Soft Tissue Laxity Following Total Knee Arthroplasty

Kappel, Andreas

Publication date:
2020

Document Version
Publisher's PDF, also known as Version of record

Link to publication from Aalborg University

Citation for published version (APA):
Kappel, A. (2020). *Soft Tissue Laxity Following Total Knee Arthroplasty*. Aalborg Universitetsforlag. Aalborg Universitet. Det Sundhedsvidenskabelige Fakultet. Ph.D.-Serien

SOFT TISSUE LAXITY FOLLOWING TOTAL KNEE ARTHROPLASTY

BY
ANDREAS KAPPEL

DISSERTATION SUBMITTED 2020

AALBORG UNIVERSITY
DENMARK

SOFT TISSUE LAXITY FOLLOWING TOTAL KNEE ARTHROPLASTY

PhD dissertation by

Andreas Kappel

Department of Clinical Medicine

AALBORG UNIVERSITY
DENMARK

AALBORG UNIVERSITY HOSPITAL
Interdisciplinary Orthopaedics

Submitted November 2020

Dissertation submitted: November 2020

PhD supervisor: Associate Prof., Consultant Orthopaedic Surgeon, PhD
Mogens Laursen
Aalborg University Hospital, Denmark

Assistant PhD supervisors: Chief Surgeon, Consultant Orthopaedic Surgeon
Poul Torben Nielsen
Aalborg University Hospital, Denmark

Prof., Consultant Orthopaedic Surgeon, FRCS, DMSc
Anders Odgaard
Rigshospitalet, Copenhagen University, Denmark

PhD committee: Clinical Associate Professor Peter Heide Pedersen
Aalborg University (chair)

Professor Martin Lind
Aarhus University

Professor Ola Rolfson
University of Gothenburg

PhD Series: Faculty of Medicine, Aalborg University

Department: Department of Clinical Medicine

ISSN (online): 2246-1302
ISBN (online): 978-87-7210-850-6

Published by:
Aalborg University Press
Kroghstræde 3
DK – 9220 Aalborg Ø
Phone: +45 99407140
aauf@forlag.aau.dk
forlag.aau.dk

Printed in Denmark by Rosendahls, 2021

“If you do something right the first time then it’s not hard enough”

Danny MacAskill, Scottish mountain bike trials legend

Table of contents

Preface and acknowledgements

As a specialized knee surgeon, different aspects of soft-tissue laxity have been increasingly puzzling me. Amongst other, my ambition to deliver impeccable surgery, have been challenged by the lack of evidence regarding optimal limits for soft tissue balancing. While my focus was clinical during surgical training and the initial time as a specialist, my interest and engagement in clinical research has evolved. These two factors where the prerequisite for this project.

The scientific work that this thesis is based upon were performed alongside my clinical work at the Department of Orthopaedic Surgery, Aalborg and Farsø Clinics, Aalborg University Hospital, during the period from 2016 to 2020. Funding and support for the studies and for clinical workload reduction was received from Region Nordjyllands forskningsfond, Augustinus fonden, Interdisciplinary Orthopaedics and the Department of Orthopaedic Surgery, Aalborg University Hospital.

My project supervisors are thanked for their support and supervision during this project. Mogens Laursen, not only my primary supervisor but also supervisor at my first sliding hip-screw operation in 1999, a good friend and former mountain-bike co-enthusiast, I owe you gratitude for your help and generosity. Poul Torben Nielsen, always being innovative and persistently pushing me towards further scientific engagement. I really appreciate your supervision, your positive mind and our cooperation both scientifically and clinically. Anders Odgaard, I had the luck to receive surgical supervision by you and Frank Madsen at Amtssygehuset “a few” years ago, back then I was not ready to engage in a project like this, fortunately you agreed to supervise when I was ready, especially thanks for your insightful feedback on my work.

Gratitude is given to project nurses Gitte Broholm Hansen, Merete Hessellund and Heidi Ladefoged Poulsen, without your incredible engagement and your handling of logistics, this project could not have been completed in the present form. Radiographers, Pia Arnskov Holm, Pia Johansen, Helle Holm Andersen and technicians from Farsoe are acknowledged for their support in establishment of the stress-radiographic set-up and thorough performance of the radiographic examinations. Fellow surgeons at clinic Farsoe, Poul Hedevang Christensen, Jesper Fuglsang Villefrance and Ole Simonsen are acknowledged for their support and for inclusion and treatment of participants in the cohort study.

Anders El-Galaly, Jacob Fyhring Mortensen and Niels Kragh Madsen are acknowledged for excellent collaboration and their contribution as co-authors on the studies.

Christian Pedersen, head of the Orthopaedic Department at Aalborg University Hospital and fellow knee surgeon, deserves special gratitude, allowing me time for research by in long periods solving the main part of our mutual clinical tasks, this despite having an already crowded schedule.

Participants in the clinical studies are especially thanked for their time and helpfulness. Indeed, all that have been supportive to this project are thanked.

My dedication to the surgical treatment of degenerative knee conditions, was nourished during surgical training at Viborg Central Sygehus, Århus Amtssygehus og Aalborg Sygehus, and I am forever grateful to the skilled surgeons who gave me their time and shared their expertise. All dedicated professionals at present and past facilities are also acknowledged, your commitment does not only contribute to excellent results, it also turns everyday routines into job satisfaction and fun.

Finally, but not least, I thank my dear family and friends for their interest and support during this project; my friends for coffee talks, walks and socializing around training/cycling, my family for long-time bearing with me and reminding me of other joys of life, and especially my wife for her love and support, always offering interesting discussions and feed-back on any projects, health-economics and life in general.

Andreas Kappel
Aalborg, November 2020

List of papers

Study	Paper
I	**Relationship between outcome scores and knee laxity following total knee arthroplasty: a systematic review.** Kappel A, Laursen M, Nielsen PT, Odgaard A. Acta Orthop. 2019 Feb;90(1):46-52
II	**Reliability of stress radiography in the assessment of coronal laxity following total knee arthroplasty.** Kappel A, Mortensen JF, Nielsen PT, Odgaard A, Laursen M. Knee. 2020 Jan;27(1):221-228
III	**Any effect of coronal laxity on outcome one year following total knee arthroplasty? A single center prospective observational cohort study with 124 participants.** Kappel A, El-Galaly A, Nielsen PT, Madsen NK, Odgaard A, Laursen M. (Submitted)

List of abbreviations and definitions

Term	Definition
Alignment	Angulation between two adjacent bones
Arthrometer	Device for sagittal laxity measurements
Arthroplasty	Artificial construction to permanently replace the whole or parts of a joint surface.
Constraint	The level of restriction/stability provided by the arthroplasty.
Coronal	Coronal plane is the plane that divided the body into back and front.
Implant	Artificial material inserted in the body. Not necessarily an arthroplasty.
Revision	Any subsequent exchange, removal, addition or modification of an arthroplasty.
Sagittal	Sagittal plane is the plane that divides the body into left and right
Stress-radiograph	Radiograph done while applying stress to a joint. Used to evaluate joint laxity.
Valgus	Coronal plane bone or joint deformity with the distal part deviating outward from the midline of the body.
Varus	Contrary to valgus.

Abbreviation

BMI	**B**ody **M**ass **I**ndex
CI	**C**onfidence **I**nterval
EV	**E**picondylar **V**iew
ICC	**I**ntraclass **C**orrelation **C**oefficient
KA	**K**nee **A**rthroplasty
TKA	**T**otal **K**nee **A**rthroplasty
CR-TKA	Posterior **C**ruciate **R**etaining
PS-TKA	**P**osterior cruciate **S**acrificing
PKA	**P**artial **K**nee **A**rthroplasty
MCID	**M**inimal **C**linically **I**mportant **D**ifference
mKL	**m**odified **K**ellgren-**L**awrence grade
OA	**O**steo**A**rthritis
KOA	**K**nee **O**steo**A**rthritis
PBT	**P**erformance **B**ased physical **T**est
PRO	**P**atient **R**eported **O**utcome
SD	**S**tandard **D**eviation
TSD	**T**elos **S**tress **D**evice

Summary

Total knee arthroplasty (TKA) is a common and proven effective procedure to relive pain and disability caused by knee joint degeneration. Following TKA, both outcome and risk of revision can be related to the balance/stability of the soft tissues surrounding the knee. However, intraoperative soft tissue balancing during TKA surgery is dependent on the surgeon's experience and preferences, and furthermore the limits of laxity that can be related to optimal function and pain relief are poorly defined.

In study I the evidence of optimal limits of knee laxity following TKA was sought after by doing a systematic review on the relation between outcome and laxity following TKA. All studies were cohort studies on supposed well-functioning TKA. The reviewed studies displayed heterogeneity regarding surgical technique, choice of outcome score and methods for laxity measurement. Methodologically concern was raised for all the studies. Qualitative meta-analysis was excluded, no evidence of any relation between laxity and outcome in the range from full extension to 60 degrees of flexion was found. In further flexion, sagittal laxity from 5 to 10 mm and medial laxity below 4 degrees could with caution be related to superior outcomes.

Reliable methods to quantify laxity following TKA are prerequisite when studying the impact of laxity. Manual assessment of laxity has been shown unreliable, and instrumented methods are used to quantify laxity. However, the stress radiographic methods used in some of the reviewed studies (study I) was not yet validated. In study II reliability and agreement for stress radiographic measurements of TKA laxity in flexion and extension was examined. In extension excellent reliability and acceptable limit of agreement was shown. In flexion, medial laxity could be measured with good to excellent reliability but lateral laxity only with moderate to good reliability. Confidence intervals in flexion and especially for the lateral laxity measurements were wide.

Results from an observational cohort study are reported in study III. Data from 124 participants with complete follow up were analyzed. Laxity was quantified with stress radiography and outcome measured with both patient reported outcomes and physical performance-based test. No differences in outcomes between TKA's tight or lax at follow up could be found. Gender, age, BMI and degree of osteoarthritis differed between groups with tight and lax knees. Mean values of medial laxity were lower than previously reported by authors using other surgical techniques. We concluded that the surgical technique used in our study (measured resection, cruciate retaining TKA), was shown effective in obtaining low levels of medial laxity, and that both demographic details and degree of osteoarthritis should be taken in consideration when planning and interpreting studies on laxity in TKA surgery.

Dansk Resume

Smerter og nedsat fysisk funktionsevne forårsaget af knæslidgigt kan ofte lindres ved operation med indsættelse af et kunstigt knæled/knæalloplastik (KA). Talrige undersøgelser har dokumenteret, at denne behandling er en effektiv metode til at lindre patientens gener, samt at den er omkostningseffektiv for samfundet. Holdbarheden af en KA er god med 10 års implantatoverlevelse over 90%. Antallet af KA operationer som udføres årligt, er stigende både i verden og i Danmark. Ifølge Dansk knæalloplastik register (DKR) blev der i 2019 udført over 11000 førstegangsoperationer med KA i Danmark. Efter en KA operation oplever de fleste patienter betydelig lindring og forbedret funktion, men det er et væsentligt problem, at cirka 20% ikke opnår tilfredshed med resultatet af operationen.

Forskellige forhold kan gøre at et knæ med KA skal opereres igen (revision). Ifølge DKR var instabilitet den hyppigste angivne årsag til revision i 2019, hvor instabilitet var anført som årsag ved 21% af revisionerne. Instabilitet er en tilstand, hvor der er smerter eller kompromitteret mekanisk funktion af en KA, som kan tilskrives manglende stabilitet af strukturer som ledbånd, sener og led kapsel omkring knæet.

Stabilitet af strukturerne omkring knæet efter KA har altså betydning for både tilfredshed og risiko for revision. I forbindelse med KA operationen kan kirurgen i et vist omfang justere stabiliteten. Denne balancering kræver både detaljeret anatomisk viden og kirurgisk erfaring. Imidlertid er den stabilitet, som giver optimal smertelindring og funktion efter en KA, ikke klart defineret, og både kirurgens justeringer og opfattelse af optimal stabilitet er underlagt en grad af subjektivitet.

Det første studie i afhandlingen er en systematisk gennemgang af tidligere publicerede studier, hvor sammenhængen mellem stabilitet og resultater efter total KA (TKA) er beskrevet. De tidligere studier viste sig at have store indbyrdes forskelle, hvad angår valg af metode til at måle stabilitet og valg af metode til at opgøre operationsresultatet på. Det var ikke muligt at foretage en samlet statistisk analyse af resultaterne fra de tidligere studier. Ud fra den systematiske gennemgang konkluderede vi, at der ikke fandtes evidens for en sammenhæng imellem stabilitet og resultat, når stabiliteten blev målt ved knæbøjninger imellem strakt ben og 60 grader bøjet knæ. Ved større grader af knæbøjning var der evidens for at konkludere at en skuffeløshed mellem 5 og 10mm samt en indvendig løshed mindre end 4 grader var relateres til de bedste resultater.

En af forudsætningerne for at undersøge sammenhængen mellem løshed og resultat efter KA er at man har pålidelige målemetoder. Undersøgelse af stabilitet ved manuel undersøgelse har vist sig at være mindre pålidelig. Studie II undersøger pålidelighed (reliability) og overensstemmelse (agreement) for stress-røntgen undersøgelser efter TKA. Ved at gentage samme undersøgelse (test-retest) og lade forskellige observatører måle på røntgenbillederne kunne dette beskrives. For stress-røntgen undersøgelse med benet strakt var pålidelighed fremragende og overensstemmelse

blev vurderet tilfredsstillende. Stress-røntgen undersøgelse af knæets indre (mediale) strukturer på bøjet ben viste god til fremragende pålidelighed, men undersøgelsen af de ydre (laterale) strukturer var med moderat til god pålidelighed. Det kunne altså vises, at stress-røntgen er en pålidelig metode til at måle stabilitet efter KA, dog skal der være opmærksomhed på den nedsatte præcision ved måling af lateral stabilitet på bøjet knæ.

Afhandlingens tredje studie er et kohortestudie, hvor en gruppe patienter opereret med TKA på Farsø sygehus blev undersøgt med et udvidet undersøgelsesprogram før og efter operationen. Stabilitet blev kvantificeret ved brug af stress-røntgen og operationsresultatet målt med både patient rapporterede oplysninger og ved fysiske funktions tests. Undersøgelsen kunne ikke påvise forskelle i resultat mellem patienterne med de mest stabile og de mindst stabile knæ. Resultaterne for stabilitet med den benyttede operationsmetode var med mindre middelværdier for løshed i forhold til tidligere undersøgelser hvor der blev benyttet en anden operationsmetode. Forhold som køn, alder, BMI og grad af slidgigt var forskellige imellem grupperne med de mest og de mindst stabile knæ. Undersøgelsen resultater bekræftede, at der med den valgte operationsteknik, i forhold til tidligere undersøgelser, kan opnås reduceret medial løshed, uden at det påvirker resultaterne negativt. Både demografi og grad af slidgigt varierende mellem grupperne, denne sammenhæng mellem præoperative faktorer og stabilitet må man være opmærksom på ved planlægning og tolkning af studier af omhandlende stabilitet efter TKA.

1. Introduction and background

Knee osteoarthritis (KOA) is a frequent cause of pain and disability in the older adults, the prevalence is rising, this being assisted by the change in age composition in the population and an increased incidence of obesity[1]. Total knee arthroplasty (TKA) is a frequent and cost-effective treatment option in end stage KOA[2]. Longevity of the TKA without additional revision procedures is high, in Denmark 93% of implants are revision free at 10 years and 87% at 20 years[3]. Most patients experience reduced knee pain and improved physical capability following TKA, it is however consistently reported that approximately 20% are dissatisfied following TKA surgery[4,5].

1.1 Knee osteoarthritis

KOA is a disease affecting the whole knee joint; i.e. hyaline cartilage, subchondral bone, joint capsule, synovium and adjacent ligaments, muscles and soft tissue. The disease is thought to arise from an imbalance between the repair mechanisms and destruction of joint tissues. Risk factors for KOA include age, female sex, obesity, previous knee injury and knee malalignment. Different risk factors might act trough different mediators promoting KOA. KOA might affect one or more of the three knee compartments. The global prevalence of KOA is rising and KOA is estimated to account for approximately 85% of the worldwide osteoarthritis burden [1].

Clinical diagnostic criteria have been set up, combining age above 50 years, the symptoms of knee pain, early morning joint stiffness, functional limitation and clinical findings of crepitus, restricted range of movement, bone enlargement, bone margin tenderness and no palpable warm to the touch. The initial diagnosis is clinical and only in atypical cases or prior to surgical evaluation radiologically examinations are needed [1,6].

Soft-tissue laxity and alignment in the osteoarthritic knee
Varus-valgus laxity in individuals with tibiofemoral KOA is systematically reviewed by Freisinger et al.[7] and increased laxity in KOA compared to non-KOA controls was reported in a majority of the 40 reviewed studies, no studies reported greater laxity in controls. Females with KOA appeared to have more laxity than males. Tanamas et al. did a systematic review on the role of knee malalignment in the development and progression of KOA, and malalignment was found to be an independent risk factor for KOA, furthermore it was stated that “loss of cartilage and bone height, may lead to further malalignment”[8]. This is consistent with the biomechanical load distribution in the knee being altered by changes in alignment and the clinical observation that malalignment increases with progressive mono compartmental tibiofemoral KOA. Bellemans et al. investigated alignment correctability in varus knees and when deformity exceeded 10 degrees of varus, they found progressive shortening of the medial collateral ligament and progressive lengthening of the lateral collateral ligament [9].

1.2 Treatment of knee osteoarthritis

Guidelines for the treatment of KOA are in broad agreement across different organizations [10]. In Denmark a national clinical guideline on the treatment of KOA was published by the Danish Health Authority in 2012 [6]. Although most cases can be treated non-surgically the incidence of knee arthroplasty has been rising through the last decades and this is expected to continue. In the year 2019, approximately 11000 primary procedures were performed in Denmark [2,3], representing a 30% increase from 2017.

Non-surgical treatment

Patient education, with the aim of improving knowledge on pathophysiology, imaging and the effect of different treatment options, might improve self-care and quality of life. Physical exercise therapy, with both strengthening and aerobic exercise, has been proven to have effect on both pain and joint motion, and although the effect is limited it is considered a key element especially in early KOA. Weight loss intervention is effective in KOA patients who are overweight or obese. The combined effect of exercise and weight loss is better than one of the interventions alone. Challenges occur with adherence to both interventions [1,6].

Pharmaceutical treatment can be used to supplement the above. Although of little proven effect, paracetamol is the first line medication, but the effect as a single agent is questioned. NSAID is more effective than paracetamol and can be used topically without the serious adverse advents observed with oral NSAIDs. However, oral NSAIDs is more effective, but the risk of adverse events limits the use to only short time use and individual smallest dose possible. Opiates are no longer recommended in the treatment of KOA, because of their limited effect on pain weighted against risk of side effects, risk of addiction and risk of over dosage [1].

Intraarticular corticosteroids are effective in the treatment of severe pain and inflammation that do not respond to oral pharmaceutical treatment. However, the effect is short-term and repeated injections might induce accelerated loss of cartilage volume. Intraarticular hyaluronans, glucosamine and chondroitin cannot be recommended [1,6].

Intraarticular injections with stem cells are given great attention, and promising short term results on both pain and function have been reported, however further evidence and long term results are demanded prior to introducing this promising treatment option in the general treatment of KOA[11,12].

Wedged insoles and braces have been used to alter load transferring through the malaligned knee, however in a recent review from the Cochrane Library the evidence for long term effect from these treatment options was deemed moderate and inconclusive [13].

Surgical treatment

The decision on surgical treatment is multifactorial and mainly based on; 1) patient complaints and expectations, 2) findings on physical examination, 3) radiological or visualized joint degeneration, and 4) risk assessment. The patient should be engaged in a shared decision-making conversation based on the balance of risk versus potential benefit and must be counselled towards realistic postoperative expectations. However the threshold for surgical intervention is not clearly defined and might be influenced by both patient and surgeon preferences as well as health-care system factors and local economics [2].

Arthroscopy

Although historically a frequent procedure with a large placebo effect, the evidence clearly indicate that the use of knee arthroscopy in the treatment of KOA should be abandoned [1,6].

Knee joint distraction

Knee joint distraction has shown short-term result comparable to high tibial osteotomy (HTO) and TKA. However, frequent adverse advents, limited number of studies and absence of randomized trials with long-term follow-up, still reserves this treatment option for controlled trials [14,15].

Osteotomies around the knee

Mechanical alignment affects the functional load distribution through the knee. The purpose of an osteotomy in the treatment of KOA, is the shift of load distribution from a diseased knee compartment to a healthier compartment. Most frequently the varus aligned knee with medial compartment KOA is treated with a valgus producing HTO [6]. While it is evident that HTO reduces pain and improves function [16], the effect compared to non-surgical treatment has only been shown in a propensity matched study [17]. The success of HTO has been linked to young age, male sex, absence of high BMI and less severe KOA [18].

Partial knee arthroplasty

Medial, lateral and patello-femoral partial knee arthroplasty (PKA) are recognized treatment options for mono compartmental KOA. Medial PKA is by way the most frequent, and in year 2019 it accounted for approximately 20% of the primary knee arthroplasties in Denmark while lateral and patella-femoral was used in only 0.6% and 1%[3]. Corresponding percentages for the use of PKA in Sweden, year 2019, are approximately half the size of the Danish percentages, witch illustrates the controversy regarding the use of PKA[19]. When compared to TKA, PKA is associated to lower incidence of short time complications [20] and slightly improved outcomes [2,21,22]. However reduced implant survival is shown in both clinical studies [23] and national joint registries [3,19]. Furthermore, revision of PKA to TKA is associated with implant survival comparable to TKA revision, which is 3-fold higher than for primary TKA [24]. Randomized controlled trials are ongoing to clarify the optimal treatment option for mono compartmental medial KOA [25].

Total knee arthroplasty

The most frequent surgical treatment of end-stage KOA is TKA, where all tibial and femoral cartilage bearing surfaces are replaced with implants. The effectiveness of this procedure in relieving pain and improving patient reported outcomes (PRO) is very well documented and the longevity is superior to other surgical treatments, with 10 and 20 year implant survival of approximately 95% and 85% [2,3]. The historical indication of intolerable pain and functional limitation has been broadened, however there is no consensus on the optimal timing to switch from non-operative treatment to TKA. Inferior outcomes have been linked to lower degrees of radiological KOA, high functional expectations, preoperative opioid consumption, depression, pain catastrophizing and obesity [2,26–28].

Adverse events following surgery

Multiple adverse events and modes of failure are recognized [19]. Immediate postoperative bleeding and minor peripheral neurological deficit might delay mobilization, but most often resolve during hospitalization. Prolonged oozing and wound healing problems are rare, but the strong association to subsequent periprosthetic joint infection is recognized. Symptomatic thromboembolic events occur with a frequency of approximately 1% [29]. Most frequent adverse events requiring revision surgery are loosening of the fixation between implant and bone without the presence of infection (aseptic loosening), periprosthetic infection (infection), lack of stability in the soft tissues surrounding the knee (instability) and persistent pain (pain) [2,3]. For all revision surgeries in Denmark the frequency of these 4 main reasons were: aseptic loosening 23%, infection 18%, instability 16% and pain 13%[3].

1.3 Results following total knee arthroplasty

Treatment with TKA should be with minimal risk of complications and high certainty of both pain relief, improved knee function and longevity for the individual. For the society the treatment should be cost effective. As stated above most of these prerequisites have been documented. Still, the unsolved problem is the persistently and consistently reported 20% of dissatisfied patients not responding to the TKA treatment.

Timing of TKA with respect to individual patient age, patient characteristics, degree of KOA, degree of pain and functional limitations is not well defined [2], and research to identify characteristics of non-responders is comprehensive. Intense preoperative knee pain, pain in other joints, low preoperative knee specific and generic scores, mental health problems alongside with less radiological degenerative changes and clinical findings of less restrictions in knee movement, have all been associated to dissatisfaction[4,30]. Decision aids have been developed to support decision making on the threshold for surgical intervention[26,31].

Technical factors, intraoperatively controllable for the surgeon, are crucial for postoperative TKA kinematics. It must be assumed that not all procedures result in optimal TKA kinematics, and while gross malalignment or severe soft tissue laxity obviously result in malfunction and dissatisfaction, the possible connection between dissatisfaction and knee kinematics in the individual patient can be obscure even for the most experienced knee surgeon.

1.4. Surgical techniques and considerations in total knee arthroplasty

It is universally accepted that the success of TKA is dependent on the surgeon’s ability and skills to control implant positioning, rotation, alignment and soft tissue balancing. However, the historical goals of neutral mechanical alignment and symmetrical medio-lateral balance in both extension and flexion have been challenged.

1.4.1 Alignment in total knee arthroplasty

Coronal plane mechanical knee alignment is defined by the angulation between the mechanical axis of the femur (a line connecting the center of the hip and the center of the knee), and tibia (a line connecting the center of the knee with the center of the ankle). The angulation can be read on the medial side of the knee and 180 degrees is considered neutral mechanical alignment, values above indicate valgus and values below indicate varus (figure 1.4.1.1). Coronal plane anatomical knee alignment is defined by the angulation between the axis of the adjacent femur and tibia. Anatomical and mechanical tibia axis are mostly identical however a difference between anatomical and mechanical femoral axis of 6 to 7 degrees is found in most individuals (figure 1.4.1.2). Joint line orientation is defined by the joint surfaces. In the native knee coronal joint line orientation is typically not perpendicular to the mechanical axis but considered normal with 3 degrees of varus, corresponding to 87 degrees tibial medial angulation. In bipedal stance the native joint line is oblique with respect to both tibia and underlying surface, however in monopodial stance this obliquity with respect to the surface is minimized due to the hip adduction necessary to balance the body weight. When walking or running the native joint line is mostly parallel to the surface. In the sagittal plane a posterior slope of 9 degrees is considered normal. Radiographs should be weight-bearing to allow measurement of functional alignment, and limb rotation should be controlled to obtain true coronal or sagittal plane projections. Anatomical alignment can be measured from short knee radiographs. For measurements of mechanical alignment, the whole extremity (hip to ankle) must be visualized. This can be done weight bearing with long standing radiographs or EOS scan and it can be done non-weight bearing with a CT-scout scan. In the non-osteoarthritic knee wide limits of alignment exist[32].

Figure 1.4.1.1: Examples of neutral-, varus- and valgus-alignment in the native knee.

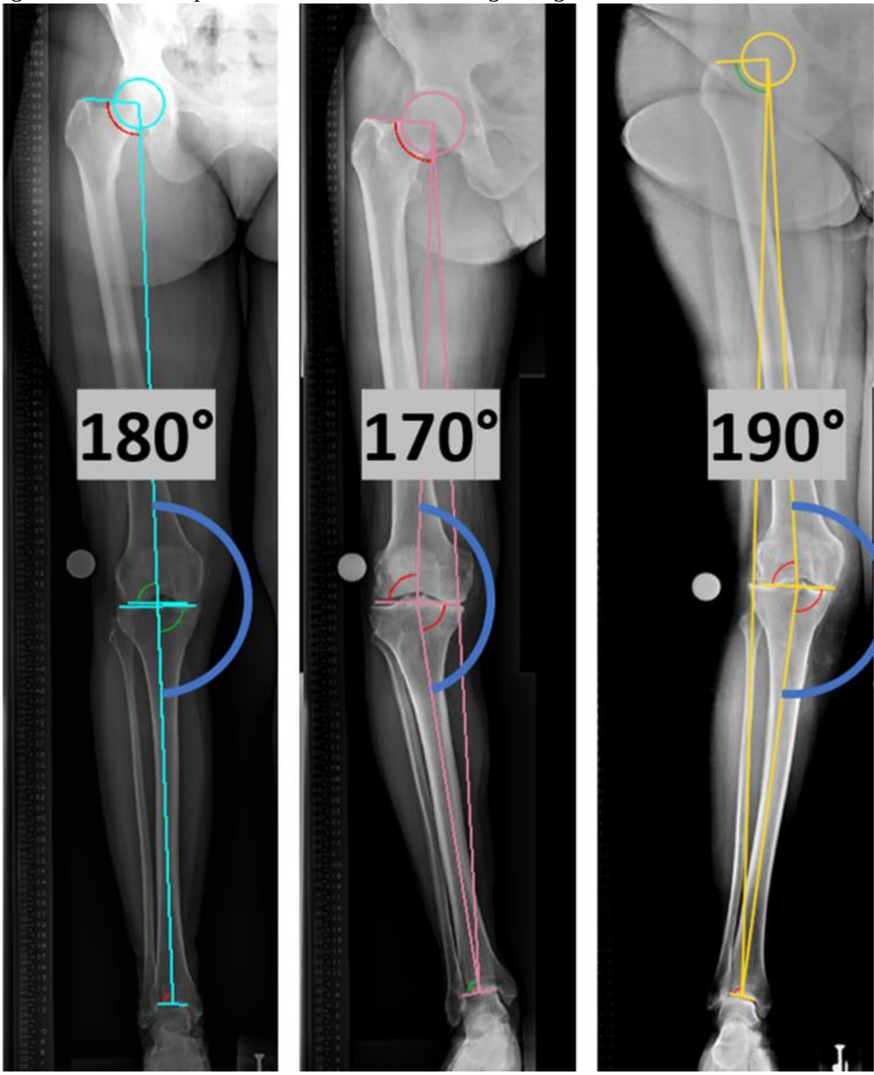
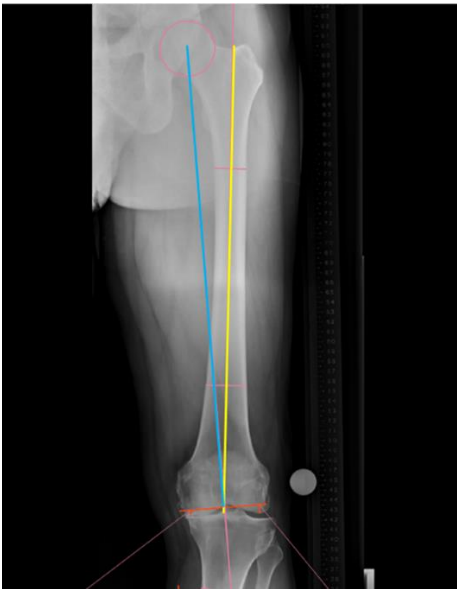


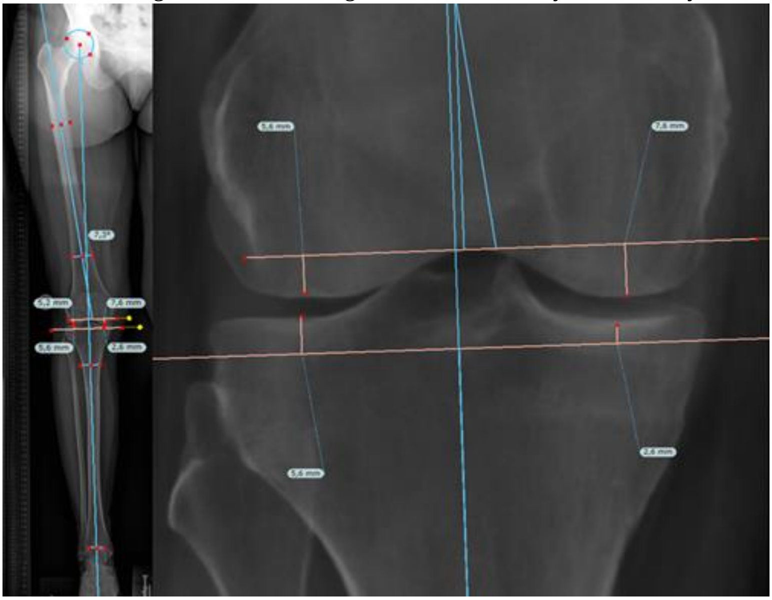
Figure 1.4.1.2: Mechanical (blue) and anatomical (yellow) femoral axis



Mechanical total knee alignment

In this approach both the tibia and the distal femur bone resections are cut perpendicular to the mechanical axis of the respective bones. This results in neutral mechanical limb alignment and introduce a change in the coronal joint line orientation from the native 3 degrees of varus to neutral, i.e. perpendicular to the mechanical axis. In a typical varus knee the bone resections will appear asymmetric with more bone removed from medial than lateral femur and opposite on the tibia (figure 1.4.1.2). In flexion the same asymmetric resections of the posterior femoral condyles compensate the tibial cut, typically with a 3-degree external rotation (figure 1.4.1.3). Femoral rotation can however be based on either anatomy or ligament laxity (section 1.4.2). The philosophy of these simplified mechanical bony resections was to promote even load distribution between the medial and lateral parts of the implants and thereby prevent both implants loosening and polyethylene wear. Historically; John Insall was a pioneer in the work [33]. Results from Behrend et al. demonstrated increased risk of failure with overall postoperative valgus alignment, tibial alignment of more than 3 degrees of valgus and BMI>34 [34]. In a more recent study on 1154 TKA's with long standing radiographs it was found that varus outliers with mechanical knee alignment lower than 177 degrees, i.e. more than 3 degrees of varus, more often suffered from tibial failure than neutrally aligned knees, however in this cohort mechanical femoral varus malpositioning was the main origin of varus outliers [35]. These results on overall alignment is further confirmed by a long-term radiostereometric study on 85 cases showing higher tibial migration in mechanical alignment outliers [36]. Mechanical total knee alignment is considered the benchmark for comparison [33].

Figure 1.4.1.2: Planning for mechanical alignment TKA, with asymmetric bony resection



Anatomic total knee alignment

This technique was described by Hungerford and Krakow 40 years ago [37,38], in this technique the aim is an overall neutral mechanical limb alignment, but with a joint line, mimicking the natural, with 3 degrees of varus. This tibial bone cut would allow the flexion or posterior femoral cut to be in line with the posterior condylar axis (figure 1.4.1.4). Technical problems especially precision when performing the tibial cut with conventional instruments caused that this approach was largely abandoned. However, this philosophy has been integrated in some modern knee implant systems, where the bone cuts are performed neutral as in mechanical alignment, but the polyethylene construct is asymmetric, thicker lateral and the femoral component correspondingly thicker on the medial side, e.g. the systems Journey™ and Physica™ KR.

Figure 1.4.1.3. Mechanical alignment, asymmetric bone resections (box)

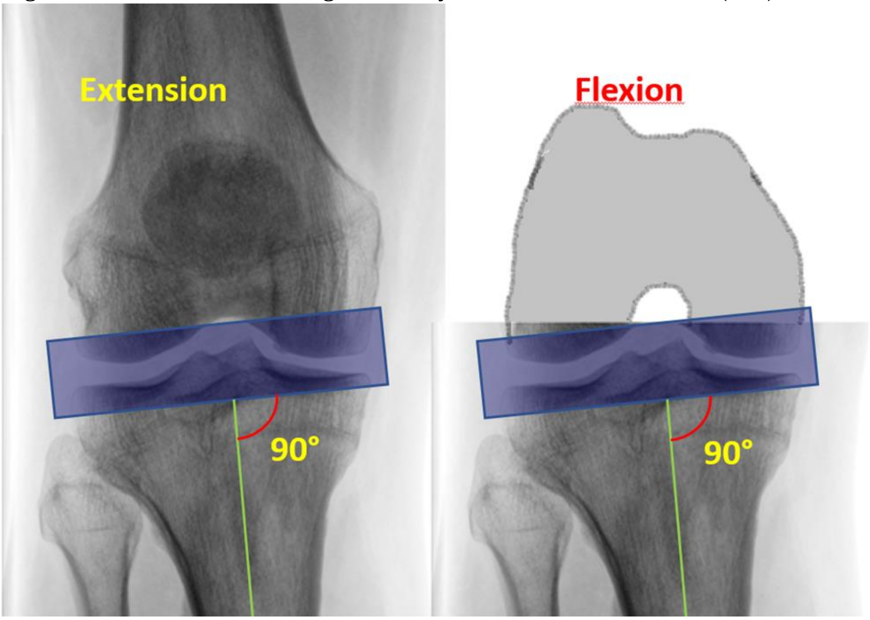
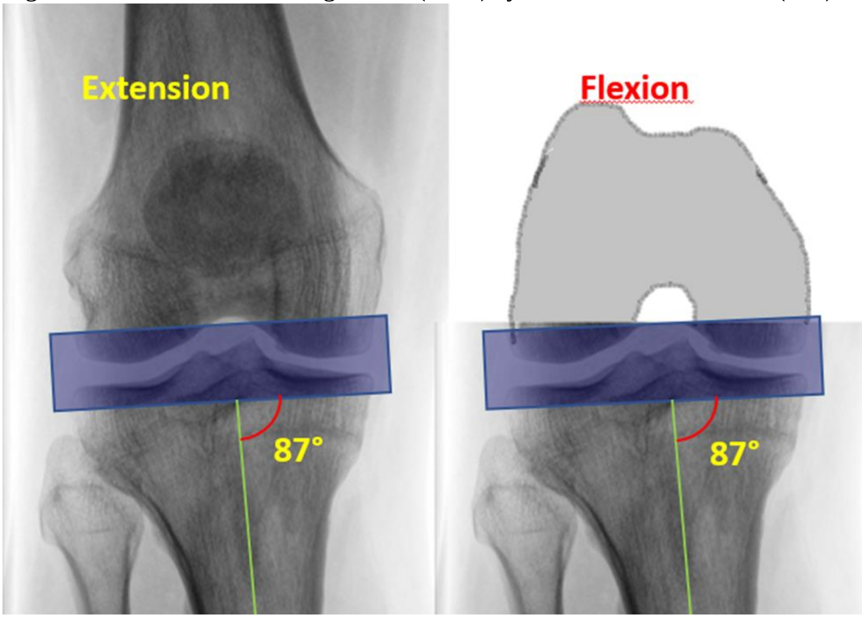


Figure 1.4.1.4. Anatomical alignment, (more) symmetric bone resection (box)



Kinematic total knee alignment
The observed individual variation in knee alignment in the non-osteoarthritic knee with 32% of males and 17% of females having more than 3 degrees of natural varus, has led to the assumption that mechanical total knee alignment would be unnatural to these subgroups [39]. In kinematic alignment, as described by Howell et al. the aim is to restore both alignment and joint line to the individual's pre-KOA condition. This is achieved by resecting the same mediolateral amount of bone from the distal and posterior femur and from the mediolateral tibia, without any restrictions on overall postoperative alignment [40]. This approach challenges the surgical precision, and the use of personalized instruments, computer guidance, caliber guidance and manual instruments have been described [40–42]. Proponents highlight that by striving to recreate pre-KOA anatomy, both laxity and kinematics are restored resulting in minimized need for soft-tissue balancing and better functional results, however concern regarding results in patients with more pronounced constitutional varus or valgus have been raised [37,43]. While kinematic alignment TKA in some studies have shown implant survival equal to mechanical alignment TKA, and excellent outcomes, the improved results have not been uniformly reproduced in randomized trials, and further studies are warranted[44].

Functional- / restricted kinematic total knee alignment
Individualized alignments goals respecting pre-KOA anatomy but restricting the postoperative limits of alignment have been described, however this technique further challenge surgical precision and might demand the use of technological aids such as personalized instruments or computer guidance[37,45].

Optimal alignment strategies in TKA are to be clarified.

1.4.2 Soft tissue balancing in total knee arthroplasty

The approach to ligament balancing is closely connected with the alignment strategy. Goals for balancing are stability, unrestricted range of movement and a well tracking patella. However the historic goals of mediolateral balance have been questioned[46,47]. The limits of coronal laxity that are acceptable, the degree of mediolateral balance that is optimal and the limits for sagittal laxity are not well defined. Soft tissue balancing might require bone resections to be modified.

Measured resection and balanced resection
In measured resection TKA bone resections are performed purely based on anatomy, and the soft tissue balancing is done subsequently. When performing balanced resection at least one initial resection is based on anatomy, and one or more of the subsequent resections adjusted to meet the actual soft tissue laxity. Most simple is the gap balancing technique where only the femoral component rotation is adjusted based on laxity.

Intra-operative evaluation of soft tissue laxity

The evaluation or feel of the soft tissue laxity, by the surgeon, must be supposed to be subjective and based on both experience and preferences. Manual surgeon assessment have been shown to be a poor predictor of more objective quantified measurements[48,49]. Simple spacer blocks can be used to evaluate flexion/extension match and balance prior to the insertion of trial implants. Another spacer technique, using spatulas inserted between trial or definitive component have been described and can deliver objective quantified measurement of laxity[50]. More advanced mechanical devices such as spreaders and tensioners are available and can be used to guide both balanced resection bone cuts and soft tissue balancing[51]. Navigation systems can also deliver surgeon feedback on laxity, either by manually testing of laxity or combined with the use of spreaders or tensioners. The use of trial inserts with integrated load sensor technology is a different approach to balancing since these trials deliver information on compartmental loads and not the laxity. This sensor technology can be combined with accelerometers, and give feedback on loads, alignment and kinematics[52]. Changes in laxity and loads might occur from trial implants to final implants due to different seating of the components[53].

Soft tissue balancing

The surgeon's profound knowledge on knee anatomy and knee biomechanics is prerequisite when balancing the TKA, regardless of the technique or technologies used. Bony corrections must be made on the femur in cases of flexion/extension mismatch and on the tibia in cases universally to tight knees. The importance of joint line restoration is commonly accepted although only documented with low levels of evidence[54]. Soft tissue releases are performed in cases where the surgeon judge imbalance inappropriate. Algorithms on sequential releases are proposed by several experts and depend on the soft tissues being tight laterally or medially and whether this is in extension or flexion[55–57].

Implant constraint

Implant design do also influence laxity. Femoral condylar shape affect laxity during changes in flexion[58]. Congruency of the polyethylene insert do mainly affect sagittal stability and different levels of insert congruency are available. The polyethylene can be medio-lateral symmetric or asymmetric, typically with the high congruency medially. Implants that can compensate for posterior cruciate ligament deficiencies, or resection, either by congruency or by a post-cam mechanism are available and preferred by some surgeons. The question whether posterior cruciate retention or sacrificing technique is superior is unsolved[59]. In cases where the soft tissues cannot be balanced sufficiently, constrained condylar knees, that can compensate for collateral insufficiencies, and hinged implants that can compensate for global instability are available. However, with increasing implant constraint follows increased functional stress on both articulation and implant fixation which might lead to early polyethylene wear and implant loosening[60]. During surgery It remains to be judged by the surgeon whether the stability is satisfactory or should be balanced, and when to increase the level of constraint. No exact limits of soft tissue laxity are recognized to justify balancing or an increase in constraint.

Although, the treatment with TKA is proven clinically successful, cost-effective and durable, important unsolved challenges are present.

The 20% dissatisfaction rate following surgery needs attention. Is the dissatisfaction rate caused by the poorly defined threshold for intervention, unrealistic patient expectations or by technical/biomechanical problems related to the implants used and the surgical performance?

Lack of TKA stability, instability, assumed to compromise TKA function is currently the most frequent cause of revision TKA surgery in Denmark. Is the instability caused by inadequate soft tissue balancing during primary surgery, does it occur subsequently or are the revisions wrongly classified?

Can the limits of soft tissue laxity that facilitate optimal function and pain relief be clarified to guide surgeons intraoperatively, and can the degree of laxity that might justify revision for instability be quantified?

2. Study aims

Soft tissue structures surrounding the knee and the conformity of the knee joint surfaces provide knee stability in both the native knee and the TKA knee. These soft tissue structures are balanced and adjusted during surgery to secure stability and function of the TKA. However, this balancing of the TKA is considered "as much" or "more art than science"[55,61] and dependent on both surgical technique and the individual surgeon's experience, preference and surgical skills. Further knowledge on which range of laxity that facilitate optimal function and pain relief are demanded to guide surgeons in optimizing results of TKA surgery.

Reliable methods for quantification of TKA laxity are prerequisite when examining impact of laxity.

Overall aim of this PhD thesis was to:

- synthesize current knowledge on optimal laxity following TKA
- to examine whether laxity around a TKA could be measured with satisfying reliability
- to investigate limits of laxity and implications in a consecutive cohort at the author's institution

2.1 Study I – Systematic review

The objective was to extract any evidence on the relationship between objective measurement of laxity following TKA and outcome scores from the current literature. Additional outcomes included conditions for soft-tissue laxity measurements, choice of outcome scores, operative techniques, types of implants and study population demographics.

2.2 Study II – Reliability study

The aim was to; 1) validate an established commercial instrumented method for quantification of coronal soft tissue laxity in extension following TKA, 2) establish a set-up for coronal laxity measurements in flexion and validate the measurements.

Primary aim was to examine test-retest reliability of the two methods and secondary aims to tests intra- and inter-rater agreement.

2.3 Study III – Cohort study

In this prospective observational cohort study, relation between follow up laxity measurements and outcome scores were investigated. Performance based physical tests (PBT) were included to investigate whether they would reveal functional differences not revealed by the patient reported outcomes (PRO). Primary aim was to examine whether outcome differed between tight and lax knees at follow up.

Secondary aims included; 1) examination of differences in pre-operative factors between tight and lax knees, and 2) determination of the range of laxity that was obtained with the technique used at our institution.

3. Methods

Different methodologies were used, study I is a literature study, study II a measurement method reliability study and study III is a prospective clinical cohort study.

3.1 Study I – Systematic review

The review was thoroughly planned, with definition of search strategy, screening method, eligibility and data collection. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was studied when planning and performing the review and followed when reporting the review. The review protocol was published on the PROSPERO database with registration number CRD42017069779.

With the assistance from university librarians the search strategy combining search words describing knee arthroplasty, soft tissue laxity and outcome was defined. 3 databases, PubMed, Embase and Cochrane, were searched. Full search strategy is listed in the supplementary data, point A. The Covidence software platform was used for primary screening of search results. Additional papers were added based on references and all references from the included papers were screened. Cross-references from all included papers were identified using Web of Science and screened for inclusion.

Studies reporting on association between quantified instrumented soft tissue laxity at follow-up and outcome scores following TKA were included. Studies reporting on soft tissue laxity based on manual physical examination were not included and ROM was not considered an outcome score. Heterogeneity of the included studies with respect to both methods and conditions for laxity measurement and choice of outcome scores was expected and it was not expected that statistical meta-analysis would be possible. Data extraction from the papers included in the review followed a strict protocol with predefined data items, table 3.1.1.

Methodological quality of the included studies was assed using the methodological index for non-randomized studies (MINORS)[62]. This assessment is based on a scoring system evaluating both reporting and methodology of the individual studies, data used for the MINORS scoring system was extracted during a second round.

The PhD student performed the initial screening for full text articles to be assessed, 2 authors should agree on inclusion of any papers to the review. Data extraction was performed by the PhD student and for each paper confirmed by one of the co-authors.

Table 3.1.1: Data extraction

Data item	Data to be extracted
Study design	rct/cohort/case series/other, prospective/retrospective, multicenter/single center, follow up time and range
Participants	Inclusion criteria, exclusion criteria, number of knees and patients included, number of knees and patients analyzed, gender distribution, mean age and range,
Surgical technique	Measured resection/gap balancing/other/not specified, surgical navigation/computerized navigation/psi/combination, use of spatulas/spreaders
Implant	CR/PS, fixed/mobile, manufacturer and implant name
Laxity measurements	Technique and instruments, sagittal/coronal, degree of flexion, load, information about validation of the method used
Outcome scores	Exact name, version and modifications of outcome scoring systems used
Statistics	Name of specific statistical tests, p-values
Results	Significant results

3.2 Study II: Reliability

Guidelines for Reporting Reliability and Agreement Studies (GRRAS)[63] were considered during planning of this study and followed when reporting the study. Study protocol was approved by the north Denmark regional committee on health research ethics (N-20180028).

Participants

Participants were recruited from the out-patient clinic at Aalborg University Hospital Farsø. Inclusion criteria were CR-TKA, follow up period more than 12 months, extension deficit less than 5 degrees, flexion more than 100 degrees, BMI less than 35 and absence of pain during manual examination of the knee.

Stress radiographs

Stress radiographs in extension were standardized using the Telos stress device (TSD), with knee flexion 10 degrees and load of 150N as described in previous papers[64,65]. Radiographers and PhD student established the method at Farsø hospital, another department with large experience with the method was visited and pilot examinations were performed before including patients in the study.

The setup to obtain stress radiographs in flexion, using the epicondylar view (EV), described by other authors was studied [66,67], and the method was established at the radiological department in Farsø. The hospital’s technical department was involved in this process. In the final setup the participant is seated on the radiographic table with a post between the thighs and both lower legs hanging freely. Traction, with a force of 50N, is then applied at the level of the ankle joint. The x-ray beam is directed from posterior to anterior with an upward angulation of 15 degrees. This setup is demonstrated in a video that is available online: https:/video.rn.dk/stress-radiographic

Both TSD and EV stress radiographs were recorded with varus and valgus stress. Following these recordings, the participant had a short break and a walked a few steps, before all radiographs were repeated (test-retest). During the examination participants were encouraged to relax the muscles and rotation were controlled by instructions from and positioning by the radiographic staff. Three dedicated radiographers performed all radiographs.

Measurements
Laxity was quantified, from the stress radiographs, by measurement of the angulation between the TKA components. Using the Easyviz viewer the radiographs were enlarged to make the space between the component fill the whole screen and the angulation between two lines, one parallel to the tibial baseplate and one connecting the most distal parts of the femoral condyles, were measured (figure 3.2.1.-2.).

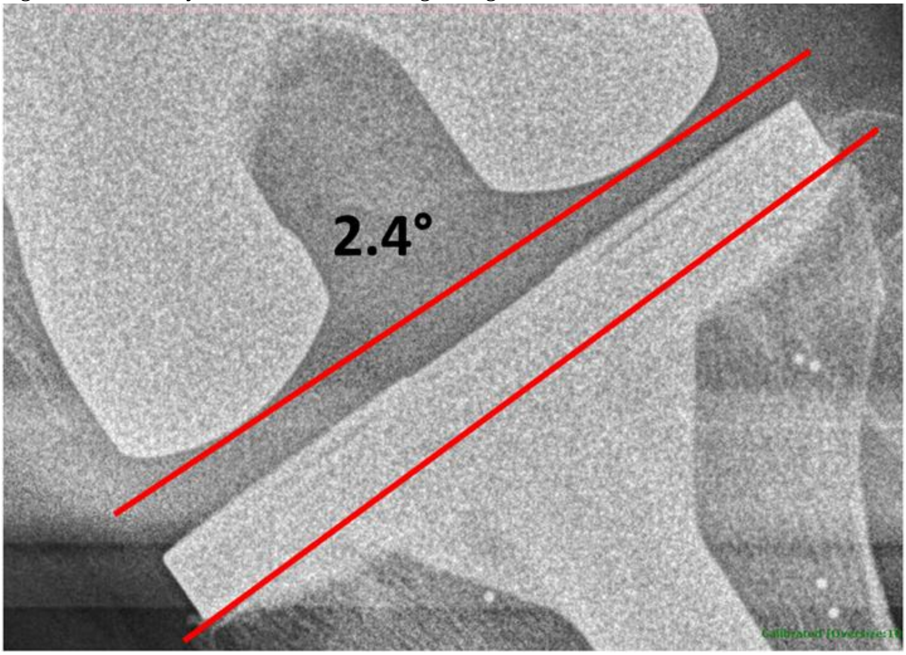
Three observers measured all radiographs in a random sequence, and after an interim period of at least two weeks measurement were repeated. Observers were blinded to results from the other observers and in the second round of measurements also to own results from the first round.

Statistical analysis
Power calculation was performed with respect to the primary aim test-retest reliability, using Bonett's method, where the expected correlation and width of the 95% confidence interval (95% CI) gives the sample size[68]. We expected the ICC to be above 0.90. The hospital's statistical team performed this analysis. A sample size of 12 participants was calculated, 15 participants were included in the study.

Data were continuous and expected to be gaussian / normally distributed. Statistical methods were chosen according to GRRAS [63]. Reliability was described by intra-class correlation coefficient (ICC). The ICC model was "Two-Way Mixed, absolute", for the inter-rater reliability based on a single measurement and for the other based on mean measurement, ICC was interpreted as proposed by Koo et al. [69]. Agreement was visualized with Bland-Altman plots, and limits of agreement (LOA) and systematic error were considered. Bland-Altman plots are constructed for the purpose of visualizing agreement between two measurements, it is a scatter plot in which the x-axis represent the average value and the y-axis the difference between the values[70]. Systematic error between measurements and LOA can be added to the plot. All analyses were conducted in STATA 15 (StataCorp, College Station, TX, USA).

Figure 3.2.1.: Flexion stress radiograph to examine medial laxity in flexion

Figure 3.2.2.: Laxity measurement following enlargement



3.3 Study III: Cohort

The study was planned to meet the methodological limitations revealed by MINORS scoring of the studies reviewed in study I. Both MINORS and guidelines from The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement were observed in the planning, and STROBE guidelines followed when reporting the results. Study design was observational cohort study with prospective inclusion of consecutive patients and surgery at a single center with 4 surgeons. Study protocol was approved by The North Denmark Regional Committee on Health Research Ethics (N-20170048).

Participants
All patients scheduled for TKA, during the study period, were screened for inclusion. Inclusion criteria was primary uncomplicated unilateral CR-TKA, and exclusion criteria were extra-articular deformity, previous osteotomy, previous multi ligament injury and participation with contralateral knee. Furthermore, participants should be able to walk 40 meters without support, understand Danish, be able to comply to protocol and answer online questionnaires.

Surgical technique and implants
All surgeons used identical technique and implants. Measured resection, femur first technique and CR implants have been used at our clinic for decades and this technique was maintained in the study. The knee was exposed with a midline incision and a medial parapatellar arthrotomy, splitting the quadriceps tendon longitudinally with approximately 5 mm of the tendon medially. Femoral resection was then done with the help of an intramedullary guide, pre-set standard resections was distal resection in 6 degrees of valgus relative to the intramedullary guide and externally rotation 3 degrees relative to the posterior condyles. Medial joint line was intended to be preserved. Tibial resection was done using an extramedullary guide, aiming for neutral, 90 degrees, frontal resection and 5 to 7 degrees posterior slope. Individual adjustments were done to meet anatomy and wear. ROM and stability were examined by the surgeon with trial implants, no instrumented laxity tests were performed. In case of extension-flexion mismatch this was solved by femoral proximalization or downsizing, and if universally tight the tibial component would be distalized. In cases of imbalance the medial or lateral structures were released gradually. 2 different implant brands were used, both standard in the department, PFC Sigma® (DePuy Synthes) and NexGen® (Zimmer Biomet).

Outcome measures
Outcome following surgery was monitored with PRO questionnaires, and physical performance tests.

PRO questionnaires were included to gain subjective measures directly from the participants. Multiple knee specific questionnaires are developed and used in KA evaluation [71], our considerations were to use questionnaires that were validated among OA and KA patients, alongside being short and relevant for the participants. The PRO chosen should reveal subtle differences between participants with supposed well-functioning TKA implants, and a major concern was the clustering of good scores (ceiling effect). The Oxford Knee Score (OKS) [72] was chosen as the historical reference questionnaire. Activity and Participation Questionnaire (OKS-APQ) [73] and Forgotten Joint Score (FJS) [74] chosen as newer questionnaires with reduced ceiling effect. All questionnaires are validated [73,75–77], however OKS-APQ not in the Danish translation. A general health (generic) questionnaire, EQ-5D-3L, supplemented the knee specific questionnaires, this questionnaire is short and simple to use [78]. Minimal clinical important difference (MCID) have been defined for OKS and FJS[79].

Performance based physical tests (PBT) were included in the hope to reveal functional differences not revealed by PRO. The use of PBT in this type of study was not identified in any previous papers. The Osteoarthritis Research Society International (OARSI), have recommended a core set of 3 PBT[80] to asses physical function in people with hip or knee OA. This core set includes activities such as walking, turning, stair climbing and raising form a chair. The core set have been found reliable for patients undergoing TKA surgery, however the validity have been questioned due to limited correlation to PRO and muscle strength measurements, and the responsiveness has also been challenged due to limited correlation with subjective improvement in performing the tasks[81]. We chose to use the OARSI recommended core of PBT as we judged this as the most established and validated. The questioned validity and responsiveness were not considered a major problem in our study as we were seeking to reveal actual functional differences not shown by the PRO questionnaires.

PRO questionnaires were answered online, using a modification of our standardized online follow up questionnaires, which is administered in the institutional database (Procordo Software Aps, Copenhagen). PBT was supervised and monitored by a team of 4 dedicated physiotherapists, following the test-guide published by OARSI [82].

Radiographic evaluation

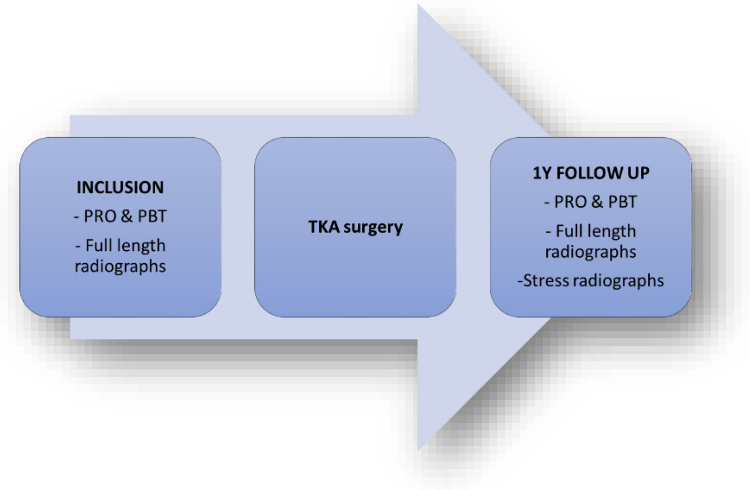
OA severity, pre- and post-TKA alignment and laxity were judged from radiographs.

OA severity was judged from the routine weight bearing knee radiographs using the modified Kellgren-Lawrence score, taking the joint space width into account as described and validated by Dowsey et al. [26]. Each radiograph was graded twice and in cases with divergence a third grading was performed.

Whole leg standing radiographs, preoperative and at follow up, were done in a standardized manner as described and validated by Skyttä et al. [83]. All angulations were measured twice, and these measurements showed excellent reliability with inter- and intra-observer agreement ICC in the range from 0.97 to 0.99. Mean values were used for analysis. Neutral mechanical alignment was defined as mechanical alignment in the range from 177 to 183 degrees, varus alignment were defined as below 177 degrees and valgus higher than 183 degrees.

Extension and flexion stress radiographs were obtained with the methods found reliable in study II. All measurement was performed twice, and the mean used for analysis.

Figure 3.3.1: Participant flow



Study size

Sample size calculation for this type of cohort studies, with no control group and without exact knowledge of the distribution and relation between the primary variables, laxity and outcome scores, was deemed both troublesome and without relevance. An estimation from previous studies succeeding in finding a relation between laxity and outcome [47,67,84] was chosen. Some dropouts were expected due to the extensive follow up program, and inclusion of 150 cases to allow analysis of at least 120 patients was intended.

Statistics

Gaussian / normality of the variables was examined using Shapiro-Wilk test and visually with histograms. Results were described by mean and standard deviation (SD) or median and interquartile range. In all other known papers, results of laxity measurements are considered normally distributed, this was not the result of Shapiro-Wilk test, histograms showed results slightly skewed, this was accepted, and they were considered parametric. Categorical outcomes were described with numbers and percentages. Each of the 4 laxity modalities was analyzed separately, and for each the results were divided into tight or lax based by the median value. Between group differences were tested with parametric or non-parametric tests as appropriate. The relation between laxity and obtaining the MCID was tested using uni- and multi-variate logistic regression, preoperative details were included as potential confounders (age, gender, BMI, mKL). Odds ratio and 95% CI described the relation between laxity and obtaining MCID. Non-complete data were excluded from the analysis. P-value below 0.05 was considered significant. STATA 15 (StataCorp, College Station, TX, USA) were used for all analyses.

4. Summary of results

4.1 Study I – Systematic review

3228 papers were screened, and 14 articles fulfilled the inclusion criteria and were included in the systematic review. Eligible studies were all cohort studies. However, heterogeneity regarding methods for laxity measurement and choice of outcome scores was obvious (table 4.1.1), furthermore, variation in patient demographics, surgical technique, choice of implant and length of follow up was found (table 4.2.1). This excluded the possibility to perform a quantitative meta-analysis.

MINORS raised methodological concerns regarding all studies, please refer to supplementary data point B. Most often patients were not enrolled consecutively, the assessment was potentially biased, and the study size was not accounted for.

In the 14 articles, 12 measurement of laxity in extension (0-30 degrees of flexion) and 10 measurement of laxity in flexion (60-90 degrees of flexion) was analyzed. No studies described mid-flexion laxity.

Laxity in extension

Sagittal laxity in 20-30 degrees of flexion was measured with arthrometers in 7 studies and no significant association to outcome could be established. Coronal laxity in 0-30 degrees of flexion was measured with stress radiography, one study used manual stress and 4 studies used the TSD. In one study a significant correlation between lateral laxity and 3 of 6 2011 KSS sub scores was found, indicating better scores for knees with lateral laxity [67], however only p-values and not confidence intervals were reported. Following stratification to tight and loose knees no significant difference in 2011 KSS sub scores was found. *Please note that this significant correlation was not mentioned in the published work as it was overseen. It does not by any way change any conclusions.* Kuster et al. examined bilateral TKA cases using coronal stress radiography with manual stress at 30 degrees of flexion. No significant differences between lax or tight knees was found, half of participants had a preferred knee and in 10 of 11 it was the more lax knee.

Sagittal laxity in flexion

Matsumoto et al.[85] analyzed Spearman rank correlation between laxity at three different degrees of flexion and KOOS sub scores using arthrometer and a PS implant. Significant correlation was found between laxity at 60 degrees of flexion and KOOS-pain, however insignificant results were obtained for all other KOOS sub scores and for measurement at 30 and 90 degrees of flexion. Ishii et al.[86] performed the same type of analysis for both CR and PS implants but insignificant correlation with the HSS score was obtained. Seon et al.[87] used stress radiographic measurement of sagittal laxity at 90 degrees of flexion and a CR implant, and reported insignificant Pearsons correlation between laxity and a modified HSS.

In 4 studies the study cohort was stratified into groups based on the results of the laxity measurement and between group differences in outcome analyzed. Seon et al.[88] again used stress radiographic measurement of sagittal laxity at 90 degrees of flexion and a CR implant, and divided into a stable group (laxity<10mm) and a unstable group (laxity≥10mm), significant better WOMAC but not HSS was found in the stable group. Seah et al.[89] used an arthrometer and measured laxity at 75 degrees. Only CR implants were used, and patients were divided in three groups, superior OKS was reported for the moderate laxity group with 5 to 10mm of laxity, however non-significant results for KSS and SF-36 was found. Jones et al.[90] used the same methodology, and reported superior KSS but not WOMAC for the moderate laxity group. Schuster et al.[91] reported on arthrometer measurements at 90 degrees of flexion and did not find significant association to KSS following stratification.

Coronal laxity in flexion

Two studies reported on coronal laxity in flexion, and both used stress radiography and epicondylar view radiographs. Tsukiyama et al.[67] reported on a PS implant (information obtained after correspondence with author) and found significant correlation between medial laxity in flexion and 5 of 6 2011 KSS sub scores. Following stratification into tight (laxity≤3degrees) and loose (laxity>3degress) groups significant better 2011 KSS sub scores was obtained for 4 of 6 sub scores. No significant results were found for lateral laxity in flexion. Oh et al.[66] used quite another path in their stratification. CR knees were divided into balanced or unbalanced depending on the difference between medial and lateral laxity in flexion. The majority, 51 of 61 knees, were classified as balanced and compared to the unbalanced knees these showed significantly less total laxity and better KSS function and WOMAC scores. Further division of the balanced knees based on total laxity showed superior results for the mid laxity group (6 to 10 degrees of total laxity) with significantly better KS pain and WOMAC scores.

Table 4.1.1: Methods and conditions for laxity measurements, outcome scores and results of reviewed studies (modified from paper I).

Author	Soft-tissue laxity measurement	Anatomical plane, flexion, mean (±SD)	Outcome scores	Statistical methods	Significant results
Matsumoto	KS Measure Arthrometer, mean of three measurements	Sagittal 30^0: 4.5±2.2mm 60^0: 3.6±1.9mm 90^0: 3.0±1.9mm	KSS, KOOS	Spearman rank correlation.	Inverse correlation between KOOS-pain score and laxity at 60^o
Tsukiyama	Stress radiographs: Telos, 150N in extension Epicondylar view, 50N in flexion	Coronal extension: Varus: $4.0±2.5^0$ Valgus: $4.0±2.4^0$ Coronal 80^0: Varus: $6.2±4.4^0$ Valgus: $3.9±2.6^0$	2011 KS	Stratification Wilcoxon rank-sum test. Pearson correlation coefficient.	4 of 6 2011 KS sub-scores better in knees medial tight in flexion.
Graff	KT-1000, 89N, mean of three measurements	Sagittal: 20^o: 3.8±2.0mm	OKS, KOOS, KSS, SF12	Pearson correlation coefficient	No correlation
Nakahara	Stress radiographs, Telos, 150N	Coronal extension: Varus: $5.9±2.7^0$ Valgus: $5.0±1.6^0$	New-KSS	Pearson correlation coefficient	No correlation
Oh	Stress radiographs, Epicondylar view, 50N	Coronal 90^0: Varus: $4.7±2.4^0$ Valgus: $4.1±2.1^0$	KSS, WOMAC	Stratification T-test Kruskall-Wallis	Superior sub scores in balanced group, and for grade II laxity
Seah	KT-1000, 89N, sum of anterior and posterior stress, mean of three measurements	Sagittal 75^o: not reported	KSS, OKS, SF-36	Stratification One-way ANOVA.	Group 2 better OKS
Schuster	Rolimeter, sum of anterior and posterior stress, mean of three measurements	Sagittal 25^0: 4.6±2.1mm 90^0: 4.9±2.2mm	KSS, VAS Pain, VAS satisfaction	Stratification Kruskall-Wallis analysis.	No differences between groups

Seon 2010	Stress radiographs, Telos, 89N, sum of anterior and posterior stress	Sagittal 90^0: 8.3mm	HSS, WOMAC	Stratification Mann Whitney U-test.	Stable group significant better WOMAC function
Seon 2007	Stress radiographs, Telos, 150N, sagittal difference between anterior and posterior stress	Sagittal 90^0: 7.1±4.1mm Coronal extension: Varus: $4.4±2.2^0$ Valgus: $3.5±1.4^0$	m-HSS	Pearson correlation coefficient.	No correlation
Van Hal	Rolimeter	Sagittal 30^0: 2.8±1.1mm	KSS	Spearman rank correlation.	No correlation
Jones	KT1000, 89N, sum of anterior and posterior translation, mean of three measurements	Sagittal 30^0: 7.3±4.0mm $75\text{-}80^0$: 4.6±3.1mm	WOMAS, KSS, SF12	Stratification. Duncan test.	Group 2 better KSS than group 3
Ishii	KT-2000, anterior force 133N, posterior force 89N sum of anterior and posterior stress, mean of three measurements,	Sagittal 30^0: CR:5.8±2.9mm, 30^0: PS:5.3±3.2mm 75^0: CR:4.8±2.3mm, 75^0: PS:3.4±1.5mm	HSS	Spearman rank correlation.	No correlation
Kuster	Manual stress radiographs	Coronal 30^0: Varus: $4.3±1.9^0$ Valgus: $4.0±2.1^0$	m-HSS, preferred knee	Stratification T-test and chi square.	No significance. Lax knees preferred over tight knee
Yamakado	KT2000, 133N, and coronal manual stress radiographs	Sagittal 30^0: 9.1±1.1mm Coronal extension: Varus: $6.2±0.9^0$ Valgus: $4.3±0.5^0$	m-KSS	Pearson correlation coefficient and multiple regression.	No correlation

Table 4.1.2: Study size, demographics and surgical details in the studies reviewed (modified from paper I).

Author	Number participants	Number Knees	Follow UP Years (range)	Mean Age Years (range)	Females	Surgical technique	Navigation	Constrained of articulation
Matsumoto	81	110	4.4 (1.1-11.5)	76.4 (26-91)	85%	GB	18%	PS-FB=23%, PS-MB=77%
Tsukiyama	41	50	4.8 (2.0-13.8)	73.0 (59-82)	76%	MR	-	PS-FB=100%
Graff	24	24	2.3 (1.0-4.8)	68.8 (54-80)	46%	-	42%	CR-FB=100%
Nakahara	68	94	4.6 (1.1-11.0)	72.5 (50-86)	85%	MR	26%	PS-FB=100%
Oh	61	61	2.2 (1.0-5.0)	68.4 (59-82)	79%	GB	0	CR-FB=100%
Seah	100	100	2 (-)	66.9 (50-83)	68%	GB	0	CR-FB=100%
Schuster	112	127	3.9 (0.8-5.0)	70.7 (50-89)	71%	GB	0	CR-FB=75%, CR-MB=25%
Seon	55	55	2.8 (2.0-4.3)	68.2 (55-81)	84%	GB	100%	CR-MB=100%
Seon	42	42	1 (-)	-	95%	GB	100%	CR-MB=100%
Van Hal	49	51	4.6 (4.1- 5.4)	72.5 (59-87)	76%	GB	0	CR-FB=100%
Jones	88	97	7 (5.4-9.9)	70.1 (-)	43%	-	0	CR-FB=100%
Ishii	71	77	6.4 (5.2-9.4)	76.6 (-.)	86%	-	0	CR=69%, PS=31%
Kuster	22	44	4.5 (2-7)	68.9 (32-82)	55%	-	0	FB=16%, MB=84%
Yamakado	15	21	7.1 (4-8)	68 (58-78)	80%	-	0	CR-FB=100%

GB=gap balancing, MR=measured resection, “-“=not specified, CR=posterior cruciate retaining, PS=posterior cruciate sacrificing, FB= fixed bearing, MB=mobile bearing

4.2 Study II: Reliability study

All participants tolerated the stress radiographic examinations. Results of the laxity measurement is listed in table 4.2.1

Table 4.2.1: Results of laxity measurements (modified from paper II).

Extension (Telos)		Flexion (Epicondylar view)	
Medial laxity	Lateral laxity	Medial laxity	Lateral laxity
4.0±2.5° (0.5-9.5°)	4.6±2.3° (0.7-10.6°)	3.8 ±2.5° (0.5-10.7°)	8.0±4.1° (1.7-17.3°)

Mean laxity ±SD (range)

Overall reliability of stress radiography was found to be good, however when looking at the individual modalities only moderate reliability was found for lateral laxity in flexion, excellent reliability was found for the other three modalities, table 4.2.2.

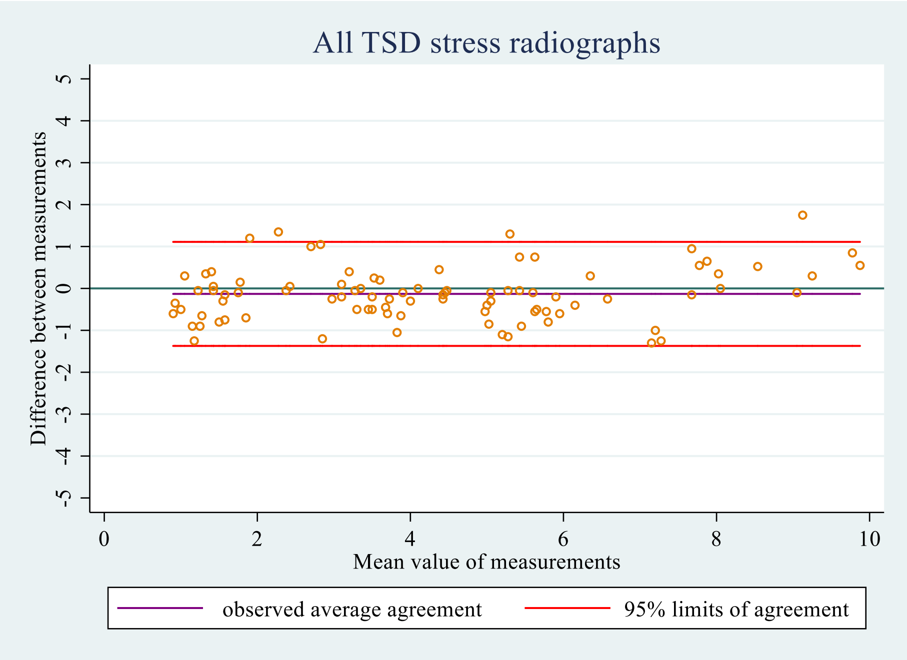
Table 4.2.2: Reliability and agreement for test-retest stress radiographs (modified from paper II).

	Telos and epicondylar	Telos		Epicondylar view	
	Med.+lat. laxity	Medial laxity	Lateral laxity	Medial laxity	Lateral laxity
ICC (95%CI)	.87 (.83-.90)	.97 (.94-.98)	.96 (.93-.98)	.94 (.89-.97)	.70 (.51-.82)
LOA	±3.4°	±1.3°	±1.3°	±1.7°	±6.3°
Systematic error	.06°	-.14°	-.12°	-.19°	.67°

Bland-Altman plots visualized agreement, figure 4.2.1 is an example of this, the systematic error of between the measurement is represented by the blue line and LOA by the red lines.

Intra-rater agreement was excellent for all raters and inter-rater agreement was found to be excellent between all raters.

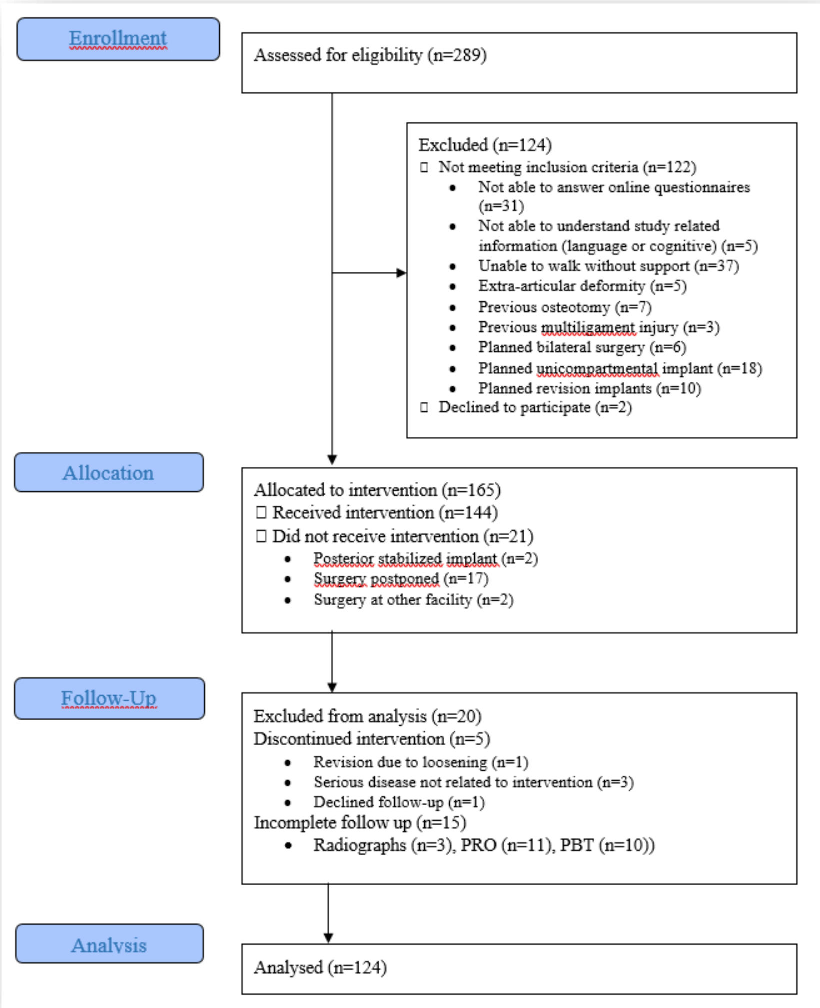
Figure 4.2.1: Bland-Altman plot showing agreement between test-retest results for all TSD stress radiographs (modified from paper II).



4.3 Study III: Cohort study

144 participants received the planned surgery, 5 discontinued the intervention and 15 cases had incomplete follow-up, this left 124 participants for analysis, please see study flow diagram, figure 4.3.1.

Figure 4.3.1. Study flow diagram (modified figure from paper III)



Baseline demographics and surgical details, for the 124 participants with complete follow-up, are listed in table 4.3.1.

Table 4.3.1: Baseline for the 124 participants analyzed (modified from paper III)

Demographics	
Age	67 (9)
Male sex	47%
BMI	30 (5)
Modified Kellgren-Lawrence grade	Grade 2 = 1% Grade 3A = 11% Grade 3B = 19% Grade 4A = 35% Grade 4B = 35%
Preoperative alignment	176 (6) Varus = 65% Neutral = 22% Valgus =13%
Surgical details	
Surgeon	Surgeon A = 31% Surgeon B = 33% Surgeon C = 15% Surgeon D = 22%
Implant	NexGen = 70% PFC Sigma = 30%

Mean (SD) or percentage

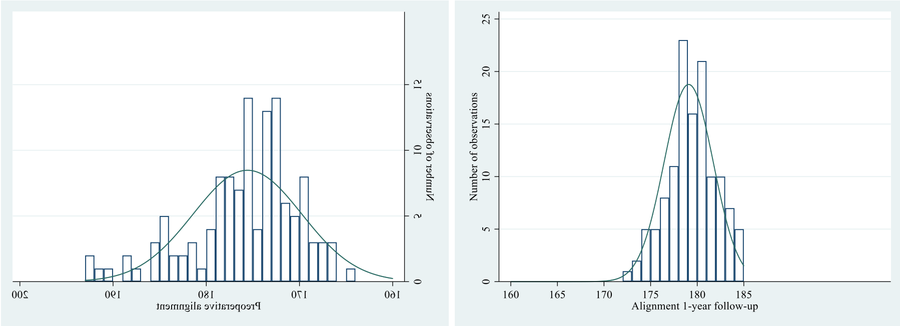
The study population achieved significant improvement in all outcomes (table 4.3.2) however 15 (12%) of the participants did reach OKS MCID of ≥ 8 points and 25 (20%) did not reach FJS MCID of ≥ 14 points[79], at the 1 year follow up. Alignment varied preoperative with most knees in varus (figure 4.3.2). At 1 year follow up 97 (78%) of the participants where aligned neutrally as intended (figure 4.3.2).

Table 4.3.2: Pre-operative, at 1-year follow-up results (modified from paper III).

	Range / units	Pre-operative	Follow-up	Δ	p
OKS	0 to 48	22 (6)	38 (7)	17 (8)	<0.001
OKS-APQ	0 to 100	10 (14)	55 (32)	45 (31)	<0.001
FJS	0 to 100	13 (13)	54 (29)	41 (28)	<0.001
EQ-5D	-0.624 to 1	0.65 (0.2)	0.83 (0.2)	0.18 (0.2)	<0.001
Extension	Degrees	4 (6)	1 (4)	-3 (7)	<0.001
Flexion	Degrees	123 (12)	123 (10)	0 (13)	0.66
30-s chair-stand	Repetitions	10 (3)	12 (3)	2 (3)	<0.001
40m fast-paced walk	Seconds	10 (4)	8 (3)	-2 (3)	<0.001
Stair-climb test	Seconds	32 (8)	27 (6)	-5 (6)	<0.001
Alignment	Degrees	176 (6)	179 (3)	4 (5)	<0.001

Mean (SD), Student's t-test

Figure 4.3.2: Preoperative alignment and alignment at follow up



Primary aim: Differences in outcome between tight and lax knees

Significant differences in follow-up outcomes between tight and lax knees were not shown (table 4.3.3. and 4.3.4). Significant differences in obtaining PRO MCID were found. In extension, more knees lateral tight than lateral lax reached the MCID in FJS, however adjusted OR did not show significance (table 4.3.3). In flexion, more knees lateral lax than lateral tight reached the MCID in OKS, this was also significant for the adjusted OR (Table 4.3.4).

Secondary aim: Differences in pre-operative factors between tight and lax knees.

Both participant characteristics (age, gender and BMI) and anatomical characteristics (degree of OA and preoperative alignment) varied between groups. Significant gender differences in 3 of 4 laxity modalities and significant differences in 1 of 4 laxity modalities for age, BMI and mKL was found (table 4.3.3 and 4.3.4).

Secondary aim: Laxity at follow up

Mean values, range and standard deviation is presented in table 4.3.5 and histograms visualize the distribution (figures 4.3.4-4.3.5).

Table 4.3.3 Comparison of tight and lax knees in extension (modified from paper III)

	EXTENSION					
	Medial laxity			Lateral laxity		
	Tight: <2.4°	Lax: >2.4°	p-value	Tight: <3.4°	Lax: >3.4°	p-value
N	62	62	-	62	62	-
	Demographics			Demographics		
Male sex	33(53%)	25(40%)	0.15[b]	38(61%)	20(32%)	0.001[b]
Age	68 (10)	66 (7)	0.65[a]	68 (9)	66 (8)	0.24[a]
BMI	31 (6)	29 (4)	0.049[a]	30 (6)	29(4)	0.29[a]
Modified KL (2, 3A, 3B, 4A, 4B)	0, 7, 17, 20, 18	1, 7, 6, 23, 25	0.08[b]	0, 6, 14 16, 26	1, 8, 9, 27, 17	0.11[b]
	Alignment			Alignment		
Preoperative	175 (5)	176 (6)	0.12[a]	176 (6)	175 (5)	0.09[a]
Follow up	179 (2)	179(3)	0.19[a]	179 (3)	179 (3)	0.09[a]
	Patient reported outcome			Patient reported outcome		
OKS	38 (7)	39 (7)	0.42[a]	39 (6)	38 (8)	0.23[a]
OKS MCID	54 (87%)	55 (89%)	0.78[b]	55 (89%)	54 (87%)	0.78[b]
Crude OR OKS MCID	0.9 (0.3-2)	Ref.	0.78[c]	1.2 (0.4-3)	Ref.	0.78[c]
Adjusted OR OKS MCID	1.1 (0.3-3)	Ref.	0.88[c]	1.2 (0.4-4)	Ref.	0.73[c]
FJS	52 (30)	56 (28)	0.37[a]	57 (26)	51 (31)	0.29[a]
FJS MCID	48 (77%)	51 (82%)	0.50[b]	54 (87%)	45 (73%)	0.04[b]
Crude OR FJS MCID	0.7 (0.3-2)	Ref.	0.50[c]	2.6 (1-7)	Ref.	0.048[c]
Adjusted OR FJS MCID	0.7 (0.3-2)	Ref.	0.44[c]	2.4 (0.9-6)	Ref.	0.09[c]
OKS APQ	51 (32)	59 (33)	0.16[a]	56 (32)	54 (33)	0.74[a]
EQ-5D	.82 (.2)	.84 (.2)	0.58[a]	.83 (.1)	.83 (.2)	0.77[a]
	Performance based outcome			Performance based outcome		
Chair-stand test	12.1 (3)	12.4 (4)	0.79[a]	12.0 (3)	12.5 (3)	0.44[a]
Fast-paced walk test	8.0 (3)	8.5 (2)	0.30[a]	8.2 (3)	8.3 (8)	0.94[a]
Stair climb test	27.3 (6)	27.1 (5)	0.59[a]	27.3 (6)	27.2 (6)	0.90[a]

Number (percentage), mean (SD) or odds ratio (95% CI), [a)]Students t-test, [b)]Chi squared test or Fischer’s exact test, [c)]logistic regression

Table 4.3.4 Comparison of tight and lax knees in flexion (modified from paper III)

	FLEXION					
	Medial laxity			**Lateral laxity**		
	Tight: <2.2°	Lax: >2.2°	p-value	Tight: <4.8°	Lax: >4.8°	p-value
N	62	62	-	62	62	-
	Demographics			Demographics		
Male sex	23 (37%)	35 (56%)	0.03[b]	40 (65%)	22 (35%)	0.000[b]
Age	68 (8)	67 (9)	0.51[a]	69 (9)	66 (8)	0.03[a]
BMI	29 (5)	30(5)	0.80[a]	29 (5)	30 (5)	0.16[a]
Modified KL (2, 3A, 3B, 4A, 4B)	0,10, 16 21, 15	1, 4, 7, 22, 28	0.02[b]	0, 6, 15, 21, 22	1, 8, 8, 22,23	0.46[b]
	Alignment			Alignment		
Preoperative	176 (6)	175 (6)	0.15[a]	176 (6)	175 (6)	0.68[a]
Follow up	180 (2)	179 (3)	0.08[a]	179 (2)	179 (3)	0.91[a]
	Patient reported outcome			Patient reported outcome		
OKS	38 (6)	39 (8)	0.42[a]	39 (7)	38 (7)	0.72[a]
OKS MCID	54 (87%)	55 (89%)	0.78[b]	50 (81%)	59 (95%)	0.01[b]
Crude OR OKS MCID	0.9 (0.3-3)	Ref.	0.78[c]	0.2 (0.1-1)	Ref.	0.02[c]
Adjusted OR OKS MCID	1.2 (0.4-4)	Ref.	0.77[c]	0.2 (0.04-1)	Ref.	0.02[c]
FJS	51 (29)	57 (28)	0.20[a]	56 (30)	52 (28)	0.39[a]
FJS MCID	48 (77%)	51 (82%)	0.50[b]	50 (81%)	49 (79%)	0.82[b]
Crude OR FJS MCID	0.7 (0.3-2)	Ref.	0.50[c]	1.1 (0.5-3)	Ref.	0.82[c]
Adjusted OR FJS MCID	0.7 (0.3-2)	Ref.	0.55[c]	0.8 (0.3-2)	Ref.	0.68[c]
OKS APQ	52 (33)	58 (32)	0.23[a]	54 (34)	56 (31)	0.81[a]
EQ-5D	.82 (.2)	.84 (.2)	0.67[a]	.83 (.2)	.83 (.2)	0.78[a]
	Performance based outcome			Performance based outcome		
Chair-stand test	12 (3)	12.5 (3)	0.35[a]	12.1 (3)	12.5 (3)	0.48[a]
Fast-paced walk test	8.4 (2)	8.0 (2)	0.38[a]	8.3 (3)	8.2 (2)	0.94[a]
Stair climb test	27.3 (5)	27.2 (6)	0.86[a]	27.6 (6)	26.6 (5)	0.50[a]

Number (percentage), mean (SD) or odds ratio (95% CI), [a)]Students t-test, [b)]Chi squared test or Fischer's exact test, [c)]logistic regression

Table 4.3.5: Results of coronal laxity measurement at 1-year follow-up (modified from paper III)

		n=124	Range
Extension	Medial	2.6 (1.2)	0.4-7.3
	Lateral	3.6 (1.6)	0.5-8.3
Flexion	Medial	2.6 (1.6)	0.3-11.5
	Lateral	5.2 (2.9)	0-17

Laxity measured in degrees, mean (SD)

Figure 4.3.4: Laxity in extension (modified from paper III)

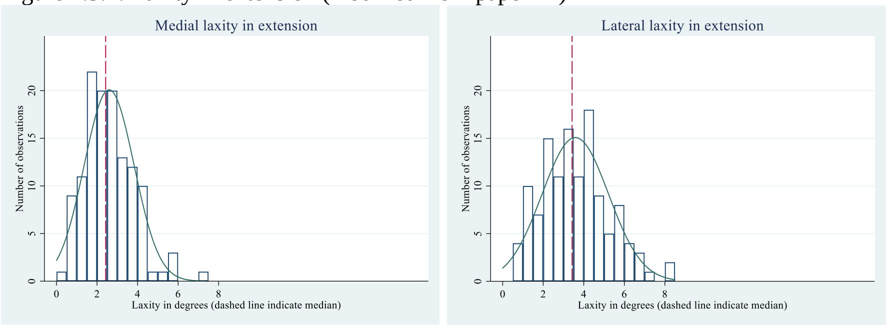
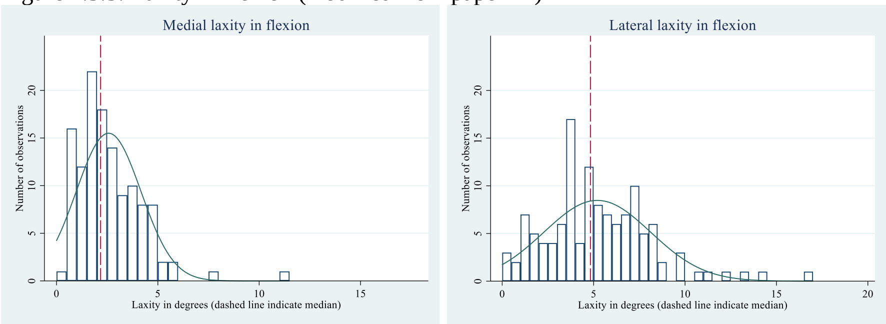


Figure 4.3.5: Laxity in flexion (modified from paper III)



5. Discussion and limitations

5.1. Study I: Systematic review

The reviewed studies were all cohort studies with follow up examinations, however heterogeneity regarding study population, surgical technique, implant constraint, time to follow up, method/conditions for laxity measurement, choice of outcome score and statistical methods was found (table 4.1.1-2). Using qualitative analysis, we conclude that from full extension to 60 degrees of flexion no significant association between laxity and outcome scores could be established. In flexion we conclude that sagittal laxity between 5 and 10mm in CR knees is associated with superior results. For coronal laxity only 2 studies reported on laxity measurement in flexion, the very different approaches for stratification in these two studies made direct comparison difficult, however we cautiously conclude that superior results were associated with medial coronal laxity below 4 degrees at 80 to 90 degrees of knee flexion.

Statistical methods differed between studies. In 9 cases Spearman or Pearson correlation was reported and in 9 cases the results were stratified based on the measured laxity and differences analyzed. In most cases laxity measurements were done under different conditions and more than one outcome score was used, this exploratory approach resulted in multiple analyses. However, this approach increases the risk of false positive results, with a significance level at 5% it can be expected that 5% of the analysis might be false positive. An example could be the paper from Matsumoto et al. [85] where laxity at 3 different angulations each are correlated to 4 KOOS sub scores, resulting in 12 analyses and only 1 significant correlation.

It must be assumed that the laxity measured at follow up is not entirely a result of the surgery, preoperative conditions such as degree of KOA, knee alignment, preoperative laxity and even patient demographics might to some extent influence this. The exact impact of all these preoperative conditions is largely unknown, however preoperative conditions might also influence outcome and must to some extent act as a confounder on the association between laxity at follow up and outcome. This is the case both when studying correlation and comparing stratified groups and this might lead to false conclusion on the impact of laxity that are in fact due to preoperative differences not accounted for.

Methods used to quantify laxity in the reviewed studies differed between sagittal measurements of laxity using arthrometer type devices or stress radiography and coronal measurement using stress radiography. Only one arthrometer devices has, to our knowledge, been validated in quantification of sagittal laxity following TKA[92]. No reports of validation of the stress radiographic methods in the assessment of TKA laxity were found.

The choice of outcome scores in the reviewed papers could also be questioned. With the aim to reveal differences in otherwise well-functioning TKA caused by variations in soft tissue laxity, the ideal outcome score should allow differentiation between these good results without clustering of these (ceiling effect). Several of the outcome scores used do not meet this criterion.

Having the ambition to identify optimal laxity following TKA further knowledge could have been extracted from studies describing the impact of intraoperative laxity measurement on outcome. This would have increased the number of eligible papers considerably, but it would also increase the number of different methods for laxity quantification correspondingly. While follow-up measurement of laxity is measured with 2 main methods (stress radiographs and arthrometer) intraoperative measurements are measured with a multitude of tools (spacer blocks, spatulas, spreaders, tensors, load-sensors, navigations systems) and further heterogeneity of methods would follow. Restricting the systematic review to studies reporting on follow-up laxity measurements was chosen as this was the method we were using for the following studies.

In conclusion: limits of optimal laxity were established from the reviewed papers in study I. However, further evidence is demanded due to several factors. The number of studies meeting criteria was only 14. Within these heterogeneity regarding methods for quantification of laxity and evaluation of outcome was obvious. Methodological concerns were raised for most studies and a number might be underpowered. Statistical methods differed, and in studies comparing groups stratified on basis of laxity measurements, between group differences were not accounted for and might bias the obtained results. Further evidence on the relationship between TKA laxity and outcome is warranted.

5.2. Study II: Reliability

Excellent reliability was demonstrated for test-retest TSD measurement, with narrow 95% CI of the ICC that did not cross the limit to good reliability. EV measurement reliability did show wider 95% CI of the ICC. EV medial laxity measurement showed excellent reliability but the 95% CI just crossed the limit to good reliability. EV lateral laxity showed moderate reliability, but the 95% CI crossed good reliability and was very wide. Larger sample size would have narrowed the 95% CI, and this would be appropriate for the EV measurements.

When using stress radiography in the evaluation of individual cases or for scientific purposes, awareness of the LOA is important. We believe that the limits of LOA for TSD and EV medial laxity allows using the methods to be used in the clinic, however the wide LOA for EV lateral laxity might limits is relevance.

Intra- and inter-rater agreement were excellent and measurements of angulation between TKA components can be done precisely with a PACS viewer that allows magnification.

The external validity of our results might be restricted by the inclusion criteria. Excessive subcutaneous tissue and weight might influence both angulation and effect of the load applied on joint. Any extremity pain or pain sensitization might cause muscle contraction and influence results.

Only one previous study reporting reliability between repeated stress radiographs could be identified [93]. In this previous study TKA knees are examined in flexion using fluoroscopy and manual stress, 12 TKA knees are examined by 2 different observers. ICC, for all the measurements was found to be 0.93 (95% CI 0.84-0.97) our comparable results for all the EV measurements are inferior with ICC of 0.83 (95% CI 0.75-0.88). It seems that this method using fluoroscopy and continuous visualization of the joint space, which might allow optimized control over both rotation of the lower leg and direction of the traction, is superior to the EV stress radiography. However; Stähelin et al., did not analyze results for medial and lateral laxity separately, and it is unclear to which extent reliability of the measurement of medial laxity are improved. Unfortunately, fluoroscopy and manual traction exposes the examiner to radiation and therefore is not feasible in most radiological departments.

Previous reports on results of stress radiography using the TSD [65,67,94–96] or the EV [66,67,95,97] view have reported consistent results, this might indicate that the results are not affected by minor methodological variations between clinics (table 5.2.1).

Manual evaluation of TKA coronal laxity in extension and flexion is the classical method to evaluate soft tissue laxity intraoperatively, the stress radiographic method replicates these examinations in a validated standardized follow up setting.

Stress radiographs can be supplemented with sagittal laxity arthrometer measurements, where the KT1000 is validated for TKA laxity[92]. Although proven reliable, both these methods are cumbersome in the clinical setting and in most clinics not available. The methods provide information on laxity in specific directions and at specific angles. The ideal laxity instrument would be clinically accessible and deliver reliable quantified information of both laxity and knee kinematics. Such an instrument would be valuable in the assessment of possible mechanical failure following TKA.

Table 5.2.1: Mean results from study II and previous studies (modified from paper II).

		Extension (Telos)		Flexion (Epicondylar view)	
		Medial laxity	Lateral laxity	Medial laxity	Lateral laxity
Current study	***N=15***	***4.0±2.5° (0.5-9.5°)***	***4.6±2.3° (0.7-10.6°)***	***3.8 ±2.5° (0.5-10.7°)***	***8.0±4.1° (1.7-17.3°)***
Tsukiyama et al. The Knee 2017	N=50	4.0±2.4° (0-9.0°)	4.0±2.5° (0-10.0°)	3.9±2.6° (0-10.0°)	6.2±4.4° (0-22.3°)
Nakahara et al. KSSTA 2015	N=15	5.0±1.6° (1.5-9.0°)	5.9±2.7° (1.0-12.7°)		
Yoshihara et al. KSSTA 2015	N=49	3±2° (0-7°)	5±3° (0–11°)	4±3° (0–9°)	6±4° (0–20°)
Oh et al. Arch Orthop Trauma Surg 2015	N=61			4.1±2.1° (0.4-12.6°)	4.7±2.4° (0.4-12.1°)
Kobayashi et al. J Arthroplasty 2012	N=41			3.4±1.4°	6.2±2.5°
Seon et al. Int Orthop. 2007	N=42	3.5±1.4° (1.1-6.8°)	4.4±1.4 (0.8-9.3°)		
Matsuda et al. Clin Orthop 2004	N=30	4.0±1.7°	3.5±1.0°		
Ishii et al. J Orthop Sci 2003	N=53	4.8±.2.1°	4.5±2.8°		

Mean laxity ±SD (range)

5.3 Study III: Cohort

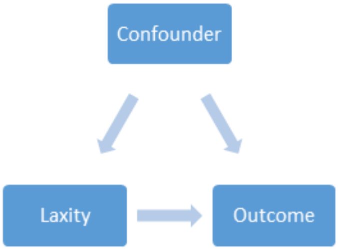
Patient baseline characteristics were comparable to values reported by DKR[3] and the number of patient not achieving MCID was similar to earlier reports[79]. The 22% alignment outliers (figure 4.3.2) is in line with previous reports using conventional instruments [98,99].

Secondary aim: Laxity at follow up
When comparing results of the laxity measurement (table 4.3.5) with previously reported values (table 5.2.1), mean medial laxity was lower and, lateral laxity comparable to the lowest numbers previously reported. SD and range were generally in the lower end when compared. Both measured resection technique and sparing of the posterior cruciate ligament might contribute to the results. Oh et al.[66], reported on balanced resection technique and succeeded in obtaining comparable values of medial and lateral laxity in flexion, our results were more medially tight and laterally loose. Reports on laxity following posterior cruciate sacrificing technique, showed more laxity than in the present study [67,94], which is to be expected [100].

Surgeon awareness of both study aims and previous reports of superior results in medial tight knees, might have affected surgeons to promote intraoperative medial stability in this prospective study.

Secondary aim: Differences in pre-operative factors between tight and lax knees.
Gender differences in preoperative laxity has been reported earlier[7], and the significant differences between lax and tight knees shown at TKA follow up might reflect this (table 4.3.3 and 4.3.4). More females had lax knees, except medial laxity in flexion where more males where lax, however, this could be a result of different wear patterns between sexes, resulting in different degrees of femoral component external rotation when using the posterior condyles as reference. OA severity did significantly differ between knees tight and lax medial in flexion, with the highest severity in the lax group. As mentioned above this might be related to femoral component rotation, and result from increased femoral external rotation in cases with more posterior femoral condyle wear medial than lateral, furthermore OA-severity has been associated to increased laxity[7,101]. Age was highest in the tight groups, but only significant for lateral laxity in flexion.

The differences in preoperative characteristics between tight and lax knees could reflect that intraoperative TKA balancing did not sufficiently correct the preoperative condition to meet goals of balancing, or that the surgeon's limits of acceptable balance intraoperatively are wide enough to include preoperative conditions. Intraoperative soft tissue balancing was performed without any objective measurement of laxity and we assume that the individual surgeon must have a range of laxity that is found to be acceptable. To minimize the effect of preoperative characteristics on follow-up laxity we believe that objective intraoperative measurement of laxity should be used to further guide the surgeons. We must assume that this observed relation between laxity and preoperative characteristics is a general phenomenon and not isolated to our study cohort. When examining any relation between laxity and outcome, preoperative factors might both be associated to laxity and outcome and act as confounders. This should be remembered when interpreting published result. In the clinical work, surgeons should be aware that both female gender and lower age could be related to increased laxity and that both have been associated with increased risk of early re-operation for instability[102].



Primary aim: Differences in outcome between tight and lax knees at follow up
In our study cohort there were no significant differences in outcome between tight and lax knees in any of the four coronal laxity modalities tested (table 4.3.3 and 4.3.4). The significant result on reaching FJS MCID for lateral laxity in extension might be caused by preoperative differences between groups lax and tight, since the adjusted OR did not reach significance, furthermore the 95% CI is wide for both the crude and adjusted OR. The results for lateral laxity in flexion, with significant more in the lax group obtaining OKS MCID, with significant crude and adjusted OR for this, might however be a false positive result (type II error). The 95% CI are wide, and the result is contradicted by insignificant results for FJS MCID and all other PRO showing differences in favor of the tight group.

Previously published results on coronal laxity in extension, correspond to our results, not showing any significant relation between laxity and outcome[67,94,103]. One previous author have compared lateral tight and lax knees in flexion, without finding significant differences in outcome[67]. In two previous reports laxity in flexion have been related to outcome. Tsukiyama et al.[67] compared tight and lax knees following measured resection, posterior cruciate sacrificing TKA and reported significant better outcomes for medial tight knees in a cohort of 50 knees. There was no significant age difference between the groups, however no other preoperative conditions were compared. Mean medial laxity in flexion was 3.9 degrees and the division between tight and lax knees was at 3 degrees, in our cohort the mean laxity was 2.6 degrees and the division between tight and lax knees was at 2.2 degrees, dividing our results at 3 degrees did not results in any significant results. Oh et al.[66] reported on laxity in flexion following balanced resection CR TKA in 61 knees, however the results were analyzed with focus on flexion balance. 51 knees were balanced with less than

3 degrees difference between medial and lateral laxity, these balanced knees were further divided into 3 subgroups based on the sum of medial and lateral laxity. Significant better results were reported for balanced knees compared to unbalanced and significant better results was reported for balanced knees with the sum of medial and lateral laxity between 6 and 10 degrees compared to less or more laxity. Mean medial laxity was 4.1 degrees. No significant differences in patient demographics between balanced and unbalanced knees were found, but only 10 participants were unbalanced, significant preoperative differences in range of motion between groups was reported, however. When using this method for analysis on the results from our cohort, we could not confirm any of the significant findings reported by Oh et al. Differences in surgical technique and mean laxity might cause that result from previous report could not be confirmed. Furthermore, gender distribution in our cohort was 47% males, but in the cohorts studied by Tsukiyama et al. and Oh et al., 22% and 21% were males. Patient demographics and threshold for intervention might vary between Asian and Danish patient[104] and the expectations towards activities demanding knee stability in flexion might also vary[105].

The inconclusive results in our study might be due to the mean values and SD obtained for medial laxity, which were lower than previously reported. No negative effect of this limited laxity was found, neither in the mean results for the cohort or in the comparison of tight and lax knees. Medial stability in flexion with laxity less than 3-4mm when measured intraoperative [55,73], and less than 3 degrees when measured at follow up, have been associated to superior results. This is further supported by kinematic analyses that emphasizes the importance of medial stability [74,75]. Results from this study are not in contradiction to this and we believe in the importance of medial knee stability and in the recommendations from previous authors.

Recently the concept of individualized alignment goals, that are based on the patients constitutional alignment, have again been given great attention in the hope that this approach where the TKA to a higher extent is adapted to the soft tissues envelope will result in better TKA kinematics and improved outcomes[37]. However, contradictory results on the superiority of this technique compared to mechanical alignment have been reported[44].

The use of OARSI core set of PBT did not reveal any differences between tight and lax knees, as this also was the case for the PRO outcomes, this study does not clarify whether the use of PBT is relevant as a supplement to the PRO.

Limitations

The complex TKA kinematics are only to some extent described by coronal laxity measured in extension and in flexion. Ideally, multidirectional laxity in the whole range of motion should be analyzed, however, clinically applicable tools for quantified follow-up measurements of laxity are limited to stress radiography and arthrometer devices.

By including a consecutive group of participants, we tried to minimize selection bias. However nearly half of the population screened for inclusion did not meet criteria, and not all allocated to intervention received surgery in the study period (study flow chart, figure 4.3.1). The inclusion criteria of both walking ability and internet use might have excluded the most elderly and weak in the population planned for TKA. The use of multiple online questionnaires might have exhausted participants and might have caused imprecisions in answers. No patient was lost in the project and only 1 patient declined physical follow-up, incomplete follow-up excluded 15 patients from analysis.
Results of the laxity measurements showed less laxity than previously reported, whether this is a result of the surgical technique that is the predominant in Denmark or only related to participating surgeons cannot be answered with certainty. However, we believe that the laxity obtained is representative of what is achieved in general using this technique, and that the external validity is high.

Outcome following TKA is affected by a multitude of factors[4,5,26,28], and we found that some of these preoperative factors could also be related to the laxity measurements. By further restriction in the inclusion criteria the effect of these confounding factors could have been reduced, however this would also reduce external validity.

6. Conclusions

The relationship between measurements of laxity and outcome following TKA was systematically reviewed in study I. Heterogeneity regarding both methods used for laxity measurements and choice of outcome measures in the reviewed studies was revealed. Methodologically concerns could be raised for all studies. *Cautiously it was concluded that favorable results following TKA could be related to sagittal laxity from 5 to 10mm in CR TKA and to medial laxity in flexion below 4 degrees. Careful intraoperative monitoring and adjustment of laxity was recommended. However further evidence on the relation between laxity and outcome was demanded.*

Agreement and reliability of coronal stress radiography following TKA, were investigated in study II. Repeated stress radiographs (test-retest) and comparison of measurement from 3 independent raters was analyzed, reliability was described with intra class correlation coefficients (ICC) and 95% CI, and agreement with Bland-Altman plots, limits of agreement and systematic error. Intra- and inter-rater reliability was excellent. *Reliability for the repeated radiographs was excellent in extension using the Telos stress device, and limits of agreement deemed satisfactory. In flexion the epicondylar view stress radiographs reliability was good to excellent for medial laxity but only moderate to good for measurements of lateral laxity, the 95% confidence intervals were especially wide for lateral laxity. Limits of agreement were satisfactory for medial laxity measurements.*

Study III was initiated to generate further evidence on the relationship between laxity and outcome following TKA, and to monitor actual limits of laxity with the surgical technique used at the PhD student's institution. *The mean values for medial laxity found were lower than those previously reported and with the laxity obtained no significant difference between tight or lax knees were found. These results might bring confidence to surgeons regarding the surgical technique used. Significant results from previous reports on the implication of medial laxity in flexion could not be confirmed. Preoperative conditions such as gender, age and degree of OA differed significantly between groups with tight and lax knees. This relation between preoperative factors and postoperative laxity should be taken into consideration when planning and interpreting studies on laxity.*

7. Future perspectives

While, further confidence in the surgical technique used at our clinic and the value of careful intraoperative monitoring of laxity in TKA surgery was supported, unsolved problems were also evident.

The percentages not attaining MCID in the outcome scores, correspond to what is consistently reported by other authors. To reduce these percentages, results from the extensive publications on this topic should be further included in the threshold for surgical intervention and in the shared decision making. Scientifically, the Nordic countries might have advantages in the further clarification of the threshold for intervention, through the accessibility of health data from national registers.

Surgical outliers were present in study III, 22% did not achieve the goal of neutral alignment, and the range of coronal laxity was wide. Surgeons must strive to reduce the occurrence of outliers. Meticulous surgery, education and sparring between specialist should be further promoted. It should be investigated whether further systemized preoperative planning, intra-operative feed-back and postoperative evaluation might be effective in reducing outliers.

Measurements of laxity by either sagittal or coronal measurement is a simplified way to quantify laxity. Much attention has been given to mid-flexion laxity, and researchers at Aalborg University have developed a set up to measure multidirectional laxity in mid-flexion, collaboration between the researchers and our study group have been initiated. Reliability and relation to outcome following TKA for this new method will be investigated.

The relation between individual factors and laxity should be investigated further, whether individual pre-OA laxity and alignment is superior to mechanical alignment and whether all will benefit from the same amount of laxity following TKA remains to be clarified. It could be hypothesized that instrumented intraoperative quantification of laxity would guide surgeons toward more balanced knees and a reduction of the impact of the preoperative factors. Another hypothesis could be that individuals with more native laxity might benefit from more TKA constraint, as provided by more congruent inserts.

Instability is internationally amongst the top 3 reasons for TKA revision and according to Danish Knee Arthroplasty Register currently the most frequent reason stated to do revision surgery in Denmark. However, the high incidence found in the register needs further attention, it is unclear whether the incidence is caused by inadequate primary surgery, changes in laxity following surgery, wrong classification or other factors. Preoperative conditions related to instability and timing of these revisions, was analyzed and presented as a poster presentation at the 2018 EFORT meeting (Supplementary material C), it was found that mean time from primary surgery to revision due to instability was 2.6 years, and it must be assumed that some of these revisions could be prevented. Research on preoperative characteristics related to early revision due to instability, analysis of the surgical techniques used in primary and revision surgery, and the degree of improvement experienced by the patients following revision also seems needed.

References

[1] Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet 2019;393:1745–59. doi:10.1016/S0140-6736(19)30417-9.

[2] Price AJ, Alvand A, Troelsen A, Katz JN, Hooper G, Gray A, et al. Knee replacement. Lancet 2018;392:1672–82.

[3] Dansk Knæalloplastikregister Årsrapport 2020.

[4] Gunaratne R, Pratt DN, Banda J, Fick DP, Khan RJK, Robertson BW. Patient Dissatisfaction Following Total Knee Arthroplasty: A Systematic Review of the Literature. J Arthroplasty 2017;32.

[5] Husain A, Lee G. Establishing Realistic Patient Expectations Following Total Knee Arthroplasty. J Am Acad Orthop Surg 2015;23:707–13.

[6] Sundhedsstyrelsen. Knæartrose - nationale kliniske retningslinjer og faglige visitationsretningslinjer. 2012. doi:papers3://publication/uuid/0F9354D1-8C22-4345-8205-13087119BACB.

[7] Freisinger GM, Schmitt LC, Wanamaker AB, Siston RA, Chaudhari AMW. Tibiofemoral Osteoarthritis and Varus-Valgus Laxity. J Knee Surg 2017;30:440–51.

[8] Tanamas S, Hanna FS, Cicuttini FM, Wluka AE, Berry P, Urquhart DM. Does knee malalignment increase the risk of development and progression of knee osteoarthritis? A systematic review. Arthritis Care Res 2009;61:459–67.

[9] Bellemans J, Vandenneucker H, Vanlauwe J, Victor J. The influence of coronal plane deformity on mediolateral ligament status: An observational study in varus knees. Knee Surgery, Sport Traumatol Arthrosc 2010;18:152–6.

[10] Nelson AE, Allen KD, Golightly YM, Goode AP, Jordan JM. A systematic review of recommendations and guidelines for the management of osteoarthritis: The Chronic Osteoarthritis Management Initiative of the U.S. Bone and Joint Initiative. Semin Arthritis Rheum 2014;43:701–12.

[11] Ha CW, Park YB, Kim SH, Lee HJ. Intra-articular Mesenchymal Stem Cells in Osteoarthritis of the Knee: A Systematic Review of Clinical Outcomes and Evidence of Cartilage Repair. Arthrosc - J Arthrosc Relat Surg 2019;35:277–288.e2.

[12] Kim SH, Djaja YP, Park YB, Park JG, Ko YB, Ha CW. Intra-articular Injection of Culture-Expanded Mesenchymal Stem Cells Without Adjuvant Surgery in Knee Osteoarthritis: A Systematic Review and Meta-analysis. Am J Sports Med 2020;48:2839–49.

[13] Duivenvoorden T, Brouwer R, Rw B, Tm VR, Ap V, Jan V, et al. Braces and orthoses for treating osteoarthritis of the knee (Review). Cochrane Database Syst Rev 2015:54 pág.

[14] Takahashi T, Baboolal TG, Lamb J, Hamilton TW, Pandit HG. Is Knee Joint Distraction a Viable Treatment Option for Knee OA?-A Literature Review and Meta-Analysis. J Knee Surg 2019;32:788–95.

[15] Goh EL, Lou WCN, Chidambaram S, Ma S. The role of joint distraction in the treatment of knee osteoarthritis: A systematic review and quantitative analysis. Orthop Res Rev 2019;11:79–92.

[16] Brouwer RW, Huizinga MR, Duivenvoorden T, van Raaij TM, Verhagen AP, Bierma-Zeinstra SMA, et al. Osteotomy for treating knee osteoarthritis. Cochrane Database Syst Rev 2014;2014.

[17] van Outeren M V., Waarsing JH, Brouwer RW, Verhaar JAN, Reijman M, Bierma-Zeinstra SMA. Is a high tibial osteotomy (HTO) superior to non-surgical treatment in patients with varus malaligned medial knee osteoarthritis (OA)? A propensity matched study using 2 randomized controlled trial (RCT) datasets. Osteoarthr Cartil 2017;25:1988–93.

[18] Amendola A, Bonasia DE. Results of high tibial osteotomy: Review of the literature. Int Orthop 2010;34:155–60.

[19] The Swedish Knee Arthroplasty Register Annual Report 2020.

[20] Murray DW, Parkinson RW. Usage of unicompartmental knee arthroplasty. Bone Jt J 2018;100B:432–5.

[21] Beard DJ, Davies LJ, Cook JA, MacLennan G, Price A, Kent S, et al. The clinical and cost-effectiveness of total versus partial knee replacement in patients with medial compartment osteoarthritis (TOPKAT): 5-year outcomes of a randomised controlled trial. Lancet 2019;394:746–56.

[22] Odgaard A, Madsen F, Kristensen PW, Kappel A, Fabrin J. The mark coventry award: Patellofemoral arthroplasty results in better range of movement and early patient-reported outcomes than TKA. Clin Orthop Relat Res 2018;476:87–100.

[23] Chawla H, van der List JP, Christ AB, Sobrero MR, Zuiderbaan HA, Pearle AD. Annual revision rates of partial versus total knee arthroplasty: A comparative meta-analysis. Knee 2017;24:179–90.

[24] El-Galaly A, Kappel A, Nielsen PT, Jensen SL. Revision Risk for Total Knee Arthroplasty Converted from Medial Unicompartmental Knee Arthroplasty. J Bone Joint Surg Am. 2019 Nov 20;101(22):1999-2006.

[25] Mortensen JF, Rasmussen LE, Østgaard SE, Kappel A, Madsen F, Schrøder HM, et al. Randomized clinical trial of medial unicompartmentel versus total knee arthroplasty for anteromedial tibio-femoral osteoarthritis. The study-protocol. BMC Musculoskelet Disord 2019;20:119.

[26] Dowsey MM, Spelman T, Choong PFM. Development of a Prognostic Nomogram for Predicting the Probability of Nonresponse to Total Knee Arthroplasty 1 Year After Surgery. J Arthroplasty 2016;31:1654–60.

[27] Smith SR, Bido J, Collins JE, Yang H, Katz JN, Losina E. Impact of Preoperative Opioid Use on Total Knee Arthroplasty Outcomes J Bone Joint Surg Am. 2017 May 17;99(10):803-808.

[28] Ba JWC, Galea VP, Ba PR, Nielsen CS, Bragdon CR, Kappel A, et al. Which Preoperative Factors are Associated with Not Attaining Acceptable Levels of Pain

and Function After TKA ? Findings from an International Multicenter Study Clin Orthop Relat Res. 2020 May;478(5):1019-1028.

[29] Jørgensen CC, Jacobsen MK, Soeballe K, Hansen TB, Husted H, Kjærsgaard-Andersen P, et al. Thromboprophylaxis only during hospitalisation in fast-track hip and knee arthroplasty, a prospective cohort study. BMJ Open 2013;3:1–10.

[30] Nakano N, Shoman H, Olavarria F, Matsumoto T, Kuroda R, Khanduja V. Why are patients dissatisfied following a total knee replacement? A systematic review. Int Orthop. 2020 Oct;44(10):1971-2007

[31] Bjerregaard HH, Svarre T, Kruse C, Gaardboe R, Laursen M. Using Patient-Reported Outcomes in Real-Time Shared Decision-Making. Proc. 17th Scand. Conf. Heal. Informatics, 12 -13 Nov 2019, Oslo Norw., 2019, p. 22–3.

[32] Paley D. Principles of Deformity Correction. 1st ed. 200. Springer-Verlag Berlin Heidelberg New York; 2002.

[33] Jaffe WL, Dundon JM, Camus T. Alignment and balance methods in total knee arthroplasty. J Am Acad Orthop Surg 2018;26:709–16.

[34] Berend ME, Ritter MA, Meding JB, Faris PM, Keating EM, Redelman R, et al. Tibial component failure mechanisms in total knee arthroplasty. Clin Orthop Relat Res 2004:26–34.

[35] Lee B, Cho H, Bin S, Kim J, Jo B. Femoral Component Varus Malposition is Associated with Tibial Aseptic Loosening After TKA. Clin Orthop Relat Res 2018;476:400–7.

[36] Pijls BG, Nelissen RGHH, Plevier JWM. RSA migration of total knee replacements: A systematic review and meta-analysis. Acta Orthop. 2018 Jun;89(3):320-328.

[37] Oussedik S, Abdel MP, Victor J, Pagnano MW, Haddad FS. Alignment in total knee arthroplasty. Bone Joint J 2020;102–B:276–9.

[38] Rivière C, Iranpour F, Auvinet E, Howell S, Vendittoli PA, Cobb J, et al. Alignment options for total knee arthroplasty: A systematic review. Orthop Traumatol Surg Res 2017;103:1047–56.

[39] Bellemans J, Colyn W, Vandenneucker H, Victor J. The Chitranjan Ranawat Award Is Neutral Mechanical Alignment Normal for All Patients? The Concept of Constitutional Varus. Clin Orthop Relat Res 2012;470:45–53.

[40] Howell SM, Papadopoulos S, Kuznik KT, Hull ML. Accurate alignment and high function after kinematically aligned TKA performed with generic instruments. Knee Surgery, Sport Traumatol Arthrosc 2013;21:2271–80.

[41] Hutt JRB, LeBlanc MA, Massé V, Lavigne M, Vendittoli PA. Kinematic TKA using navigation: Surgical technique and initial results. Orthop Traumatol Surg Res 2016;102:99–104.

[42] Nedopil AJ, Singh AK, Howell SM, Hull ML. Does Calipered Kinematically Aligned TKA Restore Native Left to Right Symmetry of the Lower Limb and Improve Function? J Arthroplasty 2018;33:398–406.

[43] Hirschmann MT, Becker R, Tandogan R, Vendittoli PA, Howell S. Alignment in TKA: what has been clear is not anymore! Knee Surgery, Sport Traumatol Arthrosc 2019;27:2037–9.

[44] Roussot MA, Vles GF, Oussedik S. Clinical outcomes of kinematic alignment versus mechanical alignment in total knee arthroplasty: A systematic review. EFORT Open Rev 2020;5:486–97.

[45] Almaawi AM, Hutt JRB, Masse V, Lavigne M, Vendittoli PA. The Impact of Mechanical and Restricted Kinematic Alignment on Knee Anatomy in Total Knee Arthroplasty. J Arthroplasty 2017;32.

[46] Tanaka Y, Nakamura S, Kuriyama S, Nishitani K, Ito H, Lyman S, et al. Intraoperative physiological lateral laxity in extension and flexion for varus knees did not affect short-term clinical outcomes and patient satisfaction. Knee Surg Sports Traumatol Arthrosc. 2020 Dec;28(12):3888-3898

[47] Aunan E, Kibsgård TJ, Diep LM, Röhrl SM. Intraoperative ligament laxity influences functional outcome 1 year after total knee arthroplasty. Knee Surgery, Sport Traumatol Arthrosc 2015;23:1684–92.

[48] Elmallah RK, Mistry JB, Cherian JJ, Chughtai M, Bhave A, Roche MW, et al. Can We Really "Feel" a Balanced Total Knee Arthroplasty? J Arthroplasty 2016;31:102–5.

[49] MacDessi SJ, Gharaibeh MA, Harris IA. How Accurately Can Soft Tissue Balance Be Determined in Total Knee Arthroplasty?v Arthroplasty. 2019 Feb;34(2):290-294.e1.

[50] Aunan E, Kibsgård T, Clarke-Jenssen J, Röhrl SM. A new method to measure ligament balancing in total knee arthroplasty: laxity measurements in 100 knees. Arch Orthop Trauma Surg 2012;132:1173–81.

[51] Matsumoto T, Muratsu H, Kawakami Y, Takayama K, Ishida K, Matsushita T, et al. Soft-tissue balancing in total knee arthroplasty: Cruciate-retaining versus posterior-stabilised, and measured-resection versus gap technique. Int Orthop 2014;38:531–7.

[52] Gustke KA. Soft-tissue and alignment correction: The use of smart trials in Total knee replacement. Bone Jt J 2014;96B:78–83.

[53] Nodzo SR, Franceschini V, Gonzalez Della Valle A. Intraoperative Load-Sensing Variability During Cemented, Posterior-Stabilized Total Knee Arthroplasty. J Arthroplasty 2016:1–5.

[54] van Lieshout WAM, Valkering KP, Koenraadt KLM, van Etten-Jamaludin FS, Kerkhoffs GMMJ, van Geenen RCI. The negative effect of joint line elevation after total knee arthroplasty on outcome. Knee Surgery, Sport Traumatol Arthrosc 2019;27:1477–86.

[55] Bottros J, Gad B, Krebs V, Barsoum WK. Gap Balancing in Total Knee Arthroplasty. J Arthroplasty 2006;21:11–5.

[56] Babazadeh S, Stoney JD, Lim K, Choong PFM. The relevance of ligament balancing in total knee arthroplasty: how important is it? A systematic review of the literature.

Orthop Rev (Pavia). 2009 Oct 10;1(2):e26.

[57] Leo A. W. Ligament balancing in total knee arthroplasty. 3rd ed. Springer -Verlag Berlin Heidelberg New York: 2004.

[58] List R, Schütz P, Angst M, Ellenberger L, Dätwyler K, Ferguson SJ, et al. Videofluoroscopic Evaluation of the Influence of a Gradually Reducing Femoral Radius on Joint Kinematics During Daily Activities in Total Knee Arthroplasty. J Arthroplasty 2020;35:3010–30.

[59] Verra WC, Van Den Boom LGH, Jacobs WCH, Schoones JW, Wymenga AB, Nelissen RGHH. Similar outcome after retention or sacrifice of the posterior cruciate ligament in total knee arthroplasty: A systematic review and meta-analysis. Acta Orthop 2015;86:195–201.

[60] Indelli PF, Giori N, Maloney W. Level of constraint in revision knee arthroplasty. Curr Rev Musculoskelet Med 2015;8:390–7.

[61] Meneghini RM, Ziemba-Davis MM, Lovro LR, Ireland PH, Damer BM. Can Intraoperative Sensors Determine the "Target" Ligament Balance? Early Outcomes in Total Knee Arthroplasty. J Arthroplasty 2016:13–8.

[62] Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (Minors): Development and validation of a new instrument. ANZ J Surg 2003;73:712–6.

[63] Kottner, J, Audigé L, Brorson S, Donner A, Gajewski BJ HA. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. J Clin Epidemiol 2011;64:96–106.

[64] Ishii Y, Matsuda Y, Ishii R, Sakata S, Omori G. Coronal laxity in extension in vivo after total knee arthroplasty. J Orthop Sci 2003;8:538–42.

[65] Matsuda Y, Ishii Y. In vivo laxity of low contact stress mobile-bearing prostheses. Clin Orthop Relat Res 2004:138–43.

[66] Oh C-S, Song E-K, Seon JK, Ahn YS. The effect of flexion balance on functional outcomes in cruciate-retaining total knee arthroplasty. Arch Orthop Trauma Surg 2015:401–6.

[67] Tsukiyama H, Kuriyama S, Kobayashi M, Nakamura S, Furu M, Ito H, et al. Medial rather than lateral knee instability correlates with inferior patient satisfaction and knee function after total knee arthroplasty. Knee 2017;24:1478–84.

[68] Bonett DG, Wright TA. Sample size requirements for estimating Pearson, Kendall and Spearman correlations. Psychometrika 2000;65:23–8.

[69] Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med 2016;15.

[70] Giavarina D. Lessons in Biostatistics Understanding Bland Altman analysis. Biochem Medica 2015;25:141–51.

[71] Theodoulou A, Bramwell D, Spiteri A, Kim SW, Krishnan J. The Use of Scoring Systems in Knee Arthroplasty: A Systematic Review of the Literature. J Arthroplasty

2016;31:2364–2370.e8.

[72] Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. J Bone Joint Surg Br 1998;80:63–9.

[73] Dawson J, Beard DJ, McKibbin H, Harris K, Jenkinson C, Price AJ. Development of a patient-reported outcome measure of activity and participation (the OKSAPQ) to supplement the Oxford knee score. Bone Jt J 2014;96 B:332–8.

[74] Behrend H, Giesinger K, Giesinger JM, Kuster MS. The "Forgotten Joint" as the Ultimate Goal in Joint Arthroplasty. Validation of a New Patient-Reported Outcome Measure. J Arthroplasty 2012;27:430–436.e1.

[75] Gagnier JJ, Mullins M, Huang H, Marinac-Dabic D, Ghambaryan A, Eloff B, et al. A Systematic Review of Measurement Properties of Patient-Reported Outcome Measures Used in Patients Undergoing Total Knee Arthroplasty. J Arthroplasty 2017;32:1688–1697.e7.

[76] Mørup-Petersen A, Krogsgaard M, Nielsen R, Paulsen A, Odgaard A. Translation and classical test theory validation of the Danish version of the Oxford Knee Score. Transl. Class. test theory Valid. Danish version Oxford Knee Score, 2019, p. http://abstract.ortopaedi.dk/k19/session16.html.

[77] Thomsen MG, Latifi R, Kallemose T, Barfod KW, Husted H, Troelsen A. Good validity and reliability of the forgotten joint score in evaluating the outcome of total knee arthroplasty: A retrospective cross-sectional survey-based study. Acta Orthop 2016;87:280–5.

[78] Group TE. EuroQol - a new facility for the measurement of health-related quality of life. Health Policy (New York) 1990;16:199–208.

[79] Ingelsrud LH, Roos EM, Terluin B, Gromov K, Husted H, Troelsen A. Minimal important change values for the Oxford Knee Score and the Forgotten Joint Score at 1 year after total knee replacement. Acta Orthop 2018;89:541–7.

[80] Dobson F, Hinman RS, Roos EM, Abbott JH, Stratford P, Davis AM, et al. OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis. Osteoarthr Cartil 2013;21:1042–52.

[81] Tolk JJ, Janssen RPA, Prinsen CAC, Latijnhouwers DAJM, van der Steen MC, Bierma-Zeinstra SMA, et al. The OARSI core set of performance-based measures for knee osteoarthritis is reliable but not valid and responsive. Knee Surgery, Sport Traumatol Arthrosc 2019;27:2898–909.

[82] Fiona Dobson, Kim L. Bennell, Rana S. Hinman, J Haxby Abbott EMR. Recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis - OARSI test manual. 2012.

[83] Skyttä ET, Haapamäki V, Koivikko M, Huhtala H, Remes V. Reliability of the hip-to-ankle radiograph in determining the knee and implant alignment after total knee arthroplasty. Acta Orthop Belg 2011;77:329–35.

[84] Matsumoto K, Ogawa H, Yoshioka H, Akiyama H. Postoperative Anteroposterior Laxity Influences Subjective Outcome After Total Knee Arthroplasty. J Arthroplasty

2017;32:1845–9.

[85] Matsumoto K, Ogawa H, Yoshioka H, Akiyama H. Postoperative Anteroposterior Laxity Influences Subjective Outcome After Total Knee Arthroplasty. J Arthroplasty 2017;32:1845–9.

[86] Ishii Y, Matsuda Y, Ishii R, Sakata S, Omori G. Sagittal laxity in vivo after total knee arthroplasty. Arch Orthop Trauma Surg 2005;125:249–53.

[87] Seon JK, Song EK, Yoon TR, Bae BH, Park SJ, Cho SG. In vivo stability of total knee arthroplasty using a navigation system. Int Orthop 2007;31:45–8.

[88] Seon JK, Park SJ, Yoon TR, Lee KB, Moon ES, Song EK. The effect of anteroposterior laxity on the range of movement and knee function following a cruciate-retaining total knee replacement. J Bone Joint Surg Br 2010;92:1090–5.

[89] Seah RB, Pang HN, Lo NN, Chong HC, Chin PL, Chia SL, et al. Evaluation of the relationship between anteroposterior translation of a posterior cruciate ligament-retaining total knee replacement and functional outcome. J Bone Jt Surg - Br Vol 2012;94–B:1362–5.

[90] Jones DPG, Locke C, Pennington J, Theis J-C. The effect of sagittal laxity on function after posterior cruciate-retaining total knee replacement. J Arthroplasty 2006;21:719–23.

[91] Schuster AJ, von Roll AL, Pfluger D, Wyss T. Anteroposterior stability after posterior cruciate-retaining total knee arthroplasty. Knee Surgery, Sport Traumatol Arthrosc 2011;19:1113–20.

[92] Mochizuki T, Tanifuji O, Sato T, Hijikata H, Koga H, Watanabe S, et al. Association between anteroposterior laxity in mid-range flexion and subjective healing of instability after total knee arthroplasty. Knee Surgery, Sport Traumatol Arthrosc 2017;25:3543–8.

[93] Stähelin T, Kessler O, Pfirrmann C, Jacob HAC, Romero J. Fluoroscopically assisted stress radiography for varus-valgus stability assessment in flexion after total knee arthroplasty. J Arthroplasty 2003;18:513–5.

[94] Nakahara H, Okazaki K, Hamai S, Okamoto S, Kuwashima U, Higaki H, et al. Does knee stability in the coronal plane in extension affect function and outcome after total knee arthroplasty? Knee Surgery, Sport Traumatol Arthrosc 2015;23:1693–8.

[95] Yoshihara Y, Arai Y, Nakagawa S, Inoue H, Ueshima K, Fujiwara H, et al. Assessing coronal laxity in extension and flexion at a minimum of 10 years after primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2016 Aug;24(8):2512-6.

[96] Ishii Y, Matsuda Y, Ishii R, Sakata S, Omori G. Coronal laxity in extension in vivo after total knee arthroplasty. J Orthop Sci 2003;8:538–42.

[97] Kobayashi T, Suzuki M, Sasho T, Nakagawa K, Tsuneizumi Y, Takahashi K. Lateral laxity in flexion increases the postoperative flexion angle in cruciate-retaining total knee arthroplasty. J Arthroplasty 2012;27:260–5.

[98] Stucinskas J, Robertsson O, Sirka A, Lebedev A, Wingstrand H, Tarasevicius S.

Moderate varus/valgus malalignment after total knee arthroplasty has little effect on knee function or muscle strength. Acta Orthop 2015;86:728–33.

[99] Magnussen RA, Weppe F, Demey G, Servien E, Lustig S. Residual varus alignment does not compromise results of TKAs in patients with preoperative varus. Clin Orthop Relat Res 2011;469:3443–50.

[100] Kayani B, Konan S, Horriat S, Ibrahim MS, Haddad FS. Posterior cruciate ligament resection in total knee arthroplasty: The effect on flexion-extension gaps, mediolateral laxity, and fixed flexion deformity. Bone Jt J 2019;101–B:1230–7.

[101] Ishii Y, Noguchi H, Sato J, Ishii H, Todoroki K, Toyabe S. Medial and lateral laxity in knees with advanced medial osteoarthritis. Osteoarthr Cartil 2018;26:666–70.

[102] Wilson CJ, Theodoulou A, Damarell RA, Krishnan J. Knee instability as the primary cause of failure following Total Knee Arthroplasty (TKA): A systematic review on the patient, surgical and implant characteristics of revised TKA patients. Knee 2017;24:1271–81.

[103] Kuster MS, Bitschnau B, Votruba T. Influence of collateral ligament laxity on patient satisfaction after total knee arthroplasty: a comparative bilateral study. Arch Orthop Trauma Surg 2004;124:415–7.

[104] Sauder N, Galea VP, Rojanasopondist P, Colon Iban YE, Florissi IS, Nielsen CS, et al. Regional differences between the US, Scandinavia, and South Korea in patient demographics and patient-reported outcomes for primary total knee arthroplasty. Arch Orthop Trauma Surg 2019;140:93–108.

[105] Mulholland SJ, Wyss UP. Activities of daily living in non-Western cultures: Range of motion requirements for hip and knee joint implants. Int J Rehabil Res 2001;24:191–8.

Supplementary material

A: Full search history for the systematic review.

Pubmed:

Search	Query
#1	Search ((oks[tw]) OR KSS[tw]) OR HSS[tw]) OR hospital for special surgery score*[tw]) OR TKFQ[tw]) OR total knee function questionnaire*[tw]) OR JKOM[tw]) OR japanese knee osteoarthritis measurement*[tw]) OR university of california los angeles activity-level rating[tw]) OR (Knee injury and Osteoarthritis Outcome Score*[tw])) OR Oxford knee score*[tw]) OR koos[tw]) OR self-report*[tw]) OR "Self Report"[Mesh]) OR Patient Outcome Assessment*[tw]) OR patient reported outcome*[tw]) OR "Health Care Surveys"[Mesh]) OR "Patient Outcome Assessment"[Mesh]) OR PROM[tw]) OR PROMs[tw]) OR oxford score*[tw]) OR WOMAC*[tw]) OR McMaster Universities Osteoarthritis Index*[tw]) OR short form[tw]) OR shortform[tw]) OR SF-36[tw]) OR SF-12[tw]) OR SF-8[tw]) OR Forgotten Joint Score*[tw]) OR fjs[tw]) OR OKS-APQ[tw]) OR VR-12[tw]) OR Rand 12[tw]) OR EQ-5D[tw]) OR Euroqol 5[tw]) OR knee society score*[tw]) OR University of California Los Angeles Activity-level Rating*[tw]) OR UCLA[tw]) OR NRS[tw]) OR VAS[tw]) OR Numerical Rating scale*[tw]) OR Visual Analog Scale*[tw]) OR "Visual Analog Scale"[Mesh])) AND (((((((((("Postural Balance"[Mesh]) OR Balanc*[tw]) OR stabilit*[tw]) OR instabilit*[tw]) OR "Joint Instability"[Mesh]) OR Laxit*[tw]) OR "Range of Motion, Articular"[Mesh]) OR Range of Motion*[tw]) OR Flexibilit*[tw])) AND (((((Knee Replacement*[tw]) OR Knee arthroplast*[tw]) OR "Arthroplasty, Replacement, Knee"[Mesh]) OR knee reconst*[tw]) OR knee joint replacement*[tw])) Filters: Publication date from 2017/06/01 to 2018/12/31

Embase:

No.	Query
#67	#6 AND #16 AND #66 AND [1-6-2017]/sd NOT [31-12-2018]/sd
#66	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65
#65	'hospital for special surgery score'/exp
#64	'hospital for special surgery scor*'
#63	kss
#62	hss
#61	tkfq
#60	'total knee function questionnaire*'
#59	'japanese knee osteoarthritis measurement*'
#58	jkom
#57	'visual analog scale'/exp
#56	'numeric rating scale'/exp
#55	'knee society score'/exp
#54	'short form 36'/exp
#53	'patient-reported outcome'/exp

#52	'self report'/exp
#51	'oxford knee score'/exp
#50	'numerical rating scale*'
#49	'visual analog* scale*'
#48	vas
#47	nrs
#46	'university of california los angeles activity-level rating*'
#45	ucla:ti,ab
#44	'knee society scor*'
#43	'euroqol 5'
#42	'eq-5d'
#41	'rand 12'
#40	'vr 12'
#39	'oks apq'
#38	fjs
#37	'forgotten joint scor*'
#36	'sf-8'
#35	'sf-12'
#34	'sf-36'
#33	shortform
#32	'short form'
#31	'mcmaster universities osteoarthritis index*'
#30	'western ontario and mcmaster universities osteoarthritis index'/exp
#29	womac*
#28	'oxford scor*'
#27	proms
#26	prom
#25	'patient reported outcome*'
#24	'patient outcome assessment*'
#23	'self-report*'
#22	koos
#21	'oxford knee score'/exp
#20	'oxford knee scor*'
#19	'knee injury and osteoarthritis outcome scor*'
#18	'knee injury and osteoarthritis outcome score'/exp
#17	oks
#16	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
#15	'range of motion*'
#14	'range of motion'/exp
#13	'knee function'/exp

#12	'joint laxity'/exp
#11	'knee instability'/exp
#10	laxit*
#9	instabilit*
#8	stabilit*
#7	balanc*
#6	#1 OR #2 OR #3 OR #4 OR #5
#5	'knee joint replacement*'
#4	'knee reconst*'
#3	'knee replacement*'
#2	'knee arthroplast*'
#1	'knee arthroplasty'/exp

Cochrane:

ID	Search
#1	MeSH descriptor: [Arthroplasty, Replacement, Knee] explode all trees
#2	"knee reconst*":ti,ab,kw (Word variations have been searched)
#3	"knee joint replacement*":ti,ab,kw (Word variations have been searched)
#4	"Knee arthroplast*":ti,ab,kw (Word variations have been searched)
#5	"Knee Replacement*":ti,ab,kw (Word variations have been searched)
#6	#1 or #2 or #3 or #4 or #5
#7	Flexibilit*:ti,ab,kw (Word variations have been searched)
#8	MeSH descriptor: [Range of Motion, Articular] explode all trees
#9	"Range of Motion*":ti,ab,kw (Word variations have been searched)
#10	Laxit*:ti,ab,kw (Word variations have been searched)
#11	MeSH descriptor: [Joint Instability] explode all trees
#12	instabilit*:ti,ab,kw (Word variations have been searched)
#13	stabilit*:ti,ab,kw (Word variations have been searched)
#14	Balanc*:ti,ab,kw (Word variations have been searched)
#15	MeSH descriptor: [Postural Balance] explode all trees
#16	#7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15
#17	#6 and #16
#18	MeSH descriptor: [Visual Analog Scale] explode all trees
#19	MeSH descriptor: [Health Care Surveys] explode all trees
#20	MeSH descriptor: [Patient Outcome Assessment] explode all trees
#21	MeSH descriptor: [Self Report] explode all trees
#22	oks:ti,ab,kw (Word variations have been searched)
#23	KSS:ti,ab,kw (Word variations have been searched)
#24	HSS:ti,ab,kw (Word variations have been searched)
#25	"hospital for special surgery score*":ti,ab,kw (Word variations have been searched)
#26	TKFQ:ti,ab,kw (Word variations have been searched)
#27	"total knee function questionnaire*":ti,ab,kw (Word variations have been searched)
#28	JKOM:ti,ab,kw (Word variations have been searched)
#29	"japanese knee osteoarthritis measurement*":ti,ab,kw (Word variations have been searched)
#30	"university of california los angeles activity-level rating":ti,ab,kw (Word variations have been searched)
#31	"Knee injury and Osteoarthritis Outcome Score*":ti,ab,kw (Word variations have been searched)
#32	"Oxford knee score*":ti,ab,kw (Word variations have been searched)

#33	koos:ti,ab,kw (Word variations have been searched)
#34	self-report*:ti,ab,kw (Word variations have been searched)
#35	"Patient Outcome Assessment*":ti,ab,kw (Word variations have been searched)
#36	"patient reported outcome*":ti,ab,kw (Word variations have been searched)
#37	PROM:ti,ab,kw (Word variations have been searched)
#38	PROMs:ti,ab,kw (Word variations have been searched)
#39	"oxford score*":ti,ab,kw (Word variations have been searched)
#40	WOMAC*:ti,ab,kw (Word variations have been searched)
#41	"McMaster Universities Osteoarthritis Index*":ti,ab,kw (Word variations have been searched)
#42	"short form":ti,ab,kw (Word variations have been searched)
#43	shortform:ti,ab,kw (Word variations have been searched)
#44	SF-36:ti,ab,kw (Word variations have been searched)
#45	SF-12:ti,ab,kw (Word variations have been searched)
#46	SF-8:ti,ab,kw (Word variations have been searched)
#47	"Forgotten Joint Score*":ti,ab,kw (Word variations have been searched)
#48	fjs:ti,ab,kw (Word variations have been searched)
#49	OKS-APQ:ti,ab,kw (Word variations have been searched)
#50	VR-12:ti,ab,kw (Word variations have been searched)
#51	"Rand 12":ti,ab,kw (Word variations have been searched)
#52	EQ-5D:ti,ab,kw (Word variations have been searched)
#53	"Euroqol 5":ti,ab,kw (Word variations have been searched)
#54	"knee society score*":ti,ab,kw (Word variations have been searched)
#55	"University of California Los Angeles Activity-level Rating*":ti,ab,kw (Word variations have been searched)
#56	UCLA:ti,ab,kw (Word variations have been searched)
#57	NRS:ti,ab,kw (Word variations have been searched)
#58	VAS:ti,ab,kw (Word variations have been searched)
#59	"Numerical Rating scale*":ti,ab,kw (Word variations have been searched)
#60	"Visual Analog Scale*":ti,ab,kw (Word variations have been searched)
#61	#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60
#62	#17 and #61 Publication Year from 2017 to 2018

B: MINORS for the studies included in the systematic review

Authors	Year	Journal	1	2	3	4	5	6	7	8	Total
Matsumoto	2017	J Arthroplasty	2	1	1	2	1	2	2	0	11
Tsukiyama	2017	Knee	2	1	1	2	1	2	2	0	11
Graff	2016	ANZ J Surg.	2	1	1	2	0	2	2	1	11
Nakahara	2015	Knee Surg Sports Traumatol Arthrosc.	2	1	1	2	0	2	2	0	10
Oh	2015	Arch Orthop Trauma Surg.	2	1	2	2	1	2	1	0	12
Seah	2012	JBJS	2	2	2	2	2	2	1	0	13
Schuster	2011	Knee Surg Sports Traumatol Arthrosc.	2	0	2	2	1	1	1	0	9
Seon	2010	JBJS	2	1	1	2	0	2	2	1	11
Seon	2007	International Orthopaedics	1	2	2	2	2	2	1	0	12
Van Hal	2007	Knee Surg Sports Traumatol Arthrosc.	2	1	1	2	1	2	2	0	11
Jones	2006	J Arthroplasty	2	1	1	2	1	2	2	0	11
Ishii	2005	Arch Orthop Trauma Surg.	1	1	1	2	1	2	2	0	10
Kuster	2004	Arch Orthop Trauma Surg.	2	0	1	2	1	2	2	0	10
Yamakado	2003	Arch Orthop Trauma Surg.	1	0	1	2	1	2	2	0	9

The non-comparative part of the MINORS criteria was used (i.e., first eight questions) as no studies analyzed the research question of this paper with use of a control group. The criteria of MINORS with 0 points when not reported, 1 when reported but not adequate, and 2 when reported and adequate. Maximum score is 16.

C: Poster presented at EFORT 2018 meeting

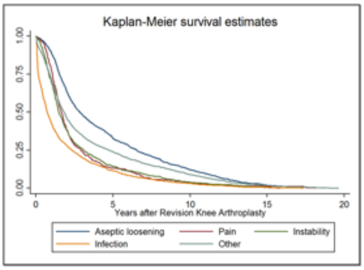
PATIENT RELATED FACTORS INFLUENCES RISK AND MODE OF SUBSEQUENT FAILURE IN PRIMARY TOTAL KNEE ARTHROPLASTY.

Results From The Danish Knee Arthroplasty Registry.

Andreas Kappel[1], Poul Torben Nielsen[1], Mogens Berg Laursen[1], Anders Odgaard[2], Anders El-Galaly[1]
[1]Aalborg University Hospital, Aalborg, Denmark,[2]Gentofte Hospital, University of Copenhagen, Denmark

Aim: To investigate differences in patient demographics and surgical details at index surgery, between not revised and revised cases.

Methods: From the Danish Knee Arthroplasty Registry, we retrieved all primary Total Knee Arthroplasty (p-TKA) procedures performed from January 1, 1997 until December 31, 2016. From these 98,629 primary procedures, we identified 5,346 subsequent first time revisions and organized these in sub-groups based on indications for revision. Continuous variable was found to be Gaussian distributed thus compared by student's t-test. Kaplan-Meier analyses and cox regression was used to Calculate survival.



Results: 5.4% of the p-TKA had a revision during the observation period; mean time to failure was 3.17 years. The revised cases were younger and weighed more, differences in age, weight, duration of surgery and time to failure were found for all the main indications of revision. All results for revised cases was found statistically significant from the not revised cases (p<.05) (table 1). HR between revised cases and not revised cases displayed multiple significant results (table 2); we present crude hazard ratios, unadjusted for possible confounders such as age. Risk factors for failure following p-TKA include young age, male sex, and prior knee surgery. Aseptic loosening was associated to young age and late failure. Infection was associated to higher age, higher weight, male sex and early failure. Instability was associated to young age and early failure.

Conclusion: This study highlights associations between patient characteristics at index surgery and subsequent revisions, this knowledge might be of benefit when planning surgery and considering risk factors for the individual case.

Table 1:

	Not revised	All revision	Loosening	Infection	Instability	Pain
	n=93283	n=5346	n=1502	n=1143	n=962	n=479
Age (years)	68.6 ±9.8	63.56 ±10.84	61.98 ±10.04	67.44 ±10.35	62.03 ±11.10	61.70 ±10.55
Body Weight (kg)	84.0 ±19.4	85.86 ±20.24	86.22 ±21.10	88.43 ±21.43	85.24 ±19.52	83.04 ±18.57
Surgical time (min)	72.3 ±22.6	77.13 ±26.83	78.38 ±25.95	78.78 ±30.94	76.16 ±26.07	74.71 ±23.62
Mean time to failure	6.46 to censor	3.17	4.63	1.90	2.63	2.59

Table 2 – crude HR:

Hazard ratio(95%CI)		All revisions	Loosening	Infection	Instability	Pain
Patient	male-sex	1.16 (1.10-1.23)***	1.01 (0.93-1.10)	1.83 (1.62-2.05)***	0.88 (0.73-1.06)	0.94 (0.76-1.17)
Diagnosis	primary OA	0.71 (0.66-0.76)***	0.75 (0.66-0.85)***	0.75 (0.66-0.85)***	0.61 (0.53-0.70)***	0.60 (0.48-0.73)***
	post fracture	2.00 (1.71-2.34)***	1.85 (1.38-2.48)***	2.83 (2.17-3.69)***	2.68 (1.99-3.60)***	1.01 (0.58-1.76)
	RA	0.80 (0.67-0.97)*	0.92 (0.72-1.19)	1.02 (0.76-1.37)	0.68 (0.43-1.07)	0.49 (0.27-0.92)*
Prior knee surgery	cruciate recon.	2.35 (1.93-2.86)***	2.40 (1.59-3.63)***	0.81 (0.49-1.36)	5.18 (4.13-6.52)***	3.03 (1.72-5.34)***
	menisctomy	1.38 (1.27-1.49)***	1.37 (1.22-1.54)***	0.96 (0.84-1.10)	1.48 (1.24-1.77)***	2.33 (1.93-2.82)***
	osteosynthesis	2.04 (1.71-2.42)***	1.67 (1.11-2.56)*	2.87 (2.19-3.77)***	3.05 (2.24-4.6)***	1.14 (0.59-2.20)
	osteotomy	1.73 (1.45-2.05)***	1.57 (1.17-2.10)**	1.56 (1.08-2.26)*	2.33 (1.77-3.07)***	1.69 (1.00-2.83)*
Surgical data	supplement	1.79 (1.44-2.23)***	2.40 (1.67-3.46)***	1.75 (1.01-3.06)*	1.78 (1.12-2.81)*	1.64 (0.78-3.46)
	CR	0.68 (0.56-0.83)***	0.65 (0.48-0.89)**	0.72 (0.60-0.87)**	0.86 (0.63-1.17)	0.56 (0.42-0.74)***

*** p<0,001, **p<0,01 and *p<0.05

Gentofte Hospital

AALBORG UNIVERSITY HOSPITAL

ISSN (online): 2246-1302
ISBN (online): 978-87-7210-850-6

AALBORG UNIVERSITY PRESS