (SAS Institute Inc., Cary, NC, USA).

In study II, crude implant survival of the cementless Oxford, cemented Oxford 3, and the cemented TKA control group were assessed by Kaplan-Meier analysis. The Cox regression model was used to assess differences in revision rates of the devices and to adjust for any confounding factors. Revisions were linked to the primary operation through the personal identification number. The survival endpoint was defined as revision. First revision for any reason served as an endpoint. Kaplan-Meier survival data were used to construct the crude survival probabilities of implants, with 95% CI. Patients who died during the follow-up period (until December 31th 2015) were censored at that point. The factors studied with the Cox model were age groups <55 years and ≧55 years, and gender.

The proportional-hazards assumption of the Cox models was checked by inspecting the Kaplan-Maier graphs. The survival rates of Oxford implants were found to intersect at roughly 18 months of follow-up. For Cox analyses comparing the cementless Oxford, cemented Oxford 3, and cemented TKA reference group, we divided the total follow-up time into two periods of 0–18 months and >18 months, because the proportional-hazards assumption was not fulfilled for the total follow-up. For the shorter follow-up, all knees with a follow-up of >18 months were excluded. For the longer time period, knees with a follow-up of <18 months were excluded from the analyses.

The Wald test was used to test the estimated hazard ratios. Differences between groups were considered to be statistically significant if the p-values were less than 0.05 in a 2-tailed test.

Study III was designed to investigate the theoretically superior functional outcome of medial unicompartmental compared to total knee arthroplasty. Baseline characteristics were described as the mean with standard deviation for continuous variables and frequencies with percentages for categorical variables. A two-sample t-test was used to compare continuous variables between the study groups and a chi-squared test or Fisher's exact test for categorical variables. The changes in the OKS, KOOS subscales, KSS, and 15D within and between the groups were analyzed with analysis of variance for repeated measurements using an unstructured covariance structure after adjustment for surgeon and stratification variables age, sex and preoperative OKS. The mean changes and between-group differences in the changes with 95% CI were calculated from the baseline to 2 and 12 months applying the Bonferroni correction. Statistical analyses were performed on an ITT basis and used all available participant data. P-values of less than 0.05 were considered statistically significant. The SAS System for Windows, version 9.4 (SAS Institute Inc., Cary, NC), was used for statistical analyses.

5 Results

5.1 Effects of preoperative osteoarthritis (Study I)

In the retrospective analysis of study I, a total of 53 out of 294 UKAs (18%) underwent revision. The average time between primary operation and revision was 3.7 years (range 0.1–10). The reasons for revision were component loosening (13 knees (12 tibial and two femoral components)), persistent pain (12 knees), progression of OA (12 knees), dislocation of the meniscal bearing (7 knees), intra-operative fracture or technical failure in the primary operation (6 knees), and infection (2 knees).

A total of 21.5% (40/186) of female patients and 12.0% (13/108) of male patients underwent a revision. Female patients had an increased risk of revision compared with male patients (OR=2.00, 95% CI 1.02–3.94, p=0.04). The age of the patients was not associated with risk of revision (OR=1.03, 95% CI 0.99–1.06, p=0.14).

Preoperative KL grade was 0–2 in 110 knees (40.7%) and 3–4 in 160 knees (59.3%). Of the knees rated KL 0–2, 23.6% (26/110) had a revision, and 13.8% (22/160) of KL 3–4 had a revision. Patients with KL 0–2 had a higher risk for revision than those with KL 3–4 (OR=1.89, 95% CI 1.03–3.45, p=0.04).

Preoperative high medial joint space or M/L ratio was associated with a higher revision rate (Figures 13 and 14). If the preoperative M/L ratio was ≤20%, the reoperation rate was 10% (n=10), and if the preoperative M/L ratio was >80%, the reoperation rate was 33% (n=4). If the preoperative medial joint space was <1 mm, the reoperation rate was 11% (n=13).

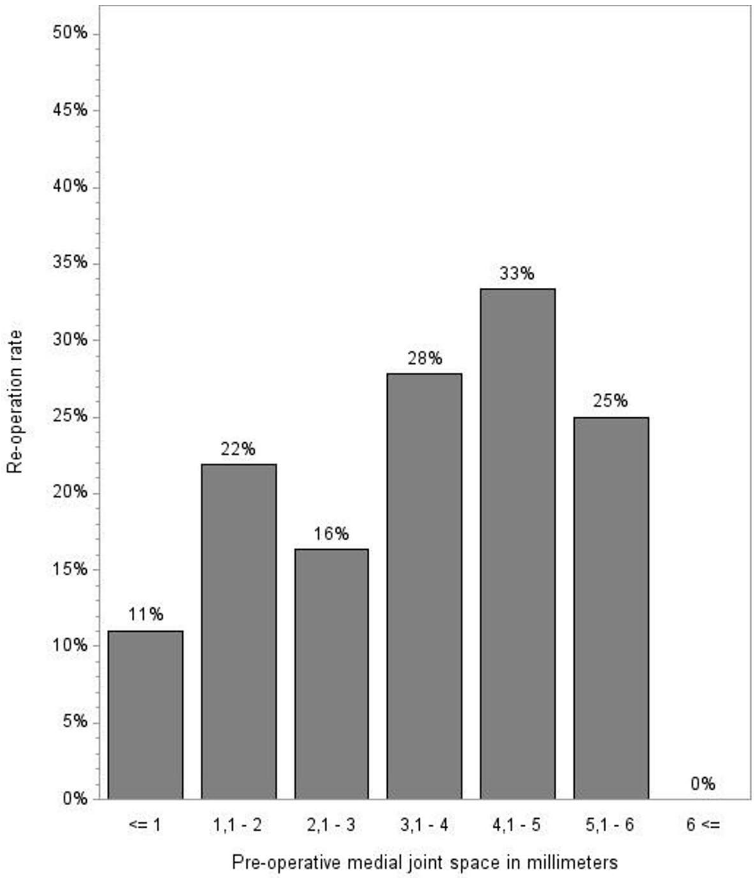


Figure 13. Preoperative medial joint space width in millimeters.

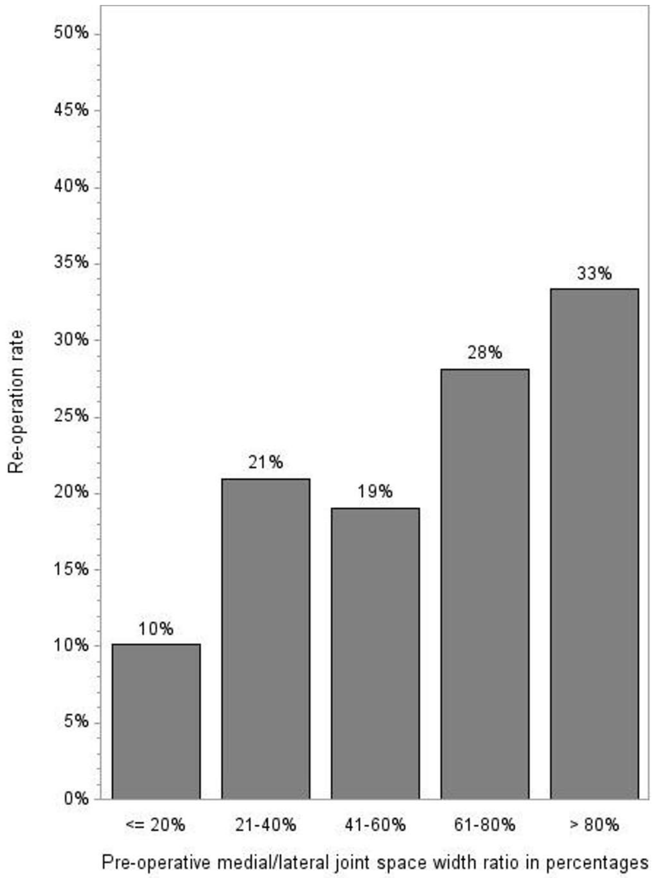


Figure 14. Preoperative medial/lateral joint space width ratio %.

5.2 Survival of cementless UKA (Study II)

The main reason for revision in the FAR data was other reason/missing data for all study groups (Table 4). The main reason for revision of diagnoses that were available for cementless Oxford was insert dislocation (16%), for cemented Oxford 3 aseptic loosening of the tibial component (10%), and for the cemented TKA reference group infection (21%).

Table 4. Reasons for revision.

Reason for revision	Cementless Oxford n (%)	Cemented Oxford 3 n (%)	Cemented TKA reference group n (%)
Insert dislocation	10 (16%)	10 (3%)	19 (1%)
Aseptic loosening of tibial component	8 (13%)	35 (10%)	50 (2%)
Malposition	7 (11%)	15 (4%)	145 (7%)
Fracture	6 (9%)	2 (1%)	46 (2%)
Pain only	6 (9%)	23 (7%)	150 (7%)
Infection	3 (5%)	12 (4%)	434 (12%)
Instability	3 (5%)	14 (4%)	171 (8%)
Aseptic loosening of femoral component	1 (2%)	27 (8%)	64 (3%)
Implant breakage	0 (0%)	1 (0%)	1 (0%)
Patellofemoral osteoarthritis progression	0 (0%)	6 (2%)	113 (5%)
Stiffness	0 (0%)	0 (0%)	12 (1%)
Other reason or missing data	20 (31%)	197 (58%)	889 (42%)
All	64 (100%)	342 (100%)	2094 (100%)

TKA=total knee arthroplasty.

The 1-year survivorship was 96.6% (CI 95.5–97.7) for cementless Oxford, 97.2% (CI 96.5–97.9) for cemented Oxford 3, and 98.9% (CI 98.8–98.9) for the cemented TKA reference group, respectively (Table 5, Figure 15).

The corresponding figures at 5 years were 92.3% (CI 90.3–94.4) for cementless Oxford, 88.9% (CI 87.6–90.2) for cemented Oxford 3, and 96.6% (CI 96.4–96.7) for the cemented TKA reference group (Table 5, Figure 15).

Table 5. Kaplan-Meier survivorship of cementless Oxford, cemented Oxford 3 and the cemented TKA reference group at 1, 3, and 5 years. Kaplan-Meier survivorship of cemented Oxford 3 and the cemented TKA reference group at 10 years is also shown.

Implant type	1 year		3 years		5 years		10 years	
	At risk	Survival % (95% CI)	At risk	Survival % (95% CI)	At risk	Survival % (95% CI)	At risk	Survival % (95% CI)
Cementless Oxford	954	96.6 (95.5-97.7)	365	93.7 (92.1-95.4)	149	92.3 (90.3-94.4)	-	-
Cemented Oxford 3	2,213	97.2 (96.5-97.9)	2,077	92.2 (91.1-93.3)	1,826	88.9 (87.6-90.2)	466	82.6 (80.8-84.5)
Cemented TKA reference group	62,106	98.9 (98.8-98.9)	44,560	97.3 (97.1-97.4)	28,801	96.6 (96.4-96.7)	3,308	95.3 (95.1-95.6)

CI=confidence interval. TKA=total knee arthroplasty.

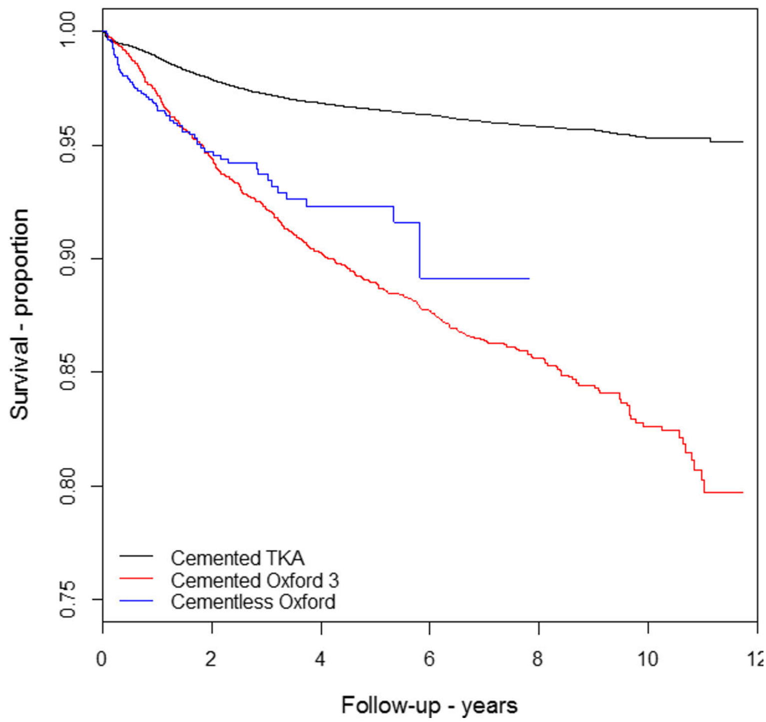


Figure 15. Kaplan-Meier survival of cementless Oxford, cemented Oxford 3, and cemented TKA as a reference group

The crude survival rates of the Oxford implants intersect at the 18-month follow-up, resulting in violation of the proportional hazards (PH) assumption in the Cox regression analysis (Figure 15). Therefore, age- and gender-adjusted comparison of the implants was performed for two separate time intervals of 0–18 months and >18 months. Both the cementless Oxford and cemented Oxford 3 had a significantly increased revision rate over that of cemented TKAs in the longer follow-up (Table 6).

Table 6. Adjusted RR (age, gender) for revision for any reason for cementless Oxford and cemented Oxford 3, and cemented TKA as the reference group.

Implant type	Follow-up overall		Follow-up 0-18 months		Follow-up >18 months	
	RR (95%CI)	p-value	RR (95%CI)	p-value	RR (95%CI)	p-value
Cemented TKA	1	-	1	-	1	-
Cemented Oxford 3	3.0 (2.7-3.4)	<0.001	3.7 (3.4-4.2)	<0.001	3.7 (3.2-4.2)	<0.001
Cementless Oxford	2.1 (1.6-2.7)	<0.001	1.7 (1.3-2.2)	<0.001	1.9 (1.2-3.0)	<0.006

RR=revision risk. TKA=total knee arthroplasty. CI=confidence interval.

5.3 Randomized assessor-blind study (Study III)

In study III, 143 patients were recruited and underwent randomization. Seventy-two patients were assigned to the medial UKA group and 71 to the TKA group (Figure 12). Three medial UKA patients did not receive their allocated device but were included in the analysis according to ITT principles. One had lateral compartment OA, one had a torn ACL, and one had posteromedial OA, all of which were revealed during surgery. The baseline characteristics of the two groups were similar with respect to age, gender, and BMI (Table 7).

Table 7. Baseline characteristics of patients by study group.

	Medial unicompartmental arthroplasty (n=72)	Total knee arthroplasty (n=71)
Age	63.3 ± 7.3	62.9 ± 8.5
Male gender - No. (%)	33 (46%)	30 (42%)
BMI	29.5 ±3.8	28.5 ±3.8
Oxford Knee Score ¤	25.0 ±6.55	26.1 ±6.5
KOOS classification §		
Symptoms	53.8 ±16.4	53.6 ±17.1
Pain	50.0 ±12.2	49.7 ±12.5
Function, Daily Living	55.8 ±14.0	58.6 ±14.0
Function, Sports	20.2 ±14.6	19.9 ±14.6
Quality of Life	28.7 ±15.3	30.8 ±13.5
Knee Society Score $	115.5 ±19.1	117.2 ±21.4
15D score £	0.84 ±0.07	0.84 ±0.08

Plus-minus values are mean ± SD. There were no significant differences in the baseline characteristics between treatment groups.

5.3.1 Primary Outcome

Clinically significant improvement from baseline to 2 and 12 months and 2 years was seen in the primary outcome in both study groups (Figure 16 and Table 8).

The functional outcome scores provided comparable scores for medial unicompartmental arthroplasty and total knee arthroplasty at 2 years. The mean difference in improvement of OKS between the study groups was 1.6 points (95% CI -0.7–3.9; p=0.175) at 2 years.

Table 8. Primary and secondary outcomes at 2 and 12 months and 2 years after surgery*.

			Improvement from baseline			
Outcome — adjusted mean (95% CI)*	Unicompartmental Knee Arthroplasty	Total Knee Arthroplasty	Unicompartmental Knee Arthroplasty	Total Knee Arthroplasty	Between-group difference, Total- vs. Unicompartmental Knee Arthroplasty	Adjusted p-value
Primary Outcome (2 years)						
Oxford knee score $	41.2 (39.7 to 42.7)	40.1 (38.7 to 41.6)	17.4 (15.8 to 19.1)	15.8 (14.2 to 17.5)	1.6 (-0.7 to 3.9)	0.175
Secondary Outcomes						
2 months						
Oxford knee score $	32.5 (30.6 to 34.4)	26.8 (24.9 to 28.7)	8.7 (6.8 to 10.6)	2.5 (0.5 to 4.4)	6.2 (3.5 to 8.9)	<0.001
Knee society score &	157.1 (150.3 to 164.0)	136.3 (129.4 to 143.1)	45.4 (38.5 to 52.3)	22.7 (15.9 to 29.6)	22.7 (13.0 to 32.4)	<0.001
KOOS Pain	72.3 (68.5 to 76.0)	59.9 (56.2 to 63.7)	24.0 (20.0 to 27.9)	12.6 (8.6 to 16.5)	11.4 (5.9 to 16.9)	<0.001
KOOS Symptoms	70.0 (65.9 to 74.1)	56.7 (52.6 to 60.8)	17.4 (12.8 to 22.0)	4.8 (0.2 to 9.4)	12.6 (6.1 to 19.1)	<0.001
KOOS Function, Daily Living	77.7 (74.0 to 81.5)	67.3 (63.6 to 71.0)	24.0 (20.0 to 28.0)	11.5 (7.5 to 15.5)	12.5 (6.8 to 18.1)	<0.001
KOOS Function, Sports	42.5 (37.0 to 48.1)	24.9 (19.4 to 30.4)	24.6 (19.3 to 30.0)	7.9 (2.6 to 13.3)	16.7 (9.1 to 24.3)	<0.001
KOOS Quality of Life	52.4 (47.7 to 57.1)	44.6 (39.9 to 49.3)	25.6 (20.9 to 30.3)	16.7 (12.0 to 21.4)	8.9 (2.3 to 15.6)	0.009
15D score	0.869 (0.852 to 0.886)	0.838 (0.821 to 0.855)	0.036 (0.020 to 0.051)	0.007 (-0.008 to 0.023)	0.028 (0.006 to 0.050)	0.013
12 months						
Oxford knee score $	41.2 (39.6 to 42.7)	38.4 (36.9 to 40.0)	17.4 (15.7 to 19.0)	14.2 (12.5 to 15.8)	3.2 (0.9 to 5.6)	0.007
Knee society score &	182.3 (177.9 to 186.8)	176.9 (172.6 to 181.3)	70.6 (65.0 to 76.2)	63.4 (57.8 to 69.0)	7.2 (-0.7 to 15.1)	0.074
KOOS Pain	87.8 (84.6 to 91.0)	81.8 (78.6 to 84.9)	39.5 (35.9 to 43.0)	34.4 (30.8 to 37.9)	5.1 (0.1 to 10.1)	0.046
KOOS Symptoms	83.1 (79.5 to 86.7)	72.6 (68.7 to 75.8)	30.4 (25.9 to 35.0)	20.3 (15.7 to 24.9)	10.1 (3.6 to 16.6)	0.003
KOOS Function, Daily Living	89.7 (86.7 to 92.7)	83.9 (80.9 to 86.9)	35.9 (32.5 to 39.3)	28.1 (24.7 to 31.5)	7.8 (3.0 to 12.7)	0.002
KOOS Function, Sports	59.5 (53.6 to 65.3)	51.6 (45.8 to 57.4)	41.6 (36.0 to 47.2)	34.6 (29.0 to 40.2)	7.0 (-0.9 to 14.9)	0.083
KOOS Quality of Life	69.4 (64.6 to 74.2)	63.9 (59.2 to 68.7)	42.6 (37.6 to 47.7)	36.0 (31.0 to 41.1)	6.6 (-0.6 to 13.8)	0.070
15D score	0.894 (0.876 to 0.912)	0.874 (0.856 to 0.893)	0.060 (0.045 to 0.076)	0.044 (0.028 to 0.059)	0.017 (-0·005 to 0.039)	0.125
2 years						
Knee society score &	180.9 (175.6 to 186.1)	178.6 (173.3 to 183.9)	69.1 (63.0 to 75.3)	65.1 (58.9 to 71.3)	4.1 (-4.7 to 12.8)	0.359
KOOS Pain	87.9 (84.7 to 91.0)	86.8 (83.7 to 90.0)	39.6 (36.1 to 43.0)	39.4 (36.0 to 42.9)	0.1 (-4.8 to 5.0)	0.959
KOOS Symptoms	85.5 (81.9 to 89.1)	77.0 (73.5 to 80.6)	32.8 (28.4 to 37.3)	25.1 (20.7 to 29.5)	7.8 (1.5 to 14.0)	0.015
KOOS Function, Daily Living	89.1 (86.2 to 92.0)	86.9 (84.0 to 89.8)	35.3 (31.9 to 38.8)	31.0 (27.6 to 34.5)	4.3 (-0.6 to 9.2)	0.084
KOOS Function, Sports	61.7 (56.1 to 67.2)	56.4 (50.9 to 61.9)	43.7 (38.6 to 48.9)	39.4 (34.3 to 44.6)	4.3 (-3.0 to 11.6)	0.245
KOOS Quality of Life	72.3 (67.9 to 76.8)	71.3 (66.9 to 75.7)	45.5 (40.6 to 50.5)	43.4 (38.5 to 48.3)	2.1 (-4.8 to 9.1)	0.547
15D score	0.894 (0.875 to 0.912)	0.889 (0.871 to 0.907)	0.060 (0.044 to 0.077)	0.058 (0.042 to 0.075)	0.002 (-0.022 to 0.025)	0.874

* Adjusted means (95% confidence intervals) from analysis of variance for repeated measurements. Analyses were adjusted for surgeon, age, sex and preoperative OKS.

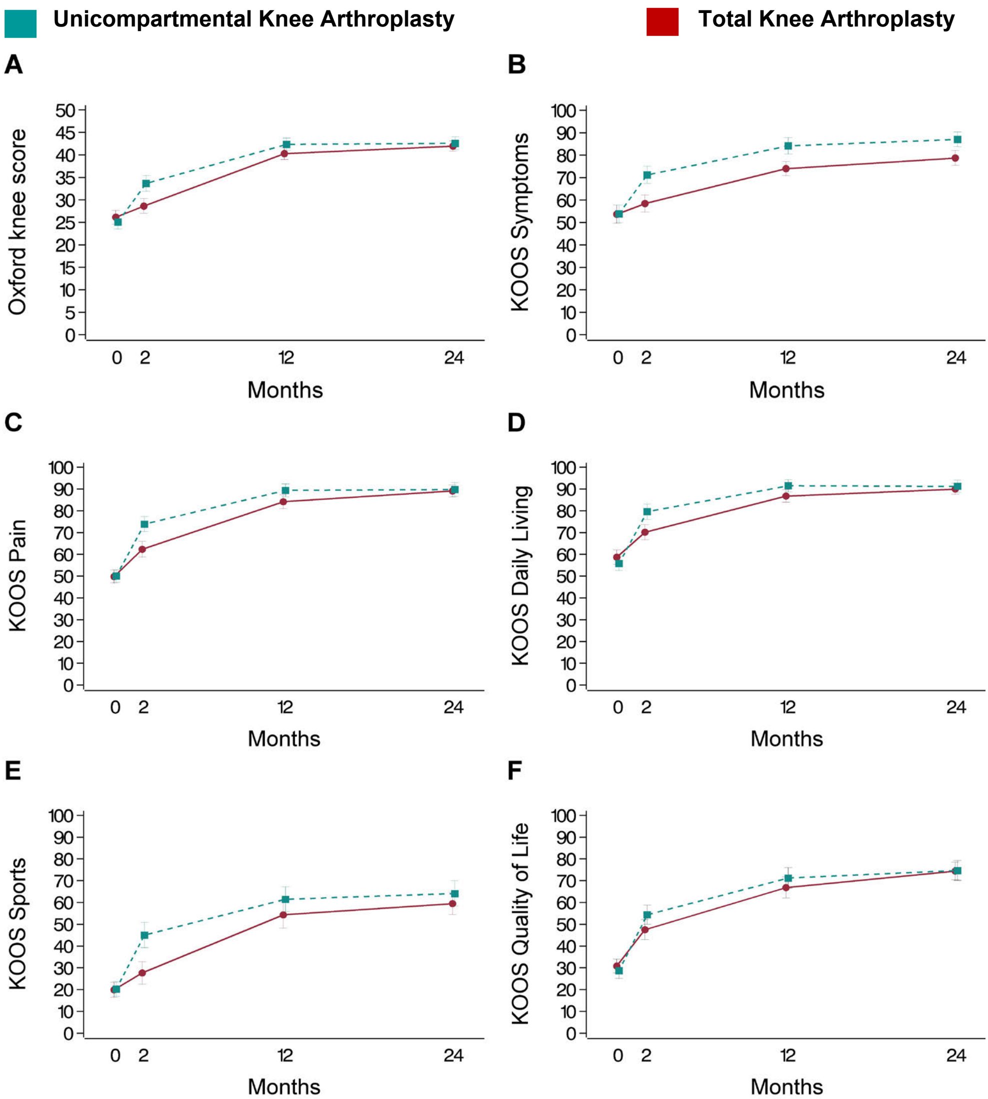


Figure 16. Primary outcomes in the UKA group and TKA Group. Values are means with 95% confidence intervals.

5.3.2 Secondary outcomes

In the KOOS subscales there were no mean differences in improvement between study groups in the pain score (0.1 points; 95% CI -4.8–5.0; p=0.96), function and daily living score (4.3 points; 95% CI -0.6–9.2; p=0.08), sports and recreation score (4.3 points; 95% CI -3.0–11.6; p=0.25), and quality of life score (2.1 points; 95% CI -4.8–9.1; p=0.55) at 2 years.

The mean difference in improvement of OKS between the study groups was 6.2 points (95% CI 3.5–8.9; p<0.001) at 2 months and 3.2 points (95% CI 0.9–5.6 p=0.007) at 12 months, favoring unicompartmental knee arthroplasty. In the KOOS subscales there were differences between the study groups in the pain score (11.4 points; 95% CI 5.9–16.9; p<0.001), symptoms score (12.6 points; 95% CI 6.1–19.1; p<0.001), function in daily living score (12.5 points; 95% CI 6.8–18.1; p<0.001), sports and recreation score (16.7 points; 95% CI 9.1–24.3; <0.001), and quality of life score (8.9 points; 95% CI 2.3–15.6; p=0.009) at 2 months and in the KOOS symptoms score (10.1 points; 95% CI 3.6–16.6 p=0.003) at 12 months. In the KOOS symptoms score the mean difference in improvement between study groups (7.7 points; 95% CI 0.02–15.3; p=0.049) favored unicompartmental arthroplasty at 2 years, but the difference was not clinically significant.

At 12 months, there were no differences between the study groups in the KOOS subscales sports and recreation score (7.0 points; 95% CI -0.9–14.9 p=0.08), and quality of life score (6.6 points; 95% CI -0.6–13.8 p=0.07). In the KOOS function and daily living score and in the pain score, the mean difference in improvement between the study groups was statistically but not clinically significant (7.8 points; 95% CI 3.0–12.7 p=0.002) and (5.1 points; 95% CI 0.1–1101 p=0.046), respectively.

Clinically significant between-group differences were found at 2 months in KSS and 15D: 22.7 points (95% CI 13.0–32.4; p<0.001) and 0.028 points (95% CI 0.006–0.050; p=0.013), respectively.

At 12 months, patients with TKA had a higher risk for limited postoperative range of movement needing manipulation under anesthesia (5 vs 0 patients, p<0.05). Three patients in the UKA group and four patients in the TKA group needed revision arthroplasty. The reasons for revision were deep infection (three in the TKA group), instability of the knee or bearing dislocation (one in the TKA and two in the medial UKA group), and hematoma evacuation (one in the medial UKA group) (Table 9.)

Table 9. Complications.

Outcome	UKA (n=69)	TKA (n=70)
Revision for any reason, No. (%) *	3 (4.2)	4 (5.6)
Infection, No. (%) §	0 (0)	3 (4.2)
Manipulation under anesthesia, No. (%)	0 (0)	5 (7.0) ¤
Postoperative hematoma (needing surgery), No. (%)	1 (1.4)	1 (1.4)
Postoperative fracture, No. (%)	0 (0)	0 (0)
Mobile bearing luxation or instability of the knee, No. (%)	2 (2.8)	1 (1.4)
Complications – Clavien-Dindo #		
Grade I, No. (%)	2 (2.8)	2 (2.8)
Grade II, No. (%)	0 (0)	5 (7.0)
Grade IIIa, No. (%)	4 (5.6)	5 (7.0)
Grade IIIb, No. (%)	0 (0)	2 (2.8)
Grade IVa, IVb and V, No. (%)	0 (0)	0 (0)

* Revisions for infection included, § Deep infections included, ¤ p=0.03

6 Discussion

The literature review provides moderate support for the use of UKA for selected patients with anteromedial knee OA. However, the main weakness of the review is the low quality of previous studies in general, and the polarity of UKA results between register-based and single-institution studies (Wilson et al., 2019). Several studies have links to the industry and thus possible bias. On the other hand, register-based studies are prone to selection bias, and lack of PROMs is justifiably criticized. There is definitely a need to make up for the paucity of literature in terms of indications and results of UKA, and especially to compare UKA to TKA in randomized controlled trial settings.

The FUNCTION study (study III) is a first assessor-blind study comparing medial unicompartmental and total knee arthroplasty in the treatment of isolated medial osteoarthrosis. The lack of blinding has been identified to be a significant source of bias in clinical trials (Hróbjartsson et al., 2014).We found that patients treated with medial unicompartmental arthroplasty did not have better patient-reported outcome scores in primary outcome OKS or secondary outcome KOOS compared to total knee arthroplasty at 2 years. Patients treated with medial unicompartmental arthroplasty had a faster postoperative recovery (better OKS and KOOS scores at 2 and 12 months) compared with patients treated with total knee arthroplasty. There was no difference in the number of revisions between the study groups.

In the stydy II we found that the short-term survivorship of the cementless Oxford UKA was higher than that of the cemented Oxford UKA. Also the overall survivorship of both UKA types was inferior to that of cemented TKAs.

In the study I we found that, the overall UKA revision rate was high (18%). All the operated patients had symptomatic OA, but a significant number of UKAs were performed on patients with radiologically mild OA (45.6%, KL 0–2). We found that in addition to female gender, radiologically mild OA (KL grade 0–2) in preoperative radiographs increased the risk of revision (OR=1.89).

6.1 Patient reported outcomes of unicompartmental versus total knee arthroplasty

To our knowledge, there are five earlier randomized trials comparing medial UKA and TKA (Sun & Jia, 2012) (Newman et al., 1998) (Newman et al., 2009) (Kulshrestha et al., 2017) (Costa et al., 2011) (Beard DJ et al. 2019). In the largest and methodologically highest quality of these randomized trials including 528 patients, UKA provided good clinical outcome with lower cost and better cost-effectiveness at 5 years compared with TKA (Beard DJ et al. 2019). In this study, OKS as the primary outcome was comparable between the study groups at 5 years postoperatively. However, patients in the UKA group were more likely to think that their knee was better than before surgery and would more often have the surgery again than patients in the TKA group (95% vs. 90%, p=0.010; 91% vs. 84%, p=0.010, respectively).

Newman et al. compared fixed-bearing UKA to TKA and reported a better range of movement (ROM) after UKA. Sun PF et al. compared mobile-bearing UKA with fixed-bearing TKA and did not find a significant difference in (ROM) or Knee Society score (KSS) postoperatively after a mean of 52 months follow-up, but the TKA group had significantly more prevalent postoperative deep vein thrombosis and greater post-operative blood loss. Kulshesrestha et al. reported similar outcomes compared fixed-bearing unicompartmental arthroplasty with total knee arthroplasty for patient with bilateral simultaneous arthroplasty. These earlier randomized control trials, except for TOPKAT, have reported single center series, without adequate blinding, with relatively small number of participants (Costa et al., 2011)(Newman et al., 1998)(Sun & Jia, 2012)(Kulshrestha et al., 2017)(Newman et al., 2009).

In our study, both UKA and TKA provided good to excellent short-term results in a assessor-blind setting. However, the UKA group had better primary outcome results at 2 months. These results were clinically significant in all primary outcome measures, suggesting faster postoperative recovery. At 12 months, the UKA group still had slightly better scores in both the OKS and KOOS, although in the OKS the difference was no longer clinically significant, but at 2 years results were comparable. UKA is significantly smaller operation than total knee arthrolasty, with preservation of patients own intact ligaments and without vastus medialis incision. These reasons might influence to faster recovery. As patient expectations have a significant effect on outcome in arthroplasty, assessor-blind studies are vital for confirming patient-reported outcome results in medial UKA with TKA (Bourne et al., 2010). The findings of our study are mainly in line with a recent literature review and meta-analysis assessing differences in patient-relevant outcomes between UKA and TKA (Wilson et al., 2019). However, medial unicompartmental arthroplasty did not provide a better functional result compared to total knee arthroplasty at 2 years in a assessor-blind randomized study setting.

Degenerative changes of the knee are relatively common findings in middle-aged and elderly people, even if the knee is asymptomatic. In symptomatic patients, degenerative changes are not always the cause of the pain and should primarily be treated conservatively. Based on the results in the extant literature, UKAs have been performed on patients for whom knee pain probably does not originate from OA, and these patients have an increased risk of unsatisfactory results and subsequent UKA revision (Niinimäki et al., 2011). This phenomenon is similar in TKA patients, as those suffering from mild or moderate OA are also at risk of dissatisfaction following TKA procedure (Schnurr et al., 2013).

The developing group of the Oxford UKA has reported a superior 94% rate of survival at 10 years when the original indications are respected (full thickness cartilage loss and anteromedial OA with bone-on-bone contact) (Pandit et al., 2015). Radiologically mild OA has been associated with high reoperation or revision rates, and there is serious concern that UKAs are performed on patients who are symptomatic but whose knee OA is radiologically not severe enough to justify UKA or any arthroplasty for that matter (Niinimäki et al., 2011)(Schnurr et al., 2013). The results of the current study support these conclusions. In addition, we observed that surgeons have expanded the UKA indications, as only half of the operated knees had KL 3–4 OA and a 33% medial joint space of 2 mm or less. Extension of the UKA indications to radiologically milder OA is a problem that needs addressing. Unfortunately, it appears that adherence to the manufacturer's instructions and educating surgeons with regard to setting indications for the Oxford UKA have not been successful. For patients with severe symptoms but mild radiological OA, other treatment options (conservative treatment, HTO, etc.) should be recommended.

UKA is a less invasive and more bone-saving operation than TKA and is therefore a tempting choice for patients with symptomatic but radiologically mild or moderate OA. Operating on these patients may partly explain the higher revision rates of UKA compared with TKA.

6.2 Cemented versus cementless unicompartmental knee arthroplasty

In the single-center series, the 5-year cumulative survival of cementless UKA has been reported to be 98.0% to 98.8%, which is comparable to the best survival for cemented TKA (Hooper et al., 2015)(Blaney et al., 2017)(Pandit et al., 2017)(NJR, 2016). It seems that cementless devices have slightly better survival than cemented.

However, the UKA procedures included in these studies were performed in high volume centers, which would explain the overall high survival of UKA compared to that in registries. The revision surgery of UKA is also clearly easier compared to revision of TKA. Radiolucent lines are commonly observed at the bone-implant interface of unicompartmental knee replacement tibial components. In total, 62% of knees with cemented Oxford UKA has complete or partial radiolucency lines. (Gulati et al., 2009). It is possible that surgeons have incorrectly interpret these to be as aseptic loosening's and it may had led to unnecessary revisions.

According to AOANJRR data, the 10-year cumulative revision frequency of the cemented Oxford 3 implant is 14.8% and of the cementless Oxford implant 13.6% (AOANJRR, 2018). The equivalent 10-year Kaplan-Meier estimate of the cumulative percentage probability of first revision in England and Wales for the Oxford 3 implant is 11.4% and in Sweden 13% (NJR, 2016)(Robertsson & Ranstam, 2003). The most common reasons for knee revision surgery were aseptic loosening (29.8%), infection (24.1%), pain (6.3%), progression of disease (6.3%) instability (5.5%) (AOANJRR, n.d.). Our data support these findings, although the revision rate of the cemented Oxford 3 implant is slightly higher (10-year estimate 17.2%) in Finland than in other countries. In the current study, the 3-year survivorship was 93.7% (95% CI 92.1-95.4) for the cementless Oxford device, 92.2% (95% CI 91.1-93.3) for the cemented Oxford 3 device, and 97.3% (95% CI 97.1– 97.4) for the cemented TKA reference group. The corresponding figures at 5 years were 92.3% (95% CI 90.3–94.4), 88.9% (95% CI 87.6–90.2), and 96.6% (95% CI 96.4–96.7).

According to New Zealand Registry, revision rate of 2,630 cementless Oxfords per 100 component years was 0.70 (0.53-0.89), whereas that of 3,940 cemented Oxford 3s was 1.40 (1.27-1.54)(NZJR 17 Year Report, n.d.). Our findings support these data, although we do not use component years in reporting. It seems that the short term implant survival of cementless Oxford has really improved compared to that of cemented Oxford 3. However, at least in Finland the use of cemented Oxford 3 has ended, and in 2015 all UKAs implanted were cementless Oxfords.

A study based on FAR data from 1985 to 2011 reported the 10-year survivorship of the cementless Oxford UKA to be around 83% (Niinimäki et al., 2014). These earlier data are consistent with current data (2005–2015) (Finnish Arthroplasty Register, n.d.). However, in a previous study it was not possible to assess separately cementless and cemented Oxford devices.

The popularity of the cementless Oxford method has grown markedly since the publication of the previous study in 2014, and practically 100% of implanted UKAs are now cementless (Finnish Arthroplasty Register, n.d.). The most common reason for revision in the earlier study based on FAR data was "aseptic loosening" (46.8%), followed by "other reason" (35%). Although the accuracy of recording reasons for revision in the FAR registry has been unsatisfactory, it seems that aseptic loosening as a major cause of failure of the cementless Oxford implant has decreased in Finland, or reporting has become more accurate. Thus the era when cemented and cementless Oxfords have been implanted is not the same. Overall indications of UKA surgery have become recently more appropriate. It has been well established that symptomatic patients who have radiologically mild OA have an increased risk for revision (Niinimäki et al., 2011)(Knifsund et al., 2017). When indications have become more appropriate, the need of "unnecessary" revisions for pain may have decreased. Systematic education of surgeons to take into account that preoperative radiologic OA grade must be bone-to-bone also in UKA surgery has been active in Finland lately. These issues have probably increased the survivorship of cementless Oxford compared to that of the cemented one in Finland.

6.3 Limitations and strengths of present studies

Our studies have some limitations. Among them is that the effect of procedure volume per surgeon on revision rate was not separately assessed. Further, the study I design was observational and retrospective, and therefore also vulnerable to other omitted variables, which may have confounded our findings. Information regarding potentially important variables, such as comorbidity, was unavailable. Further, preoperative radiographs in study I were taken with each patient standing upright in front of the film cassette with the knee in full extension or 20 degrees flexion. Radiographs taken in full extension may underestimate the degree of OA. In register-based studies, implant survival is the only outcome we are able to assess. Patient-reported outcome measures are not included in the available long-term data. In the register data on patients' medical histories, comorbidities, and knee radiographs are not strictly available, and even if patients are matched for age and gender, the characteristics of patients undergoing arthroplasty may be quite different. On the other hand, this study reports reliable the indications and revisios from single center. After publication it has changed the treatment protocol and indications for UKA, in this center. Further, the UKA operations are now focused to the three orthopedic surgeons to reach sufficient amount of operations per year per surgeon.

The accuracy of reporting the indication for revision in register-based studies is based on the revision surgeon's opinion and is prone to error. Second, the era when cemented and cementless UKAs were implanted in study II is different. Indications for UKA may have become more stringent. These circumstances could have increased the survivorship of the cementless device compared to the cemented one in Finland. The strengths of these register-based studies are the population-based design, prospective collection of data, and the large and comprehensive sample size.

Further, patients with pain following UKA may be more likely to have a revision than patients with pain following TKA (Liddle et al., 2015). Dissatisfied patients without any abnormal radiological findings are at risk of unnecessary revisions and subsequent unsatisfactory results. An example of this is misdiagnosis of loosening; radiolucent lines are a common finding adjacent to cemented UKAs and may be falsely diagnosed as component loosening, particularly on the tibial side (Tibrewal et al., 1984).

In study III, 2 years is a relatively short follow-up time for an arthroplasty. However, one of the main potential benefits of UKA is faster postoperative recovery, which can be assessed during the first two postoperative years. Second, there was only one uncemented mobile-bearing medial UKA device included in the study; thus caution should be applied when extrapolating these results to other unicompartmental device types such as lateral, cemented, or fixed-bearing unicompartmental devices. The main strength of our study was the assessor-blind setup, which is the most reliable method for comparing these devices. Patient expectations might have an effect on the results (Bourne et al., 2010). Another strength of our study is that it was conducted in the public sector in publicly funded hospitals and the authors did not receive any grants or other funding from industry.

6.4 Summary

The current study supports the recommendation that in preoperative, standing, weight-bearing radiographs, the degree of knee OA should be KL 3 or 4, the thickness of the medial joint space should be less than 20% of the thickness of the lateral joint space, and the medial joint space must be less than 1 mm. Other treatment choices such as conservative treatment or HTO should be considered in patients not meeting these criteria.

The cementless Oxford method has better survivorship than that of the cemented Oxford 3 in the short term. However, overall survivorship of both UKA types remained inferior to that of contemporary cemented TKAs. Survival of UKA will be always be lower compared to TKA due to the risk of progression of lateral compartment OA. This should be taken into account and discussed preoperatively with patients.

Medial unicompartmental arthroplasty provides a better short-term outcome and faster postoperative recovery with low risk of complications than total knee arthroplasty. These studies support the use of medial UKA in patients with anteromedial osteoarthritis. However, more long-term data from randomized trials is needed to assess the later revision burden.

When deciding between the two treatment options of TKA or UKA for the same condition, the decision should be made between the patient and the orthopedic surgeon. Every surgeon offering knee arthroplasty should have both treatment options available, at least in the operative unit. Patients should be able to understand

and compare the risks and benefits of both treatment options. A wide range of outcomes, relative risks, and potential benefits of each treatment option must be understood and applied to each individual patient.

7 Conclusions

The following conclusions can be drawn from the present study:

1) When considering UKA the following criteria should be fulfilled in preoperative standing, weight-bearing radiographs: a) the degree of knee osteoarthritis should be Kellgren-Lawrence 3 or 4, b) the thickness of the medial joint space should be less than 20% of the thickness of the lateral joint space, c) the medial joint space must be less than 1 mm.

2) In the short term, use of the cementless Oxford implant is associated with increased survivorship compared to the cemented Oxford 3. However, overall survivorship of both mobile-bearing unicompartmental arthroplasty types is still inferior to contemporary cemented total knee arthroplasties.

3) Medial unicompartmental arthroplasty provided a good outcome at 2 years and faster postoperative recovery than total knee arthroplasty. The present study supports the use of medial unicompartmental arthroplasty in patients with anteromedial osteoarthritis. In patients who are suitable for unicompartmental arthroplasty, faster recovery and lower risk of complications but also comparable 2 year functional results should be part of the shared dissension making prior to the operation and when deciding between unicompartmental and total knee arthroplasty. Also, the higher revision risk must be taken into consideration.

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