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CONTENTS

LIST OF ORIGINAL PUBLICATIONS

1. Metsna V, Vorobjov S, Märtson A. Prevalence of anterior knee pain among patients following total knee arthroplasty with nonreplaced patella: a retrospective study of 1778 knees. Medicina (Kaunas). 2014;50(2):82–6.

2. Metsna V, Vorobjov S, Lepik K, Märtson A. Anterior knee pain following total knee replacement correlates with the OARSI score of the cartilage of the patella. Acta Orthop. 2014;85(4):427–32.

3. Metsna V, Sarap P, Vorobjov S, Tootsi K, Märtson A. The patellar shift index: a reliable and valid measure for patellofemoral congruence following total knee arthroplasty with unresurfaced patella. Acta Orthop Traumatol Turc. 2013;47(5):323–9.

Contribution of Vahur Metsna to original publications

Paper 1: study design, data collection, data analysis, writing the paper

Paper 2: study design, performing the surgeries, obtaining the biopsies of the patella, clinical evaluation of patients, data collection, data analysis, writing the paper

Paper 3: study design, data collection, data analysis, writing the paper

ABBREVIATIONS

AKP	anterior knee pain
AKPQ	anterior knee pain questionnaire
AP	anterior to posterior
CI	confidence interval
HSS	Hospital for Special Surgery (New York)
ICC	intraclass correlation coefficient
ISN	infrapatellar branch of the saphenous nerve
Kα	Krippendorff's alpha
LPT	lateral patellar tilt
OARSI	Osteoarthritis Research Society International
PD	patellar displacement
PF	patellofemoral
PFPS	patellofemoral pain syndrome
PR	prevalence ratio
PSI	patellar shift index
SD	standard deviation
TKA	total knee arthroplasty

INTRODUCTION

Anterior knee pain (AKP) is the cause of dissatisfaction with an artificial joint in more than half of patients following total knee arthroplasty (TKA) (van Jonbergen et al. 2012). AKP is indistinctly specified as a construct, which makes the estimation of its prevalence difficult. However, increasing numbers of knee replacements performed each year due to an aging population (Robertsson 2013, Leonardi et al. 2014) make AKP, as one of the most prevalent complication of TKA, an important topic to study. The majority of research covering AKP comes from high performing specialised centres in countries with racially and ethnically diverse patient populations. Dissimilarities in institutional, physician and patient characteristics may cause differences in TKA performance between the sites of care. The prevalence of AKP following TKA has not been studied in Estonia and this thesis aims to ascertain whether results obtained in Estonia are comparable to the findings in other care settings worldwide.

Degeneration of the articular cartilage of the patella may be one cause of AKP (Picetti et al. 1990, Rodriguez-Merchan and Gomez-Cardero 2010). The dilemma of resurfacing versus not resurfacing the patella has been the subject of numerous studies. Although there is a trend towards less revisions (Pilling et al. 2012) and slightly better patient satisfaction (Schindler 2012) in cases of resurfaced patella, many unanswered questions remain regarding the role of patellar cartilage in the evolution of AKP. Research focusing on the correlation of macroscopic cartilage defects and AKP has provided conflicting results (van Jonbergen et al. 2012). Histological changes precede macroscopic degeneration of the cartilage (Bentley and Hill 2007) and this is why visual inspection of the cartilage may not be adequate. In this study an approach proposed by the Osteoarthritis Research Society International (OARSI), which combines the histologic assessment of depth with visual inspection of the extent of the cartilage impairment (Pritzker et al. 2006), was used to find out whether patellar cartilage defects characterised this way correlate significantly with postoperative AKP following knee replacement. Clarifying the role of cartilage defects in the evolution of AKP should aid surgeons in the optimal handling of the patella during knee replacement.

Examination of a patient with a painful knee includes taking radiographs in anterior to posterior (AP), lateral and patellofemoral (PF) axial projections. Patellar maltracking in knees with AKP may express several possible causes of complaints. Resection of the joint surfaces during knee replacement and stress-induced remodelling of the unresurfaced patella distort the landmarks currently necessary for measuring PF congruence. Interpretation of the measures expressing patellar translation in absolute numbers (millimetres) instead of proportions is also influenced by radiographic magnification and knee dimensions, making it unhelpful to compare the results of different studies. The need has emerged for a new reliable radiographic measurement tool, which would enable practitioners to make judgements upon the patellofemoral congruence of a replaced knee joint and quantify patellar displacement.

This thesis focuses on three aspects of AKP following TKA with unresurfaced patella: the prevalence, correlation with patellar cartilage defects and measurement of PF congruence.

REVIEW OF THE LITERATURE

1. Definition of AKP and PFPS

Anterior knee pain (AKP) refers to pain in the front part of the knee. AKP is a general term incorporating all possible pathologies that might cause the anterior of the knee to hurt (Witvrouw et al. 2005).

Patellofemoral pain syndrome (PFPS) is a narrower term than AKP, emphasizing the patellofemoral (PF) joint as the source of pain. PFPS however does not specify which structure of the patella or femur is impaired. The word 'syndrome' stands for the conglomeration of symptoms and signs in addition to pain and instability (Witvrouw et al. 2005). PFPS manifests as activity related AKP and grows worse with activities (*e.g.* descending the stairs) that put greater strain on the PF joint. Sitting for a longer time may also elicit PFPS symptoms (Petersen et al. 2013, Sanchis-Alfonso 2014).

In the orthopaedic literature AKP and PFPS are frequently used as synonyms. In the current thesis the term AKP is used only when specifying the location of pain in the front aspect of the knee; the term PFPS is reserved for describing pain of PF origin.

2. Patellofemoral anatomy

2.1. General aspects

The PF joint forwards the forces generated by the quadriceps femoris muscle to the shank through a lever system, where patella functions like a fulcrum.

There is a trilaminar arrangement of fibrous soft-tissue structures between the skin and the anterior surface of the patella. The most superficial is a transversely orientated fascia, next layer is an aponeurosis with obliquely orientated fibers and the deepest of the three is rectus femoris tendon with its longitudinal fibers. The spaces between these three fibrous layers comprise of three bursas: a prepatellar subcutaneous bursa, a prepatellar subfascial bursa, and a prepatellar subaponeurotic bursa. The bursas' main idea is reducing friction (Dye et al. 2003).

The infrapatellar fat pad lies between the patellar ligament and anterior side of the proximal tibia. It is richly innervated with sensory nerve endings and may be the source of AKP (Kramers-de Quervain et al. 2005).

The convex posterior side of the patella and the concave femoral trochlea constitute the PF articulation. The posterior surface of the knee cap has three facets: medial facet is isolated from the lateral by median ridge, odd facet is small and located on the medial edge (Scott 2012).

Wiberg (1941) has classified patellar shape into three: "1 – the median ridge lies in the centre of patella and the medial and lateral facets are of the same size, 2 – the median ridge is situated slightly medial and the lateral facet is bigger than the medial one, 3 – the median ridge is displaced far medially so the medial facet is nearly absent". Wiberg (1941) type 3 patellas have reduced

constraint due to the small medial facet and are therefore more predisposed to lateral subluxation (Wiberg 1941, Panni et al. 2011). Bony and cartilaginous contours of the patella do not coincide. This is why it is easy to misinterpret plain radiographs when estimating the PF congruence based on the lowest points of trochlea and patella (Staubli et al. 1999).

The patellar articular surface has the widest contact area with the trochlea when the knee is in 90 degrees of flexion: in this knee position also the PF contact pressure is the highest. The area of the patellar articular cartilage in contact with the trochlea is relatively small and changes constantly during knee motion (Müller and Wirz 2001). At full extension inferior part of the patella is in contact with the trochlea. As the knee flexes, the contact point shifts in the superior direction on the patella (Stiehl 2005). The thicker cartilage in the superior part of the patella helps to neutralise the higher PF contact forces in deeper flexion (Luyckx et al. 2009). The PF joint has to cope with the highest stresses in the human organism, amounting even to 20 times the body weight (Schindler 2012).

The direction of PF forces varies during knee motion because of internal and external rotation of the tibial tubercle relative to femur caused by the thigh muscles crossing the knee joint (Müller and Wirz 2001). Also alterations in patellar height may create severe disturbances in force transmission through knee flexion (Stiehl et al. 2001).

In a prosthetic knee the PF joint is stabilised by the geometry of the trochlear groove and the posterior side of the patella, medial and lateral soft tissue restraints, the quadriceps muscle and patellar tendon (Andrikoula et al. 2006, Barink et al. 2006).

Abnormal PF forces may cause PF symptoms following knee replacement (Iranpour et al. 2010). TKA's with unresurfaced patella or anatomic shaped re-surfacings retain close to normal PF contact pattern, wheras dome-shaped patellas transfer the contact point on the patella more superior (Stiehl et al. 2001).

A lot of importance is attached to the design of the trochlear groove of the femoral component in ensuring the optimal tracking pattern of patella and minimising postoperative PF complaints. It should be emphasized, however, that besides trochlear design, also alignment of the components, soft tissue balance, scar tissue and surgical techniqe in general affect the PF function (Kulkarni et al. 2000, Iranpour et al. 2010).

2.2. Blood supply of the patella

The patellar blood supply derives from the vessels originating from the popliteal artery proximal to the femoral condyles: the superior genicular, medial superior genicular, medial inferior genicular, lateral superior genicular, lateral inferior genicular and the anterior tibial recurrent artery. These arteries form a vascular anastomotic ring around patella. The medial and lateral genicular arteries give off transverse branches anastomosing behind the patellar ligament (Scapinelli 1967).

Intraosseus perfusion consists of two connected systems: the mid-patellar vessels entering 10–12 vascular foramina on the anterior surface of patella and the vessels of the inferior third of the patella arising from the transverse branches behind the patellar ligament. The intrinsic vessels supply cancellous bone up to the chondro-osseus junction (Gelfer et al. 2003, Naslund et al. 2007).

2.3. Innervation of the patella

The anterior part of the knee is innervated by the articular branches of the femoral, the common peroneal and the saphenous nerve (Hirasawa et al. 2000, Damarey et al. 2013). Nerves have been found to enter patella in supero-medial and supero-lateral quadrants (Maralcan et al. 2005) and medially (Barton et al. 2007). Most of the intraosseous nerves are accompanied by vessels. Medial and central patella are more densly innervated compared to the lateral part, there are no large nerves adjacent to the subchondral plate (Barton et al. 2007). There are three types of nerve endings in the knee: Ruffini's corpuscles, free nerve endings and Pacinian corpuscles. Free nerve endings are associated with pain detection (Hirasawa et al. 2000). Most well-known neuropeptides involved in the transmission of pain by peripheral nerves are substance P and calcitonin gene related peptide (Hirasawa et al. 2000, Bohnsack et al. 2005). Nerve endings accompany blood vessels and are far-spread in periarticular soft tissues of the knee: the retinaculum, synovium, fat pad and the pes anserinus (Witonski and Wagrowska-Danielewicz 1999, Bohnsack et al. 2005). In patients with AKP the concentration of nociceptive nerve fibers increases in the fat pad and medial retinaculum (Witonski and Wagrowska-Danielewicz 1999).

2.4. Architecture of the articular cartilage

Patellar cartilage is the thickest in the human body, amounting to 6,5mm (Scott 2012). Hyaline cartilage consists of extracellular matrix and chondrocytes. The extracellular matrix is synthesized by the chondrocytes and constitutes 95% of the cartilage volume being principally comprised of water, type 2 collagen and proteoglycans.

The chondrocytes are organised into 4 zones. The superficial zone contains high number of flattened chondrocytes and the collagen fibers aligned parallel to the articular surface. The superficial layer protects deeper zones from share forces. In the middle zone the chondrocytes are spherical and their density is low, collagen is organised obliquely. In the deep zone the chondrocytes together with the collagen fibers are both arrranged in columns and perpendicular to the joint line. The role of the deep zone is resistance to compressive forces. The calcified layer secures the cartilage to bone and is separated from the deep zone by the tide mark. There are small numbers of hypertrophic chondrocytes in the calcified layer (Alford 2005, Sophia Fox et al. 2009).

Normal articular cartilage is avascular, aneural and without lymphatics. In osteoarthritis the erosion channels containing blood vessels together with nerves

may run through the subchondral plate and invade the cartilage (Witonski and Wagrowska-Danielewicz 1999, Suri et al. 2007). Angiogenesis is a prerequisite for the innervation of the articular cartilage. The erosion channels may contain vessels without nerves, but never nerves without vessels (Suri et al. 2007, Sophia Fox et al. 2009).

3. Causes of AKP

The etiology of AKP is multifactorial and this is why determination of its immediate cause may be difficult. Previous research describes an abundance of possible causes, but the actual reason for the evolution of anterior knee complaints may be a combination of several factors unique to each case (Bourne 2011, Meftah et al. 2011).

3.1. Classification

The causes of AKP following TKA may be classified as follows:

Imbalance of soft tissues
- Dynamic valgus of the knee
- Imbalance of vastus medialis and lateralis
- Lateral patellar facet syndrome (tight lateral retinaculum)

Implant-specific
- Design
- Malpositioning
- Sizing

Patella-specific
- Cartilage
- Height
- Fracture
- Ischemia
- Tumor

Synovial proliferation
- Synovial entrapment
- Patellar clunc syndrome
- Notch stenosis

Fat pad pathology
Neuropathic pain
Unknown cause

3.2. Imbalance of soft tissues

Soft tissue imbalance and implant-specific problems both lead to PF maltracking, which may cause pain through increasing focal bone stresses and streching the retinacular structures. The genesis of pain in cases of PF instability has been associated with hyperinnervation (nerve ingrowth) of the lateral retinaculum as a result of chronic stretching and with stimulation of subchondral nerves of the patella in response to constant overload of the articular surfaces (Sanchis-Alfonso 2014). The relationship between PF maltracking and pain is not so definite. There are studies stating that even mild patellar maltracking causes pain (Lakstein et al. 2014) concurrently with data suggesting to explore other causative mechanisms of complaints in the front part of the knee (MacIntyre et al. 2006).

PF soft tissue balance may be altered also by dynamic valgus of the knee, which is the sequelae of the weakness of hip abductors and external rotators, causing adduction and internal rotation of the femur. Other abnormalities associated with this pathology are internal rotation and abduction of the tibia, hyperpronation of the foot, contralateral pelvic drop and excessive hip adduction and ipsilateral trunc inclination (Sanchis-Alfonso 2014).

In situations where the decreased activity of vastus medialis is not able to equilibrate the force of vastus lateralis, patella is pulled excessively laterally, causing unphysiological strain in the PF joint. Often such imbalance of the quadriceps is present in arthritic knees already preoperatively and worsens after the joint replacement (Petersen et al. 2014, Sanchis-Alfonso 2014).

Lateral patellar facet syndrome may be diagnosed if in addition to pain experienced by the patient in the front part of the knee also palpation of the lateral side of patella is painful and the lateral facet of the patella is in contact with the prosthetic femoral trochlea on axial X-ray (Cercek et al. 2011, Zhang et al. 2012, Nikolaus et al. 2014, Pagenstert et al. 2014). Other possible causes of pain like infection, component malpositioning and metal allergy have to be eliminated beforehand (Pagenstert et al. 2014). Relief of symptoms after decompression of lateral PF joint by lateral patellar facetectomy and medial patellar reefing refers to the role of tight lateral retinaculum in the evolution of lateral patellar facet syndrome (Zhang et al. 2012, Pagenstert et al. 2014). Although lateral patellar facetectomy seems to be the preferred method due to retaining the lateral blood flow, there is also data about the positive effect of lateral retinacular release in lowering the incidence of AKP following TKA (Zha et al. 2014).

3.3. Implant-specific causes

3.3.1. Design

PF problems have been attributed to several design features of the femoral, tibial and patellar components. Following the faultless knee replacement with balanced soft tissues and correctly mounted implants, the design of the femoral component is the most important determinant of optimal patellofemoral stress.

More anatomical femoral component is advisable when not replacing the patella (Ma et al. 2007).

Anterodistally facing corner along the trochlear floor of the posterior stabilised femoral components may interfer with patellar tracking and in the presence of suprapatellar synovial tissue be responsible for the patellar clunc syndrome or synovial entrapment (Kulkarni et al. 2000, Pollock et al. 2002, Dajani et al. 2010, Peralta-Molero et al. 2014).

The length of the trochlea has been shown to influence patellar kinematics. Too short trochlea proximally hinders the patellar secure entering into the trochlear groove at the start of extension. On the other hand, ending the distal trochler groove too proximally will disturb patellar tracking in deep flexion. Too flat lateral flange of the trochlea may fail to offer enough constraint for the prevention of lateral displacement of the patella (Kulkarni et al. 2000).

Multiradius femoral components have a relatively anterior and changing extension-flexion axis while in single radius femoral implants knee movement occurs around one relatively posterior rotation centre. The more posterior rotation axis of the femoral component ensures longer and more efficient extensor mechanism's moment arm. Longer moment arm exerts less pressure on the PF joint and reduces AKP. Therefore single radius femoral components may be preferred when trying to gain optimal PF kinematics (Mahoney et al. 2002).

It has also been shown by Mugnai et al. (2014) that more anatomic bearing geometry of both femoral and tibial components can lower the prevalence of AKP. However, a meta-analysis by Pavlou et al. (2011) comparing patella-friendly and patella non-friendly TKA designs didn't find any difference in the incidence of AKP between groups.

3.3.2. Position

While performing the knee replacement surgery, it is vital to choose the correct implant size and to place the components in correct rotation and medio-lateral as well as AP position. Errors in implant sizing and positioning will lead to either instability or overstuffing of the PF or tibiofemoral compartments. The association between rotational malalignment of the components of the total knee implant and chronic postoperative knee pain has been recorded convincingly (Czurda et al. 2010, Vanbiervliet et al. 2011). PF lateral share-forces can be minimised by rotating the femoral component laterally and in cases of patellar resurfacing, placing the patellar component medially (D'Lima et al. 2003). Steinbruck et al. (2014) proved in a cadaver study that placement of the femoral component in 6 degrees of external rotation relative to transepicondylar axis will result in significantly reduced PF pressure compared to neutral or 3 degrees external rotation. Figgie et al. (1986) showed that AKP may be almost eliminated, if the tibial component is inserted neutral or posterior to the center of tibia, the joint line is not changed more than 8 mm and patellar height remains between 10–30 mm. Somewhat surprisingly van de Groes et al. (2014) reported less postoperative pain when the femoral component was placed in a

more medial position. They speculated, that the reason might be the more lateral orientation of the prosthetic trochlea compared to the native knee.

3.3.3. Size

Tibio-femoral instability created by too loose flexion gap compromises the PF joint through reduced femoral roll-back in flexion. When the knee is unstable in flexion, the posteriorly subluxed tibia icreases PF contact pressure. In a well functioning knee femoral rollback improves the efficiency of the extensor mechanism and therefore reduces PF strain (D'Lima et al. 2003, Petersen et al. 2014). The placement of the femoral component excessively anteriorly or oversizing either the femoral or patellar component will result in redundantly tight soft tissues and increase in contact pressure between the articulating surfaces of the patella and femur, which is called overstuffing (Ghosh et al. 2009, Steinbruck et al. 2013, Petersen et al. 2014). The same is true about tibiofemoral compartment, when too thick insert is implanted (Babazadeh et al. 2013). Several authors have shown that overstretching the knee compartment during arthroplasty is a strong predictor of pain in that compartment postsurgically (Ghosh et al. 2009, Babazadeh et al. 2013, Steinbruck et al. 2013). However, Pierson et al. (2007) do not support the belief that overstuffing the PF joint has any adverse effects on the results of TKA.

3.4. Patella-specific causes

3.4.1. Cartilage

Without doubt, most of the patellas show some type of cartilage damage on visual inspection at the time of surgery (Rodriguez-Merchan and Gomez-Cardero 2010). Furthermore, radiographic studies have demosntrated remodelling of patellar shape in a replaced knee with unresurfaced knee cap: these are changes extending far beyond the articular cartilage (Shih et al. 2004). The link between AKP and PF osteoarthritis has been well established in a native knee (Thomas et al. 2010), but this relationship cannot be carried over to the artificial joint due to the replaced articulating surfaces. In general terms, the medical literature is dubious regarding the role of patellar cartilage defects in the evolution of AKP in a replaced knee.

3.4.2. Height

Patellar height changes more than 10% in a substantial amount of patients following TKA (Jawhar et al. 2014). Mostly patella baja (abnormally low positioned patella) is held responsible for AKP (Jawhar et al. 2014), but also patella alta (abnormally high positioned patella) may cause pain in the front part of the knee (Luyckx et al. 2009). Patella baja evolves in 9.8% of knees after TKA (Meneghini et al. 2006) and is the result of either joint line elevation (Bieger et

al. 2014) or contracture of the patellar tendon (Petersen et al. 2014). Inferiorly located patella increases PF contact stress and impinges on the tibial component provoking AKP (Bieger et al. 2014). Patella alta follows extensor mechanism elongation or placement of the joint line too distally (Luyckx et al. 2009). Greater height of the patella disturbs its engagement into the trochlear groove, predisposing thisway PF instability (Jawhar et al. 2014). Greater patellar height increases PF contact forces in deep flexion and this is thought to be the biomechanical explanation for AKP in patients with patella alta (Luyckx et al. 2009).

3.4.3. Fracture

Patellar fracture as a complication of TKA is relatively rare, occuring within the first two years following surgery and mostly in resurfaced patellas. Patellar fracture does not have to be accompanied by clinical symptoms (Melloni et al. 2008). Patella may fracture due to direct trauma, because of the disruption of its blood supply after lateral retinacular release or certain exposures like quadriceps turntown and following the sudden forceful contraction of quadriceps femoris (Smith et al. 2004, Melloni et al. 2008).

3.4.4. Ischemia

Patellar blood supply in a replaced knee may be reduced by exposure (Hasegawa et al. 2009), lateral retinacular release (Strachan et al. 2009, Molyneux and Brenkel 2012) and knee flexion (Naslund et al. 2007, Hasegawa et al. 2009). Exposure-related reduction of patellar blood flow is only temporary, as the patella is being everted in the process of medial parapatellar exposure (Hasegawa et al. 2009). Neither medial parapatellar or subvastus approach will impair the patellar vascular status permanently (Gelfer et al. 2003, Kohl et al. 2011). However transient hypovascularisation of the patella has been noted in approximately 10% of patients after knee replacement, resolving within 4–6 weeks postoperatively. These transient ischemic episodes correlate with AKP (Gelfer et al. 2003). In a flexed position the patellar blood flow diminishes to an average 65% and in a quarter of patients drops even to zero at flexion of 100 degrees and above (Kohl et al. 2011). The patellar perfusion of patients with AKP is reduced in flexion to greater extent compared to symptomless individuals (Naslund et al. 2007). Kohl et al. (2011) report no correlation between decreased patellar blood flow and AKP following TKA.

3.4.5. Tumor

Although tumors rarely cause AKP, they should still be considered in differential diagnosis. The following tumors of patella are mentioned in the literature as causes of AKP: aneurysmal bone cyst (Balke et al. 2010), osteoid osteoma (Chillemi et al. 2013) and extraskeletal ossifying chondroma (Singh et al. 2009).

3.5. Synovial proliferation

3.5.1. Synovial entrapment

Hypertrophic synovial tissue behind the quadriceps tendon at the superior pole of the patella may cause crepitus and pain in the front part of the knee. These patients can usually walk painfree, symptoms come up during active extension of the knee from a 90 degrees flexed position while climbing the stairs or rising from the chair. It is mostly related to posterior-stabilised knee implants (Dajani et al. 2010).

3.5.2. Patellar clunc syndrome

Patellar clunc syndrome and synovial entrapment probably share the same etiology (Pollock et al. 2002). Patellar clunc syndrome manifests as a painful and audible clunc during knee extension at 30–45 degrees when suprapatellar fibrous nodule entraps into the intercondylar notch of the femoral component (Dajani et al. 2010, Peralta-Molero et al. 2014). It usually develops within one year following TKA. High-flex mobile bearing knees demonstrate especially high incidence of patellar clunc (Snir et al. 2014).

3.5.3. Notch stenosis

Notch stenosis evolves not earlier than three months following posterior-stabilised knee replacement as a consequence of synovial tissue impingement in the femoral notch between the stabilising box of the femoral component and polyethylene post of the tibial insert. AKP, crepitation and progressive loss of knee extension are the main symptoms (Bonutti et al. 2010).

3.5.4. Fat pad

Surgeons either remove the fat pad to enhance the exposure or leave it in place. After resecting the fat pad the patellar tendon may shorten because of scarring and lead to patella baja and AKP (Meneghini et al. 2007, Pinsornsak et al. 2014). The retained infrapatellar fat pad on the other hand may provoke AKP through compression between the anterior side of the polyethylene insert and inferior pole of patella (Bohnsack et al. 2005, Kramers-de Quervain et al. 2005). Mobile and meniscal bearing designs seem to be more fat pad friendly with less impingement (Kramers-de Quervain et al. 2005). Histochemic reactions in the edematous fat pad may also be responsible for the chronic pain in the anterior part of the knee (Bohnsack et al. 2009). A recent metaanalyses states that patients undergoing TKA because of osteoarthritis will have the same outcome irrespecive of whether the fat pad is resected or not, but in rheumatoid patients the fat pad resection will have deleterious effect on pain (van Beeck et al. 2013).

3.6. Neuropathic pain

Neuropathic pain in the anterior part of the knee mainly occurs as a result of the lesion of the infrapatellar branch of the saphenous nerve (ISN) during knee arthroplasty (Kachar et al. 2008, Ackmann et al. 2014) with an incidence up to 70% (Ackmann et al. 2014). The formation of a painful ISN neuroma is much more likely with the medial parapatellar approach and therefore straight midline skin incision should be preferred (Kachar et al. 2008).

3.7. Unknown cause

In more than 10% of cases AKP of moderate intensity may occur without any known cause (Meftah et al. 2012).

4. Burden of AKP and TKA

Prevalence is one way of measuring disease burden (Helmick et al. 2008, Kestenbaum 2009), *i.e.* the proportion of people in the population at one point in time who have the disease. Prevalence (%) is calculated:

number of people with the disease / number of people in the population x 100
(Kestenbaum 2009).

Prevalence takes into account persons with both existing and new disease (Helmick et al. 2008).

AKP may comprise the outcome of TKA in more than half of patients (van Jonbergen et al. 2012) and its burden to health service is expected to increase in the future due to an ageing population (Leonardi et al. 2014) and the increase of knee osteoarthritis with age (Lawrence et al. 2008). The percentage of people older than 60 years of age are projected to increase in Europe from 20.3% in the year 2000 to 28.8% in 2025, with the median age rising from 37.7 to 45.4 years (Leonardi et al. 2014). The lifetime risk of symptomatic knee osteoarthritis is 44.7%, but risk is greater in obese patients and for people who have experienced previous knee trauma (Murphy et al. 2008, Niu et al. 2009). The prevalence of symptomatic knee osteoarthritis among adults ranges from 10–47% (Fernandez-Lopez et al. 2008, Helmick et al. 2008, Lawrence et al. 2008, Sudo et al. 2008, Quintana et al. 2008, Kim et al. 2010, Salve et al. 2010, Jiang et al. 2012). The number of people affected by symptomatic knee osteoarthritis is projected to increase by 40% over the next 25 years in the United States (Helmick et al. 2008). More cases of knee osteoarthritis can elicit an increase in the incidence of knee replacements together with accompanying complications (Robertsson 2013). In the United States the demand for primary TKA is predicted to increase by 673% by year 2030 compared to 2005 (Kurtz et al. 2007). TKA is a fast growing intervention (Leskinen et al. 2012, Parvizi et al. 2014) that has been documented by national joint replacement registries (Odgaard 2010, Wiig

2010, Graves 2013, Powers-Freeling 2013, Robertsson 2013). In Denmark the incidence of knee replacement per 100,000 inhabitants increased from 142 in 2008 to 163 in 2009 (Odgaard 2010). In Australia the amount of total knee arthroplasties has increased by 69.1% since 2003 (Graves 2013) and the trend is likely to continue (Robertsson 2013). Some authors report the fastest growth of the incidence of knee arthroplasty among younger patients (Parvizi et al. 2014).

The lifetime risk of knee replacement is growing (Bohensky et al. 2014) and is somewhat higher for women (10–12%) compared to men (7–10%) (Bohensky et al. 2014, Weinstein et al. 2013). According to Weinstein et al. (2013) the lifetime risk of revision TKA is 1.0% for men and 1.7% for women; approximately 50% of patients with the diagnosis of symptomatic knee osteoarthritis will go through TKA and the risk of subsequent revision is around 15%; 4% of the adult population has a replaced knee joint. The prevalence of having at least one knee arthroplasty is highest around 80–85 years of age, at 6% for men and 8% for women (Robertsson 2013).

5. Predictors of AKP

Due to its multifactorial nature, the occurrence of AKP may depend on several variables.

5.1. Treatment of the patella

It is not currently clear in what way the patellofemoral joint contributes to AKP. Proponents of the knee cap as the main source of pain prescribe resurfacing of the patella, but not all surgeons agree with this theory and will usually leave the patella untouched (Deirmengian and Lonner 2013). There is also a third option, *i.e.* selective resurfacing. The rationale for always resurfacing the patella is a smaller incidence of AKP, reduced risk of reoperation due to patellar problems and better overall patient satisfaction with the procedure (Mayman et al. 2003, Patel and Raut 2011, Hwang et al. 2012, Schindler 2012). As research has not shown convincingly that leaving the patella unreplaced will produce inferior results, it might be decided not to resurface the patella. Circumventing patellar replacement will moreover avoid some potentially serious complications, like patellar fracture, rupture of the patellar tendon, overstuffing of the PF joint, PF instability, osteolysis, component fracture and polyethylene wear (Mayman et al. 2003, Meneghini 2008, Patel and Raut 2011, Hwang et al. 2012, Schindler 2012).

An unresurfaced patella may be treated in two different ways using either the conventional method or patelloplasty. The conventional handling of unresurfaced patella means the resection of its osteophytes. Patelloplasty consists of reshaping the patellar facets with a saw so the patella will better conform to the contours of the femoral trochlea, denervation of the patellar rim by electrocautery is also included (Hwang et al. 2012, Zupan et al. 2014). The results of studies comparing relief of knee pain following patelloplasty and patellar osteophyte removal have yielded conflicting results. In a retrospective study of

89 patients by Zupan et al. (2014), patelloplasty significantly outperformed the removal of osteophytes in regard to postoperative knee pain. The work of Sun et al (2012), which analysed 152 patients retrospectively, did not however reach a statistically significant result. Two retrospective studies (Hwang et al. 2012, Li et al. 2012) and one prospective study (Liu et al. 2012) that assessed the advantage of patelloplasty or patellar resurfacing in diminishing AKP following TKA all reached a similar conclusion, *i.e.* there is no significant difference in the success of either procedure in diminishing AKP.

The idea behind selective resurfacing is to perform the procedure in patients who would benefit from replacing the patella whilst avoiding unnecessary surgery and patella-related complications in individuals who would do well with the native patella (Schindler 2012). Suggested patient-specific and surgery related prerequisites for the retention of patella are: an age younger than 65; an absence of preoperative AKP; no cristallarthropathy; well preserved patellar thickness and shape; normal PF tracking; Outerbridge (1961) 1–3 patellar cartilage defects not extending to the subchondral bone; correct alignment of prosthesis components; balanced ligaments; avoiding the violation of the extensor mechanism during exposure (Müller and Wirz 2001, Rodriguez-Merchan and Gomez-Cardero 2010, Schindler 2012). Anatomical design of the trochlear groove and physiological tibiofemoral rotation are the two most important implant specific characteristics vital for ensuring a painless PF joint following TKA without resurfacing the patella (Müller and Wirz 2001, Ma et al. 2007). Misra et al. (2003) showed in a prospective study of 129 cruciate retaining press-fit condylar total knee implantations with a mean follow-up of 57 months, that by applying selective resurfacing equally good results in regard to postoperative AKP may be achieved in patients with different severity of patellar cartilage impairment. The patellar articular surface was retained in Outerbridge (1961) grades 0, 1, 2, but replaced for grades 3 and 4. Both the 0–2 and 3–4 Outerbridge (1961) grade groups had a similar incidence of post-operative AKP at around 4%, which is less than reported in most studies. AKP thus evolves independently of whether the patella is resurfaced or not, and patient selection is essential when selectively resurfacing the patella (Misra et al. 2003). Using MRI Kumahashi et al. (2013) compared preoperative patellar cartilage thickness with thickness up to a year following TKA with unre-surfaced patella, and found that the cartilage of the lateral facet was signifi-cantly thinner post-surgery. The thickness of the cartilage of the patella as evaluated during knee replacement surgery, might be one variable to consider when deciding between resurfacing the patella or not (Kumahashi et al. 2013).

Leichtle et al. (2014) executed a biomechanical study comparing PF pressure between native knees, replacement knees without patellar resurfacing and arthroplasty knees with a replaced patella. Despite correct positioning of the implants and avoidance of PF overstuffing, peak PF pressure increased vague in a replaced knee without patellar resurfacing and 1.5–2.5 fold in knees with a resurfaced patella. In the absence of serious cartilage defects, patellar re-surfacing from a biomechanical point of view was not recommended.

The results of studies examining AKP and patellar resurfacing are controversial. Barrac et al. (2001) examined 118 patients with Miller-Galante II (Zimmer, Warsaw, USA) posterior cruciate-retaining knee replacements into patellar resurfacing and retaining groups. There was no significant difference in postoperative AKP between the patellar resurfacing and retaining groups (Barrack et al. 2001), a conclusion also drawn in studies with 10 years of follow-up (Beaupre et al. 2012, O'Brien et al. 2012). A prospective randomised study by Smith et al. (2008) of 181 knees replaced with the Profix Total Knee System (Smith & Nephew Richards Inc., Memphis, Tennessee) demonstrated an increased incidence of AKP in patients with resurfaced patella. 30.1% of knee replacement patients with resurfaced patella and 20.9% without patella resurfacing had AKP. The study however reported only short term results (mean of four years) and the outcome for AKP in the non-resurfaced patella group may worsen with time. A study was performed by Patel et al. (2011) that included 65 patients who had both knees replaced in stages, but with resurfacing of the patella only performed on one knee. Press-fit condylar prosthesis was used in all cases. The mean follow-up was 4.5 years. Patients preferred the knee with resurfaced patella and the incidence of AKP was also smaller. A retrospective randomised study of 100 patients receiving an Anatomic Medullary Knee (DePuy, Warsaw, IN) with 8–10 years follow-up demonstrated significantly less AKP with walking and stair climbing in a group with resurfaced patella compared to not replacing the knee cap (Mayman et al. 2003).

When residual AKP compromises daily quality of life surgeons are too often incapable of resisting the temptation to provide the patient a relatively simple and quick solution, *i.e.* secondary resurfacing of the patella. The revision rate of primarily unresurfaced patella is between 0.4–7.5% (Müller and Wirz 2001, Mockford and Beverland 2005, Parvizi et al. 2012). In cases where primary knee replacement with unreplaced patella has not eliminated AKP, the success rate of secondary patellar resurfacing is also poor (Mockford and Beverland 2005). 14–50% of patients continue to have pain in the front part of the knee even after secondary resurfacing (Müller and Wirz 2001, Mockford and Beverland 2005, Munoz-Mahamud et al. 2011, Correia et al. 2012, Daniilidis et al. 2012, Parvizi et al. 2012, Petersen et al. 2014). The disappointing outcome of secondary resurfacing suggests that not all AKP can be attributed to the cartilage of patella (Petersen et al. 2014).

Systematic reviews and meta-analyses generally endorse the use of a patellar implant (Swan et al. 2010, Leichtle et al. 2014), convincingly demonstrate an increased reoperation rate associated with unresurfaced patella (Meneghini 2008, Calvisi et al. 2009, Fu et al. 2011, He et al. 2011, Li et al. 2011, Pavlou et al. 2011, Pilling et al. 2012, Chen et al. 2013, Petersen et al. 2014), but do not agree on the causes of postsurgical AKP. An early work (Calvisi et al. 2009) favours resurfacing, but more recent studies (Fu et al. 2011, He et al. 2011, Li et al. 2011, Pavlou et al. 2011, Pilling et al. 2012, Chen et al. 2013, Petersen et al. 2014) have been unable to confirm the advantage of either patellar resurfacing or retention in reducing AKP. One viewpoint to the reoperation rate is that it may be artificially increased due to the perception that only the articulation

between patella and femoral trochlea is the cause of AKP. The same rates of AKP in patella resurfaced and retaining groups, together with poor results of secondary resurfacing, indicate that the etiology of AKP is multifactorial and the overall balance of the knee is important in avoiding AKP (Pavlou et al. 2011).

National joint registries are a valuable source for observing how patellar replacement differs between countries. In Sweden the use of a patellar button has constantly decreased over the years and constituted only 2.6% of knee replacements performed in 2012 (Robertsson 2013). A similar situation has occurred in Norway, where the use of patellar resurfacing decreased from 35.8% in 1994 to 2.2% in 2009 (Wiig 2010). In Australia and Denmark however the proportion of patellar resurfacing grew from 41.5% in 2005 to 54% in 2012 (Graves 2013) and from 69% in 1997–2000 to 80% in 2009 respectively (Odgaard 2010). In Great Britain 86 % of all knee replacements are cemented total knees, of which 38% had the patella replaced. 3% of all knee replacements in Great Britain are cementless total knees, of which only 7% of patella's get the button (Powers-Freeling 2013). 76% of the members of American Association of Hip and Knee Surgeons always resurface the patella, 16% implant the patellar button in >90% of surgeries and 5% replace the patella in <10% of cases (Johnson et al. 2012). In Estonia the patella is usually not resurfaced during primary knee replacement.

5.2. Condition of the patellar cartilage

When the patella remains unresurfaced, AKP following TKA may always be ascribed to the impairment of the cartilage of the patella (Seil and Pape 2011). Two of the most exploited systems for macroscopic grading of cartilage lesions are the Outerbridge (1961) classification and its modification by Beguin and Locker (1983). The Outerbridge classification defines the cartilage lesion as: "grade 1 – softening and swelling of the cartilage, grade 2 – fragmentation and fissuring in an area 13 mm or less in diameter, grade 3 – fragmentation and fissuring in an area more than 13 mm in diameter, grade 4 – erosion of cartilage down to bone" (Outerbridge 1961). The Beguin and Locker classification also distinguishes 4 grades: "grade 1 – softening and swelling, grade 2 – superficial chondral fissuring, grade 3 – deep chondral fissuring, grade 4 – erosion with exposed subchondral bone" (Beguin and Locker 1983). Compared to the Outerbridge (1961) classification, the Beguin and Locker (1983) system characterizes only the depth of the lesion, eliminating its extent as a component. Han et al. (2006) studied the visual assessment of cartilage defects and concluded it is generally reliable. Three investigators assessed the depth and extent of the cartilage lesion on 80 photographs of the patella, taken during knee replacement. The assessments resulted in substantial intra-observer and moderate inter-observer reliability.

Osteoarthritic defects of the patellofemoral joint can be prevalent among older populations. Iriuchishima et al. (2013) studied 203 cadaveric PF joints of

Japanese patients with a median age of 84 years. 76% of all subjects had cartilage defects of grade 2 and over according to the Outerbridge (1961) scale. The defects were almost always on the medial facet, with only 3% of lesions on the lateral side. The incidence of PF cartilage defects was also higher in females compared to males. Such a large proportion of PF cartilage impairment post mortem may indirectly confirm the symptomless nature of the majority of these lesions during a subject's lifetime (Beard et al. 2007). Beard et al. (2007) documented a series of 824 unicondylar knee replacements of patients with a median age of 66 years and found full thickness cartilage loss (Outerbridge grade 3 and 4) on the medial facet of the patella in 9% of cases and on the lateral facet in 4% cases. A much lower incidence of cartilage defects found by Beard et al. (2007) compared to Iriuchishima et al. (2013) may be attributed to the younger age of patients and exclusion of Outerbridge (1961) 2 defects in the former study. The distribution pattern of lesions between medial and lateral facets was however similar in both studies.

On visual inspection at the time of surgery most patella show some type of cartilage damage (Rodriguez-Merchan and Gomez-Cardero 2010). Radiologic studies have also demonstrated that changes to patellar cartilage continue after implantation of the prosthesis in cases where the patella is left unresurfaced. Kumahashi et al. (2013) evaluated the cartilage thickness of twelve unresurfaced patellae preoperatively using MRI and again a year post-surgery in patients who received a zirconia ceramic knee implant. The measurements showed significantly thinner cartilage of the lateral facet of the patella postoperatively, which was interpreted as a results of osteoarthritic changes. In extreme cases the articular surface of the patellar may entirely lose its original shape in the process of remodelling (Shih et al. 2004). Postoperative degradation of the articular cartilage of the unresurfaced patella may be ascribed to ongoing biological process, or more often to mechanical factors such as incorrect rotation of the femoral component (Seil and Pape 2011).

The link between AKP and PF osteoarthritis has been well established in a native knee (Thomas et al. 2010). The association between AKP and radiological changes was investigated in a study of 151 knees of 107 patients undergoing total joint replacement owing to osteoarthritis. Preoperative Merchant views were performed and PF symptoms evaluated. Joint space obliteration correlated significantly with increased postoperative AKP, but joint space narrowing did not (Chang et al. 2007). The accuracy of predicting cartilage changes by evaluating radiographic joint space narrowing was however questioned in a later study that used the same cohort of 151 knees to study the use of preoperative Merchant views and registering of gross cartilage changes during surgery (Chang et al. 2008). The small agreement between the raadiographic joint space narrowing and the degree of cartilage degeneration, together with the inferior diagnostic accuracy of the assessment of the severity of cartilage defects by radiography alone, demonstrates the inadequacy of relying only on radiographic findings when deciding upon the degree of cartilage impairment (Chang et al. 2008).

There are several studies of the relation between preoperative AKP and degeneration of the PF joint. Han et al. (2005) investigated 87 knees in 58 patients undergoing TKA. PF pain was evaluated by an independent investigator before operation and cartilage defects of the patella were assessed during surgery. The cartilage lesion's size, location and depth according to Outerbridge (1961) was registered. The depth and size of the patellar cartilage defect had a significant, although weak, positive correlation with AKP preoperatively (Han et al. 2005). In a further study Han et al. (2007) investigated the correlation of PF osteophytes and AKP in 77 knees of 60 patients. The proportion of the margin of the patella rimmed by osteophytes was registered and cartilage impairment was assessed by visual inspection at surgery. The degree of osteophytes had a weak positive correlation with the status of the cartilage of the patella and the relationship between osteophytes and preoperative AKP was missing.

The Oxford Group has performed several studies to ascertain the role of PF cartilage defects in the evolution of anterior knee pain symptoms. One of their works investigated 824 knees of 793 patients undergoing medial unicompartmental arthroplasty with an Oxford UKR implant (Biomet, Bridgend, United Kingdom) and after an average follow-up period of two years later, produced a somewhat paradoxical result with significantly less anterior knee pain reported by patients with full thickness cartilage loss anywhere in the PF joint compared to normal cartilage. It was concluded that PF cartilage loss does not compromise the outcome of medial unicondylar replacement with the Oxford knee (Beard et al. 2007). In another study of 91 patients (100 knees) receiving an Oxford UKR medial unicompartmental knee implant (Biomet, Bridgend, United Kingdom), the relationship between PF cartilage degeneration and postoperative AKP was investigated. After two years the prevalence of AKP in patients with cartilage defects on the medial facet did not differ from individuals with unimpaired patella. Patients with lateral patellar defects however had more often AKP than in cases with a normal knee-cap (Beard et al. 2007).

The relationship between AKP and PF osteoarthritis in a native knee or following unicondylar replacement cannot be meaningfully compared to total arthroplasty as the biomechanics and contact surfaces of the PF joint are different. To date attempts to establish a link between the state of the patellar cartilage at the time of TKA and postoperative AKP have produced ambiguous results (van Jonbergen et al. 2012). One of the studies affirming patellar cartilage degeneration as a cause of AKP following TKA recruited 100 knees of 84 patients receiving a Total Condylar Knee prosthesis (Johnson and Johnson, New Brunswick, New Jersey, USA and Howmedica, Rutherford, New Jersey, USA) without resurfacing (Picetti et al. 1990). Patellar cartilage degeneration was recorded during surgery and patients were followed for a minimum of 2 years. A strong association between postoperative AKP and full thickness patellar cartilage defects exceeding 25% of the surface area was reported. It was proposed that all such patella be resurfaced (Picetti et al. 1990). The most extensive work to date exploring the role of the cartilage defects of the patella in the evolution of AKP following TKA has been carried out by Rodríguez-

Merchán and Gomez-Cardero (2010). 500 patients undergoing TKA with a NexGen PS (Zimmer, Warsaw, Indiana, USA) implant were recruited and divided into two groups based on the condition of the patellar articular cartilage at surgery: group A = individuals with Outerbridge (1961) grade 1–3 defects; group B = individuals with grade 4 defects. Patients in both groups were randomised either to have the patella resurfaced or not. After five years rates of AKP brought about a 21% higher risk of patellar resurfacing in group B compared to group A. Shih et al. (2004) performed a radiologic study where they studied 235 knees of 187 patients for a minimum of 5 years after implantation of the Porous Coated Anatomic (PCA; Howmedica, Rutherford, New Jersey, USA) total knee prosthesis. Patients with more advanced loss of patellar cartilage thickness on a Merchant axial view had a significantly higher incidence of AKP. Anterior knee pain symptoms were attributed to the erosion of patellar cartilage.

There are also a handful of studies refuting patellar cartilage changes as a cause of AKP. At surgery Barrack et al. (1997) recorded patellar cartilage defects of 118 knees in 86 patients that received a Miller-Galante II (Zimmer, Warsaw, Indiana, USA) total knee implant and diagnosed AKP after a mean follow-up time of 30 months. No association between patellar cartilage defects as graded by Outerbridge (1961) and postoperative pain in the front part of the knee was found (Barrack et al. 1997). Campbell et al. (2006) also found no association between patellar cartilage and postoperative frontal knee pain with the Miller-Galante II (Zimmer, Warsaw, Indiana, USA) implant over a longer follow-up period of 10 years. Wood et al. (2002) also studied the prevalence of AKP in a prospective randomised way in 221 patients with the Miller-Galante II (Zimmer, Warsaw, Indiana, USA) implant and an average follow-up of 48 months. The absence of patellar resurfacing was the only significant predictor of AKP, the impairment of patellar cartilage recorded at surgery as described by Outerbridge was not. At 10 years follow-up Burnett et al. (2004) reported no significant difference in the prevalence of AKP between resurfaced and retained patella in their prospective randomised double-blind study of patients with the cruciate retaining Anatomical Medullary Knee (DePuy, Warsaw, Indiana, USA) implant.

Meta-analyses of patellar resurfacing (Pavlou et al. 2011) and poor results of secondary patellar resurfacing produce evidence that AKP is likely to result from other causes rather than the impairment of the cartilage of the patella.

5.3. Preoperative AKP

Most studies show no correlation between preoperative AKP and pain in the front part of the knee following joint replacement (Barrack et al. 1997, Barrack et al. 2001, Wood et al. 2002, Campbell et al. 2006). However also contrary viewpoint exists. Picetti et al. (1990) reported 25 of the 27 patients with preoperative AKP having the same complaints also after TKA with unresurfaced

patella. Burnett et al. (2004) discovered that patients without AKP preoperetively will neither experience it in the postoperative period.

5.4. Obesity

The prevalence of obesity increases worldwide (Dewan et al. 2009). There is evidence following TKA, that compared to individuals with normal weight, the patients with higher than normal body mass will have more perioperative complications and overall revisons, the midterm results are the same regardless of body weight (Lizaur-Utrilla et al. 2014), and long term the incidence of aseptic loosening is bigger in obese (Foran et al. 2004). Studies generally report no significant relationship between obesity and the incidence of postoperative AKP following knee replacement (Barrack et al. 2001, Singh et al. 2011, Hwang et al. 2012). However, Dewan et al. (2009) showed in their study of 169 TKA patients with BMI exceeding 20, that at mean follow-up of 5.4 years only morbidly obese patients with BMI over 40 will experience more postopeartive AKP compared to patients with BMI 20–29. Wood et al. (2002) have come up with an interesting finding about patients' weight, not body mass index, as the only preoperative variable influencing the incidence of postsurgical AKP. Also taller height has been highlighted as a predictor of AKP following knee replacement (Schindler 2012). The higher incidence of AKP in taller and heavier patients may be attributed to bigger PF forces generated by increased leaver arms and total joint loading (Wood et al. 2002, Schindler 2012).

5.5. Surgical approach

Medial parapatellar, medial subvastus and midvastus approaches are the most utilised methods for gaining access to the knee joint in performing arthroplasty (Liu et al. 2013). There is a trend towards less invasive approaches in order to save as much as possible of the integrity of the extensor mechanism. Such minimally invasive techniques include the mini-medial parapatellar, mini-midvastus, mini-subvastus and "quadriceps-sparing" approaches (Lai et al. 2014). None of the beforementioned approaches, either standard or minimally invasive, has proved superior long-term in regard to postoperative knee pain (Nestor et al. 2010, Hu et al. 2013, Pongcharoen et al. 2013, Zhang et al. 2013, Heekin and Fokin 2014, Jenkins et al. 2014, Lai et al. 2014). Compared to standard approaches, minimally invasive surgery may result in less knee pain within a couple of weeks after the operation (Liu et al. 2013), but at the same time limited visualisation of the knee joint predisposes component malpositioning, which in turn may compromise implant longevity (Zhang et al. 2013, Lai et al. 2014). Lateral parapatellar approach with or without the osteotomy of tuberositas tibiae is an option, besides medial approaches, when operating on a valgus knee. The best approach for performing arthroplasty in valgus knees is still debatable (Rossi et al. 2014). As seen in the study of Satish et al. (2013), lateral approach may eliminate postsurgical AKP. They report 5

year results of the knee replacement with different implants and unresurfaced patella in 32 arthritic valgus knees, according to which none of the patients complained of AKP. Hirschmann et al. (2010) prospectively compared medial parapatellar and lateral approaches in 143 valgus knees of 133 patients using cruciate retaining BalanSys® (Mathys Ltd, Bettlach, Switzerland) implant. Patella was resurfaced in 6 knees. Patients were not randomised: the approach was chosen according to surgeon's preference in each case. At two years, the patients who received their knee implant through the lateral approach, showed significantly smaller VAS pain scores, although AKP was not individually analysed. Several studies, however, have not succeeded to allege the superiority of the lateral approach over medial ones in replacing valgus deformed knees (Nikolopoulos et al. 2011, Sekiya et al. 2014).

As all approaches capacitate comparable long-term results, the surgeons should use an approach with which they are most accustomed to (Heekin and Fokin 2014).

5.6. Lateral release

Lateral release denotes severing of tight soft tissue structures on the outer side of the patella and it serves the concept of improved patellar tracking together with reduced PF pressure, which may led to less AKP. In a prospective study by Zha et al. (2014) with the Gemini MK II (Link, Germany) mobile bearing prosthesis with unresurfaced patella, 148 patients were randomised either to receive the retinacular release or not. At 18 months follow-up the patients in a lateral retinacular release group experienced significantly less AKP compared to the other group. Peretz et al. (2012) showed in a cadaveric study, comparing native knees with traditional standard implants and gender specific designs, that most effective reduction of PF pressure after lateral release occurs in knees with standard components.

5.7. Gender

Compared to men, women have a reduced medial-lateral to AP femoral condylar aspect ratio. This difference is very small and its clinical significance is dubious. Q-angle and the prominence of anterior femoral condyles are patient's height-related variables, not gender specific (Merchant et al. 2008, Dargel et al. 2011, Johnson et al. 2011). Ignorance of the height of the anterior femoral condyles may theoretically lead to PF overstuffing and anterior knee symptoms, but it has not been confimed in clincal studies yet (Dargel et al. 2011, Johnson et al. 2011). Based on the anatomic pequliarity of the female knee, gender specific implants have been elaborated, but unfortunately without any effect on clinical outcome (Johnson et al. 2011, Xie et al. 2013). The studies comparing the results of TKA using gender specific and uni-sex implants show equal postoperative results (Johnson et al. 2011, Xie et al. 2013). The results of TKA are similar in both genders (MacDonald et al. 2008, Merchant et al. 2008). When interpreting the results of TKA in terms of gender, the difference of pre- and post-operative scores requires particular conside-

ration. Women usually start and also end in lower score levels, but the change in the postoperative status compared to preoperative, is equal to men (MacDonald et al. 2008). There is one study specifically looking for the effect of gender on PF function after TKA. Sensi et al. (2011) recruited 50 male and 50 female patients undrgoing TKA and implanted them Nex Gen Legacy Posterior Stabilized (Zimmer, Warsaw, Indiana, USA) prothesis with resurfaced patella. The AKP was diagnosed using HSS patella score. At mean follow-up of 6 years, the prevalence of AKP was bigger in women compared to men, 12% and 4% respectively. However the difference was statistically insignificant.

5.8. Bearing mobility

The rationale behind mobile bearings is to physiologically imitate the internal rotation of the tibia relative to the femur during knee flexion, and the external rotation while extending the knee (Wasielewski et al. 2008). Theoretically the rotation between the tibial base plate and polyethylene insert allows self-alignment of the prosthesis into an optimal position and may in this way compensate for slight malpositioning of the components (Heinert et al. 2011). In case of patellar resurfacing mobile bearing designs have been shown to result in smaller PF contact stress compared to fixed tibial implants (Skwara et al. 2009). Clinical studies however have revealed no advantage of bearing mobility in PF or femorotibial kinematics compared to fixed bearings (Heinert et al. 2011). Wasielewski et al. (2008) conducted an in vivo study of 527 knees with different types of mobile bearing knee implants and determined the amount of axial rotation. Average rotation in a native knee ranged from 16–23 degrees during deep knee bending. Only 12% of the knees with mobile bearing implants studied rotated more than 10 degrees, with the rotation in most of the knees only around 3–5 degrees.

The postulated advantages of rotating tibial polyethylene inserts have not manifested in the reduction of AKP either. Breugen et al. (2008) compared the Nexgen Complete Knee Solution Legacy Posterior Stabilized Fixed and the Nexgen Complete Knee Solution Legacy Posterior Stabilized Mobile (Zimmer, Warsaw, Indiana, USA) implants. The patella was resurfaced in all patients. A year after surgery the mobile bearing design was associated with significantly less AKP than the fixed design (Breugem et al. 2008), but after an average of 7.9 years post-surgery this difference had become non-significant (Breugem et al. 2014). A study of 50 patients undergoing bilateral knee replacement with a PFC Sigma rotating platform implant (DePuy, Warsaw, Indiana, USA) in one knee and a PFC Sigma fixed bearing prosthesis (DePuy, Warsaw, Indiana, USA) in the other knee, with no patella resurfacing in any case, found after a mean follow-up period of 40 months the prevalence of AKP in the mobile bearing group was 14% and in the fixed platform 12% (Jawed et al. 2012). Studies resulting in a non-significant difference in the prevalence of AKP have also been conducted by comparing: *a*) Scorpio Single Axis mobile bearing system knees (Stryker Howmedica Osteonics, Allendale, New Jersey, USA) to

Duracon fixed bearing implant system knees (Stryker Howmedica Osteonics, Allendale, New Jersey, USA) (Aggarwal and Agrawal 2013); *b*) Scorpio Total Knee Arthroplasty (Stryker; Mahwah, New Jersey, USA) fixed bearing system knees with Scorpio Plus (Stryker; Mahwah, New Jersey, USA) rotating platform implant knees (Ball et al. 2011).

Meta-analyses have emphasised there is no additional benefit of mobile bearing polyethylene inserts compared to fixed tibial component designs in improving the clinical results of TKA (Oh et al. 2009, Smith et al. 2011).

5.9. Circumpatellar electrocautery

One means of reducing the prevalence of AKP following TKA is patellar denervation in the form of rim cauterisation (Gupta et al. 2010, van Jonbergen et al. 2010). The idea behind circumpatellar electrocauterisation is to interrupt the pain pathways by destroying the substance-P nociceptive afferent fibers in peripatellar tissues (van Jonbergen et al. 2011, Li et al. 2014). However, the translation of patellar rim electrocauterisation into improved outcomes is uncertain (Baliga et al. 2012). Van Jonbergen et al. (2011) have conducted two consecutive studies in 300 patients undergoing TKA with NexGen LPS posterior stabilised fixed bearing implant (Zimmer, Warsaw, Indiana, USA) without patellar resurfacing. The patients were randomised into two groups, with and without patellar denervation. Patient-reported outcomes were used for diagnosing AKP. The first study estimated the results one year since surgery. The overall prevalence of AKP was 26%, being significantly higher in the patients who were not assigned to circumpatellar electocauterisation. In the following study the same patient cochorts were analysed at mean follow-up of 3.7 years. The overall prevalence of AKP had increased somewhat to 32% (95% CI 26 to 39) and the statistically significant difference between groups had been lost. The authors concluded, that the benefit of reducing postsurgical AKP by patellar rim denervation will not last (van Jonbergen et al. 2014). Similar results were obtained in a study by Pulavarti et al. by randomising 126 patients according to patellar denervation. NexGen cruciate retaining prothesis (Zimmer, Warsaw, Indiana, USA) was implanted in all cases. The patellar denervation group had significantly less AKP shortly after surgery at 3 months follow-up, but at 12 and 24 months since knee replacement the prevalence of AKP was identical in both groups (Pulavarti et al. 2014). Baliga et al. (2012) were also unable to demonstrate the superiority of circumpatellar electrocauterisation over not denervating the patella in terms of reducing AKP at one year follow-up in a prospective randomised study recruiting 200 patients undergoing TKA with Low Contact Stress (DePuy, Leeds,United Kingdom) or Kinemax (Zimmer, Warsaw, Indiana, USA) implants.

Metaanalyses and systematic reviews provide conflicting results regarding the efect of patellar electrocauterisation. As it reduces AKP short-term and no harm is done with the procedure, van Jonbergen et al. (2014) and Li et.al (2014) recommend for denervation of the patella during knee raplacement. Cheng et al.

(2013) are not in favour of circumpatellar electrocauterisation, because the technique does not result in improved outcome and its possible negative effects are of concern. The effect of denervation on the patellar cartilage has been investigated in 20 rabbits. The subjects were randomised into case and control groups. The subjects in the case group underwent anteromedial arthrotomy of the knee together with patellar denervation, in the control group only knee arthrotomy was performed. At 12 weeks the rabbits were sacrificed and patellar cartilage microscoped. There were statistically significant differences of cartilage degeneration in the electrocauterisation group like loss of matrix and clustering of chondrocytes. This study indicates that denervation of the patella may result in cartilage damage (Namazi et al. 2014).

6. Diagnosis of AKP

6.1. Symptoms and signs

Patients suffering from AKP usually complain about pain behind the patella when descending and ascending the stairs, sitting with the bent knees, squatting, running and rising from a sitting position. At clinical examination patellar mobility is tested, painful areas are located with palpation and patellofemoral crepitus is evaluated. The best diagnostic test of provoking PF pain is resisted knee extension (Smith et al. 2013).

6.2. Diagnostic scores

There is no widely acnowledged and validated instrument for diagnosing AKP (Gupta et al. 2010). We are not aware of any discriminative outcome measure for diagnosing AKP following TKA. It is widely used practice in orthopaedic literature to diagnose AKP relying on few items reflecting PF pain within a multi-item evaluative instrument (Pilling et al. 2012).

There are three scores initially conceived to be used in arthroplasty patients and containing AKP specific items: the Bartlett score (Feller et al. 1996), the HSS patella score (Baldini et al. 2006) and the Ranawat PAQ-knee score (Mancuso et al. 2012). The Bartlett and the HSS patella scores record both examiner performed and patient reported items, the Ranawat PAQ-knee score relies purely on patient reported information. The abovementioned three scores ask precisely, whether the patient experiences pain in the front part of the knee.

A group of tools enables the diagnosis of AKP indirectly by questionning the patients about pain during activities overloading the PF joint (like squatting, rising from the chair, climbing the stairs, etc.). Such questionnaires are the Womac score (Bellamy et al. 1988), the KOOS score (Roos et al. 1998), the Lysholm score (Lysholm and Gillquist 1982), the Hughston score (Flandry et al. 1991), the Kujala score (Kujala et al. 1993), the Oxford knee score (Dawson et al. 1998), the Knee pain scale (Rejeski et al. 1995) and the ADLS score (Irrgang

et al. 1998). Only the Oxford score from the last mentioned instruments has been elaborated for use in knee arthroplasty patients.

The third type of instruments register only the existence and severity of pain in the knee without further localising it. In this case an extra question should be asked or clinical test performed for identifying whether the anterior part of the knee hurts or not. The Knee Society score (Insall et al. 1989), the International Knee Documentation Committee subjective knee form (Hefti et al. 1993), the Fulkerson score (Fulkerson et al. 1990), the Hungerford score (Hungerford and Kenna 1983), the Hospital of Special Surgery score (Ranawat and Shine 1973), the Hofmann score (Hofmann et al. 1991), the Edinburgh score (Leigh Brown et al. 1999), the ACL quality of life questionnaire (Mohtadi 1998), the British Orthopaedic Association knee function assessment chart (Aichroth et al. 1978) and the Bristol knee score (Mackinnon et al. 1988) fall into this category.

6.3. Imaging

6.3.1. The need for patellofemoral axial imaging

Radiography is usually the first imaging study available when examining patients with PF complaints (Davies et al. 2000, Melloni et al. 2008). The evolution of AKP in cases of patellar lateral translation have been attributed to two theories (O'Donnell et al. 2005): *i*) that pain may arise from cartilage damage caused by the increased contact pressure of the PF articulating surfaces in the incongruent joint; *ii*) that the stretching of the contracted lateral retinaculum may cause pain through irritation of the nerve endings in peri-patellar soft tissues. Radiography is unlikely however to yield an instant diagnosis about the source of pain, it rather provides a general overview of the joint and indicates the need for further analysis (Grelsamer 2000). The patella may be considered malaligned if positioned abnormally in any plane and maltracked if falling out of the normal range at any point in the flexion-extension cycle (Wilson 2007).

Although imaging can quantify malalignment (Grelsamer 2000), the definition of what constitutes normal PF tracking still remains an elusive goal (Katchburian et al. 2003). After analysing 40 knees of asymptomatic patients during weight-bearing in MRI, Tennant et al. (2001) proposed that in normal PF kinematics: a straight and fully relaxed knee patella is located at the proximal margin of the trochlea and in half of the people is in a laterally displaced position; as the knee flexes, the patella engages into the trochlea; at 10–30 degrees of flexion the patella is centred in the trochlea; with flexion beyond 30 degrees the patella medialises slightly.

Even in cases of perfect positioning of the components, TKA changes PF kinematics considerably compared to a native knee (Barink et al. 2007). Barink et al. (2007) compared the patellar kinematics of the knees of five cadavers in three situations: without an implant; with an implanted Continuum Knee System endoprothesis (Biomet/STRATEC, Warsaw, Indiana, USA) with symmetrical femoral component; with a Continuum Knee System endoprothesis

prototype with asymmetrical patellar groove. The femorral component with an asymmetrical femoral groove had seven degrees of lateral orientation of the anterior flange. In the scenario with endoprothesis in situ, the patella was located more medially in a deeper flexion (between 65–90 degrees) and tilted more laterally at lower flexion (between 10–45 degrees) compared to the native knee. There were no statistically significant differences in patellar motion between the symmetrical and asymmetrical femoral components. It was concluded that despite the anatomic design claimed by the manufacturers of the implants, the arthroplasty was not capable of reproducing physiological patellar kinematics. Similar results were generated by Belvedere et al. (2007) in a study of 6 cadavers, by using computer navigation to compare the PF kinematics of native knees and knees replaced with a cruciate retaining Scorpio (Stryker, Allendale, New Jersey, USA) implant including patellar resurfacing. The replaced knees showed increased patellar tilt of 5–10 degrees and a more lateral shift of the patella up to 12 mm in comparison to the native knees.

PF imaging may reveal patellar maltracking, signs of patellar avascular necrosis (sclerosis, flattening, fragmentation, fracture) (Smith et al. 2004), fracture of the patella or patellar component (Figgie et al. 1989), and dissociation of the patellar component and patella baja or alta (Schindler 2012, Petersen et al. 2014). PF axial incongruence may be a sign of malpositioning of the femoral and tibial components in the axial or frontal plane, imbalance of peripatellar soft tissues, incorrect placement of the patellar component and an overstuffed anterior compartment (Jazrawi et al. 2000, Hatayama et al. 2011). Patella alta may be the consequence of too distal a placement of the joint line and rupture of the extensor mechanism. Contracture or scarring of the patellar tendon and elevation of the joint line can cause patella baja (Hofmann et al. 2006, Dennis et al. 2011).

Conflicting data exists regarding the effect of femoral component rotation on patellofemoral alignment. According to some studies, external rotation of the femoral component improves patellar tracking by lateralizing the trochlear groove (Figgie et al. 1989, Abadie et al. 2009). Kessler et al. (2008) reached diametrically different conclusions in a study where six knees of cadavers were replaced with a fixed-bearing Scorpio CR (Stryker, Mahwah, New Jersey, USA) prosthesis and patellar kinematics in cases of different positions of knee implants were recorded. The external rotation of the femoral component increased the tilt and lateral displacement of the patella, while internal rotation did the opposite.

There are also studies that report no effect on the rotation of the femoral component on PF kinematics. In their retrospective study of 62 knees of 52 patients following TKA with a Kirchner Performance Knee system (Kirschner Medical Corporation, Timonium, MD, USA) and resurfaced patella, Kawano et al. (2002) were unable to find any significant correlation between femoral component rotation and patella tracking. The displacement was assessed using skyline view with the knee in 60 degrees of flexion. As femoral component rotation has the greatest effect on patellar tracking when the knee is nearly extended, the imaging in 60 degrees of flexion might have been the reason for

no significant relationship between femoral component rotation and patellar position relative to trochlea (Kawano et al. 2002).

Besides axial rotation it is also important to watch for the correct positioning of the implants in the coronal plane. Fukagawa et al. (2011) studied retrospectively 56 knees of 40 patients who had received a NexGen Legacy posterior-stabilized prosthesis (Zimmer, Warsaw, Indiana, USA). After a mean postoperative period of 5.3 years full-length weight-bearing AP radiographs of the leg and PF axial view according to Laurin with the knee in 60 degrees of flexion was performed. Femoro-tibial varus alignment was found to correlate significantly with the medial displacement of the patella and patellar lateral tilt.

Surgical approach has also been considered as a variable influencing patellar tracking, but the results of studies concerning this matter are conflicting. Ozkoc et al. (2005) recruited 21 patients undergoing simultaneous bilateral knee replacement with a Genesis II (Smith& Nephew, Memphis, TN, USA) prosthesis. Surgery was performed using a midvastus approach in one knee and a medial parapatellar approach in the other knee. Preoperative radiographs were compared to postoperative radiographs after a mean period of 22 months following surgery in both knee type groups. There were no changes of patellar tracking in replacement knees inserted with the midvastus approach. Medial parapatellar surgery tended to result however in lateral subluxation of the patella. Pongcharoen et al. (2013) in a prospective randomised study however found no radiographic difference in pre- and post-operative patellar tracking when comparing the outcome of knee replacements of 60 patients with a NexGenI LPS Hi-Flex (Zimmer, Inc, Warsaw, Indiana, USA) implant, performed with either a limited medial parapatellar or mini-midvastus surgical approach.

6.3.2. Radiographic views of the patellofemoral joint

Finding the relationship between PF congruence and AKP is dependent not only on the way of describing the X-ray findings, but also on the circumstances in which the image has been taken. The process of reliable PF imaging starts with a team of skilled radiographers ensuring the depiction of the joint in a standardized manner (Davies et al. 2000). The other variables affecting images of the position of the patella relative to the trochlear groove in the axial plane are the flexion angle of the knee, contraction of the quadriceps, varus-valgus alignment of the knee, rotation of the tibia (Katchburian et al. 2003) and whether the image was taken in a standing or lying position (Baldini et al. 2007). Most important abnormalities of patellar tracking occur at the beginning of knee flexion, *i.e.* between 0–20 degrees, when only soft tissues stabilise the patella (Katchburian et al. 2003).

Standard radiographic techniques produce only static images and are not capable of revealing dynamic disturbances of PF tracking that occur during knee motion (Katchburian et al. 2003). Currently two of the most frequently used projections are the Merchant view (Merchant et al. 1974) and the Laurin

technique (Laurin et al. 1979). The Merchant view (Figure 1), also known as the Mountain view (Bradley and Ominsky 1981), is taken with the patient lying supine and knees flexed at 45 degrees over the edge of the imaging table. The X-ray beam passes through the femur at an angle of 30 degrees from proximal to distal. The film cassette is placed distal to the knee and perpendicular to the X-ray beam (Merchant et al. 1974).

Figure 1. Technique of the Merchant view

When visualising the PF joint with the Laurin technique the patient sits on the imaging table with the knees flexed at 20 degrees and feet exactly at the edge of the table. The X-ray beam is directed from distal to proximal and adjusted parallel to the long axis of the tibia. The patient is holding the film cassette above the knees at a 90 degree angle to the X-rays (Laurin et al. 1979).

It has been debated whether weight-bearing axial radiographs replicate the PF joint loading in a better way than supine views (Tennant et al. 2001). Baldini et al. (2007) introduced an axial weight-bearing Merchant view of the PF joint, performing it axially in both a supine and standing position with 100 knees of 69 patients who had received a total knee implant. In the weight-bearing views the patellar lateral subluxation and tilt were significantly reduced compared to unloaded images. The weight-bearing views correlated with postsurgical AKP, but the supine views did not. Powers et al. (2003) conducted an MRI study on six patients suffering from AKP and found less lateral displacement of the patella under weight-bearing only in knee flexion angles of 12 and 30 degrees. In knee positions throughout the range of 0–45 degrees however, joint loading did not influence patellar tracking compared to supine images.

6.3.3. Measures of patellofemoral congruence

Patellar position relative to trochlea may be characterized in many ways: in the form of angles, as displacement in millimeters or as ratios. Radiographic measurement techniques in use today for evaluation of the PF congruence in a replaced knee are methodologies elaborated originally for a native joint.

The sulcus angle (Figure 2) forms between the two lines from the deepest point of the trochlear groove to the highest points of both femoral condyles (Merchant et al. 1974).

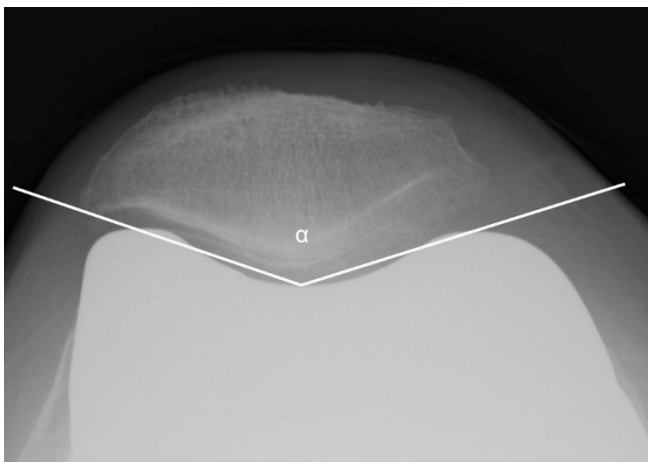

Figure 2. The sulcus angle

The congruence angle (Figure 3) is the angle created by the line bisecting the sulcus angle and the line from the lowest point of the trochlear groove to the lowest point of the median ridge of the patella (Merchant et al. 1974).

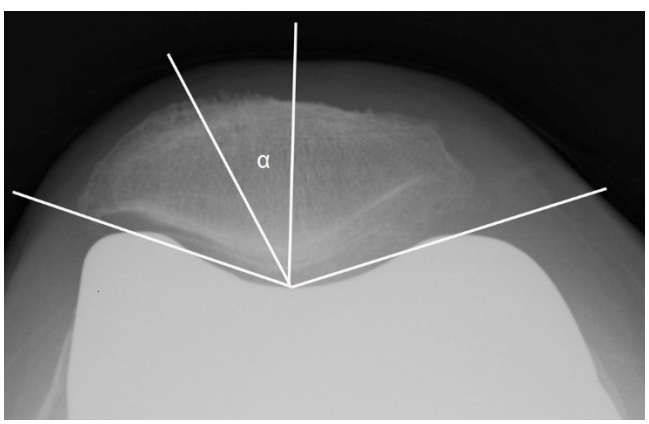

Figure 3. The congruence angle

The lateral patellar displacement (Figure 4) is the distance between two lines drawn at right angle from the line connecting the anterior limits of the femoral condyles: the first line touches the medial limit of patella and the other starts from the most prominent part of the medial femoral condyle (Laurin et al. 1979).

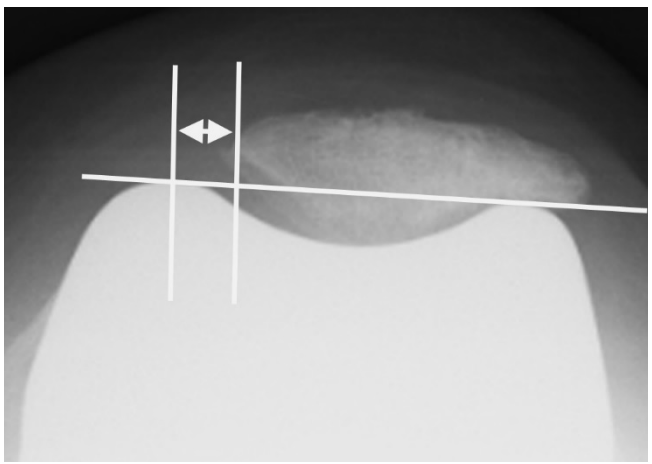

Figure 4. The lateral patellar displacement

The patellar displacement (Figure 5) is the horizontal distance either between the centres of the patella and trochlea (Heesterbeek et al. 2007) or between the lowest point of the median ridge of the patella and the deepest point of the trochlear groove (Chia et al. 2009, Urch et al. 2009).

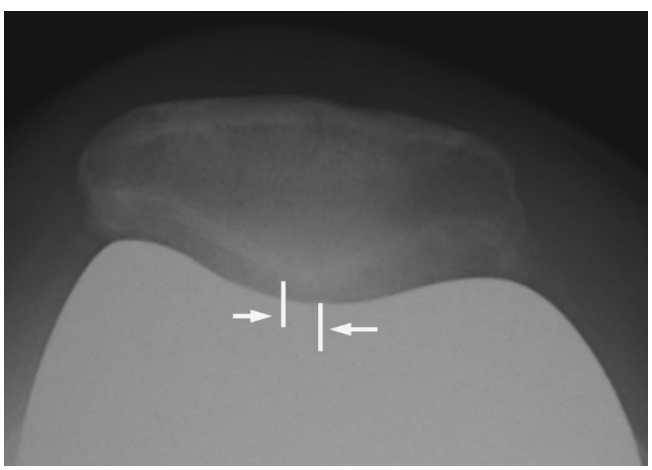

Figure 5. The patellar displacement

The lateral PF angle (Figure 6) is created by the lateral facet of the patella and the line connecting the apices of the anterior femoral condyles (Laurin et al. 1979).

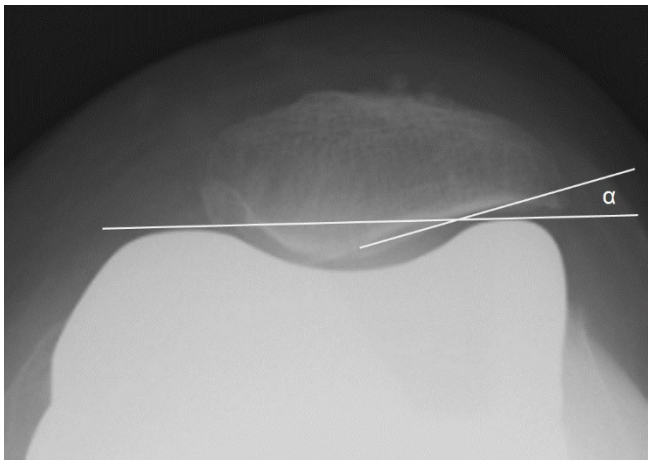

Figure 6. The lateral PF angle

The lateral patellar tilt (Figure 7) is an angle formed between the horizonlat plane (lower margin of the radiograph) and line connecting the two edges of the patella. In the absence of well discernable patellar edges, the line parellel to the anterior cortex of the patella may be used instead of the line between patellar edges (Grelsamer et al. 1993). The hosrisontal plane may be referenced also from the posterior condylar reference line or from the line joining anterior limits of the femoral condyles (Katchburian et al. 2003, Heesterbeek et al. 2007).

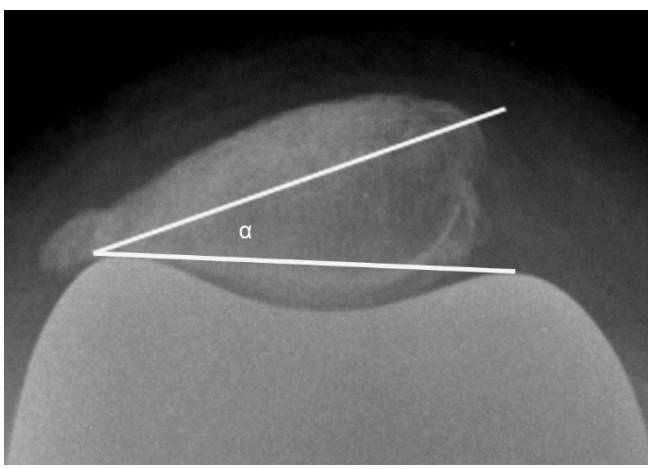

Figure 7. The lateral patellar tilt

AIMS OF THE STUDY

The general aims of this research were to estimate the prevalence of anterior knee pain following total knee arthroplasty with unresurfaced patella among patients operated on in East-Tallinn Central Hospital, to study the correlation between the state of patellar cartilage at knee replacement with postsurgical AKP and to propose a new radiographic method for measuring patellofemoral congruence in the axial plane.

The specific objectives of this study were to:

1) Estimate the prevalence of anterior knee pain following total knee arthroplasty without patellar resurfacing with a patient-administered questionnaire and physician-based clinical information.
2) Determine whether there is a significant correlation between the condition of the cartilage of unresurfaced patella at the time of knee replacement (as assessed by the OARSI score and Outerbridge classification) and postsurgical anterior knee pain.
3) Develop a new method (the patellar shift index or PSI) for the measurement of patellar medio-lateral alignment relative to the femoral groove on radiographs.
4) Estimate the validity and reliability of PSI and to compare the reliability of PSI to that of the lateral patellar tilt and the patellar displacement.

MATERIALS AND METHODS

7. Estimation of the prevalence of AKP by a patient-administered questionnaire

We carried out a retrospective analysis of 1778 consecutive primary TKA's without patellar replacement performed from January 1, 2000 – December 31, 2009 on 1431 patients in East-Tallinn Central Hospital. The primary outcome included the prevalence of AKP. Subgroup analysis specified data concerning the prevalence of AKP by age, by diagnosis and by implants. The secondary outcome included the severity of PF symptoms assessed by the Kujala Score. The knee was the unit of analysis. Implants were inserted using a medial para-patellar approach, fixed to the bone with cement and the patella was not replaced. By the time of the beginning of the study, 213 patients (250 knees) were deceased, 16 knees were revised and contact information of 7 patients (7 knees) was missing. 274 (18.2%) primary unrevised total knee arthroplasties performed on men and 1231 (81.8%) on women were available for the study. 1505 sets of two self-report measures, the Anterior knee pain questionnaire (AKPQ) and the Kujala score, were sent to 1200 patients by ordinary mail. Patients with both knees replaced received two sets of measures: one for each knee. The AKPQ (Table 1) developed for the current study is based on a reflective model measuring AKP as an indirect construct by observable items.

Table 1. The Anterior knee pain questionnaire (AKPQ)

1.	**When did the knee pain arise following arthroplasty?**
	a. the knee does not hurt (0)
	b. the knee remained painful right after arthroplasty(1)
	c. within 1–5 years following arthroplasty (2)
	d. more than 5 years following arthroplasty (3)
2.	**Does the knee hurt when rising from the chair or coach?**
	a. never (0)
	b. sometimes (1)
	c. always (2)
3.	**Does the knee hurt when ascending or descending the stairs?**
	a. never (0)
	b. sometimes (1)
	c. always (2)
4.	**Is touching of the knee cap painful?**
	a. never (0)
	b. sometimes (1)
	c. always (2)
5.	**Does the knee hurt when squatting?**
	a. never (0)
	b. sometimes (1)
	c. always (2)
6.	**Do You feel pain mostly in the anterior part of the knee?**
	a. never (0)
	b. sometimes (1)
	c. always (2)

The AKPQ consisted of the activities exerting the greatest strain on the PF joint. On the basis of the responses to the AKPQ, the knees were grouped into three pain related categories: 1) painfree, 2) AKP and 3) knee pain of some other origin than PF joint. Knees marked with "0" to question 1 were considered as painfree. The remaining group with responses "1", "2" or "3" to question 1 consisted of painful knees and was further subdivided into two. AKP was diagnosed if in addition to response "1", "2" or "3" to question 1 either "1" or "2" was chosen to all of the remaining questions (2,3,4,5,6) of the AKPQ. The rest of the knees with the responses "1", "2" or "3" to question 1 denoted knee pain of some origin other than PF joint.

The Kujala score (Table 2) evaluates subjective symptoms and functional limitations in patellofemoral disorders (Kujala et al. 1993).

Table 2. The original version of the Kujala Score (Kujala et al. 1993)

Anterior knee pain (Sheet code: _____)	Name: _____ Date: _____
Age _____	Knee: L / R
Duration of symptoms: ____years _____ months	
For each question, circle the latest choice (letter) which corresponds to your knee symptoms.	
1. Limp a. None (5) b. Slight or periodical (3) c. Constant (0)	**8. Prolonged sitting with the knees flexed** a. No difficulty (10) b. Pain after exercise (8) c. Constant pain (6) d. Pain forces to extend knees temporarily (4) e. Unable (0)
2. Support a. Full support without pain (5) b. Painful (3) c. Weight bearing impossible (0)	**9. Pain** a. None (10) b. Slight and occasional (8) c. Interferes with sleep (6) d. Occasionally severe (3) e. Constant and severe (0)
3. Walking a. Unlimited (5) b. More than 2 km (3) c. 1–2 km (2) d. Unable (0)	**10. Swelling** a. None (10) b. After severe exertion (8) c. After daily activities (6) d. Every evening (4) e. Constant (0)
4. Stairs a. No difficulty (10) b. Slight pain when descending (8) c. Pain both when descending and ascending (5) d. Unable (0)	**11. Abnormal painful kneecap (patellar) movements (subluxations)** a. None (10) b. Occasionally in sports activities (6) c. Occasionally in daily activities (4) d. At least one documented dislocation (2) e. More than two dislocations (0)
5. Squatting a. No difficulty (5) b. Repeated squatting painful (4) c. Painful each time (3) d. Possible with partial weight bearing (2) e. Unable (0)	**12. Atrophy of thigh** a. None (5) b. Slight (3) c. Severe (0)

6. Running	**13. Flexion deficiency**
a. No difficulty (10)	a. None (5)
b. Pain after more than 2 km (8)	b. Slight (3)
c. Slight pain from start (6)	c. Severe (0)
d. Severe pain (3)	
e. Unable (0)	
7. Jumping	
a. No difficulty (10)	
b. Slight difficulty (7)	
c. Constant pain (2)	
d. Unable (0)	

With Urho M. Kujala's consent, the questionnaire was adapted to the local language. To ensure that the original and the translated questionnaire were identical, forward and back translation method was used (Beaton et al. 2000). The sum of the Kujala score ranges from 0 to 100, where the greater value indicates a better PF function. Mean of the Kujala score was calculated for each of the abovementioned three knee categories.

Figure 8 describes how the study sample was developed.

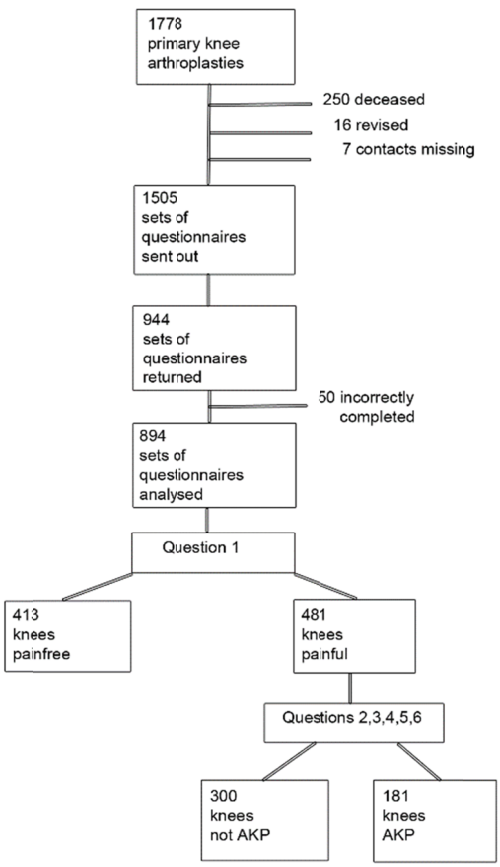

Figure 8. Algorithm of the study

Descriptive statistics, including mean and standard deviation (SD) were used for continuous variables. For categorical variables, percentages (%) and absolute (n) frequencies were presented. 95% confidence intervals (95%CI) were calculated to provide an estimate of population parameters. Chi-squared test, t-test and ANOVA were used to test the statistical significance. Two-tailed P values less than 0.05 were considered statistically significant.

8. Estimation of the prevalence of AKP by physician-based information

We prospectively included 100 consecutive patients suffering from osteo-arthritis and undergoing total knee replacement in the study. The patients were operated on by one surgeon (Vahur Metsna) in East-Tallinn Central Hospital between January 2011 and May 2012. The same surgeon who performed the arthroplasties also reviewed the patients in the outpatient clinic 1 year after the knee replacement. At follow-up we discriminated patients with AKP from symptomless ones using the HSS patella score (Table 3) (Baldini et al. 2006). This is a physician administered multi-item questionnaire rating subjective and objective aspects of PF function on a scale from 0–100, with higher values indicating a better result. 2 items of the HSS questionnaire are directly concerning AKP: pain in the front part of the knee while rising from a low chair and tenderness to palpation of the medial or lateral facets of the patella. We diagnosed AKP if at least 1 of these 2 tests was painful.

All patients also underwent radiographic evaluation of the knee joint in AP and lateral projections to exclude periprosthetic osteolysis as a potential source of pain. We performed Merchant patellofemoral axial views to see whether patellofemoral malalignment had any correlation with AKP. PSI was the measure of patellofemoral congruence in our study.

Table 3. The HSS patella score (Baldini et al. 2006)

Type of score	Variable	Score	Points	Max	Min
Subjective	Anterior knee pain How do you rate the pain on the front of your knee while rising from this low chair?	VAS score 0–10 50 – (5 x VAS score)		50	0
	Functional limitations Do you feel that the anterior part of your knee is limiting you while: – Climbing stairs – Descending stairs – Sitting for prolonged time (30 minutes at 90°)	No functional limitations Limitation in one function Limitation in two functions Limitation in all functions	15 10 5 0	15	0
Objective	Tenderness (palpation of medial and/or lateral patellar retinaculum-facet)	Absent Present	10 0	10	0
	Crepitus (during active ROM)	None Mild (for a limited ROM) Moderate (throughout entire ROM) Severe (catching/clunk)	15 10 5 0	15	0
	Quadriceps strength	Normal (5/5) Reduced (3–4/5) Deficient (1–2/5)	10 5 0	10	0
Total				100	0

9. Assessment of the condition of the cartilage of the patella

We performed the study on the same 100 patients, mentioned in the previous section. We inserted all implants through a standard medial parapatellar approach and cemented to bone. The patella was handled in a standardized way. We left the patella unresurfaced and resected only its osteophytes together with the Hoffa's fat pad. We didn't perform patellar rim electrocautery, but removed the synovial tissue around the margins of the patella. All patients received the PFC Sigma (DePuy, Warsaw, Indiana, USA) posterior stabilized mobile bearing implant. We aimed to place the femoral component parallel to the epicondylar axis and perpendicular to the Whiteside line. Following the eversion of patella and before removal of the osteophytes the operating surgeon evaluated the macroscopic impairment of the patellar cartilage according to the original Outerbridge (1961) classification: "grade 1-softening and swelling of the cartilage, grade 2-fragmentation and fissuring in an area 13 mm or less in diameter, grade 3- fragmentation and fissuring in an area more than 13 mm in diameter, grade 4-erosion of cartilage down to bone" (Outerbridge 1961). Intraoperative grading of the cartilage defects of the patella was necessary for location of the most damaged area in order to obtain the biopsy. An operation theatre nurse, specially trained in intraoperative photography, took pictures of the articular surface of the everted patella.

The operating surgeon took 1 biopsy of the patella from the macroscopically most advanced area of chondromalacia, as assessed by the Outerbridge classification (Outerbridge 1961), using a 10G bone biopsy kit (Figure 9). We excluded osteophytes from sampling.

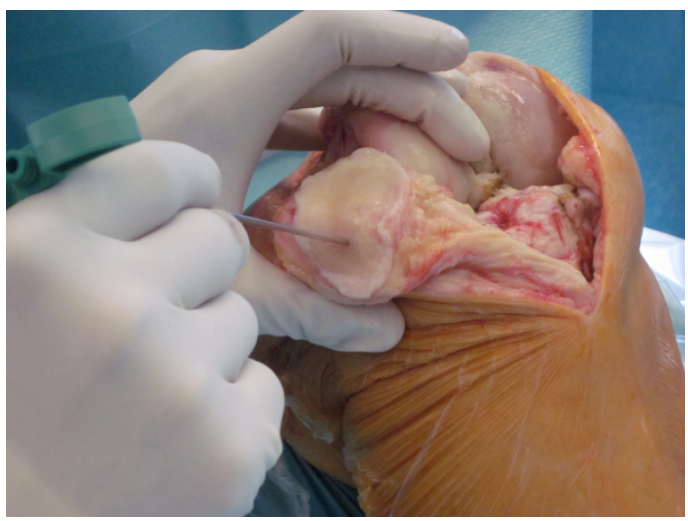

Figure 9. Obtaining the biopsy of the patella

The procedure resulted in a cylinder of 1.5 mm in diameter and 10–15 mm in length extending from the articular surface of the patella to the subchondral bone. The tissue specimens were placed in a receptacle filled with 10% buffered formalin. In the laboratory the histology technician applied the samples to decalcifying solution for 30 min and then washed the samples in water for 15 min. We used conventional tissue processing and embedded the samples in paraffin blocks. 4 micrometer thick serial sections were mounted on glass slides and stained with haematoxylin and eosin.

We evaluated the condition of the cartilage of the patella using the OARSI Osteoarthritis Cartilage Histopathology Assessment System (Pritzker et al. 2006), which incorporates 3 variables: the stage, the grade and the score.

The stage is the lesion's horizontal extent over the cartilage surface irrespective of the underlying grade. The operating surgeon measured the extent of the loss of the surface integrity of the patellar cartilage on photographs taken intraoperatively, distinguishing the normal cartilage from the impaired one using the original Outerbridge classification (Outerbridge 1961). We analysed the photographs using Adobe Photoshop CS5 Extended (Adobe Systems Incorporated 345 Park Avenue, San Jose, CA 95110-2704 USA) software and its lasso tool functionality. The lasso tool enables the selection of an irregular portion of an image as well as the counting of the pixels of the marked area. First, we delineated the imaginary perimeter of the articular surface of the patella as it would look like after resecting the osteophytes. We excluded the osteophytes outside the perimeter from the analysis and classified the osteophytes inside the perimeter as Outerbridge (1961) grade 4 chondromalacia (Figure 10).

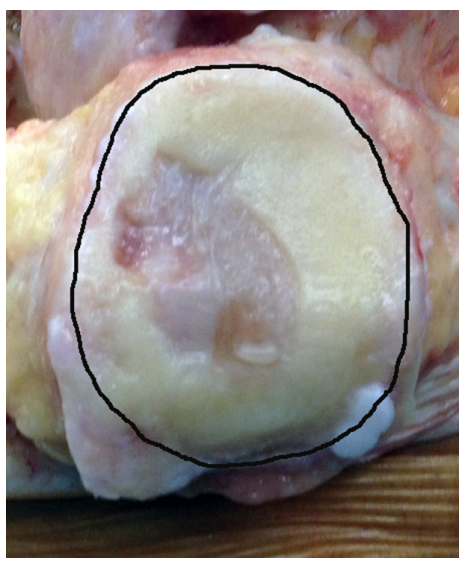

Figure 10. Delineation of the perimeter of the articular surface of the patella

Second, we marked the area of a normal cartilage (Figure 11). If present, we added together the discontinuous areas of the undamaged cartilage. We specified areas with grades worse than Outerbridge (1961) grade 1 as a lesion.

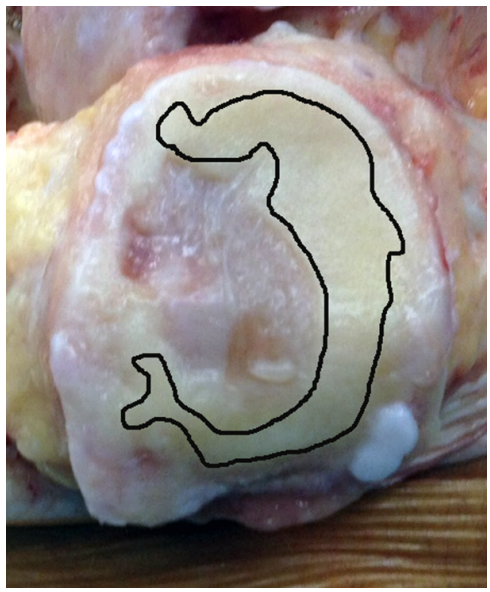

Figure 11. Marking of the normal cartilage of the patella

We recorded the amount of pixels of the 2 delineated areas and calculated the percentage of the damaged articular surface area of the patella as follows:

100 – (pixels of normal cartilage / pixels of perimeter x 100).

We categorized the extent of the cartilage involvement into 5 OARSI stages: stage 0 no involvement, stage 1 < 10%, stage 2 10–25%, stage 3 25–50%, stage 4 > 50%.

6 grades depict the lesion's histologic progression into the depth of the cartilage from intact cartilage morphology to subchondral bone remodelling. A pathologist, blinded to the patient's clinical information and OARSI stage of the articular cartilage, performed the microscopic examination under the standard light microscope. The pathologist assigned the grade to all samples: a grade 1 specimen had to have intact cartilage surface, grade 2 (Figure 12) denoted cartilage surface discontinuity, grade 3 vertical fissuring, grade 4 cartilage erosions and grade 5 bone denudation. The biopsies were not informative enough to differentiate between grades 5 and 6 therefore all biopsies with denuded bone and reparative tissue were classified as grade 5. We did not apply subgrading.

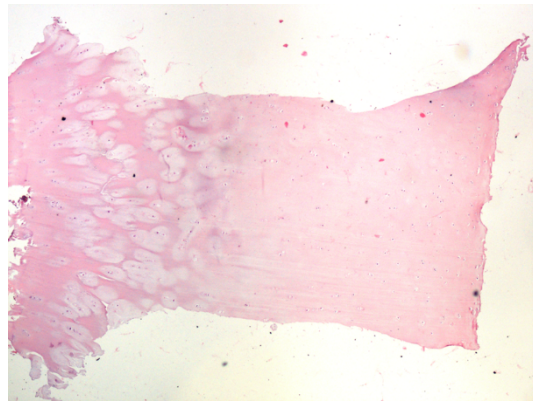

Figure 12. OARSI grade 2

The OARSI score combines the grade with the stage of the cartilage lesion and it is calculated by using a formula: score = grade x stage. The score ranges from 0 to 24, with the higher values indicating more advanced cartilage injury.

10. Determination of the correlation between the defects of the cartilage of the patella and AKP

We used descriptive statistics including mean, SD and range for continuous variables. We present the percentages and absolute frequencies for categorical variables. We used the Student's t-test to determine whether the OARSI score of painless patients differed significantly from the OARSI score of patients experiencing postsurgical AKP and for the comparison of PSI. We assessed the relationship between Outerbridge (1961) grade 4 cartilage defects and AKP using the Spearman correlation coefficient. We divided the patients into 2 groups based on the OARSI score and analyzed the difference of AKP prevalence between these groups by calculating the prevalence ratio (PR) together with 95% confidence intervals (CI) exerting the Poisson regression with robust variance. We considered the differences statistically significant if p-values were less than 0.05 and analyzed the data with Stata 9 software.

11. Development of the PSI

The study included 51 PF axial X-rays (Merchant view) of patients with PF pain syndrome following TKA. Radiographs were obtained from our digital database and analyzed. Only patients with unresurfaced patellae were included in the study. The mediolateral position of the patella relative to the trochlea was investigated. A new measure, the PSI, was developed.

The calculation of the PSI is described in Figure 13. Lines 1 and 2 are drawn parallel to the medial and lateral trochlear shoulders. Line 3 joins the apices of the anterior femoral condyles. The intersection of first three lines creates two

distinct reference points at the level of the anterior femoral condyles, determining the trochlear width. Line 4 is drawn from the most medial edge of the patella to its most lateral border to determine the patellar width. The center of the trochlea is calculated on Line 3 by bisecting the distance between the two anterior reference points. Line 5 is drawn from the center of the trochlea at a right angle to Line 3. The center of the patella is identified by bisecting Line 4. Line 6 is drawn from the center of the patella at a right angle to Line 3. The distance between Lines 5 and 6 is called the patellar shift. Trochlear width and patellar shift are measured. The PSI is calculated by dividing the patellar shift with the trochlear width (PSI = patellar shift / trochlear width). The index is rounded up to two decimal points. Patellar shift can be either medial or lateral with medial patellar shift marked with a "-" sign.

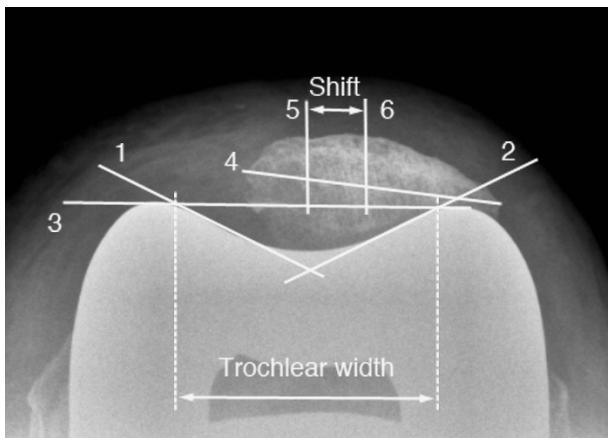

Figure 13. Measurement technique for the PSI

12. Estimation of the validity and reliability of the PSI and comparison of the reliability of PSI to that of LPT and PD

The intra-rater and inter-rater reliability of the PSI were estimated by one orthopedic surgeon, one radiologist and two medical students. The value of the PSI was calculated twice at a two-week interval with each researcher working independently of the others. Radiographs were printed on an A4-size sheet of paper. Measurements were carried out by hand using the technique described above with a pencil and a transparent ruler.

The reliability of the PSI was compared to the reliability of the LPT and the PD. The LPT (Figure 14) is the angle between the transverse axis of the patella and the anterior intercondylar line. The patellar transverse axis is defined as the line between the medial and lateral patellar corners (Grelsamer et al. 1993).

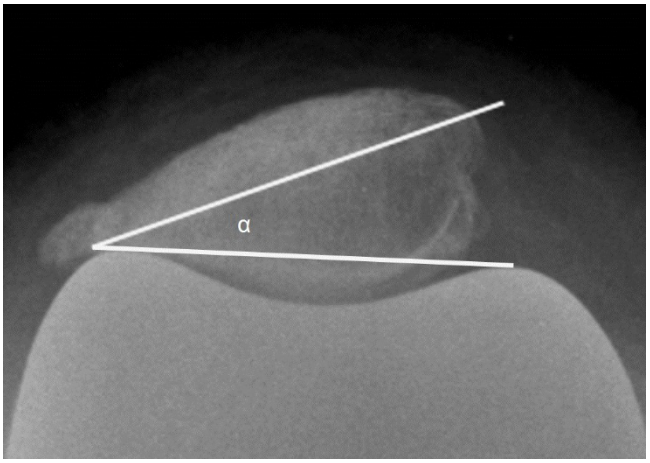

Figure 14. The lateral patellar tilt (LPT)

The PD (Figure 15) is the distance between the deepest point of the trochlear groove and the lowest point of the articular ridge of the patella (Heesterbeek et al. 2007).

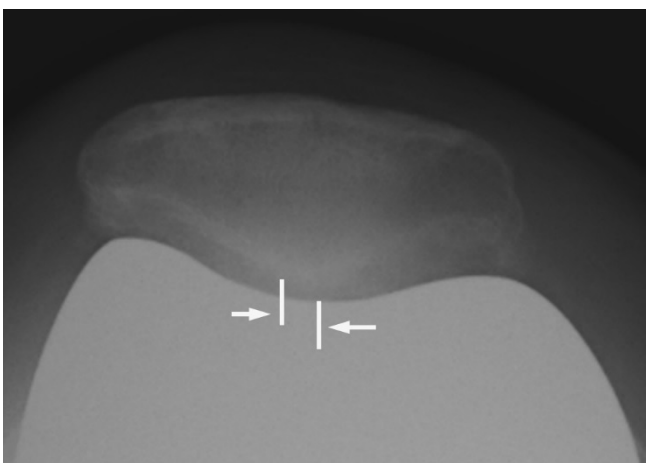

Figure 15. The patellar displacement (PD)

LPT and PD values were also calculated twice at a two-week interval by the same researchers engaged in the measurement of the PSI.

PSI face validity was tested by 4 orthopedic surgeons not involved in the calculation of radiographic PF congruence measures. Each surgeon was asked to visually evaluate 5 images of the 51 radiographs of their own choice and rank them in a descending order in terms of the magnitude of patellar displacement.

Each surgeon created a unique set of 5 images out of 51. The mean PSI (2 measurements by all 4 investigators) of each selected image was compared to the visual ranking of the respective radiograph. The image with greater displacement on visual inspection was assumed to have a higher PSI value. The intraclass correlation coefficient (ICC), a two-way mixed model on absolute agreement, with 95% confidence intervals was used to analyze the intra-rater reliability (Shrout and Fleiss 1979). ICC values can range from 0 to 1, with a higher value indicating greater reliability.

Krippendorff`s alpha (Kα) is a reliability coefficient developed to estimate reliability regardless of the number of observers, levels of measurement, sample sizes and the presence or absence of missing data (Hayes and Krippendorff 2007). Inter-rater reliability is usually regarded as being sufficient if alpha is greater than 0.70. Confidence intervals of 95% were calculated.

The consistency of PD measurements was verified by calculating the proportion of agreement indicating the number of measurements of the PD for which observers agreed over the total amount of observations. An agreement above 70% was considered acceptable (De Vet HCW 2011).

13. Ethics

We obtained approval for the study from the Tallinn Medical Research Ethics Committee (nr. 2230-20.12.2010, nr. 2398-19.05.2011) and the East-Tallinn Central Hospital Medical Review Board. All patients signed informed consent.

RESULTS

14. Prevalence of AKP

14.1. Patient-reported outcome

Patients returned 944 sets (171 male and 773 female knees) of completed measures (AKPQ, Kujala score) to investigators, thus resulting in a 62.7% response rate. The response rate was fairly similar among men and women, 62.4% and 62.8% respectively. 50 sets of the returned and filled-in measures (6 male and 44 female knees) were defective and therefore excluded from the study. 894 sets (165 male and 729 female) of properly completed questionnaires were left for the final analysis, constituting 59.4% of all questionnaires sent out initially.

Mean follow-up time from knee arthroplasty until completing the questionnaires was 69 (SD=33, range 19–137) months. The mean age was 72 years for male respondents (SD=9, range 43–88) and 73 years for female (SD=8, range 42–92).

Less than half of the knees were painfree and one third had pain originating from a source other than PF joint. Relying on the diagnostic criteria established in the present study, the prevalence of AKP did not differ significantly between genders, p=0.578 (Table 4).

Table 4. Pain related categories

	Male knees		Female knees		Total	
	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
Painfree	72	43.6 (35.9−51.6)	341	46.8 (43.1−50.5)	413	46.2 (43.0−49.5)
AKP	36	21.8 (15.8−28.9)	145	19.9 (17.1−23.0)	181	20.2 (17.7−23.0)
Painful, not AKP	57	34.6 (27.3−42.3)	243	33.3 (29.9−36.9)	300	33.6 (30.5−36.6)
Total	165		729		894	

The highest prevalence of AKP was noted among men below 60 years of age. Also women younger than 60 years experienced more AKP compared to the other age groups of the same gender. Women aged 81 and over were least affected by AKP (Table 5).

Table 5. Prevalence of AKP by age

	Male knees			Female knees		
Age (y)	n	AKP	% (95%CI)	n	AKP	% (95%CI)
< 60	18	7	38.9 (17.3–64.3)	57	17	29.8 (18.4–43.4)
61 – 70	53	9	17.0 (8.1–29.8)	200	42	21.0 (15.6–27.3)
71 – 80	71	15	21.1 (12.3–32.4)	348	67	19.3 (15.2–23.8)
> 81	23	5	21.7 (7.4–43.7)	124	19	15.3 (9.5–22.9)

There was a statistically significant (p=0.010) difference between the mean age of patients with AKP (n=181) and the rest of the study group (n=713), 71.4 and 73.2 years respectively. 90.7% of knees involved in the study suffered from osteoarthritis, 8.2% from rheumatoid arthritis and the remaining 1.1% were impaired either by arthritis secondary to ankylosing spondylitis, psoriatic arthritis or knee dysplasia. The osteoarthritis group showed higher prevalence of AKP compared to rheumatoid knees, 20.5% (95%CI 17.7–23.4) and 15.1% (95%CI 7.8–25.4) respectively. The difference was not statistically significant (p=0.269). The prevalence of AKP was 40.0% (95%CI 12.2–73.8) in the third group of patients. Due to the small number of knees involved and the heterogenicity of diagnoses, the results of the smallest group should be interpreted with caution.

The two most frequently used implants were PFCΣ-CS fixed bearing (J&J) prosthesis in 70.6% of the cases and PFCΣ-CS mobile bearing (J&J) prosthesis in 23.0% of arthroplasties. The prevalence of AKP in the fixed bearing group was 20.1% (95%CI 17.1–23.5) and in the mobile bearing group 21.4% (95%CI 16.0–27.6). We were unable to show any significant (p=0.703) difference in the prevalence of AKP between mobile and fixed bearing implants.

AKP occurred early following the arthroplasty. In 49.2% (95%CI 41.7–56.7) of the cases of AKP the knee remained painful right after the surgery, 38.1% (95%CI 31.0–45.6) became symptomatic within 1–5 years following the knee replacement and in only 12.7% (95%CI 8.2–18.5) of patients' knees AKP emerged more than 5 years since the operation.

The mean of the Kujala score differed significantly (p<0.001) among pain related knee categories. As expected, symptomless knees had the highest mean of the Kujala score 74.6 (95%CI 72.5–76.7). The Kujala score of the knees with pain of some other origin than the PF joint was 55.8 (95%CI 53.6–58.0) and AKP lessened the outcome to 45.5 (95%CI 43.0–48.1).

14.2. Physician-based outcome

95 out of the 100 patients were available for follow-up 1 year after surgery. 2 patients died from reasons not related to TKA, 1 patient was revised due to infection and 2 patients withdrew their consent. The mean age was 66 (45–79) years for the 15 male patients and 69 (49–87) years for the 80 female patients. Relying on the results of HSS patella score, 38 of the reviewed patients were symptomless and 57 had pain in the front part of the knee. Of the 57 patients with painful knees, 3 had AKP when rising from a low chair, 38 had pain at palpation of the patella and in 16 cases the patients experienced pain in both tests.

15. Correlation of the condition of the cartilage of the patella with AKP

The same 95 patients described in the previous section "Physician based outcome" were used in the analysis.

We classified the extent of the damage of the surface area of the cartilage as OARSI stage 3 in 7 patellas and stage 4 in 88 patellas.

Histologic assessment of the biopsies of the patella revealed the following OARSI grades: grade 2 in 13 knees, 3 in 19 knees, 4 in 47 knees and grade 5 in 11 knees. Due to the shortfall of histologic processing of the biopsies we were unable to determine the histologic grade of cartilage impairment of 5 patellas.

The mean OARSI score was 14 (6–20, SD=3.8). Due to the missing histologic grades of 5 patients we managed to calculate scores of 90 patellas, of which 36 were painless and 54 having AKP. The mean OARSI score of painless patients was 13 (6–20) and of patients with AKP 15 (6–20). The difference was statistically significant (p=0.04). Macroscopic Outerbridge grade 4 cartilage defects did not correlate with postsurgical AKP (Spearman ρ=0.1, p= 0.5).

We estimated AKP in 2 groups of patients according to the OARSI score: the first group had scores 0–12 and the second group had scores 13–24 (Table 6).

Table 6. AKP and the OARSI score

	OARSI 0–12	OARSI 13–24
	n	n
No AKP	18	18
AKP	15	39
Total	33	57

The second group of patients had a 50% higher risk of AKP with borderline significance (PR=1.5, CI 1.0–2.3).

The assessment of conventional radiographs excluded osteolysis and patellar maltracking as a possible source of knee pain. The PF congruence in axial radiographs measured by the PSI method was similar between the symptomless patients and those experiencing painful knees.

16. Validity and reliability of PSI

The intra-rater reliability of the LPT, the PD and the PSI are presented in Table 7. Results were excellent for all three methods.

Table 7. Intraclass correlation coefficients (ICCs)

	Rater 1		Rater 2		Rater 3		Rater 4		Mean
	ICC	**95% CI**	**ICC**	**95% CI**	**ICC**	**95% CI**	**ICC**	**95% CI**	
Lateral patellar tilt	0.99	0.98– 0.99	0.94	0.89–0.96	0.97	0.95–0.98	0.95	0.91–0.97	0.96
Patellar displacement*	0.99	0.98–0.99	0.97	0.92–0.98	0.98	0.93–0.99	0.98	0.90–0.99	0.98
Patellar shift index	0.85	0.75–0.91	0.85	0.76–0.92	0.97	0.94–0.98	0.99	0.97–0.99	0.91

**Images with missing landmarks were excluded from analysis.*

The inter-rater reliability, characterized by Kα, was high for all three measurements (Table 8).

Table 8. Kα coefficients.

	Kα	**95% CI**
Lateral patellar tilt	0.89	0.84–0.92
Patellar displacement	0.97*	0.96–0.99
Patellar shift index	0.92	0.88–0.94

**Images with missing landmarks were excluded from analysis.*

Indefinable landmarks did not allow for the measurement of PD in a substantial number of radiographs. These images were excluded from the reliability analysis of the displacement technique.

In the calculation of PD, 16 of 51 radiographs were noted to having missing landmarks and all necessary landmarks were found in only 8 images by all investigators. The proportion of agreement for measurements of PD remained as low as ((16+8)/51) × 100=47.1%.

Table 9 summarizes the results of the face validity test.

Table 9. Visual ranking of the radiographs and corresponding mean values of the PSI

Surgeon 1		**Surgeon 2**		**Surgeon 3**		**Surgeon 4**	
Visual	**PSI**	**Visual**	**PSI**	**Visual**	**PSI**	**Visual**	**PSI**
X-ray 29	1.20	X-ray 29	1.20	X-ray 29	1.20	X-ray 29	1.20
X-ray 53	0.33	X-ray 3	0.60	X-ray 3	0.60	X-ray 3	0.60
X-ray 83	0.32	X-ray 45	0.27	X-ray 67	0.23	X-ray 10	0.30
X-ray 50	0.30	X-ray 66	0.17	X-ray 82	0.24	X-ray 67	0.23
X-ray 49	0.09	X-ray 88	0.09	X-ray 8	0.04	X-ray 8	0.04

In general, images displaying larger PF incongruity on visual inspection had higher PSI values. Although there was a difference between the surgeon's estimation and the PSI value in one case, the results were quite similar and did not diverge from the general pattern.

DISCUSSION

17. Prevalence of AKP

We estimated the prevalence of AKP in patients following TKA using the patient specific Anterior knee pain questionnaire (AKPQ) and the clinician based Hospital for Special Surgery (HSS) patella score, resulting in prevalence rates of 20% and 60% respectively. Our data reflect the trend in other studies, *i.e.* that patient reported outcomes yield smaller prevalence of AKP (Burnett et al. 2007, Epinette and Manley 2008) compared to works recording both patient and clinician based data (Baldini et al. 2006, Campbell et al. 2006).

At the time of designing the study a literature review did not reveal any patient specific outcome measures for diagnosing AKP following TKA. Manusco et al. (2012) however has published a patient-reported PAQ-knee scale, which among other items contained specific questions about AKP. It is a widely used practice in orthopaedic literature to diagnose AKP relying on a few items that reflect PF pain within a multi-item evaluative instrument (Barrack et al. 2001, Zupan et al. 2014). We therefore had to compose our own questionnaire for discerning AKP in patients. Although not an externally validated tool, we believe our questionnaire was fit for purpose as the content was composed of feasible activities for patients with a replaced knee to exert increased strain on the patellofemoral joint in order to produce AKP.

For the assessment of the severity of PF symptoms we used the Kujala score (Kujala et al. 1993). The perfect match of the results of the Kujala score with pain related knee categories served as a validation tool of diagnostic criteria of pain established in the current study. We admit, however, that as the Kujala score was originally conceived to be used in young patients with high expectations of physical activity, the item content is not perfect for application to mostly low-demand sedentary patients after knee replacement.

The HSS patella score is a clinician based questionnaire for diagnosing AKP in patients following TKA (Baldini et al. 2006). We choose HSS because it is reliable tool, was conceived to be used on patients with a replaced knee, specifically asks questions about the location of pain in the front part of the knee, and detects both objective and subjective PF pain.

Patient satisfaction should be the ultimate goal of TKA. Quite often patient and physician perceptions of a positive outcome of TKA do not coincide (Falez 2014). Excessive focus on what the physician thinks about the performance of the implant may easily overlook patient dissatisfaction. In recent years therefore the focus of research has shifted from surgical outcomes to patient opinion, with an emphasis on patient quality of life and overall satisfaction than clinical symptoms and signs (Mancuso et al. 2012, Falez 2014). Until uniform diagnostic criteria of AKP are agreed upon, the results of different studies will remain difficult to compare. Further work should examine which diagnostic tools of AKP are appropriate in clinical practice and whether patient-reported outcomes, clinician-specific signs or the combination of clinical tests and questionnaires are accurate enough.

Probably the most important issue in the process of establishing a diagnosis of AKP is the precise location of pain in the knee. Patients may face difficulties in determining where the knee exactly hurts, when replying to the questions of the self-report measures. Therefore methods comprising clinical tests, performed by the examining physician, seem to be more eligible in diagnosing AKP. Pain maps, which are photographic images or drawings of the contours of the knee where the pain sites can be marked either by the patient or the examiner, is a promising solution to the problem (Creamer et al. 1998, Elson et al. 2011).

In the current work we studied several variables that may predict the evolution of AKP following knee replacement. Similar to published literature we did not find patient gender correlating significantly with postsurgical AKP. However subgroup analysis of the responses to AKPQ by gender and age revealed the highest prevalence of AKP among men under 60 years of age. Also among women below 60 there was higher than average proportion of patients with AKP. The higher prevalence of AKP in the younger age group is probably explained by greater strain on PF joint due to a physically more active way of life. Sedentary lifestyle, on the other hand, prevents overloading the knee and therefore results in fewer cases of AKP. None of the patients engaged in our study had a gender-specific implant. In common to the current trend of TKA (Dargel et al. 2011), instead of gender specifics we aimed at replicating the native knee anatomy as closely as possible by adapting the prosthesis to variations in knee anatomy irrespective of gender. The theoretical advantage of mobile bearing tibial inserts in terms of self-alignment that compensates for small rotational errors in component positioning (Heinert et al. 2011), did not result in a lower prevalence of AKP in our study either.

According to Leichtle et al. (2014) the results of isolated studies should be interpreted with caution as most are implant specific and results may differ between dissimilar prosthetic designs. For example a study that evaluated 5 patella-friendly implants from a number of producers found substantial differences of patellofemoral tracking in all of them (Ma et al. 2007). Interpretation of our results take into consideration that the vast majority of implants studied were PFC Sigma (DePuy, Warsaw, Indiana, USA) fixed and mobile bearing designs. Another important methodological factor for the estimation of the prevalence of AKP in our retrospective survey using AKPQ was that the response rate of 60% may have produced selection bias.

Our data support previous research stating that despite TKA has proved to be an effective treatment option for end-stage arthritis unresponsive to medical therapy (Waimann et al. 2014), it does not restore the function of the knee to normal (Stiehl 2005) and a substantial amount of TKA recipients continue to have residual knee symptoms leading to dissatisfaction with the procedure (Parvizi et al. 2014). Patients undergoing TKA should be therefore appraised of the high probability of experiencing pain in the front part of the knee following the surgery.

18. Measurement of PF congruence

An incongruent PF joint may be the expression of an imbalance of the peri-patellar soft tissue envelope or malposition of the components of the knee prosthesis. The lack of a difference in PF alignment between asymptomatic and symptomatic patients is seen not as an absence of correlation, but rather as an insufficiency of the current measurement techniques (Wilson 2007). We believe the confusion in this matter is generated by three main factors: *i*) that the definition of a norm is difficult to establish due to the variety of patellar tracking patterns among asymptomatic individuals (Katchburian et al. 2003, Kong et al. 2014); *ii*) that the orthopaedic community has not been able to agree upon a single technique as a standard for measurement of PF congruence. PF axial views are being captured in different positions of knee flexion under weight-bearing or non-weight-bearing conditions and the analysis of the images is being conducted using a variety of indices (Wilson 2007); *iii*) that the reliability and validity of currently available PF axial measuring techniques is questionable (Wilson 2007, Heesterbeek et al. 2007).

In the search for possible causes of complaints in patients with AKP following TKA, it is ineluctable to assess PF kinematics in the axial plane. As AKP can also be caused by alteration of the height of the patella, the PF joint should also be evaluated in the saggital plane. Similar to axial plane measurements, none of the patellar height ratios has been accepted as a standard and correlation of patellar height ratios with AKP is weak (Narkbunnam et al. 2013).

Heesterbeek et al. (2007) found lateral patellar tilt (LPT) and patellar displacement (PD) more successful than other techniques when assessing PF congruence in patients following TKA with unresurfaced patella. Tilting of the patella is however not related to displacement (Chia et al. 2009). Figures 16a and 16b present luxated patella with a smaller tilt angle than the subluxed knee cap.

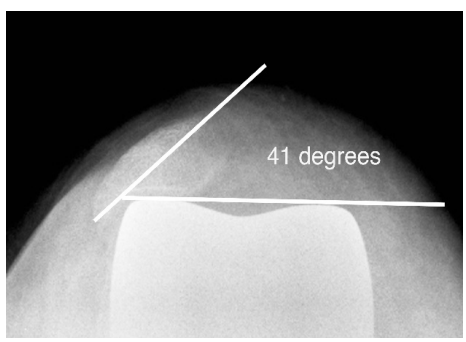

Figure 16a

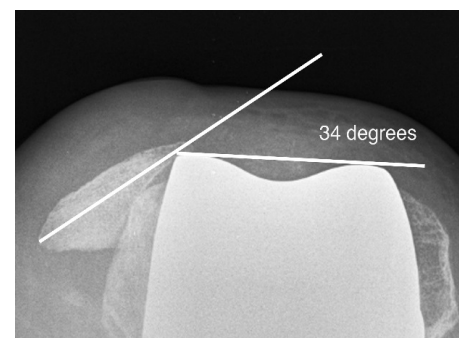

Figure 16b

In this work we introduced a valid and reliable method for the measurement of PF congruence following TKA with unresurfaced patella: the PSI. Compared to previously described methods, the PSI has several advantages. Trochlear contours of the femoral component are relatively flat, which makes pinpointing the highest extremum of the femoral condyles and the lowest point of the trochlear groove difficult. Additionally, the bony and cartilaginous geometry of the patella does not match (Figure 17) and therefore it is misleading to judge the conformity of the lowest points of the patella and the trochlea relying on bony landmarks only (Staubli et al. 1999). With our PSI however all landmarks necessary for the calculation of the index are always easily discernible.

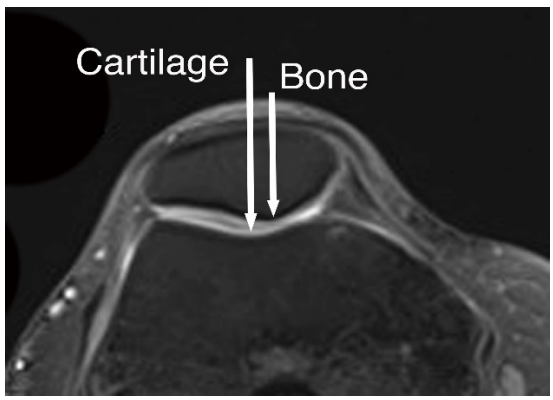

Figure 17. Non-matching cartilaginous and osseus geometry of the patella on axial MRI

Unresurfaced patella also loses its original shape (Figure 18) in the process of stress-induced remodelling or disruption of blood supply in 40–85% of TKA cases (Smith et al. 1989, Shih et al. 2004, Smith et al. 2004, Melloni et al. 2008).

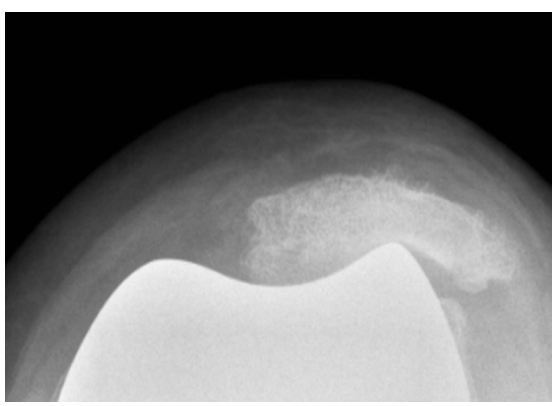

Figure 18. Remodelling of the laterally subluxed patella

The high intra- and inter-reliability rate of the PD technique was only achieved by excluding images that did not qualify due to indefinable landmarks. The low proportion of agreement (47.1%) among investigators reflects the difficulty in interpreting radiographic landmarks and should be considered a limitation of the PD measurement technique. Katchburian et al. (2003) propose using posterior instead of anterior condyles of the femur as more reproducible references, but such an idea is not applicable to X-rays as posterior condyles are not visible on PF axial radiographs. According to the PSI methodology, the centre of the trochlear groove is found according to the landmarks arising from the intersection of lines drawn on the radiograph and the midpoint of the knee cap is determined by bisecting the line connecting the two edges of the patella, thus avoiding the indistinct contours of the replaced knee joint.

PSI relies on proportions rather than expressing displacement of the patella in millimetres. Radiographic magnification may cause variability in linear measurements of patellar displacement. Displacements of an equal number of millimetres may also have a larger effect on knees with smaller dimensions. As a ratio, PSI is independent of radiographic magnification and circumvents the effect of knee size, allowing for the comparison of results between patients and studies.

PSI has uses beyond simply analysing the radiograph of a replaced knee with unresurfaced patella. Although the PSI method was created for describing the position of the patella relative to trochlea in a replaced knee with an unresurfaced patella, there is no reason why it cannot also be used in cases with a resurfaced patella or in a native knee. The images obtained by X-ray, CT or MRI may be analysed either on a computer or on print-outs using a ruler and pencil.

PSI has proved to be a valid and reliable tool to serve the purpose of characterizing the position of the patella relative to the trochlea.

19. Correlation of the state of the patellar cartilage with AKP

The results of our study indicate that structural changes of the patellar cartilage may contribute to the evolvement of AKP following TKA. Our study however does not elucidate on the long-term relationship between structural changes of the patellar cartilage and AKP. Information concerning time-dependent prevalence of AKP is conflicting. Meftah et al. (2011) have documented an almost 3-fold decrease of AKP 10 years following TKA, while van Jonbergen et al. (2012) found in a meta-analysis that the relationship between AKP and time of assessment is inconclusive. Studies show that the degradation of the cartilage of the unresurfaced patella continues after TKA (Shih et al. 2004). One year following joint replacement should be a good milestone to assess the relationship of postsurgical AKP and the state of patellar cartilage recorded at surgery. A year post-surgery the patient will have recovered from the surgical trauma

and the state of the patellar cartilage is more like the situation encountered at surgery than after a longer period.

The scientific literature provides convincing arguments both for and against patellar resurfacing (Schindler 2012), often leaving the reader uncertain about the optimal way of treating the patella during knee replacement. It is disputable to relate the reduction of AKP following patellar replacement solely to the substitution of the cartilage with plastic. The theoretical advantage of patellar resurfacing in regard to reduction of postsurgical AKP lies not only in clearing away the damaged patellar cartilage, but also in improved patellar tracking because of better conformity of the patellar button and the trochlear groove. Conversely the improved PF biomechanics in cases of replaced patella has been questioned, because despite avoidance of overstuffing and correct positioning of the implants the PF peak pressure may rise 2,5-fold (Leichtle et al. 2014). Results of secondary resurfacing (Parvizi et al. 2012) and the high prevalence of post mortem cartilage defects of the patella, which were likely asymptomatic during a subjects lifetime (Iriuchishima et al. 2013), means that factors besides articular cartilage may influence the evolution of pain in the front part of the knee following TKA.

So far attempts to relate intraoperative cartilage changes to postoperative AKP have led to conflicting results (van Jonbergen et al. 2012), but the absence of significant correlations may be owing to insufficient evaluation methods. Previous studies (Picetti et al. 1990, Barrack et al. 1997, Barrack et al. 2001, Wood et al. 2002, Burnett et al. 2004, Campbell et al. 2006, Rodriguez-Merchan and Gomez-Cardero 2010) have used the original Outerbridge (1961) classification and its modification by Beguin and Locker (1983) that enable macroscopic assessment of cartilage defects. Macroscopic evaluation alone may not provide enough information about cartilage impairment, as microscopic changes at the cellular level may be quite advanced before any change detectable by the human eye becomes visible (Agha and Webb 2006, Bentley and Hill 2007). We decided therefore to grade the cartilage pathology using the OARSI system, which combines the microscopic changes of the depth of the cartilage and the macroscopic extent of arthritic changes over the joint surface into an overall score (Pritzker et al. 2006). The OARSI system is considered a valid way of evaluating cartilage impairment (Pearson et al. 2011, Pauli et al. 2012). The cartilage defect usually contains areas of different stages of cartilage impairment. We took the biopsy from the most damaged location of the cartilage as assessed macroscopically and in this way only the histological grade of the most degenerated surface area was used for calculation of the OARSI score (Pritzker et al. 2006).

The assessment of articular surface defects on photographs resembles the situation encountered during surgery. The continuum of cartilage changes from fissures to subchondral bone exposure are clearly visible on the photographs. Only softening of the cartilage cannot be estimated because of the absence of tactile feedback. Drawing of the virtual resection line of the patellar osteophytes is also relatively simple for a surgeon experienced in knee replacement. Digital images may offer additional benefits as they enable zooming in or out on the

photograph and the usage of other functions of the image processing software. Han et al. (2005) found photographic assessment of cartilage defects both valid and reliable.

Our study is the first to utilise a combined approach of microscopic and macroscopic cartilage assessment in patients following TKA with unresurfaced patella. We demonstrated that patients with extensively impaired cartilage of the patella, as expressed by the OARSI score, have a higher risk of AKP. The lower limit of the confidence interval of the prevalence ratio of AKP was 1.0. We would like to emphasize that such a borderline significance does not exclude the probable effect of the impairment of the patellar cartilage on the development of postsurgical AKP, because the actual effect lies within the range of the confidence interval with unequal probability. The real value is more likely to be around the estimated prevalence ratio of 1.5 rather than at either end of the confidence interval (Hackshaw and Kirkwood 2011).

Unfortunately knowledge about the relationship between impairment of the microarchitecture of the patellar cartilage and postsurgical AKP does not help in decision making during surgery. The OARSI system is too complex and time consuming to be applied in everyday clinical practice (Pauli et al. 2012). Higher risk of AKP in patients with bigger OARSI scores and the absence of a significant correlation between Outerbridge (1961) grade 4 defects and AKP in our study show, that analysing the same data with different methodologies may lead to dissimilar outcomes. The key-point is the creation of a valid and reliable grading system of patellar cartilage impairment that would best correlate with patients' symptoms. Further research should focus on finding potential relationships between microscopic and macroscopic changes of the patella cartilage. Acebes et al. (2009) have already started the process by investigating the correlation between macroscopic alteration of the cartilage as classified by the Beguin-Locker (1983) and Mankin (1971) histopathology grading systems. The authors pointed out a tendency to over-evaluate cartilage impairment in the Beguin-Locker (1983) grades 3–4 owing to the difficulty in determining the border between cartilage and subchondral bone, the correlation between microscopic and macroscopic appearance of the cartilage was strong in case of lower grades of cartilage impairment (Acebes et al. 2009). Identifying the macroscopic expression of histologic changes should enable the elaboration of cartilage-related criteria for selective resurfacing of the patella during knee replacement that could result in a significant reduction of postsurgical AKP.

We believe our work has added a valuable piece of knowledge to support the theory of patellar cartilage impairment as one of the causes of AKP following TKA.

CONCLUSIONS

1) Patients undergoing total knee arthroplasty (TKA) with unresurfaced patella should be appraised of the high probability of experiencing pain in the front part of the knee after surgery. We diagnosed a 20.2% prevalence of AKP in a postal survey based solely on patient reported data and a 60% prevalence of AKP by using physician specific information.

   Neither a patients' gender, the mobility of the tibial insert nor Outerbridge (1961) grade 4 cartilage defects of the patella diagnosed at knee replacement predicted the incidence of postsurgical AKP following TKA without patellar resurfacing.
2) The Osteoarthritis Research Society International (OARSI) score of the patellar cartilage, which combines the microscopic severity and macroscopic extent of the lesion, correlated positively with postoperative AKP following TKA with unresurfaced patella. Patients with greater patellar cartilage impairment, as expressed by higher OARSI scores, had a higher risk of AKP.
3) We introduced a new radiographic measure for patellofemoral congruence to evaluate patellar alignment in the axial plane following TKA with unresurfaced patella – the patellar shift index (PSI). The necessary landmarks for the calculation of PSI were always present and easily discernible. PSI is independent of radiographic magnification or knee dimensions and is applicable to different media, like digital images and printed radiographs.
4) PSI was found to be a valid and reliable diagnostic tool of patellofemoral congruence. The radiographic landmarks of patellar displacement are frequently difficult to interpret and therefore it is not a suitable measure for patellar medio-lateral shift. Lateral patellar tilt is a reliable measure of patellofemoral congruence, but does not allow for the quantification of patellar displacement because the inclination of the patella does not correlate with maltracking.

SUMMARY IN ESTONIAN

Eesmine põlvevalu endoproteesitud põlveliigesega patsientidel: levimus, seos põlvekedra kõhre kahjustusega ja patellofemoraalse kongruentsuse aspektid

Sissejuhatus

Levimus

Eesmine põlvevalu (EPV) põhjustab rahulolematust rohkem kui poolel põlve endoproteesiga patsientidest (van Jonbergen *et al.* 2012). EPV on põlve eespinna valu sõltumata selle tekkepõhjusest (Witvrouw *et al.* 2005). Patellofemoraalne valusündroom (PFVS) on kitsam mõiste kui EPV. PFVS-iks loetakse põlvekedra ja trohlea vahelisest liigesest pärinevaid kaebusi, samas täpsustamata, millise konkreetse struktuuri kahjustus sümptomeid põhjustab (Witvrouw *et al.* 2005). PFVS tekib ennekõike koormusel ja ägeneb põlveketra koormavate tegevuste korral, näiteks trepist laskumisel. Kirjanduses kasutatakse EPV-d ja PFVS-i sageli sünonüümidena.

Vananeva rahvastiku (Leonardi *et al.* 2014) tõttu suureneb artroosi esmashaigestumus (Lawrence *et al.* 2008). Degenereerunud põlvekõhrega patsientide hulga suurenemine tingib omakorda põlveliigese endoproteesimise juhtude kasvu. See trend kajastub ka kõigis proteesiregistrites. Eesti Haigekassa rahastamispoliitikast tulenevalt on Eestis liigesevahetuse operatsioonide arv püsinud viimastel aastatel samal tasemel. Põlveliigese endoproteesimise sagenemisega kaasneb ka võimalike komplikatsioonide, sealhulgas EPV juhtude arvu suurenemine.

Patsiendiküsimustikel baseeruvates uuringutes on EPV levimusmäär väiksem (Burnett *et al.* 2007, Epinette, Manley 2008) kui nendes uuringutes, mis arvestavad nii subjektiivseid kui ka objektiivseid haigustunnuseid (Baldini *et al.* 2006, Campbell *et al.* 2006). Eestis on põlveliigeseid endoproteesitud ligi 20 aastat, kuid EPV levimust põlveproteesiga patsientidel seni uuritud pole.

Kõhrekahjustus

EPV etioloogia on mitmeteguriline. Igal konkreetsel juhul võib kaebuste vallandajaks olla erinevate tegurite unikaalne kombinatsioon. Seetõttu on EPV täpse põhjuse väljaselgitamine sageli keeruline (Bourne 2011, Meftah *et al.* 2011). Põlve eespinnale kiirguvat valu võib tekitada peripatellaarsete pehmete kudede düsbalanss, proteesiga seotud tegurid, põlvekedraspetsiifilised faktorid, sünoovia proliferatsioon, infrapatellaarse rasvpadjandi patoloogia või neuropaatia. 10% juhtudest võib EPV põhjus jääda selgusetuks.

Üks võimalik EPV põhjus on põlvekedra kõhrekahjustus (Picetti *et al.* 1990, Rodriguez-Merchan, Gomez-Cardero 2010). Patellofemoraalsed kõhredefektid on levinud, enamasti asuvad need põlvekedra mediaalsel fassetil (Iriuchishima

et al. 2013) ja suurel osal patsientidest need kaebusi ei põhjusta (Beard *et al.* 2007). Samas jääb nende patsientide puhul, kellel põlveliigese vahetamisel põlvekedra liigespinda pole asendatud, alati võimalus operatsioonijärgset EPV-d patella kõhrekahjustusega seostada (Seil, Pape 2011). Asendatud põlvekedra liigespinnaga patsiendid on põlveartroplastika tulemustega rohkem rahul (Schindler 2012) ja neil esineb vähem revisjonlõikusi (Pilling *et al.* 2012) kui säilitatud patella liigespinnaga patsientidel.

Põlvekedra kõhre seisundi ja EPV seostes on veel palju lahendamata küsimusi. Senistes uuringutes on saadud vastakaid tulemusi põlve endoproteesimisel täheldatavate patella kõhre silmaga nähtavate muutuste ja operatsioonijärgse EPV seose kohta (van Jonbergen *et al.* 2012). Makroskoopilisele kahjustusele eelnevad muutused rakkude tasandil ja ainult makroskoopiliste kõhremuutuste hindamine ei pruugi anda kõhre seisundist terviklikku pilti (Bentley 2007).

Kaks enim kasutust leidnud kõhrekahjustuse makroskoopilise hindamise klassifikatsiooni on Outerbridge'i (Outerbridge 1961) ja Beguin-Lockeri (Beguin, Locker 1983) klassifikatsioonid. Kõhredefektide visuaalset hindamist peetakse üldiselt usaldusväärseks (Han *et al.* 2006). Käesolevas väitekirjas kasutasime põlvekedra kõhre seisundi määramiseks OARSI (Osteoarthritis Research Society International) metoodikat (Pritzker *et al.* 2006), milles on ühendatud kõhrekahjustuse sügavuse mikroskoopiline analüüs ja muutuste leviku pindala hindamine. Põlvekedra kõhrekahjustuse ja eesmise põlvevalu seoste parem tundmine võimaldab põlveliigese endoproteesimisel argumenteeritult otsustada, kas põlvekedra liigespind säilitada või vahetada.

Patellofemoraalne kongruentsus

EPV-ga patsiendi kliiniline uurimine eeldab ka põlveliigese röntgeniülesvõtteid eest taha ja külgsuunas ning patellofemoraalset aksiaalset projektsiooni (Melloni *et al.* 2008, Davies *et al.* 2000). Röntgenipildi alusel pole võimalik kohe valu põhjust määrata: pigem annab see üldise ülevaate põlvest ja suuna edasiseks uuringuks (Grelsamer 2000). Patellofemoraalse kongruentsuse hindamise röntgenoloogilised meetodid on algselt välja töötatud kasutamiseks loomulike liigespindadega põlvel. Põlveliigese endoproteesimise käigus resetseeritavate liigespindade ja patella remodelleerumise tulemusel vajalikud röntgenoloogilised orientiirid kaovad. Samuti mõjutab seniste meetoditega saadud tulemusi röntgeniülesvõtete suurendus ja põlve mõõtmed. Seni puudub valiidne ja reliaabne röntgenmetoodika, mis võimaldaks hinnata endoproteesitud põlveliigese patellofemoraalset kongruentsust ning võrrelda eri uuringute tulemusi.

Käesolev väitekiri käsitleb põlveproteesimise järgset EPV levimust Eestis, EPV ja põlvekedra kõhrekahjustuse seost ning patellofemoraalse kongruentsuse aspekte.

Uurimuse eesmärgid

Uurimuse eesmärgiks oli hinnata operatsioonijärgset eesmise põlvevalu levimust Ida-Tallinna Keskhaigla patsientide seas, kellel oli paigaldatud põlveprotees, asendamata patella liigespinda. Samuti uurida põlveliigese endoproteesimise ajal diagnoositud põlvekedra kõhrekahjustuse seost operatsioonijärgse EPV-ga ja luua uus patellofemoraalse kongruentsuse hindamise röntgenmeetod.

Uurimuse täpsemad ülesanded olid:

1) hinnata EPV levimust patsientidel, kellel on teostatud põlveartroplastika patella liigespinna asendamiseta, nii subjektiivse, patsiendi täidetava küsimustiku abil kui ka objektiivse, arstidele mõeldud küsimustikuga;
2) hinnata seost operatsioonijärgse EPV ja patella kõhre seisundi vahel, mis on määratud OARSI skoori või Outerbridge'i klassifikatsiooni alusel põlvekedra liigespinna asendamiseta teostatud põlveartroplastika ajal;
3) töötada välja uus röntgenmeetod, põlvekedra nihkeindeks (PNI), millega on võimalik hinnata aksiaaltasapinnas patella asetsust trohlea suhtes;
4) hinnata PNI valiidsust ja reliaabsust ning võrrelda neid patella lateraalse kalde (PLK) ja patella nihkumise (PN) analoogsete näitajatega.

Uuritav materjal ja meetodid

Patsiendipõhisesse, subjektiivsesse EPV levimusuuringusse kaasati retrospektiivselt 1431 patsienti, kellel teostati ajavahemikus 01.01.2000–31.12.2009 Ida-Tallinna Keskhaiglas 1778 järjestikust põlveartroplastikat patella liigespinda asendamata. Patsientidelt koguti andmeid posti teel saadetud EPV küsimustikuga ja Kujala küsimustikuga. Küsimustikud saadeti1200 patsiendile, andmeid koguti 1505 põlve kohta. Mõlema põlve endoproteesiga patsiendid said kaks komplekti küsimustikke, kummagi põlve jaoks ühe. Patsiendid tagastasid 944 küsimustike komplekti, seega oli küsitluses osalemismäär 62,7%. 50 komplekti olid vigaselt täidetud ja seetõttu jäi lõplikuks andmeanalüüsiks informatsioon 894 põlve kohta.

Arstide kogutud objektiivsete andmete alusel uurisime EPV levimust prospektiivselt kaasatud 100 gonartroosi patsiendil, kellel teostati ajavahemikus 01.01.2011–31.05.2012 Ida-Tallinna Keskhaiglas 100 põlveartroplastikat patella liigespinda asendamata. Kõiki patsiente opereeris sama kirurg (Vahur Metsna). Ühe aasta möödudes põlveartroplastikast hindas kirurg EPV levimust patsientide seas HSS (Hospital for Special Surgery) patella küsimustikuga. Operatsioonijärgsed andmed koguti 95 patsiendilt.

Põlvekedra kõhre operatsiooniaegset seisundit hinnati samal 100 patsiendil, kes olid kaasatud ka EPV arstipõhisesse levimusuuringusse. Põlveliigese endoproteesimisel resetseeriti patella osteofüüdid, tehti digifoto patella kõhrest ja võeti patella silinderbiopsia kõhre piirkonnast, mis oli visuaalsel vaatlusel Outerbridge'i klassifikatsiooni järgi kõige rohkem kahjustunud. Digifoto alusel määrasime Outerbridge'i klassifikatsioonist lähtuvalt, kui suure osa protsentuaalselt moodustab säilinud kõhrega ala põlvekedra liigespinna kogupindalast. Patella bioptaadid värviti hematoksüliin-eosiiniga ja kõhrekahjustuse sügavust

hinnati preparaate mikroskopeerides. Kõhrekahjustuse sügavuse ja pindala astmete korrutisena arvutati OARSI skoori. Asümptoomsete ja EPV-ga patsintide OARSI skoori statistilist erinevust hinnati Studenti t-testiga. EPV seost Outerbridge 4 kõhredefektidega hindasime Spearmani korrelatsioonikoefitsiendiga. Jagasime patsiendid OARSI skoori alusel kahte rühma ja määrasime levimuskordaja.

PNI väljatöötamisel kasutasime 51 patellofemoraalset aksiaalset Merchant'i röntgenülesvõtet säilitatud patella liigespinnaga endoproteesitud põlveliigestest. PNI arvutamine on kujutatud joonisel 13. Jooned 1 ja 2 tõmmatakse paralleelselt trohlea mediaalse ja lateraalse servaga. Joon 3 puudutab reiekondüülide eesmisi tippe. Joonte 1,2 ja 3 lõikumisel tekkivad kaks punkti reie eesmiste kondüülide kõrgusel tähistavad trohlea laiust. Trohlea keskpunkt määratakse trohlea laiuse poolitamisel. Põlvekedra mediaalse ja lateraalse serva vahele tõmmatud joon 4 märgib patella laiust. Põlvekedra keskpunkt määratakse joone 4 poolitamisel. Joon 5 tõmmatakse trohlea keskpunktist ja joon 6 põlvekedra keskpunktist, mõlemad risti joonega 3. Joonte 5 ja 6 vaheline kaugus on põlvekedra nihe. Mõõdetakse trohlea laius ja põlvekedra nihe. PNI arvutatakse põlvekedra nihke jagamisel trohlea laiusega. (PNI = patella nihe ÷ trohlea laius). Indeks ümardatakse kahe komakohani. Põlvekedra nihe võib olla kas mediaalne või lateraalne, mediaalne nihe märgitakse märgiga "–".

PNI, LPK ja PNi hindamise ja hindaja reliaablust määrasid kahenädalase intervalliga röntgenipilte mõõtes üks ortopeed, üks radioloog ja kaks meditsiinitudengit. PNI näivvaliidsust hindasid neli uuringuga mitteseotud ortopeedi, reastades patellofemoraalsed aksiaalsed röntgenipildid visuaalsel vaatlusel põlvekedra nihke alusel. Seejärel analüüsiti kas vaatlustulemuste põhjal koostatud röntgenipiltide järjestus ühtib PNI-põhise järjestusega.

Uuringuks andis loa Tallinna Meditsiiniuuringute Eetikakomitee (nr 2230-20.12.2010, nr 2398-19.05.2011) ja Ida-Tallinna Keskhaigla uurimistööde hindamise komisjon. Kõik uuringus osalenud patsiendid allkirjastasid teavitatud nõusoleku vormi.

Uurimuse tulemused ja järeldused

Käesolev väitekiri on esimene põlveliigese endoproteesimise järgset EPV-d käsitlev uurimistöö Eestis. Selle käigus määrati põlvekedra liigespinna asendamiseta teostatud põlveliigese endoproteesimise järgse EPV levimuse, uurisime EPV seost patella kõhre kahjustusega ja töötasime välja uue röntgenmetoodika patellofemoraalse kongruentsuse hindamiseks.

1) Enne põlveliigese endoproteesimist on soovitav patsiente informeerida operatsioonijärgse EPV esinemise suurest tõenäosusest. Siinses uurimuses diagnoositi patsientide esitatud andmete alusel EPV 20,2% juhtudest, arstide täidetava küsimustiku kasutamisel oli EPV levimus 60%. Patsiendi sugu, põlveproteesi säärekomponendi mobiilsus ja Outerbridge'i 4. staadiumi kõhredefektid ei mõjuta põlvekedra liigespinna asendamiseta teostatud põlveproteesimise järgset EPV levimust.

2) Põlvekedra kõhre kahjustuse sügavuse mikroskoopilist ja leviku makroskoopilist hindamist ühendav OARSI skoor seostub põlvekedra liigespinna asendamiseta teostatud põlveproteesimise järgse EPV-ga. Suurema OARSI skooriga patsientidel on EPV risk suurem.
3) Töötasime välja patellofemoraalse aksiaaltasapinnalise kongruentsuse hindamise röntgenmeetodi – PNI, mille arvutamiseks on kõik orientiirid alati hästi eristatavad. PNI ei sõltu röntgenoloogilisest suurendusest ega põlveproteesi mõõtudest ning on kasutatav nii digitaalsete kui ka trükitud röntgenipiltide korral.
4) PNI on valiidne ja reliaabne meetod. PLK on samuti reliaabne, kuid selle alusel pole võimalik põlvekedra liikumist kvantitatiivselt iseloomustada. PNi on puuduvate orientiiride tõttu sageli raske määrata ja seetõttu ei sobi see meetod põlvekedra medio-lateraalsuunalise liikumise hindamiseks.

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REFERENCES

Abadie P, Galaud B, Michaut M, Fallet L, Boisrenoult P, Beaufils P. Distal femur rotational alignment and patellar subluxation: a CT scan in vivo assessment. Orthop Traumatol Surg Res. 2009;95(4):267–71.

Acebes C, Roman-Blas JA, Delgado-Baeza E, Palacios I, Herrero-Beaumont G. Correlation between arthroscopic and histopathological grading systems of articular cartilage lesions in knee osteoarthritis. Osteoarthritis Cartilage. 2009;17(2):205–12.

Ackmann T, Von During M, Teske W, Ackermann O, Muller P, Von Schulze Pellengahr C. Anatomy of the infrapatellar branch in relation to skin incisions and as the basis to treat neuropathic pain by cryodenervation. Pain Physician. 2014;17(3): E339–48.

Aggarwal AK, Agrawal A. Mobile vs fixed-bearing total knee arthroplasty performed by a single surgeon: a 4- to 6.5-year randomized, prospective, controlled, double-blinded study. J Arthroplasty. 2013;28(10):1712–6.

Agha RA, Webb B. A cadaveric investigation into the links between macroscopic and microscopic osteoarthritic changes at the hip. Clin Anat. 2006;19(2):115–24.

Aichroth P, Freeman MA, Smillie IS, Souter WA. A knee function assessment chart. J Bone Joint Surg Br. 1978;60(3):308–9.

Alford JW. Cartilage Restoration, Part 1: Basic Science, Historical Perspective, Patient Evaluation, and Treatment Options. American Journal of Sports Medicine. 2005; 33(2):295–306.

Andrikoula S, Tokis A, Vasiliadis HS, Georgoulis A. The extensor mechanism of the knee joint: an anatomical study. Knee Surg Sports Traumatol Arthrosc. 2006; 14(3):214–20.

Babazadeh S, Dowsey MM, Stoney JD, Choong PF. The effect of tibio-femoral over-distraction in primary knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2013;21(12):2810–6.

Baldini A, Anderson JA, Cerulli-Mariani P, Kalyvas J, Pavlov H, Sculco TP. Patello-femoral evaluation after total knee arthroplasty. Validation of a new weight-bearing axial radiographic view. J Bone Joint Surg Am. 2007;89(8):1810–7.

Baldini A, Anderson JA, Zampetti P, Pavlov H, Sculco TP. A new patellofemoral scoring system for total knee arthroplasty. Clin Orthop Relat Res. 2006;452:150–4.

Baliga S, McNair CJ, Barnett KJ, MacLeod J, Humphry RW, Finlayson D. Does circumpatellar electrocautery improve the outcome after total knee replacement?: a prospective, randomised, blinded controlled trial. J Bone Joint Surg Br. 2012; 94(9):1228–33.

Balke M, Dedy N, Mueller-Huebenthal J, Liem D, Hardes J, Hoeher J. Uncommon cause for anterior knee pain – Aggressive aneurysmal bone cyst of the patella. Sports Med Arthrosc Rehabil Ther Technol. 2010;2:9.

Ball ST, Sanchez HB, Mahoney OM, Schmalzried TP. Fixed versus rotating platform total knee arthroplasty: a prospective, randomized, single-blind study. J Arthroplasty. 2011;26(4):531–6.

Barink M, Meijerink H, Verdonschot N, van Kampen A, de Waal Malefijt M. Asymmetrical total knee arthroplasty does not improve patella tracking: a study without patella resurfacing. Knee Surg Sports Traumatol Arthrosc. 2007;15(2):184–91.

Barink M, Van de Groes S, Verdonschot N, De Waal Malefijt M. The difference in trochlear orientation between the natural knee and current prosthetic knee designs; towards a truly physiological prosthetic groove orientation. J Biomech. 2006; 39(9):1708–15.

Barrack RL, Bertot AJ, Wolfe MW, Waldman DA, Milicic M, Myers L. Patellar re-surfacing in total knee arthroplasty. A prospective, randomized, double-blind study with five to seven years of follow-up. J Bone Joint Surg Am. 2001;83-A(9):1376–81.

Barrack RL, Wolfe MW, Waldman DA, Milicic M, Bertot AJ, Myers L. Resurfacing of the patella in total knee arthroplasty. A prospective, randomized, double-blind study. J Bone Joint Surg Am. 1997;79(8):1121–31.

Barton RS, Ostrowski ML, Anderson TD, Ilahi OA, Heggeness MH. Intraosseous innervation of the human patella: a histologic study. Am J Sports Med. 2007; 35(2):307–11.

Beard DJ, Pandit H, Gill HS, Hollinghurst D, Dodd CA, Murray DW. The influence of the presence and severity of pre-existing patellofemoral degenerative changes on the outcome of the Oxford medial unicompartmental knee replacement. J Bone Joint Surg Br. 2007;89(12):1597–601.

Beard DJ, Pandit H, Ostlere S, Jenkins C, Dodd CA, Murray DW. Pre-operative clinical and radiological assessment of the patellofemoral joint in unicompartmental knee replacement and its influence on outcome. J Bone Joint Surg Br. 2007;89(12):1602–7.

Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine (Phila Pa 1976). 2000; 25(24):3186–91.

Beaupre L, Secretan C, Johnston DW, Lavoie G. A randomized controlled trial comparing patellar retention versus patellar resurfacing in primary total knee arthroplasty: 5–10 year follow-up. BMC Res Notes. 2012;5:273.

Beguin J, Locker B. Chondropathie rotoulienne. 2e me Journee d'Arthroscopie du Genou. 1983;1:88–90.

Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol. 1988;15(12):1833–40.

Belvedere C, Catani F, Ensini A, Moctezuma de la Barrera JL, Leardini A. Patellar tracking during total knee arthroplasty: an in vitro feasibility study. Knee Surg Sports Traumatol Arthrosc. 2007;15(8):985–93.

Bentley BS, Hill RV. Assessing macroscopic and microscopic indicators of osteo-arthritis in the distal interphalangeal joints: a cadaveric study. Clin Anat. 2007; 20(7):799–807.

Bieger R, Huch K, Kocak S, Jung S, Reichel H, Kappe T. The influence of joint line restoration on the results of revision total knee arthroplasty: comparison between distance and ratio-methods. Arch Orthop Trauma Surg. 2014;134(4):537–41.

Bohensky MA, Ackerman I, DeSteiger R, Gorelik A, Brand CA. Lifetime risk of total knee replacement and temporal trends in incidence by health care setting, socio-economic status, and geographic location. Arthritis Care Res (Hoboken). 2014; 66(3):424–31.

Bohnsack M, Hurschler C, Demirtas T, Ruhmann O, Stukenborg-Colsman C, Wirth CJ. Infrapatellar fat pad pressure and volume changes of the anterior compartment during knee motion: possible clinical consequences to the anterior knee pain syndrome. Knee Surg Sports Traumatol Arthrosc. 2005;13(2):135–41.

Bohnsack M, Klages P, Hurschler C, Halcour A, Wilharm A, Ostermeier S, et al. Influence of an infrapatellar fat pad edema on patellofemoral biomechanics and knee kinematics: a possible relation to the anterior knee pain syndrome. Arch Orthop Trauma Surg. 2009;129(8):1025–30.

Bohnsack M, Meier F, Walter GF, Hurschler C, Schmolke S, Wirth CJ, et al. Distribution of substance-P nerves inside the infrapatellar fat pad and the adjacent synovial tissue: a neurohistological approach to anterior knee pain syndrome. Arch Orthop Trauma Surg. 2005;125(9):592–7.

Bonutti PM, Zywiel MG, Rudert LA, Gough AK, McGrath MS, Mont MA. Femoral notch stenosis caused by soft tissue impingement in semi or open-box posterior-stabilized total knee arthroplasty. J Arthroplasty. 2010;25(7):1061-5.

Bourne RB. To resurface the patella or not? Better assessments needed to address the benefits for total knee replacement: commentary on an article by George Pavlou, BSc, MRCS, et al.: "Patellar resurfacing in total knee arthroplasty: does design matter? A meta-analysis of 7075 cases". J Bone Joint Surg Am. 2011;93(14):e82.

Bradley WG, Ominsky SH. Mountain view of the patella. AJR Am J Roentgenol. 1981;136(1):53–8.

Breugem SJ, Sierevelt IN, Schafroth MU, Blankevoort L, Schaap GR, van Dijk CN. Less anterior knee pain with a mobile-bearing prosthesis compared with a fixed-bearing prosthesis. Clin Orthop Relat Res. 2008;466(8):1959–65.

Breugem SJ, van Ooij B, Haverkamp D, Sierevelt IN, van Dijk CN. No difference in anterior knee pain between a fixed and a mobile posterior stabilized total knee arthroplasty after 7.9 years. Knee Surg Sports Traumatol Arthrosc. 2014;22(3):509–16.

Burnett RS, Boone JL, McCarthy KP, Rosenzweig S, Barrack RL. A prospective randomized clinical trial of patellar resurfacing and nonresurfacing in bilateral TKA. Clin Orthop Relat Res. 2007;464:65–72.

Burnett RS, Haydon CM, Rorabeck CH, Bourne RB. Patella resurfacing versus nonresurfacing in total knee arthroplasty: results of a randomized controlled clinical trial at a minimum of 10 years' followup. Clin Orthop Relat Res. 2004(428):12–25.

Calvisi V, Camillieri G, Lupparelli S. Resurfacing versus nonresurfacing the patella in total knee arthroplasty: a critical appraisal of the available evidence. Arch Orthop Trauma Surg. 2009;129(9):1261–70.

Campbell DG, Duncan WW, Ashworth M, Mintz A, Stirling J, Wakefield L, et al. Patellar resurfacing in total knee replacement: a ten-year randomised prospective trial. J Bone Joint Surg Br. 2006;88(6):734–9.

Cercek R, Jacofsky D, Kieffer K, Larsen B, Jacofsky M. Lateral patellofemoral impingement: a cause of treatable pain after TKA. J Knee Surg. 2011;24(3):181–4.

Chang CB, Han I, Kim SJ, Seong SC, Kim TK. Association between radiological findings and symptoms at the patellofemoral joint in advanced knee osteoarthritis. J Bone Joint Surg Br. 2007;89(10):1324–8.

Chang CB, Seong SC, Kim TK. Evaluations of radiographic joint space--do they adequately predict cartilage conditions in the patellofemoral joint of the patients undergoing total knee arthroplasty for advanced knee osteoarthritis? Osteoarthritis Cartilage. 2008;16(10):1160–6.

Chen K, Li G, Fu D, Yuan C, Zhang Q, Cai Z. Patellar resurfacing versus non-resurfacing in total knee arthroplasty: a meta-analysis of randomised controlled trials. Int Orthop. 2013;37(6):1075–83.

Cheng T, Zhu C, Guo Y, Shi S, Chen D, Zhang X. Patellar denervation with electrocautery in total knee arthroplasty without patellar resurfacing: a meta-analysis. Knee Surg Sports Traumatol Arthrosc. 2013.

Chia SL, Merican AM, Devadasan B, Strachan RK, Amis AA. Radiographic features predictive of patellar maltracking during total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2009;17(10):1217–24.

Chillemi C, Franceschini V, D'Erme M, Ippolito G, Farsetti P. Patellar osteoid osteoma as a cause of anterior knee pain in adolescents: a case report and literature review. Case Rep Med. 2013;2013:746472.
Correia J, Sieder M, Kendoff D, Citak M, Gehrke T, Klauser W, et al. Secondary Patellar Resurfacing after Primary Bicondylar Knee Arthroplasty did Not Meet Patients' Expectations. Open Orthop J. 2012;6:414–8.
Creamer P, Lethbridge-Cejku M, Hochberg MC. Where does it hurt? Pain localization in osteoarthritis of the knee. Osteoarthritis Cartilage. 1998;6(5):318–23.
Czurda T, Fennema P, Baumgartner M, Ritschl P. The association between component malalignment and post-operative pain following navigation-assisted total knee arthroplasty: results of a cohort/nested case-control study. Knee Surg Sports Traumatol Arthrosc. 2010;18(7):863–9.
D'Lima DD, Chen PC, Kester MA, Colwell CW, Jr. Impact of patellofemoral design on patellofemoral forces and polyethylene stresses. J Bone Joint Surg Am. 2003;85-A Suppl 4:85–93.
Dajani KA, Stuart MJ, Dahm DL, Levy BA. Arthroscopic treatment of patellar clunk and synovial hyperplasia after total knee arthroplasty. J Arthroplasty. 2010;25(1): 97–103.
Damarey B, Demondion X, Wavreille G, Pansini V, Balbi V, Cotten A. Imaging of the nerves of the knee region. Eur J Radiol. 2013;82(1):27–37.
Daniilidis K, Vogt B, Gosheger G, Henrichs M, Dieckmann R, Schulz D, et al. Patellar resurfacing as a second stage procedure for persistent anterior knee pain after primary total knee arthroplasty. Int Orthop. 2012;36(6):1181–3.
Dargel J, Michael JW, Feiser J, Ivo R, Koebke J. Human knee joint anatomy revisited: morphometry in the light of sex-specific total knee arthroplasty. J Arthroplasty. 2011;26(3):346–53.
Davies AP, Costa ML, Shepstone L, Glasgow MM, Donell S. The sulcus angle and malalignment of the extensor mechanism of the knee. J Bone Joint Surg Br. 2000;82(8):1162–6.
Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. J Bone Joint Surg Br. 1998;80(1):63–9.
De Vet HCW TC, Mokkink LB, Knol DL. Measurement in medicine. A practical guide. Cambridge: Cambridge University Press; 2011.
Deirmengian CA, Lonner JH. What's new in adult reconstructive knee surgery. J Bone Joint Surg Am. 2013;95(2):184–90.
Dennis DA, Kim RH, Johnson DR, Springer BD, Fehring TK, Sharma A. The John Insall Award: control-matched evaluation of painful patellar Crepitus after total knee arthroplasty. Clin Orthop Relat Res. 2011;469(1):10–7.
Dewan A, Bertolusso R, Karastinos A, Conditt M, Noble PC, Parsley BS. Implant durability and knee function after total knee arthroplasty in the morbidly obese patient. J Arthroplasty. 2009;24(6 Suppl):89–94, e1–3.
Dye SF, Campagna-Pinto D, Dye CC, Shifflett S, Eiman T. Soft-tissue anatomy anterior to the human patella. J Bone Joint Surg Am. 2003;85-A(6):1012–7.
Elson DW, Jones S, Caplan N, Stewart S, St Clair Gibson A, Kader DF. The photographic knee pain map: locating knee pain with an instrument developed for diagnostic, communication and research purposes. Knee. 2011;18(6):417–23.
Epinette JA, Manley MT. Outcomes of patellar resurfacing versus nonresurfacing in total knee arthroplasty: a 9-year experience based on a case series of scorpio PS knees. J Knee Surg. 2008;21(4):293–8.
Falez F. Knee arthroplasty today. Int Orthop. 2014;38(2):221–5.

Feller JA, Bartlett RJ, Lang DM. Patellar resurfacing versus retention in total knee arthroplasty. J Bone Joint Surg Br. 1996;78(2):226–8.
Fernandez-Lopez JC, Laffon A, Blanco FJ, Carmona L, Group ES. Prevalence, risk factors, and impact of knee pain suggesting osteoarthritis in Spain. Clin Exp Rheumatol. 2008;26(2):324–32.
Figgie HE, 3rd, Goldberg VM, Figgie MP, Inglis AE, Kelly M, Sobel M. The effect of alignment of the implant on fractures of the patella after condylar total knee arthroplasty. J Bone Joint Surg Am. 1989;71(7):1031–9.
Figgie HE, 3rd, Goldberg VM, Heiple KG, Moller HS, 3rd, Gordon NH. The influence of tibial-patellofemoral location on function of the knee in patients with the posterior stabilized condylar knee prosthesis. J Bone Joint Surg Am. 1986;68(7):1035–40.
Flandry F, Hunt JP, Terry GC, Hughston JC. Analysis of subjective knee complaints using visual analog scales. Am J Sports Med. 1991;19(2):112–8.
Foran JRH, Mont MA, Rajadhyaksha AD, Jones LC, Etienne G, Hungerford DS. Total knee arthroplasty in obese patients. The Journal of Arthroplasty. 2004;19(7):817–24.
Fu Y, Wang G, Fu Q. Patellar resurfacing in total knee arthroplasty for osteoarthritis: a meta-analysis. Knee Surg Sports Traumatol Arthrosc. 2011;19(9):1460–6.
Fukagawa S, Matsuda S, Mizu-uchi H, Miura H, Okazaki K, Iwamoto Y. Changes in patellar alignment after total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2011;19(1):99–104.
Fulkerson JP, Becker GJ, Meaney JA, Miranda M, Folcik MA. Anteromedial tibial tubercle transfer without bone graft. Am J Sports Med. 1990;18(5):490–6; discussion 6–7.
Gelfer Y, Pinkas L, Horne T, Halperin N, Alk D, Robinson D. Symptomatic transient patellar ischemia following total knee replacement as detected by scintigraphy. The Knee. 2003;10(4):341–5.
Ghosh KM, Merican AM, Iranpour F, Deehan DJ, Amis AA. The effect of overstuffing the patellofemoral joint on the extensor retinaculum of the knee. Knee Surg Sports Traumatol Arthrosc. 2009;17(10):1211–6.
Graves S. Australian Orthopaedic Association National Joint Replacement Registry. Annual Report. 2013.
Grelsamer RP. Patellar malalignment. J Bone Joint Surg Am. 2000;82-A(11):1639–50.
Grelsamer RP, Bazos AN, Proctor CS. Radiographic analysis of patellar tilt. J Bone Joint Surg Br. 1993;75(5):822–4.
Gupta S, Augustine A, Horey L, Meek RM, Hullin MG, Mohammed A. Electrocautery of the patellar rim in primary total knee replacement: beneficial or unnecessary? J Bone Joint Surg Br. 2010;92(9):1259–61.
Hackshaw A, Kirkwood A. Interpreting and reporting clinical trials with results of borderline significance. BMJ. 2011;343:d3340.
Han I, Chang CB, Choi JA, Kang YG, Seong SC, Kim TK. Is the degree of osteophyte formation associated with the symptoms and functions in the patellofemoral joint in patients undergoing total knee arthroplasty? Knee Surg Sports Traumatol Arthrosc. 2007;15(4):372–7.
Han I, Chang CB, Kang YG, Yoon SW, Seong SC, Kim TK. Intraobserver and interobserver reliability of the assessment of the patellar articular cartilage in osteo-arthritic patients undergoing total knee arthroplasty. J Arthroplasty. 2006;21(4):567–71.
Han I, Chang CB, Lee S, Lee MC, Seong SC, Kim TK. Correlation of the condition of the patellar articular cartilage and patellofemoral symptoms and function in osteo-arthritic patients undergoing total knee arthroplasty. J Bone Joint Surg Br. 2005;87(8):1081–4.

Hasegawa M, Kawamura G, Wakabayashi H, Sudo A, Uchida A. Changes to patellar blood flow after minimally invasive total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2009;17(10):1195–8.
Hatayama K, Terauchi M, Higuchi H, Yanagisawa S, Saito K, Takagishi K. Relationship between femoral component rotation and total knee flexion gap balance on modified axial radiographs. J Arthroplasty. 2011;26(4):649–53.
Hayes AF, Krippendorff K. Answering the call for a standard reliability measure for coding data. Communication Methods and Measures. 2007;1(1):77–89.
He JY, Jiang LS, Dai LY. Is patellar resurfacing superior than nonresurfacing in total knee arthroplasty? A meta-analysis of randomized trials. Knee. 2011;18(3):137–44.
Heekin RD, Fokin AA. Mini-midvastus versus mini-medial parapatellar approach for minimally invasive total knee arthroplasty: outcomes pendulum is at equilibrium. J Arthroplasty. 2014;29(2):339–42.
Heesterbeek PJ, Beumers MP, Jacobs WC, Havinga ME, Wymenga AB. A comparison of reproducibility of measurement techniques for patella position on axial radiographs after total knee arthroplasty. Knee. 2007;14(5):411–6.
Hefti F, Muller W, Jakob RP, Staubli HU. Evaluation of knee ligament injuries with the IKDC form. Knee Surg Sports Traumatol Arthrosc. 1993;1(3–4):226–34.
Heinert G, Kendoff D, Preiss S, Gehrke T, Sussmann P. Patellofemoral kinematics in mobile-bearing and fixed-bearing posterior stabilised total knee replacements: a cadaveric study. Knee Surg Sports Traumatol Arthrosc. 2011;19(6):967–72.
Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. Arthritis Rheum. 2008;58(1):15–25.
Hirasawa Y, Okajima S, Ohta M, Tokioka T. Nerve distribution to the human knee joint: anatomical and immunohistochemical study. Int Orthop. 2000;24(1):1–4.
Hirschmann M. Anterolateral approach with tibial tubercle osteotomy versus ... BMC Musculoskelet Disord. 2010.
Hofmann AA, Kurtin SM, Lyons S, Tanner AM, Bolognesi MP. Clinical and radiographic analysis of accurate restoration of the joint line in revision total knee arthroplasty. J Arthroplasty. 2006;21(8):1154–62.
Hofmann AA, Murdock LE, Wyatt RW, Alpert JP. Total knee arthroplasty. Two- to four-year experience using an asymmetric tibial tray and a deep trochlear-grooved femoral component. Clin Orthop Relat Res. 1991(269):78–88.
Hu X, Wang G, Pei F, Shen B, Yang J, Zhou Z, et al. A meta-analysis of the sub-vastus approach and medial parapatellar approach in total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2013;21(10):2398–404.
Hungerford DS, Kenna RV. Preliminary experience with a total knee prosthesis with porous coating used without cement. Clin Orthop Relat Res. 1983(176):95–107.
Hwang BH, Yang IH, Han CD. Comparison of patellar retention versus resurfacing in LCS mobile-bearing total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2012;20(3):524–31.
Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. Clin Orthop Relat Res. 1989(248):13–4.
Iranpour F, Merican AM, Dandachli W, Amis AA, Cobb JP. The geometry of the trochlear groove. Clin Orthop Relat Res. 2010;468(3):782–8.
Iriuchishima T, Ryu K, Aizawa S, Yorifuji H. Cadaveric assessment of osteoarthritic changes in the patello-femoral joint: evaluation of 203 knees. Knee Surg Sports Traumatol Arthrosc. 2013;21(9):2172–6.

Irrgang JJ, Snyder-Mackler L, Wainner RS, Fu FH, Harner CD. Development of a patient-reported measure of function of the knee. J Bone Joint Surg Am. 1998;80(8):1132–45.

Jazrawi LM, Birdzell L, Kummer FJ, Di Cesare PE. The accuracy of computed tomography for determining femoral and tibial total knee arthroplasty component rotation. J Arthroplasty. 2000;15(6):761–6.

Jawed A, Kumar V, Malhotra R, Yadav CS, Bhan S. A comparative analysis between fixed bearing total knee arthroplasty (PFC Sigma) and rotating platform total knee arthroplasty (PFC-RP) with minimum 3-year follow-up. Arch Orthop Trauma Surg. 2012;132(6):875–81.

Jawhar A, Sohoni S, Shah V, Scharf HP. Alteration of the patellar height following total knee arthroplasty. Arch Orthop Trauma Surg. 2014;134(1):91–7.

Jenkins D, Rodriguez J, Ranawat A, Alexiades M, Deshmukh A, Fukunaga T, et al. A randomized, controlled, prospective study evaluating the effect of patellar eversion on functional outcomes in primary total knee arthroplasty. J Bone Joint Surg Am. 2014;96(10):851–8.

Jiang L, Rong J, Zhang Q, Hu F, Zhang S, Li X, et al. Prevalence and associated factors of knee osteoarthritis in a community-based population in Heilongjiang, Northeast China. Rheumatol Int. 2012;32(5):1189–95.

Johnson AJ, Costa CR, Mont MA. Do we need gender-specific total joint arthroplasty? Clin Orthop Relat Res. 2011;469(7):1852–8.

Johnson TC, Tatman PJ, Mehle S, Gioe TJ. Revision surgery for patellofemoral problems: should we always resurface? Clin Orthop Relat Res. 2012;470(1):211–9.

Kachar SM, Williams KM, Finn HA. Neuroma of the infrapatellar branch of the saphenous nerve a cause of reversible knee stiffness after total knee arthroplasty. J Arthroplasty. 2008;23(6):927–30.

Kalichman L, Zhu Y, Zhang Y, Niu J, Gale D, Felson DT, et al. The association between patella alignment and knee pain and function: an MRI study in persons with symptomatic knee osteoarthritis. Osteoarthritis Cartilage. 2007;15(11):1235–40.

Katchburian MV, Bull AM, Shih YF, Heatley FW, Amis AA. Measurement of patellar tracking: assessment and analysis of the literature. Clin Orthop Relat Res. 2003(412):241–59.

Kawano T, Miura H, Nagamine R, Urabe K, Matsuda S, Mawatari T, et al. Factors affecting patellar tracking after total knee arthroplasty. The Journal of Arthroplasty. 2002;17(7):942–7.

Kessler O, Patil S, Colwell CW, Jr., D'Lima DD. The effect of femoral component malrotation on patellar biomechanics. J Biomech. 2008;41(16):3332–9.

Kestenbaum B. Epidemiology and biostatistics. An introduction to clinical research.: Springer; 2009.

Kim I, Kim HA, Seo YI, Song YW, Jeong JY, Kim DH. The prevalence of knee osteoarthritis in elderly community residents in Korea. J Korean Med Sci. 2010; 25(2):293–8.

Kohl S, Evangelopoulos DS, Hartel M, Kohlhof H, Roeder C, Eggli S. Anterior knee pain after total knee arthroplasty: does it correlate with patellar blood flow? Knee Surg Sports Traumatol Arthrosc. 2011;19(9):1453–9.

Kong CG, Park SW, Yang H, In Y. The effect of femoral component design on patellar tracking in total knee arthroplasty: Genesis II prosthesis versus Vanguard prosthesis. Arch Orthop Trauma Surg. 2014;134(4):571–6.

Kramers-de Quervain IA, Engel-Bicik I, Miehlke W, Drobny T, Munzinger U. Fat-pad impingement after total knee arthroplasty with the LCS A/P-Glide system. Knee Surg Sports Traumatol Arthrosc. 2005;13(3):174–8.

Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. Arthroscopy. 1993;9(2):159–63.
Kulkarni SK, Freeman MA, Poal-Manresa JC, Asencio JI, Rodriguez JJ. The patellofemoral joint in total knee arthroplasty: is the design of the trochlea the critical factor? J Arthroplasty. 2000;15(4):424–9.
Kumahashi N, Tadenuma T, Kuwata S, Fukuba E, Uchio Y. A longitudinal study of the quantitative evaluation of patella cartilage after total knee replacement by delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) and T2 mapping at 3.0 T: preliminary results. Osteoarthritis Cartilage. 2013;21(1):126–35.
Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am. 2007;89(4):780–5.
Lai Z, Shi S, Fei J, Wei W. Total knee arthroplasty performed with either a mini-subvastus or a standard approach: a prospective randomized controlled study with a minimum follow-up of 2 years. Arch Orthop Trauma Surg. 2014.
Lakstein D, Naser M, Adar E, Atoun E, Edelman A, Hendel D. Partial lateral patellar facetectomy as an alternative to lateral release in total knee arthroplasty (TKA). The Journal of Arthroplasty. 2014.
Laurin CA, Dussault R, Levesque HP. The tangential x-ray investigation of the patello-femoral joint: x-ray technique, diagnostic criteria and their interpretation. Clin Orthop Relat Res. 1979(144):16–26.
Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum. 2008;58(1):26–35.
Leichtle UG, Wunschel M, Leichtle CI, Muller O, Kohler P, Wulker N, et al. Increased patellofemoral pressure after TKA: an in vitro study. Knee Surg Sports Traumatol Arthrosc. 2014;22(3):500–8.
Leigh Brown AP, Kennedy ADM, Grant AM, Campbell J, Macnicol MF, Torgerson DJ. The development and validation of the Edinburgh Knee Function Scale: a simple tool for outcome measurement in non-surgical patients. The Knee. 1999;6:115–23.
Leonardi M, Chatterji S, Koskinen S, Ayuso-Mateos JL, Haro JM, Frisoni G, et al. Determinants of health and disability in ageing population: the COURAGE in Europe Project (collaborative research on ageing in Europe). Clin Psychol Psychother. 2014;21(3):193–8.
Leskinen J, Eskelinen A, Huhtala H, Paavolainen P, Remes V. The incidence of knee arthroplasty for primary osteoarthritis grows rapidly among baby boomers: a population-based study in Finland. Arthritis Rheum. 2012;64(2):423–8.
Li B, Bai L, Fu Y, Wang G, He M, Wang J. Comparison of clinical outcomes between patellar resurfacing and nonresurfacing in total knee arthroplasty: retrospective study of 130 cases. J Int Med Res. 2012;40(5):1794–803.
Li S, Chen Y, Su W, Zhao J, He S, Luo X. Systematic review of patellar resurfacing in total knee arthroplasty. Int Orthop. 2011;35(3):305–16.
Li T, Zhou L, Zhuang Q, Weng X, Bian Y. Patellar Denervation in Total Knee Arthroplasty Without Patellar Resurfacing and Postoperative Anterior Knee Pain: A Meta-Analysis of Randomized Controlled Trials. J Arthroplasty. 2014.
Lizaur-Utrilla A, Miralles-Munoz FA, Sanz-Reig J, Collados-Maestre I. Cementless total knee arthroplasty in obese patients: a prospective matched study with follow-up of 5–10 years. J Arthroplasty. 2014;29(6):1192–6.
Liu HW, Gu WD, Xu NW, Sun JY. Surgical Approaches in Total Knee Arthroplasty: A Meta-Analysis Comparing the Midvastus and Subvastus to the Medial Peripatellar Approach. J Arthroplasty. 2013.

Liu ZT, Fu PL, Wu HS, Zhu Y. Patellar reshaping versus resurfacing in total knee arthroplasty – Results of a randomized prospective trial at a minimum of 7 years' follow-up. Knee. 2012;19(3):198–202.

Luyckx T, Didden K, Vandenneucker H, Labey L, Innocenti B, Bellemans J. Is there a biomechanical explanation for anterior knee pain in patients with patella alta?: influence of patellar height on patellofemoral contact force, contact area and contact pressure. J Bone Joint Surg Br. 2009;91(3):344–50.

Lysholm J, Gillquist J. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. Am J Sports Med. 1982;10(3):150–4.

Ma HM, Lu YC, Kwok TG, Ho FY, Huang CY, Huang CH. The effect of the design of the femoral component on the conformity of the patellofemoral joint in total knee replacement. J Bone Joint Surg Br. 2007;89(3):408–12.

MacDonald SJ, Charron KD, Bourne RB, Naudie DD, McCalden RW, Rorabeck CH. The John Insall Award: gender-specific total knee replacement: prospectively collected clinical outcomes. Clin Orthop Relat Res. 2008;466(11):2612–6.

MacIntyre NJ, Hill NA, Fellows RA, Ellis RE, Wilson DR. Patellofemoral joint kinematics in individuals with and without patellofemoral pain syndrome. J Bone Joint Surg Am. 2006;88(12):2596–605.

Mackinnon J, Young S, Baily RA. The St Georg sledge for unicompartmental replacement of the knee. A prospective study of 115 cases. J Bone Joint Surg Br. 1988;70(2):217–23.

Mahoney OM, McClung CD, dela Rosa MA, Schmalzried TP. The effect of total knee arthroplasty design on extensor mechanism function. J Arthroplasty. 2002;17(4): 416–21.

Mancuso CA, Ranawat AS, Meftah M, Koob TW, Ranawat CS. Properties of the patient administered questionnaires: new scales measuring physical and psychological symptoms of hip and knee disorders. J Arthroplasty. 2012;27(4):575–82 e6.

Maralcan G, Kuru I, Issi S, Esmer AF, Tekdemir I, Evcik D. The innervation of patella: anatomical and clinical study. Surg Radiol Anat. 2005;27(4):331–5.

Mayman D, Bourne RB, Rorabeck CH, Vaz M, Kramer J. Resurfacing versus not resurfacing the patella in total knee arthroplasty. The Journal of Arthroplasty. 2003;18(5):541–5.

Meftah M, Jhurani A, Bhat JA, Ranawat AS, Ranawat CS. The effect of patellar replacement technique on patellofemoral complications and anterior knee pain. J Arthroplasty. 2012;27(6):1075–80 e1.

Meftah M, Ranawat AS, Ranawat CS. The natural history of anterior knee pain in 2 posterior-stabilized, modular total knee arthroplasty designs. J Arthroplasty. 2011; 26(8):1145–8.

Melloni P, Valls R, Veintemillas M. Imaging patellar complications after knee arthroplasty. Eur J Radiol. 2008;65(3):478–82.

Meneghini RM. Should the patella be resurfaced in primary total knee arthroplasty? An evidence-based analysis. J Arthroplasty. 2008;23(7 Suppl):11–4.

Meneghini RM, Pierson JL, Bagsby D, Berend ME, Ritter MA, Meding JB. The effect of retropatellar fat pad excision on patellar tendon contracture and functional outcomes after total knee arthroplasty. J Arthroplasty. 2007;22(6 Suppl 2):47–50.

Meneghini RM, Ritter MA, Pierson JL, Meding JB, Berend ME, Faris PM. The effect of the Insall-Salvati ratio on outcome after total knee arthroplasty. J Arthroplasty. 2006;21(6 Suppl 2):116–20.

Merchant AC, Arendt EA, Dye SF, Fredericson M, Grelsamer RP, Leadbetter WB, et al. The female knee: anatomic variations and the female-specific total knee design. Clin Orthop Relat Res. 2008;466(12):3059–65.

Merchant AC, Mercer RL, Jacobsen RH, Cool CR. Roentgenographic analysis of patellofemoral congruence. J Bone Joint Surg Am. 1974;56(7):1391–6.
Misra AN, Smith RB, Fiddian NJ. Five year results of selective patellar resurfacing in cruciate sparing total knee replacements. Knee. 2003;10(2):199–203.
Mockford BJ, Beverland DE. Secondary resurfacing of the patella in mobile-bearing total knee arthroplasty. J Arthroplasty. 2005;20(7):898–902.
Mohtadi N. Development and validation of the quality of life outcome measure (questionnaire) for chronic anterior cruciate ligament deficiency. Am J Sports Med. 1998;26(3):350–9.
Molyneux S, Brenkel I. Predictors and outcomes of lateral release in total knee arthroplasty: a cohort study of 1859 knees. Knee. 2012;19(5):688–91.
Mugnai R, Digennaro V, Ensini A, Leardini A, Catani F. Can TKA design affect the clinical outcome? Comparison between two guided-motion systems. Knee Surg Sports Traumatol Arthrosc. 2014;22(3):581–9.
Munoz-Mahamud E, Popescu D, Nunez E, Lozano LM, Nunez M, Sastre S, et al. Secondary patellar resurfacing in the treatment of patellofemoral pain after total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2011;19(9):1467–72.
Murphy L, Schwartz TA, Helmick CG, Renner JB, Tudor G, Koch G, et al. Lifetime risk of symptomatic knee osteoarthritis. Arthritis Rheum. 2008;59(9):1207–13.
Müller W, Wirz D. The patella in total knee replacement: does it matter? 750 LCS total knee replacements without resurfacing of the patella. Knee Surgery, Sports Traumatology, Arthroscopy. 2001;9(S1):S24-S6.
Namazi N, Jaberi FM, Pakbaz S, Vosoughi AR, Jaberi MM. Does patellar rim electro-cautery have deleterious effects on patellar cartilage? Knee. 2014;21(2):524–8.
Narkbunnam R, Chareancholvanich K, Hanroongroj T. Sagittal plane evaluation of patellofemoral movement in patellofemoral pain patients with no evidence of maltracking. Knee Surg Sports Traumatol Arthrosc. 2013.
Naslund J, Walden M, Lindberg LG. Decreased pulsatile blood flow in the patella in patellofemoral pain syndrome. Am J Sports Med. 2007;35(10):1668–73.
Nestor BJ, Toulson CE, Backus SI, Lyman SL, Foote KL, Windsor RE. Mini-midvastus vs standard medial parapatellar approach: a prospective, randomized, double-blinded study in patients undergoing bilateral total knee arthroplasty. J Arthroplasty. 2010;25(6 Suppl):5–11, e1.
Nikolaus OB, Larson DR, Hanssen AD, Trousdale RT, Sierra RJ. Lateral patellar facet impingement after primary total knee arthroplasty: it does exist. J Arthroplasty. 2014;29(5):970–6.
Nikolopoulos DD, Polyzois I, Apostolopoulos AP, Rossas C, Moutsios-Rentzos A, Michos IV. Total knee arthroplasty in severe valgus knee deformity: comparison of a standard medial parapatellar approach combined with tibial tubercle osteotomy. Knee Surg Sports Traumatol Arthrosc. 2011;19(11):1834–42.
Niu J, Zhang YQ, Torner J, Nevitt M, Lewis CE, Aliabadi P, et al. Is obesity a risk factor for progressive radiographic knee osteoarthritis? Arthritis Rheum. 2009;61(3): 329–35.
O'Brien S, Spence DJ, Ogonda LO, Beverland DE. LCS mobile bearing total knee arthroplasty without patellar resurfacing. Does the unresurfaced patella affect outcome? Survivorship at a minimum 10-year follow-up. Knee. 2012;19(4):335–8.
O'Donnell P, Johnstone C, Watson M, McNally E, Ostlere S. Evaluation of patellar tracking in symptomatic and asymptomatic individuals by magnetic resonance imaging. Skeletal Radiol. 2005;34(3):130–5.
Odgaard A. Danish Knee Arthroplasty Register. Annual Report. 2010.

Oh KJ, Pandher DS, Lee SH, Sung Joon SD, Jr., Lee ST. Meta-analysis comparing outcomes of fixed-bearing and mobile-bearing prostheses in total knee arthroplasty. J Arthroplasty. 2009;24(6):873–84.

Ozkoc G, Hersekli MA, Akpinar S, Ozalay M, Uysal M, Cesur N, et al. Time dependent changes in patellar tracking with medial parapatellar and midvastus approaches. Knee Surg Sports Traumatol Arthrosc. 2005;13(8):654–7.

Outerbridge RE. The etiology of chondromalacia patellae. J Bone Joint Surg Br. 1961;43-B:752–7.

Outerbridge RE. Further Studies on the Etiology of Chondromalacia Patellae. J Bone Joint Surg Br. 1964;46:179–90.

Pagenstert G, Seelhoff J, Henninger HB, Wirtz DC, Valderrabano V, Barg A. Lateral patellar facetectomy and medial reefing in patients with lateral facet syndrome after patellar-retaining total knee arthroplasty. The Journal of Arthroplasty. 2014.

Panni AS, Cerciello S, Maffulli N, Di Cesare M, Servien E, Neyret P. Patellar shape can be a predisposing factor in patellar instability. Knee Surg Sports Traumatol Arthrosc. 2011;19(4):663–70.

Parvizi J, Mortazavi SM, Devulapalli C, Hozack WJ, Sharkey PF, Rothman RH. Secondary resurfacing of the patella after primary total knee arthroplasty does the anterior knee pain resolve? J Arthroplasty. 2012;27(1):21–6.

Parvizi J, Nunley RM, Berend KR, Lombardi AV, Jr., Ruh EL, Clohisy JC, et al. High level of residual symptoms in young patients after total knee arthroplasty. Clin Orthop Relat Res. 2014;472(1):133–7.

Patel K, Raut V. Patella in total knee arthroplasty: to resurface or not to--a cohort study of staged bilateral total knee arthroplasty. Int Orthop. 2011;35(3):349–53.

Pauli C, Whiteside R, Heras FL, Nesic D, Koziol J, Grogan SP, et al. Comparison of cartilage histopathology assessment systems on human knee joints at all stages of osteoarthritis development. Osteoarthritis Cartilage. 2012;20(6):476–85.

Pavlou G, Meyer C, Leonidou A, As-Sultany M, West R, Tsiridis E. Patellar resurfacing in total knee arthroplasty: does design matter? A meta-analysis of 7075 cases. J Bone Joint Surg Am. 2011;93(14):1301–9.

Pearson RG, Kurien T, Shu KS, Scammell BE. Histopathology grading systems for characterisation of human knee osteoarthritis--reproducibility, variability, reliability, correlation, and validity. Osteoarthritis Cartilage. 2011;19(3):324–31.

Peralta-Molero JV, Gladnick BP, Lee YY, Ferrer AV, Lyman S, Gonzalez Della Valle A. Patellofemoral crepitation and clunk following modern, fixed-bearing total knee arthroplasty. J Arthroplasty. 2014;29(3):535–40.

Peretz JI, Driftmier KR, Cerynik DL, Kumar NS, Johanson NA. Does lateral release change patellofemoral forces and pressures?: a pilot study. Clin Orthop Relat Res. 2012;470(3):903–9.

Petersen W, Ellermann A, Gosele-Koppenburg A, Best R, Rembitzki IV, Bruggemann GP, et al. Patellofemoral pain syndrome. Knee Surg Sports Traumatol Arthrosc. 2013.

Petersen W, Rembitzki IV, Bruggemann GP, Ellermann A, Best R, Koppenburg AG, et al. Anterior knee pain after total knee arthroplasty: a narrative review. Int Orthop. 2014;38(2):319–28.

Picetti GD, 3rd, McGann WA, Welch RB. The patellofemoral joint after total knee arthroplasty without patellar resurfacing. J Bone Joint Surg Am. 1990;72(9):1379–82.

Pierson JL, Ritter MA, Keating EM, Faris PM, Meding JB, Berend ME, et al. The effect of stuffing the patellofemoral compartment on the outcome of total knee arthroplasty. J Bone Joint Surg Am. 2007;89(10):2195–203.

Pilling RW, Moulder E, Allgar V, Messner J, Sun Z, Mohsen A. Patellar resurfacing in primary total knee replacement: a meta-analysis. J Bone Joint Surg Am. 2012; 94(24):2270–8.
Pinsornsak P, Naratrikun K, Chumchuen S. The effect of infrapatellar fat pad excision on complications after minimally invasive TKA: a randomized controlled trial. Clin Orthop Relat Res. 2014;472(2):695–701.
Pollock DC, Ammeen DJ, Engh GA. Synovial entrapment: a complication of posterior stabilized total knee arthroplasty. J Bone Joint Surg Am. 2002;84-A(12):2174–8.
Pongcharoen B, Yakampor T, Charoencholvanish K. Patellar tracking and anterior knee pain are similar after medial parapatellar and midvastus approaches in minimally invasive TKA. Clin Orthop Relat Res. 2013;471(5):1654–60.
Powers-Freeling L. National Joint Registry for England, Wales and Northern Ireland. 10-th Annual Report. 2013.
Powers CM, Ward SR, Fredericson M, Guillet M, Shellock FG. Patellofemoral kinematics during weight-bearing and non-weight-bearing knee extension in persons with lateral subluxation of the patella: a preliminary study. J Orthop Sports Phys Ther. 2003;33(11):677–85.
Pritzker KP, Gay S, Jimenez SA, Ostergaard K, Pelletier JP, Revell PA, et al. Osteoarthritis cartilage histopathology: grading and staging. Osteoarthritis Cartilage. 2006;14(1):13–29.
Pulavarti RS, Raut VV, McLauchlan GJ. Patella denervation in primary total knee arthroplasty – a randomized controlled trial with 2 years of follow-up. J Arthroplasty. 2014;29(5):977–81.
Quintana JM, Arostegui I, Escobar A, Azkarate J, Goenaga JI, Lafuente I. Prevalence of knee and hip osteoarthritis and the appropriateness of joint replacement in an older population. Arch Intern Med. 2008;168(14):1576–84.
Ranawat CS, Shine JJ. Duo-condylar total knee arthroplasty. Clin Orthop Relat Res. 1973(94):185–95.
Rejeski WJ, Ettinger WH, Jr., Shumaker S, Heuser MD, James P, Monu J, et al. The evaluation of pain in patients with knee osteoarthritis: the knee pain scale. J Rheumatol. 1995;22(6):1124–9.
Robertsson O. The Swedish Knee Arthroplasty Register. Annual Report. 2013.
Rodriguez-Merchan EC, Gomez-Cardero P. The outerbridge classification predicts the need for patellar resurfacing in TKA. Clin Orthop Relat Res. 2010;468(5):1254–7.
Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. J Orthop Sports Phys Ther. 1998;28(2):88–96.
Rossi R, Rosso F, Cottino U, Dettoni F, Bonasia DE, Bruzzone M. Total knee arthroplasty in the valgus knee. Int Orthop. 2014;38(2):273–83.
Salve H, Gupta V, Palanivel C, Yadav K, Singh B. Prevalence of knee osteoarthritis amongst perimenopausal women in an urban resettlement colony in South Delhi. Indian J Public Health. 2010;54(3):155–7.
Sanchis-Alfonso V. Holistic approach to understanding anterior knee pain. Clinical implications. Knee Surg Sports Traumatol Arthrosc. 2014.
Satish BR, Ganesan JC, Chandran P, Basanagoudar PL, Balachandar D. Efficacy and mid term results of lateral parapatellar approach without tibial tubercle osteotomy for primary total knee arthroplasty in fixed valgus knees. J Arthroplasty. 2013; 28(10):1751–6.
Scapinelli R. Blood supply of the human patella. Its relation to ischaemic necrosis after fracture. J Bone Joint Surg Br. 1967;49(3):563–70.

Schindler OS. The controversy of patellar resurfacing in total knee arthroplasty: Ibisne in medio tutissimus? Knee Surg Sports Traumatol Arthrosc. 2012;20(7):1227–44.
Scott WN. Insall & Scott Surgery of the Knee. Fifth Edition ed. Scott WN, editor: Elsevier; 2012.
Seil R, Pape D. Causes of failure and etiology of painful primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2011;19(9):1418–32.
Sekiya H, Takatoku K, Takada H, Sugimoto N, Hoshino Y. Lateral approach is advantageous in total knee arthroplasty for valgus deformed knee. Eur J Orthop Surg Traumatol. 2014;24(1):111–5.
Sensi L, Buzzi R, Giron F, De Luca L, Aglietti P. Patellofemoral function after total knee arthroplasty: gender-related differences. J Arthroplasty. 2011;26(8):1475–80.
Shih HN, Shih LY, Wong YC, Hsu RW. Long-term changes of the nonresurfaced patella after total knee arthroplasty. J Bone Joint Surg Am. 2004;86-A(5):935–9.
Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol Bull. 1979;86(2):420–8.
Singh JA, Gabriel SE, Lewallen DG. Higher body mass index is not associated with worse pain outcomes after primary or revision total knee arthroplasty. J Arthroplasty. 2011;26(3):366–74 e1.
Singh VK, Shah G, Singh PK, Saran D. Extraskeletal ossifying chondroma in Hoffa's fat pad: an unusual cause of anterior knee pain. Singapore Med J. 2009;50(5):e189–92.
Skwara A, Tibesku CO, Ostermeier S, Stukenborg-Colsman C, Fuchs-Winkelmann S. Differences in patellofemoral contact stresses between mobile-bearing and fixed-bearing total knee arthroplasties: a dynamic in vitro measurement. Arch Orthop Trauma Surg. 2009;129(7):901–7.
Smith AJ, Wood DJ, Li MG. Total knee replacement with and without patellar resurfacing: a prospective, randomised trial using the profix total knee system. J Bone Joint Surg Br. 2008;90(1):43–9.
Smith H, Jan M, Mahomed NN, Davey JR, Gandhi R. Meta-analysis and systematic review of clinical outcomes comparing mobile bearing and fixed bearing total knee arthroplasty. J Arthroplasty. 2011;26(8):1205–13.
Smith PN, Parker DA, Gelinas J, Rorabeck CH, Bourne RB. Radiographic changes in the patella following quadriceps turndown for revision total knee arthroplasty. The Journal of Arthroplasty. 2004;19(6):714–9.
Smith SR, Stuart P, Pinder IM. Nonresurfaced patella in total knee arthroplasty. J Arthroplasty. 1989;4 Suppl:S81–6.
Smith TO, Davies L, Toms AP, Hing CB, Donell ST. The reliability and validity of radiological assessment for patellar instability. A systematic review and meta-analysis. Skeletal Radiol. 2011;40(4):399–414.
Smith TO, McNamara I, Donell ST. The contemporary management of anterior knee pain and
patellofemoral instability. The Knee. 2013;20:S3-S15.
Snir N, Schwarzkopf R, Diskin B, Takemoto R, Hamula M, Meere PA. Incidence of Patellar Clunk Syndrome in Fixed Versus High-Flex Mobile Bearing Posterior-Stabilized Total Knee Arthroplasty. J Arthroplasty. 2014.
Sophia Fox AJ, Bedi A, Rodeo SA. The basic science of articular cartilage: structure, composition, and function. Sports Health. 2009;1(6):461–8.
Staubli HU, Durrenmatt U, Porcellini B, Rauschning W. Anatomy and surface geometry of the patellofemoral joint in the axial plane. J Bone Joint Surg Br. 1999;81(3):452–8.

Steinbruck A, Schroder C, Woiczinski M, Fottner A, Muller PE, Jansson V. Patello-femoral contact patterns before and after total knee arthroplasty: an in vitro measurement. Biomed Eng Online. 2013;12:58.
Steinbruck A, Schroder C, Woiczinski M, Fottner A, Muller PE, Jansson V. The effect of trochlea tilting on patellofemoral contact patterns after total knee arthroplasty: an in vitro study. Arch Orthop Trauma Surg. 2014;134(6):867–72.
Stiehl JB. A clinical overview patellofemoral joint and application to total knee arthroplasty. J Biomech. 2005;38(2):209–14.
Stiehl JB, Komistek RD, Dennis DA, Keblish PA. Kinematics of the patellofemoral joint in total knee arthroplasty. J Arthroplasty. 2001;16(6):706–14.
Strachan RK, Merican AM, Devadasan B, Maheshwari R, Amis AA. A technique of staged lateral release to correct patellar tracking in total knee arthroplasty. J Arthroplasty. 2009;24(5):735–42.
Sudo A, Miyamoto N, Horikawa K, Urawa M, Yamakawa T, Yamada T, et al. Prevalence and risk factors for knee osteoarthritis in elderly Japanese men and women. J Orthop Sci. 2008;13(5):413–8.
Sun YQ, Yang B, Tong SL, Sun J, Zhu YC. Patelloplasty versus traditional total knee arthroplasty for osteoarthritis. Orthopedics. 2012;35(3):e343–8.
Suri S, Gill SE, Massena de Camin S, Wilson D, McWilliams DF, Walsh DA. Neurovascular invasion at the osteochondral junction and in osteophytes in osteoarthritis. Ann Rheum Dis. 2007;66(11):1423–8.
Swan JD, Stoney JD, Lim K, Dowsey MM, Choong PF. The need for patellar resurfacing in total knee arthroplasty: a literature review. ANZ J Surg. 2010; 80(4):223–33.
Zha GC, Sun JY, Dong SJ. Less anterior knee pain with a routine lateral release in total knee arthroplasty without patellar resurfacing: a prospective, randomized study. Knee Surg Sports Traumatol Arthrosc. 2014;22(3):517–25.
Zhang LZ, Zhang XL, Jiang Y, Wang Q, Chen YS, Shen H. Lateral patellar facetectomy had improved clinical results in patients with patellar-retaining total knee arthroplasty. J Arthroplasty. 2012;27(8):1442–7.
Zhang Z, Zhu W, Gu B, Zhu L, Chen C. Mini-midvastus versus mini-medial parapatellar approach in total knee arthroplasty: a prospective, randomized study. Arch Orthop Trauma Surg. 2013;133(3):389–95.
Zupan A, Snoj Z, Antolic V, Pompe B. Better results with patelloplasty compared to traditional total knee arthroplasty. Int Orthop. 2014.
Tennant S, Williams A, Vedi V, Kinmont C, Gedroyc W, Hunt D. Patello-femoral tracking in the weight-bearing knee: a study of asymptomatic volunteers utilising dynamic magnetic resonance imaging: a preliminary report. Knee Surgery, Sports Traumatology, Arthroscopy. 2001;9(3):155–62.
Thomas MJ, Wood L, Selfe J, Peat G. Anterior knee pain in younger adults as a precursor to subsequent patellofemoral osteoarthritis: a systematic review. BMC Musculoskelet Disord. 2010;11:201.
Urch SE, Tritle BA, Shelbourne KD, Gray T. Axial linear patellar displacement: a new measurement of patellofemoral congruence. Am J Sports Med. 2009;37(5):970–3.
Waimann CA, Fernandez-Mazarambroz RJ, Cantor SB, Lopez-Olivo MA, Zhang H, Landon GC, et al. Cost-effectiveness of total knee replacement: a prospective cohort study. Arthritis Care Res (Hoboken). 2014;66(4):592–9.
van Beeck A, Clockaerts S, Somville J, Van Heeswijk JH, Van Glabbeek F, Bos PK, et al. Does infrapatellar fat pad resection in total knee arthroplasty impair clinical outcome? A systematic review. Knee. 2013;20(4):226–31.

van de Groes SA, Koeter S, de Waal Malefijt M, Verdonschot N. Effect of medial-lateral malpositioning of the femoral component in total knee arthroplasty on anterior knee pain at greater than 8years of follow-up. Knee. 2014.
van Jonbergen HP, Barnaart AF, Verheyen CC. A dutch survey on circumpatellar electrocautery in total knee arthroplasty. Open Orthop J. 2010;4:201–3.
van Jonbergen HP, Reuver JM, Mutsaerts EL, Poolman RW. Determinants of anterior knee pain following total knee replacement: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2012;22(3):478–99.
van Jonbergen HP, Reuver JM, Mutsaerts EL, Poolman RW. Determinants of anterior knee pain following total knee replacement: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2014;22(3):478–99.
van Jonbergen HP, Scholtes VA, Poolman RW. A randomised, controlled trial of circumpatellar electrocautery in total knee replacement without patellar resurfacing: a concise follow-up at a mean of 3.7 years. Bone Joint J. 2014;96-B(4):473–8.
van Jonbergen HP, Scholtes VA, van Kampen A, Poolman RW. A randomised, controlled trial of circumpatellar electrocautery in total knee replacement without patellar resurfacing. J Bone Joint Surg Br. 2011;93(8):1054–9.
Vanbiervliet J, Bellemans J, Verlinden C, Luyckx JP, Labey L, Innocenti B, et al. The influence of malrotation and femoral component material on patellofemoral wear during gait. J Bone Joint Surg Br. 2011;93(10):1348–54.
Wasielewski RC, Komistek RD, Zingde SM, Sheridan KC, Mahfouz MR. Lack of axial rotation in mobile-bearing knee designs. Clin Orthop Relat Res. 2008;466(11): 2662–8.
Weinstein AM, Rome BN, Reichmann WM, Collins JE, Burbine SA, Thornhill TS, et al. Estimating the burden of total knee replacement in the United States. J Bone Joint Surg Am. 2013;95(5):385–92.
Wiberg G. Roentgenographic and anatomic studies on the femoropatellar joint: with special reference to chondromalacia patellae. Acta Orthop. 1941;12:319–410.
Wiig O. The Norwegian Arthroplasty Register. Annual Report. 2010.
Wilson T. The measurement of patellar alignment in patellofemoral pain syndrome: are we confusing assumptions with evidence? J Orthop Sports Phys Ther. 2007;37(6): 330–41.
Witonski D, Wagrowska-Danielewicz M. Distribution of substance-P nerve fibers in the knee joint in patients with anterior knee pain syndrome. A preliminary report. Knee Surg Sports Traumatol Arthrosc. 1999;7(3):177–83.
Witvrouw E, Werner S, Mikkelsen C, Van Tiggelen D, Vanden Berghe L, Cerulli G. Clinical classification of patellofemoral pain syndrome: guidelines for non-operative treatment. Knee Surg Sports Traumatol Arthrosc. 2005;13(2):122–30.
Wood DJ, Smith AJ, Collopy D, White B, Brankov B, Bulsara MK. Patellar resurfacing in total knee arthroplasty: a prospective, randomized trial. J Bone Joint Surg Am. 2002;84-A(2):187–93.
Xie X, Lin L, Zhu B, Lu Y, Lin Z, Li Q. Will gender-specific total knee arthroplasty be a better choice for women? A systematic review and meta-analysis. Eur J Orthop Surg Traumatol. 2013.

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1989–1995	University of Tartu, Faculty of Medicine
1978–1989	Tallinn Inglish College

Professional employment:

2006–…	East-Tallinn Central Hospital; orthopedic surgeon
1999–2001	Tallinn Pelgulinna Hospital, Linnamõisa Family Medicine Center; general practitioner
1996–2001	MS Prim Ltd.; member of board
1989–1994	Tartu Maarjamõisa Hospital; nurse's assistant, nurse
1986–1989	Seppo Clinic; nurse's assistant

Membership in scientific organizations:
Estonian Medical Association
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Estonian Arthroplasty Society

Publications:

1. Metsna V, Vorobjov S, Märtson A. Prevalence of anterior knee pain among patients following total knee arthroplasty with nonreplaced patella: a retrospective study of 1778 knees. Medicina (Kaunas). 2014;50(2):82–6.
2. Metsna V, Vorobjov S, Lepik K, Märtson A. Anterior knee pain following total knee replacement correlates with the OARSI score of the cartilage of the patella. Acta Orthop. 2014;85(4):427–32.
3. Metsna V, Sarap P, Vorobjov S, Tootsi K, Märtson A. The patellar shift index: a reliable and valid measure for patellofemoral congruence following total knee arthroplasty with unresurfaced patella. Acta Orthop Traumatol Turc. 2013;47(5):323–9.
4. Metsna V. Eespõia deformatsioonide diagnostika ja kompleksne kirurgiline ravi. Eesti Arst. 2006;Lisa 9.

5. Metsna V, Linnamägi R, Kööp A, Parv M. Ida-Tallinna Keskhaiglasse aastatel 2001–2002 reieluukaela murruga hospitaliseeritud patsientide ravi retrospektiivne analüüs. Eesti Arst. 2003;Lisa 6.

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Haridus:

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2001–2006	Tartu Ülikool, arstiteaduskond, ortopeedia residentuur; ortopeed
1999–2001	Tartu Ülikool, arstiteaduskond, perearstide spetsialiseerumiskursus; perearst
1996–1997	Internatuur Tallinna Keskhaiglas
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1978–1989	Tallinna Inglise Kolledz

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1999–2001	Tallinna Pelgulinna Haigla, Linnamõisa Pereartsikeskus; üld-arst
1996–2001	MS Prim OÜ; juhatuse liige
1989–1994	Tartu Maarjamõisa Haigla traumapunkt; sanitar, õde
1986–1989	Seppo Kliinik; operatsioonitoa sanitar

Osalemine erialaseltsides:
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Eesti Traumatoloogide-Ortopeedide Selts
Eesti Artroplastika Selts

Publikatsioonid:

1. Metsna V, Vorobjov S, Märtson A. Prevalence of anterior knee pain among patients following total knee arthroplasty with nonreplaced patella: a retrospective study of 1778 knees. Medicina (Kaunas). 2014;50(2):82–6.
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