Aus dem Zentrum für Orthopädie und Unfallchirurgie der
Universitätsmedizin der Johannes Gutenberg-Universität Mainz

Moderne Methoden zur Verbesserung der Patientenzufriedenheit in der Gelenkendoprothetik und Messinstrumente zu deren Bestimmung

Habilitationsschrift

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II. Wunderlich F, Azad M, Westphal R, Klonschinski T, Belikan P, Drees P, **Eckhard L**; Comparison of Postoperative Coronal Leg Alignment in Customized Individually Made and Conventional Total Knee Arthroplasty; J Pers Med. 2021 Jun 12;11(6):549. doi: 10.3390/jpm11060549.

III. **Eckhard L**, Munir S, Wood D, Talbot S, Brighton R, Walter B, Baré J; The ceiling effects of patient reported outcome measures for total knee arthroplasty; Orthop Traumatol Surg Res. 2021 May;107(3):102758. doi: 10.1016/j.otsr.2020.102758.

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V. **Eckhard L**, Munir S, Wood D, Talbot S, Brighton R, Walter B, Baré J; The KOOS-12 shortform shows no ceiling effect, good responsiveness and construct validity compared to standard outcome measures after total knee arthroplasty;

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VI. **Eckhard L**, Jones T, Collins JE, Shrestha S, Fitz W; Increased postoperative dexamethasone and gabapentin reduces opioid consumption after total knee arthroplasty; Knee Surg Sports Traumatol Arthrosc. 2019 Jul;27(7):2167-2172. doi: 10.1007/s00167-019-05449-8.

Inhalt

2 Einleitung

Sind konservative Behandlungsoptionen ausgereizt, stellt der endoprothetische Gelenkersatz heutzutage eine erfolgreiche Behandlung endgradiger Arthrosen des Knie- und Hüftgelenks dar. Durch ihn können Schmerzen dauerhaft gelindert, die funktionelle Lebensqualität gesteigert und die Selbstständigkeit von Patienten wiederhergestellt werden[1].

Am Knie finden sich erste Beschreibungen einer Arthroplastik Mitte des neunzehnten Jahrhunderts. Ferguson beschrieb 1861 eine Resektionsarthroplastik, welche in einer belastungsfähigen Pseudarthrose ausheilen sollte. Da Resektionsarthroplastiken allerdings regelmäßig in einer Ankylose oder Fusion endeten, wurden in der Folge diverse Techniken der Interposition von Weichteilen, entweder mit Fettgewebe oder Kapselanteilen, beschrieben und bis in die 1950er Jahre – ohne zufriedenstellende Ergebnisse – durchgeführt. In Ermangelung anderer Alternativen wurden sogar vollständige Kniegelenkstransplantationen, teils sogar der Gegenseite, unternommen, was jedoch häufig bereits nach kurzer Zeit zu einer Amputation des funktionslos gewordenen Beins führte.

Mitte des 20. Jahrhunderts finden sich erste Berichte über Knie-Totalendoprothesen. Diese waren zunächst noch aus Acryl und später Vitallium geformte einfache Scharniergelenke. Durch die Einführung von Polymethylmetacrylat als Knochenzement in den 1970er Jahren entstand neue Hoffnung, der universell und früh einsetzenden Lockerung der Scharnierprothesen endlich mit einer stabilen Fixierung zu begegnen. Dies scheiterte jedoch ebenfalls, da die über die Prothese eingeleiteten Rotationskräfte auf das starre Scharnier auch für die Zementfixierung zu hoch waren. Nicht-anatomische und anatomische unicondyläre Prothesenentwicklungen folgten und eine Kombination aus metallenen femoralen Komponenten und Polyethylen-Tibiaplateaus wurde verfolgt. Insall gelang schließlich ein Durchbruch mit dem Design eines „Total Condylar Knee“ Systems, das erstmals auch das Patellofemoralgelenk vollständig ersetzte. Mit dem Folgedesign, der Insall-Burnstein Prothese, wurde 1982 schließlich das erste „posterior-stabilized“ Design, welches beide Kreuzbänder ersetzt und durch einen cam-post Mechanismus das natürliche femorale rollback imitiert, vorgestellt und die moderne Kniegelenksendoprothetik eingeleitet. Neben der Robotik zählen patientenindividuell angefertigte Endoprothesen zu den aktuellen Innovationen und stellen auch in der vorliegenden Arbeit einen Anteil dar.

Auch an der Hüfte begann zu Beginn des 18. Jahrhunderts die Geschichte der Arthroplastik zunächst mit der Resektion des Gelenks, analog zum Vorgehen am Knie mit dem Versuch eine fibröse Pseudarthrose zu schaffen. Die Technik wurde insbesondere in den 1940er Jahren, mehr zur Behandlung von septischen oder tuberkulösen Arthritiden als Coxarthrosen, durch Girdlestone bekannt.

Nachdem auch am Hüftgelenk zunächst Versuche des Gelenkerhalts durch Weichteilinterposition folgten und scheiterten, war Smith-Petersen 1925 der erste, der einen Oberflächenersatz mit Glas durchführte. Da dies zwar zur Ausbildung einer fibrösen Gleitmembran führte, die Implantate jedoch schnell versagten, experimentierte Smith-Peterson zunächst mit diversen Materialien, bevor er 1937 auf Empfehlung seines Zahnarztes Vitallium zur Herstellung von Interpositionsimplantaten nutzte.

Die moderne Hüftendoprothetik begann schließlich mit John Charnleys „low friction arthroplasty“, die durch den Einsatz von deutlich kleineren Prothesenköpfen, die Fixierung der Implantate mit Knochenzement und die Einführung von hoch dichtem Polyethylen als Gleitpartner beachtliche Standzeiten von etwa 80% zum 25-Jahres follow up erreichte.

Verschiedene Evolutionen an Gleitpaarungen wurden von den 1960er bis zu den 1980er Jahren entwickelt. Metall-auf-Metall Gleitpaarungen aus Cobalt-Chrom-Legierungen brachten das Problem des metallischen Abriebs und der dadurch ausgelösten inflammatorisch vermittelten „Partikelkrankheit“ mit periprothetischen Osteolysen mit sich. Keramik-auf-Keramik Paarungen sollten zwar dieses Problem lösen, jedoch hatten die frühen Keramikgenerationen in Form von Keramikbruch und Quietschen neue Versagensursachen. Moderne Gleitpaarungen aus 4. Generationskeramik und mit Vitamin E angereichertem, ultra-hoch vernetztem Polyethylen stellen schließlich seit Beginn der 2000er Jahre den Standard dar und scheinen die Suche nach der optimalen Gleitpaarung vorerst gelöst zu haben.

In der Hüftgelenksendoprothetik durchlief neben den genannten Gleitpaarungen insbesondere das Design des femoralen Schaftes diverse Evolutionsprozesse. In den 1970er Jahren waren zementierte Schäfte populär. Neben diesen Geradschäften, wie zum Beispiel dem erfolgreichen Müller-Schaft, folgten anatomische, konisch zulaufende und zylindrisch designte Schäfte. Zudem wurden Schäfte porös beschichtet um ein knöchernes Einwachsen und damit eine zementfreie Fixierung zu erzielen. In der Folge nahm der Anteil zementierter primärer Versorgungen stetig ab. Aufgrund der nun

reproduzierbar guten Ergebnisse bewerteten Learmonth et al. die Hüft-TEP 2007 in einem viel beachteten und seither unzählige Male zitierten Artikel schließlich sogar als „operation of the century“[2].

Jedoch gibt es sowohl in der Knie-, als auch in der Hüftendoprothetik einen relevanten Anteil an Patienten, die mit dem Ergebnis ihrer Operation nicht zufrieden sind. Während die Erwartungen an den Gelenkersatz bei Hüft- und Kniearthrosepatienten gleichermaßen hoch sind, ist der Anteil unzufriedener Patienten nach Hüftendoprothetik in der Regel geringer (Neuprez PLOS 2016).

Bourne et al. gaben an, dass zwischen 11-19% der Patienten nach primärem Ersatz des Kniegelenks mittels Totalendoprothese mit dem Ergebnis des Eingriffs nicht zufrieden sind[3]. Auch nach dem Einsatz moderner Implantate durch besonders erfahrene Operateure beobachteten Parvizi et al. in einer amerikanischen Multicenter-Studie, dass 33% der Patienten verbleibende Schmerzen, 41% eine Steifigkeit des Gelenks, 33% Knirschen oder andere Geräusche sowie 33% eine anhaltende Schwellungsneigung hatten[4].

In Anbetracht des demographischen Wandels und des zunehmenden Aktivitätsbedürfnisses auch im Alter, ist in den nächsten Jahrzehnten mit einer deutlichen Zunahme der endoprothetischen Versorgungen zu rechnen. Für Deutschland wird eine Steigerung der Versorgungszahlen bis 2040 um 45% (Knie-TEP) bzw. 23% (Hüft-TEP) erwartet[5]. Im gleichen Zeitraum wird in den USA mit einer Steigerung der Patienten, die eine Knie-TEP benötigen um 401% und derer, die eine Hüft-TEP benötigen um 284% gerechnet[6].

Damit erlangt die Unzufriedenheit nach Gelenkersatz nicht nur auf Patientenniveau, sondern aufgrund der damit verbundenen sozioökonomischen Kosten auch für die Gesellschaft als Ganzes eine steigende Bedeutung. Neben den indirekten Kosten, welche etwa durch eine Arbeitsunfähigkeit verursacht durch eine schlechte Gelenkfunktion entstehen, sind insbesondere Revisionsoperationen kostspielig.

Die Kosten für eine Revisionsoperation nach fehlgeschlagener oder nicht zufriedenstellender Primärversorgung mit Hüft- oder Knie-TEP haben sich im Zeitraum von 10 Jahren verdreifacht[7]. Im Mittel kostet eine Revisionsoperation gemäß einer Analyse der National Inpatient Sample Datenbank am Knie in den USA 75.000US$ und an der Hüfte 78.000US$[8,9]. Den Hauptanteil der Kosten machen hierbei perioperative

Kosten (33%), Implantatkosten (28%) und Kosten für den stationären Aufenthalt (22%) aus[10].

Trotz Fortschritten in der operativen Technik, als auch im Implantatdesign ist die „Revisionslast“ – der Anteil an Patienten, der eine Revisionsoperation erhält, im Vergleich zur Anzahl der erfolgten Primäroperationen – nicht gesunken[7]. In Deutschland stieg die Anzahl der Revisionsknieendoprothesen von 2008 bis 2018 um 20,76% auf 23.812[11].

Mögliche Ansatzpunkte zur Steigerung der Patientenzufriedenheit sind vielfältig. Revisionsoperationen beispielsweise führen neben einer Zunahme von Morbidität und Mortalität regelhaft zu Unzufriedenheit auf Seiten des Patienten. Im Jahr 2020 stellten Revisionsoperationen an Hüft- und Kniegelenk 10,6% aller im deutschen Endoprothesenregister erfassten endoprothetischen Eingriffe dar[12]. Die Revisionsursachen unterscheiden sich hierbei zwischen Knie- und Hüftendoprothetik. In der Hüftendoprothetik stellten 2021 in Deutschland Lockerungen (24,7%), Infektionen (15,8%), periprothetische Frakturen (13,4%) und Luxationen (13,0%) die häufigsten Revisionsursachen dar[12]. Dahingegen zeigten sich nach Knie-Totalendoprothesen Lockerungen (23,4%), Infektionen (14,9%) und Bandinstabilitäten (8,9%) als die häufigsten Gründe für eine Revisionsoperation[12]. Während sich die unter 3.1 zusammengefasste Arbeit dem Problem der Luxation nach Hüftendoprothetik widmet, behandelt Arbeit 3.2 eine mögliche Ursache der aseptischen Lockerung nach Knie-Endoprothetik.

Postoperative Schmerzen sind eine der häufigsten Ursachen anhaltender Unzufriedenheit nach endoprothetischem Gelenkersatz[13]. Insbesondere, wenn die beim Patienten vorhandenen Erwartungen an die postoperative Schmerzlinderung nicht erfüllt werden, kommt es zu Unzufriedenheit[3]. Da unmittelbare postoperative Schmerzen einen Risikofaktor für die spätere Entwicklung chronischer Schmerzen darstellen[14], kommt neben einer adäquaten Beratung des Patienten zu realistischen postoperativen Erwartungen insbesondere der perioperativen Schmerzkontrolle eine entscheidende Bedeutung in der Steigerung der Patientenzufriedenheit zu.

Gerade vor dem Hintergrund der, vor allem in den USA herrschenden, Opioid-Krise wurden alternative und multimodale Schmerzbehandlungskonzepte entwickelt[15]. Multimodale Schmerzbehandlungskonzepte nutzen neben klassischen Analgetika aus den Gruppen der nicht steroidalen Antirheumatika (NSARs) und Opioide auch Co-

Analgetika wie z.B. NMDA-Antagonisten, Serotonin-Inhibitoren oder regionale Anästhesieverfahren. Eine Fortentwicklung im Bereich des Co-Analgetika Einsatzes zur Verringerung des Opioid-Bedarfs nach Knieendoprothetik beschreibt Arbeit 3.3.

In der Vergangenheit wurde der Therapieerfolg nach Gelenkendoprothetik typischerweise aus Sicht des Chirurgen anhand objektiver Parameter wie der Implantatpositionierung, Implantatstandzeit, Transfusionsraten oder dem Auftreten von Komplikationen gemessen[16,17]. Sicherlich hatte dieser Ansatz seine Berechtigung in der Evaluation operationstechnischer oder Prothesendesign-bedingter Aspekte, ließ allerdings die Bewertung des erhaltenen Eingriffs durch den Patienten außen vor. Insbesondere, da es bei endoprothetischen Eingriffen um die Wiederherstellung der Gelenkfunktion sowie der Lebensqualität des Patienten geht, sollte diese Perspektive jedoch eine wesentliche Rolle spielen.

In den letzten Jahren zeigt sich ein zunehmender Wandel hin zu einer Patienten-zentrierten Bewertung der Ergebnisse nach Hüft- und Knietotalendoprothetik. Mit „patient reported outcome measures“ (PROMs) wird es ermöglicht, die Einschätzung des Behandlungsergebnisses direkt vom Patienten, ohne Beeinflussung durch den Untersucher, zu bekommen. Zahlreiche Messinstrumente, in der Regel Fragebögen, zur Erhebung gelenk- sowie erkrankungsspezifischer oder genereller Gesundheits-Outcomes wurden publiziert und validiert.

Den Stellenwert von PROMs in der Bewertung des Therapieerfolges nach Hüft- und Knie-TEP zeigt nicht nur die fortschreitende Fokussierung auf die Patientenzufriedenheit bei der Darstellung von Studienergebnissen, sondern auch die zunehmende Implementierung in Endoprothesenregistern weltweit[18].

Damit PROMs nicht nur im Rahmen von Studien und Registern, sondern auch routinemäßig im klinischen Alltag eingesetzt werden können, muss der Aufwand für Behandelnde wie Patienten gleichermaßen gering sein. Es wird daher versucht Kurzversionen häufig eingesetzter PROMs zu generieren, die trotz einer geringeren Anzahl an Fragen an den Patienten ihre Aussagekraft nicht verlieren. Ein Beispiel hierfür ist die nur 12 anstatt 42 Fragen umfassende Kurzversion des Knee Injury and Osteoarthritis Outcome Scores (KOOS-12)[19–21].

Um den Einfluss von Innovationen, zum Beispiel operationstechnischer Art oder in der perioperativen Behandlung, auf die Patientenzufriedenheit adäquat bestimmen zu

können, bedarf es vor dem breiten klinischen Einsatz neuer Messinstrumente zunächst einer Validierung[22]. Die drei wichtigsten psychometrischen Eigenschaften sind hierbei Objektivität, Reliabilität und Validität[23–26]. Die unter 3.4 dargestellte Arbeit nimmt eine solche Validierung für den KOOS-12 vor.

Während der Wandel hin zu einer PROM-basierten Bewertung des Behandlungserfolges in den letzten Jahren mittlerweile breiten Anklang gefunden hat, herrscht noch Unsicherheit darüber, in welcher Situation welches Messinstrument am geeignetsten ist[27]. Nachdem der KOOS-12 im Rahmen der unter 3.4 dargestellten externen Validierung vielversprechende psychometrische Eigenschaften gezeigt hatte, sollte die unter 3.5 zusammengefasste Arbeit hier eine wissenschaftlich fundierte Entscheidungshilfe liefern. Untersucht wurde die gerade in der Endoprothetik bedeutende Fähigkeit eines PROMs zur Diskrimination guter von sehr guten Ergebnissen, psychometrisch beschrieben durch den „ceiling effect“[28,29]. Eine breite Auswahl häufig nach Knie-TEP verwendeter PROMs wurde gleichzeitig untersucht, um einen direkten Vergleich der ceiling Effekte zu erlangen.

Nicht nur die Auswahl der verwendeten PROMs sollte adäquat für den Untersuchungszeitpunkt und die untersuchte Kohorte sein, sondern auch die Einschätzung der erzielten Ergebnisse über eine simple Beschreibung statistischer Signifikanz hinausgehen. Ausschlaggebend für Patienten ist nicht das Erreichen eines p-Wertes, sondern ob eine Verbesserung spürbar ist und als klinisch relevant eingeschätzt wird [30]. Die Begriffe des „minimal important change“ (MIC) und der „minimum clinically important difference“ (MCID) beschreiben hierbei für Kliniker und Wissenschaftler gleichermaßen wichtige Maßzahlen, welche in der unter 3.6 beschriebenen Arbeit zum einen erklärt und zum anderen erstmals für den KOOS-12 etabliert wurden.

3 Synopsis

3.1 Der Einsatz von Computer Navigation in der Hüft-Totalendoprothetik ist mit einem reduzierten Revisionsrisiko auf Grund von Luxationen assoziiert

Agarwal S*, Eckhard L*[§] et al., J Bone Joint Surg Am. 2021

(*equally contributed; [§]corresponding author)

Die korrekte Positionierung der Hüftpfanne ist wesentlich für eine gute postoperative Beweglichkeit des künstlichen Hüftgelenks. Eine Fehlpositionierung wiederum kann zum Anschlagen des Prothesenhalses an die Pfanne (Impingement), Instabilität mit dem Risiko der Luxation des Prothesenkopfes aus der Prothesenpfanne und „edge-loading" (Überbelastung der Kanten-nahen Anteile der Prothesenpfanne) verbunden mit einem beschleunigten Verschleiß, Quietschen und Prothesenbruch, führen.

Zur Einordnung der postoperativen Pfannenpositionierung wurden von Lewinnek et al. „safe zones" definiert und in der Folge von Operateuren als Ziel verfolgt. Eine Positionierung der Pfanne mit einer Inklination von 45° ± 10° und einer Anteversion von 15° ± 10° wird als sicher erachtet. Eine Positionierung der Pfanne außerhalb der „safe zones" wurde in Studien mit höheren Revisionsraten und vermehrten Luxationen assoziiert. Eine zu hohe Inklination begünstigt insbesondere eine Luxation nach cranial, eine zu geringe Anteversion eine Luxation nach dorsal.

Luxationen sind, wie in der Einleitung dargestellt, eine der häufigsten Revisionsursachen nach Hüft-Totalendoprothetik (Hüft-TEP). Die Fehlpositionierung der Pfanne wiederum ist ein Hauptrisikofaktor für Luxationen der Prothese. Etwa 50% der frühen Revisionen werden als vermeidbar eingeschätzt und eine Fehlpositionierung der azetabulären Komponente gilt mit einem Anteil von 48% als die häufigste Ursache einer vermeidbaren frühen Revision.

Erstmals wurde Computer Navigation von Nolte et al. zur korrekten Positionierung von Pedikelschrauben in der Wirbelsäulenchirurgie eingesetzt[31]. Für das Hüftgelenk wurde 1992 mit dem ROBODOC das erste System zur Anwendung von Computer Navigation, damals zur exakten aktiven Präparation des Femurkanals für zementfreie Schäfte mit einem robotischen Arm, vorgestellt[32]. Nicht selbst aktive Systeme, die dem Chirurgen nur eine Hilfe zur Orientierung der Komponenten im Raum geben, wurden in der Folge durch Verbesserungen in der 3D-Sensortechnologie möglich. Hier werden CT-basierte

Systeme und Systeme ohne die Nutzung von präoperativer Bildgebung („imageless“) unterschieden. Optische oder magnetische Sensoren werden als 3D-Positionssensoren zur Positionsbestimmung der zu operierenden Knochen sowie der chirurgischen Instrumente genutzt. Beim Einsatz CT-basierter Systeme ist neben der präoperativen CT und der damit verbundenen Strahlenbelastung eine aufwändige computergestützte Planung notwendig. Daher stellen imageless-Systeme, bei denen lediglich zu Beginn der Operation eine Referenzierung des 3D-Koordinatensystems an anatomischen Landmarken zu erfolgen hat, eine einfacher zu handhabende Technik dar, die zu einem vermehrten Einsatz der Computer Navigation geführt hat.

Mehrere Studien konnten bereits belegen, dass der Einsatz von Computer Navigation zu einer präziseren Pfannenpositionierung führt. Insbesondere werden durch Computer Navigation die Variabilität der Pfannenpositionierung und der Anteil von außerhalb der safe zone gelegenen Implantaten verringert[33]. Bisher fehlte jedoch der klinische Nachweis, dass dies zu einem verminderten Auftreten von luxationsbedingten Revisionen führen kann.

Das australische Endoprothesenregister (Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR)) begann 2003 damit Daten zur Computer Navigation zu erheben. Weniger als 2% der Hüfttotalendoprothesen wurden seitdem mit der Hilfe von Computer Navigation implantiert. Der Mangel an belastbaren klinischen Daten zum Nutzen der Technik wird hier neben dem apparativen sowie zeitlichen Aufwand und den damit verbundenen Kosten immer wieder als Hindernis für eine verbreitetere Anwendung angeführt.

Um den Einfluss der Computer Navigation auf die Revisionsrate nach Hüft-TEP zu untersuchen, wurden Daten des australischen Endoprothesenregisters zu 269.848 Hüft-TEPs aus den Jahren 2009-2019 ausgewertet. 2,6% der Eingriffe erfolgte mit Computer Navigation. Zum Vergleich von navigierten und nicht-navigierten Eingriffen wurden hazard ratios (HRs) aus einem Cox-Modell adjustiert nach Alter, Geschlecht und Prothesenkopf-Größe berechnet.

Eingeschlossen wurden nur Operationen, bei denen moderne Gleitpaarungen, definiert als Keramik-Keramik, Metall-Polyethylen oder Keramik-Polyethylen, eingesetzt wurden. Da Metall-Metall-Gleitpaarungen bekanntermaßen aufgrund des erhöhten Materialabriebs eine erhöhte Revisionsrate mit sich bringen, wurden diese Eingriffe von der Analyse ausgeschlossen. Auch dual-mobility Implantate, bei denen eine

Kombination aus zwei Gleitpaarungen besteht, als auch constrained liner, bei denen überhöhte Inlays im Bereich der Hüftpfanne eingesetzt werden, wurden aufgrund bekannter bautechnischer Besonderheiten von der Analyse ausgeschlossen.

Insgesamt wurden 160 von 6912 navigierten Hüft-TEPs revidiert. Es zeigte sich keine Differenz in der Gesamt-Revisionsrate zwischen navigierten und nicht-navigierten Hüft-TEPs und die kumulative Revisionsrate betrug nach 10 Jahren 4,0% (95% CI, 3,2% bis 4,9%) für navigierte, verglichen mit 4,6% (95% CI, 4,4% bis 4,7%) für nicht-navigierte Hüft-TEPs (HR, 0,89; 95% CI, 0,76 bis 1,04; p = 0,138) (Abbildung 1).

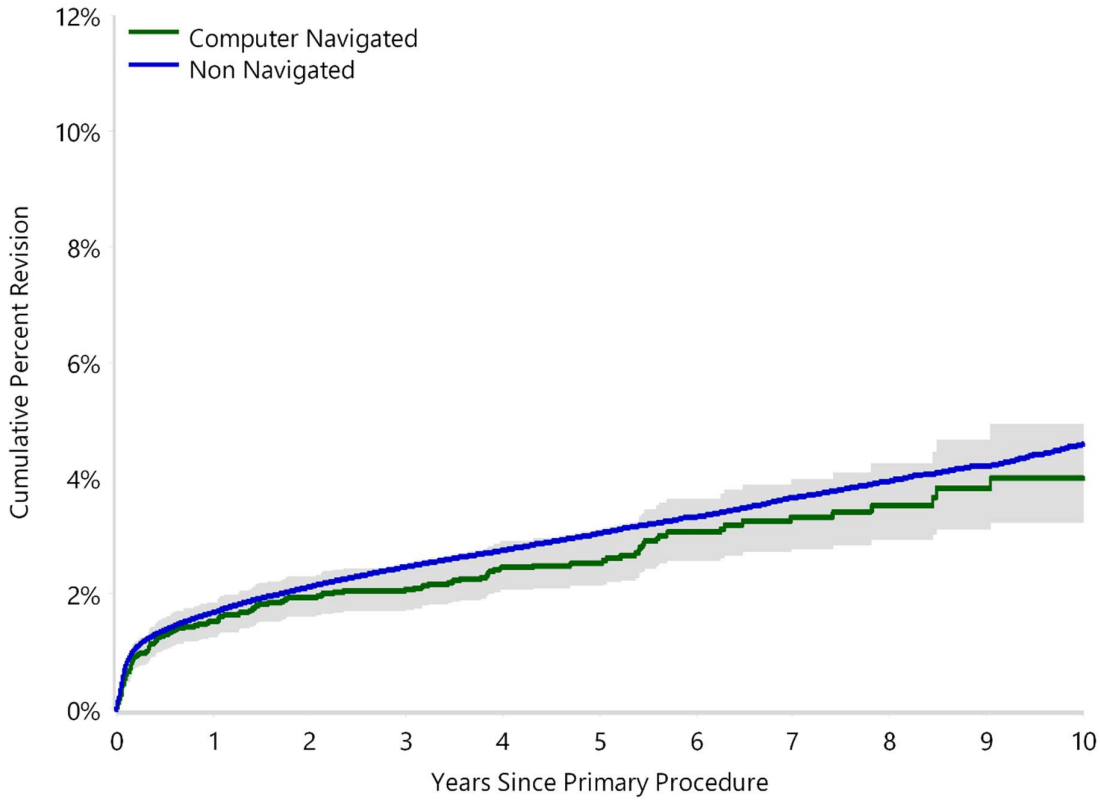

Abbildung 1: Graph zur Darstellung der kumulativen Gesamt-Revisionsrate

Die Rate an Revisionen aufgrund von Luxationen war geringer in der Gruppe der navigierten Hüft-TEPs. Die kumulative luxationsbedingte Revisionsrate betrug nach 10 Jahren in dieser Gruppe 0,4% (95% CI, 0,2% bis 0,6%) verglichen mit 0,8% (95% CI, 0,8% bis 0,9%) in der Gruppe der nicht-navigierten Hüft-TEPs (HR, 0,46; 95% CI, 0,29 bis 0,74; p = 0,002) (Abbildung 2).

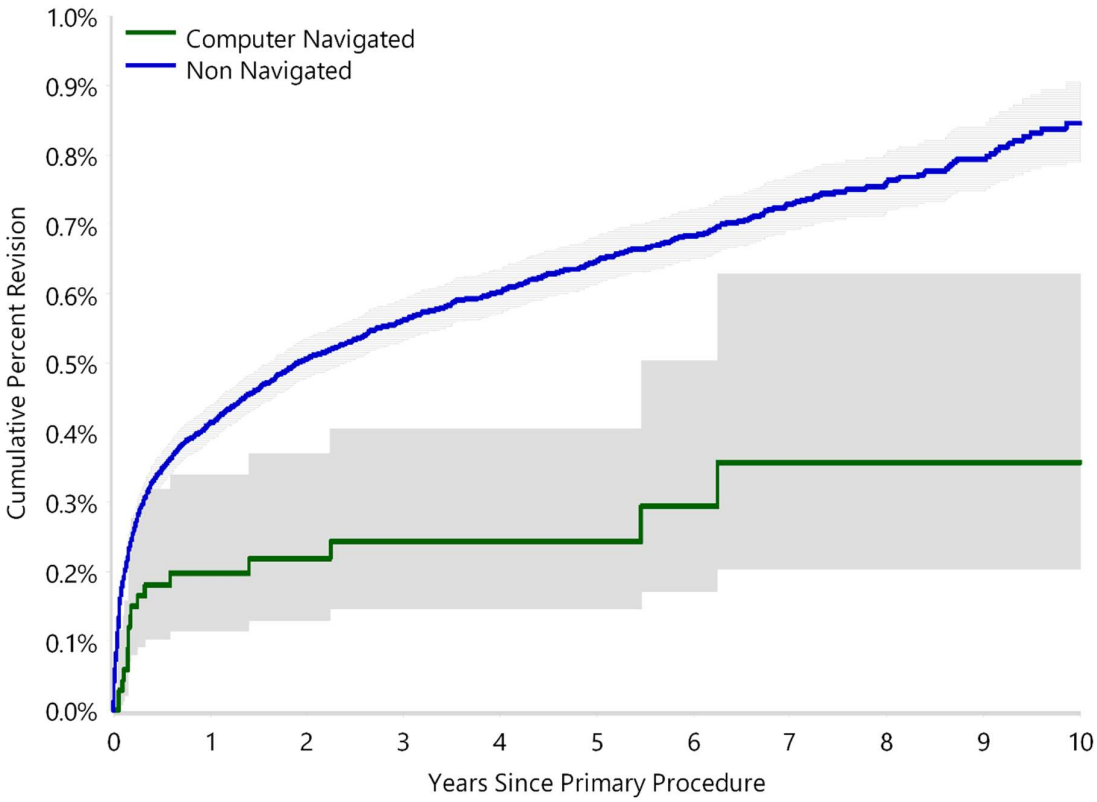

Abbildung 2: Graph zur Darstellung der luxationsbedingten kumulativen Revisionsrate

Aufgrund bekannter Prothesen-spezifischer Unterschiede in den Ergebnissen nach Hüft-TEP wurde zudem eine Subanalyse der fünf am häufigsten mit und ohne Navigation eingesetzten Implantat-Kombinationen durchgeführt. Diese Implantatkobinationen waren Trident und Exeter V40 (Stryker), Pinnacle und Corail (DePuy Synthes), Trident und Accolade II (Stryker), Continuum und M/L Taper Kinectiv (Zimmer Biomet) sowie Fitmore und CLS (Zimmer Biomet). Hier zeigte sich sowohl für die Gesamt-Revisionsrate als auch für die Rate an Revisionen aufgrund von Luxation eine signifikant niedrigere Revisionsrate in der Gruppe der navigierten Hüft-TEPs. Die Gesamtrevisionsrate lag nach 10 Jahren in der Gruppe navigierter Hüft-TEPs bei 2,4% (95% CI, 1,6% bis 3,4%) und in der Gruppe nicht-navigierter Hüft-TEPs bei 4,2% (95% CI, 4,0% bis 4,5%; HR 0,64; 95% CI, 0,48 bis 0,86; p = 0,003). Die Rate der Revisionen aufgrund von Luxationen in der Subanalyse der fünf am häufigsten mit und ohne Navigation eingesetzten Implantat-Kombinationen lag in der Gruppe der navigierten Hüft-TEPs nach zehn Jahren bei 0,3% (95% CI, 0,1% bis 0,8%) und in der

Gruppe der nicht-navigierten Hüft-TEPs bei 0,9% (95% CI, 0,8% bis 1,0%; HR 0,37; 95% CI, 0,16 bis 0,82; p = 0,014).

Auch der Einfluss der chirurgischen Expertise des Operateurs sollte berücksichtigt werden, weshalb eine Analyse beschränkt auf die Eingriffe, welche von Operateuren die Hüft-TEPs sowohl mit als auch ohne Navigation operiert hatten durchgeführt wurde. Hier zeigte sich kein Unterschied in der Gesamt-Revisionsrate, jedoch erneut ein signifikanter Unterschied in der Rate an Revisionen aufgrund von Luxationen.

Es wird häufig diskutiert, ob der operative Zugangsweg einen Einfluss auf die Luxationsrate nach Hüft-TEP hat. Pincus et al. gaben etwa an, die Luxationsrate sei bei Patienten, die über einen anterioren Zugang operiert wurden, geringer als bei Patienten, die einen lateralen oder posterioren Zugang erhielten[34]. In der vorliegenden Studie zeigte sich kein Unterschied in der Revisionsrate zwischen anteriorem, lateralem oder posteriorem Zugang.

Eine Stärke dieser Studie war die Möglichkeit die gesamte Erfahrung einer Nation mit der Technik der Computer Navigation abzubilden. Neben der damit verbundenen Größe des Datenpools – die vorliegende Studie ist die zweitgrößte zu Computer Navigation bei Hüft-TEP – konnten somit auch mögliche Bias-Gründe, wie etwa Besonderheiten einzelner Technologien, regionale Unterschiede oder Operateurs-bedingte Abweichungen ausgeschlossen werden. Zudem konnte auf das längste follow up im Vergleich zu ähnlichen Studien zurückgegriffen werden.

In einer kürzlich veröffentlichten Studie, die ebenfalls die Auswirkung der Computer Navigation auf die Luxationsrate nach Hüftendoprothesen untersuchte, analysierten Bohl et al. mehr als 800.000 Eingriffe aus dem U.S. Medicare Kollektiv. Auch sie fanden eine geringere Luxationsrate für Hüftendoprothesen, welche mit Computer Navigation implantiert wurden, im Vergleich zu jenen, welche ohne Computer Navigation implantiert wurden. Im Gegensatz zur vorliegenden Studie hatten Bohl et al. aufgrund der verwendeten Medicare Daten jedoch keine Informationen über Patienten jünger als 65 Jahre oder isolierte Revisionen des Prothesenkopfes oder des Pfanneninlays. Eine weitere Stärke der aktuellen Studie, im Vergleich zur Studie von Bohl et al., war die Adjustierung nach der verwendeten Kopfgröße, welche die Luxationswahrscheinlichkeit erheblich beeinflusst. Es ist bekannt, dass größere Kopfgrößen seltener luxieren als kleinere.

Die vorliegende Studie ist nicht ohne Limitationen. So war etwa eine Adjustierung nach Häufigkeit der durchgeführten Operationen je Operateur oder je Krankenhaus nicht möglich. Aufgrund der Komplexität der Technik und der damit verbundenen Kosten sind Operateure, die Computer Navigation einsetzen wahrscheinlich „high volume" Chirurgen. Dies könnte ein Bias hin zu einer niedrigeren Revisionsrate bei navigierten Hüft-TEPs darstellen. Jedoch zeigten die Daten des Australian Orthopaedic Association National Joint Replacement Registry, dass Computer Navigation in mehr als der Hälfte der Krankenhäuser in Australien, in denen Hüftendoprothetik durchgeführt wird, genutzt wird. Die Technologie ist also nicht auf spezialisierte Zentren, Universitätsklinika oder Lehrkrankenhäuser beschränkt. In einer vergleichbaren Studie zur Verwendung von Computer Navigation in der Knieendoprothetik konnte ebenfalls anhand von Daten des Australian Orthopaedic Association National Joint Replacement Registry gezeigt werden, dass die Fallzahl eines Operateurs keine Auswirkung auf die Revisionswahrscheinlichkeit hatte. Weiterhin wurde wie oben geschildert eine Analyse beschränkt auf Operateure, die sowohl Fälle mit als auch ohne Computer Navigation operiert hatten durchgeführt. Hier zeigte sich kein anderes Ergebnis, als in der unbeschränkten Hauptanalyse. Es wird daher davon ausgegangen, dass dieses mögliche Bias keinen relevanten Effekt auf das Studienergebnis hatte.

Eine weitere Limitation der Studie war, dass in den Daten des australischen Endoprothesenregisters keine Informationen zum chirurgischen Entscheidungsprozess für oder gegen Computer Navigation vorlagen. Es ist wahrscheinlich, dass Operateure Computer Navigation eher bei komplexen Fällen anwendeten, was die verminderte Rate an Revisionen aufgrund von Luxationen umso klinisch relevanter erscheinen lässt.

Das AOANJRR erfasst nur operative Revisionen aufgrund von Luxationen. Luxationen, welche ausschließlich konservativ mittels geschlossener Reposition behandelt wurden, werden nicht registriert. Der Effekt der Computer Navigation auf die Gefahr der Luxation könnte somit in Realität größer, als anhand der operativen Revisionen aufgrund von Luxation verdeutlicht, gewesen sein.

Zu Beginn dieses Kapitels wurde geschildert, welchen Einfluss eine korrekte und präzise Positionierung der Hüftgelenkspfanne auf das Luxationsrisiko, das Phänomen des „edge loagings" sowie die Beweglichkeit hat. Da im AOANJRR keine radiologischen Daten erfasst werden, konnten in dieser Studie keine Rückschlüsse auf die Beziehung zwischen Computer Navigation und Präzision der Pfannenpositionierung

gezogen werden. Eine direkte Korrelation zwischen präziserer Pfannenpositionierung und geringerer Revisionsrate aufgrund von Luxationen kann daher nicht gezogen werden.

Aufgrund der geringen Fallzahlen bei einer Aufschlüsselung der Ergebnisse nach den verschiedenen verfügbaren Systemen der Computer Navigation war eine Aussage hinsichtlich einer möglichen Über- oder Unterlegenheit einzelner Technologien nicht möglich.

Zwar darf der in dieser Studie aufgezeigte Zusammenhang zwischen dem Einsatz von Computer Navigation und einer geringeren Rate an Revisionen aufgrund von Luxation nicht mit einer Kausalität verwechselt werden. Jedoch legen die Ergebnisse nahe, dass Navigation ein nützliches Instrument sein kann für Operateure, die Luxationen vermeiden wollen.

3.2 Vergleich des postoperativen coronaren Alignments in patientenindividuell angefertigter und konventioneller Knie-Totalendoprothetik

Wunderlich F, Eckhard L* et al., J Pers Med. 2021 (*senior author)

Die Wiederherstellung einer neutralen mechanischen Beinachse in der Coronarebene im Rahmen des endoprothetischen Gelenkersatzes am Knie gilt als ein wichtiger prädiktiver Faktor für die Standzeit der Prothese. Ein Abweichen von der Neutralen von weniger als 3° in Varus oder Valgus wird empfohlen. Bei Abweichungen darüber ist mit vermehrter Belastung einzelner Prothesenbestandteile zu rechnen. Dies hat wiederum eine erhöhte Krafteinleitung auf das Interface Prothese-Zement-Knochen zur Folge, was in einer verfrühten aseptischen Lockerung der Prothese enden kann. Weiterhin wird das einliegende Polyethylen-Inlay asymmetrisch belastet, was ebenfalls zu einem verfrühten Verschleiß der Prothese führen kann.

Die Entwicklung patientenindividueller Kniegelenkstotalendoprothesen gehört zu den jüngeren Innovationen zur Steigerung der Patientenzufriedenheit und um noch zuverlässiger gute Operationsergebnisse in der Knieendoprothetik zu erzielen. Patientenindividuell angefertigte Knie-Totalendoprothesen werden mit Hilfe ebenfalls patientenindividuell angefertigter Instrumente und Sägelehren implantiert. Die Planung erfolgt durch den Hersteller anhand einer präoperativ angefertigten, CT-basierten 3D-Rekonstruktion der knöchernen Anatomie des Patienten.

Waren patientenspezifisch gefertigte Operationsinstrumente bereits seit Anfang der 2000er Jahre verfügbar, sind seit 2011 nun auch patientenindividuell angefertigte Implantate verfügbar. Neben der Wiederherstellung der mutmaßlichen präarthrotischen Gelenkgeometrie sowie der damit verbundenen natürlichen Bandspannung und einer knochensparenden Resektion an Femur und Tibia ist auch die neutrale mechanische Achsausrichtung in der Coronarebene ein Ziel der Design-Philosophie dieser Implantate.

Inwiefern das Ziel der neutralen mechanischen Beinachse durch patientenindividuell angefertigte Implantate und Instrumente häufiger erreicht wird als durch konventionelle Knie-TEP und Instrumentierung wurde in dieser Studie untersucht.

Die coronare Beinachse, bestimmt auf postoperativen Ganzbein-Standaufnahmen, von 283 mit patientenindividuellen Knie-TEPs (Fa. Conformis, iTotal CR) versorgten

Patienten wurde verglichen mit der von 283 mit konventionellen Knie-TEPs (Fa. ZimmerBiomet, Vanguard CR) versorgten Patienten. Bestimmt wurde der „hip-knee-ankle-angle“ (HKA) als Winkel zwischen der mechanischen Achse des Femurs (Verbindung des Femurkopfzentrums zum Zentrum der femoralen Kniegelenksbasis) und der mechanischen Achse der Tibia (Verbindung des Zentrums der tibialen Kniebasis zum Zentrum der talaren Gelenkfläche). Um eine besonders präzise Messung zu gewährleisten erfolgten die Messungen mittels Computer-gestützter CAD-Planung mit anschließender Rotationskorrektur (Abbildung 3). Die Rotation des Kniegelenks wurde hierbei anhand der Überlappung des Fibulakopfes durch die proximale Tibia bestimmt und mit der Formel zur Rotationskorrektur nach Maderbacher et al. korrigiert.

Postoperative Ganzbein-Standaufnahmen, die eine geringe Bildqualität z.B. durch exzessive Weichteilverschattung im Bereich des Hüftkopfes oder einen nicht adäquat zu korrigierenden übermäßigen Rotationsfehler aufwiesen, wurden von der Analyse ausgeschlossen.

Das mittlere Alter zum Zeitpunkt der Operation betrug in der Gruppe patientenindividueller Knie-TEPs 69,4 ± 10,31 Jahre (Variation 24-89 Jahre) mit einer Geschlechterverteilung von 149 Frauen zu 134 Männern. In der Gruppe der konventionellen Knie-TEPs betrug das mittlere Alter zum Zeitpunkt der Operation 71,7 ± 10,43 Jahre (Variation 35-92 Jahre). Hier waren 105 männliche und 174 weibliche Patienten eingeschlossen worden.

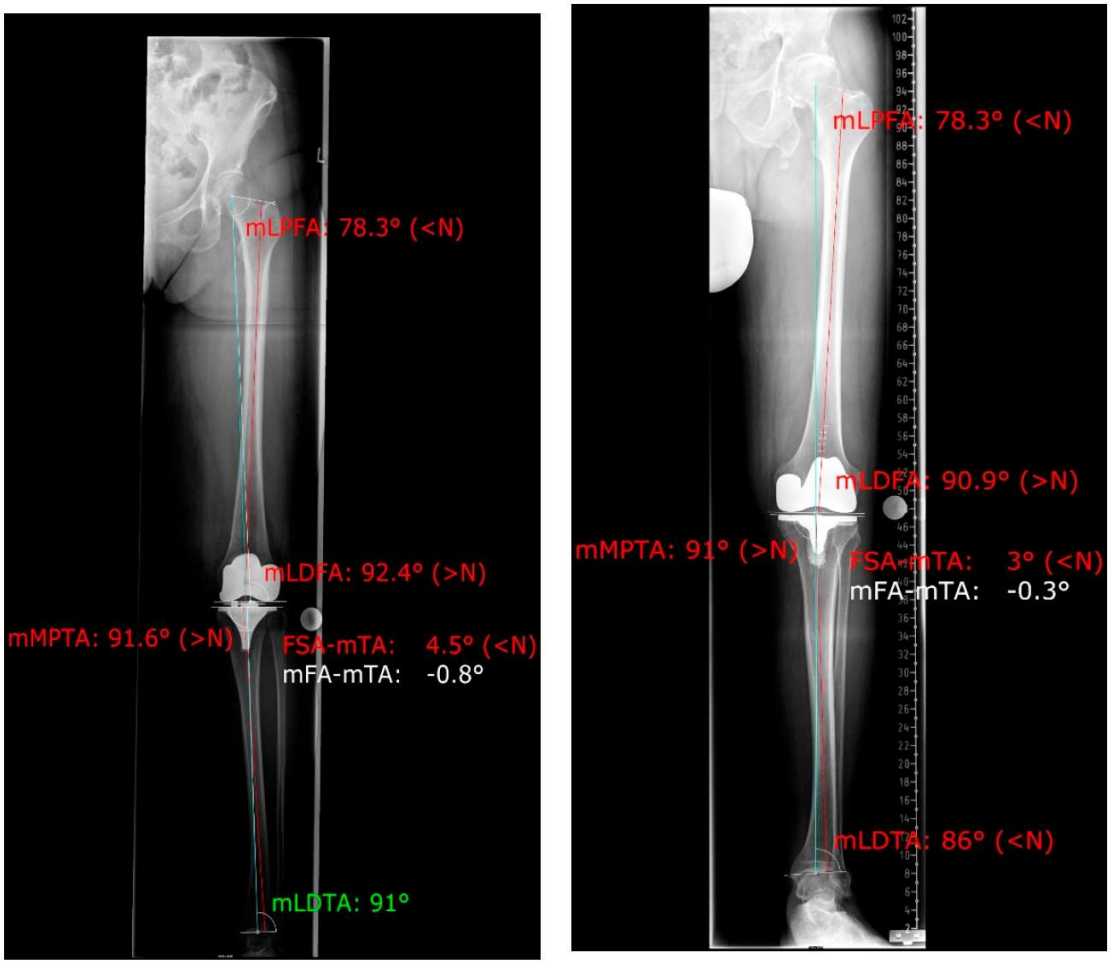

Abbildung 3: Messung der coronaren Beinachse mittels mediCAD 2D Planungssoftware; a) ZimmerBiomet Vanguard CR (konventionelles Implantat); b) Conformis iTotal CR (patientenindividuelles Implantat)

Die mittlere postoperative Beinachse betrug in der Gruppe der patientenindividuellen Knie-TEP 179,0° (SD 2,8°) und in der Gruppe der konventionellen Knie-TEP 179,2° (SD 3,1°) und war somit sowohl vom mittleren Ergebnis als auch von der Streuung her vergleichbar (Abbildung 4). Die maximalen Varus- bzw. Valgusachsen waren in beiden Gruppen ähnlich und betrugen 171.2° und 190.1° in der Gruppe konventioneller Knie-TEP sowie 168.6° und 187.7° in der Gruppe patientenindividueller Knie-TEP.

Auch der Anteil der Ausreißer mit Beinachsen-Abweichungen von mehr als 3° in Varus oder Valgus war in beiden Gruppen gleich und betrug 32,9%.

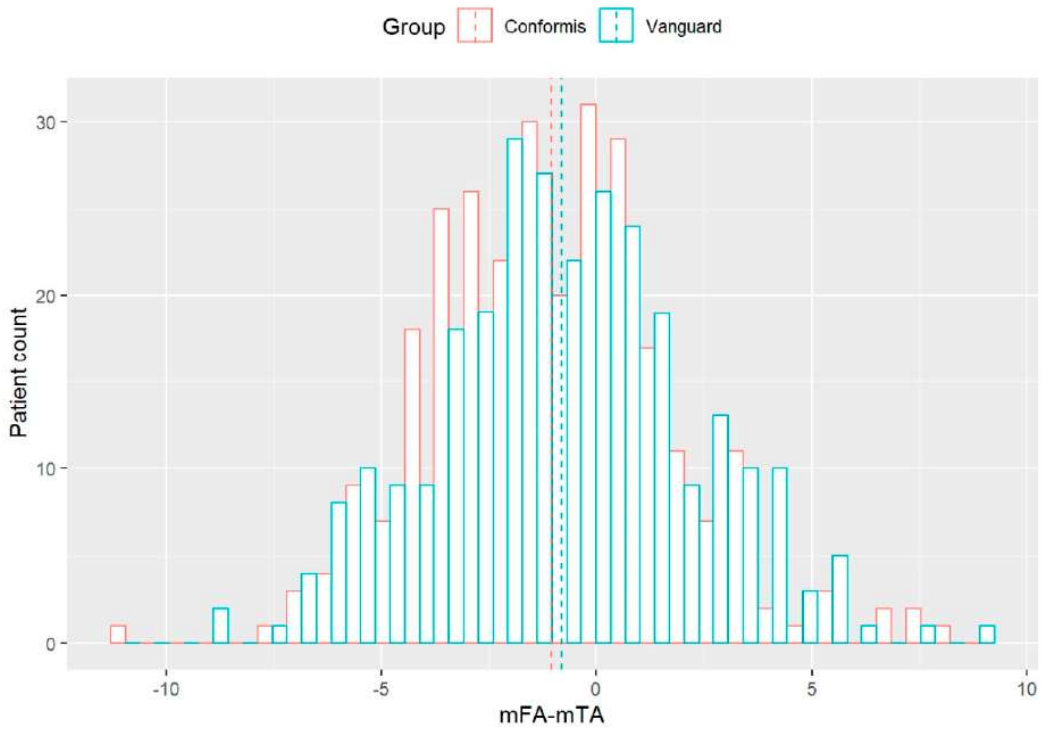

Abbildung 4: Verteilung der postoperativen Beinachsen nach patientenindividueller (rot) und konventioneller (türkis) Knie-TEP. O auf der X-Achse entspricht einer geraden Beinachse von 180°, die gepunkteten Linien zeigen den jeweiligen Mittelwert der beiden Gruppen.

Es zeigte sich somit zumindest hinsichtlich der postoperativen coronaren Beinachse kein Benefit durch die Nutzung patientenindividueller Implantate und Instrumente. Ob jedoch ein Einfluss auf die Standzeit der Implantate oder die Patientenzufriedenheit besteht, ist Gegenstand aktueller Forschung.

3.3 Erhöhte Dosierungen von Dexamethason und Gabapentin reduzieren den Opioid Verbrauch nach Knie-Totalendoprothetik

Eckhard L et al., Knee Surg Sports Traumatol Arthrosc. 2019

Die Implantation einer Knie-TEP zählt zu den schmerzhaftesten orthopädischen Eingriffen. Der akute postoperative Schmerz behindert nicht nur eine zügige Rehabilitation nach der Operation und führt zu einer schlechten Patientenzufriedenheit, sondern stellt auch einen bedeutenden Risikofaktor für das Auftreten von chronischem postoperativem Schmerz dar. Die zur Linderung der Beschwerden verbreitet eingesetzten Opioid-Analgetika besitzen neben ihrer guten Wirksamkeit allerdings auch ein erhebliches Nebenwirkungspotential. Übelkeit, Erbrechen, Obstipation, Sedierung und ein nicht zu vernachlässigendes Abhängigkeitspotential stellen gute Gründe dar, den Einsatz von Opioiden möglichst gering zu halten. Gleichzeitig darf eine Reduktion der Opioidmedikation nicht zu einem vermehrten Auftreten von postoperativen Schmerzen führen.

Daher sind moderne Schmerzbehandlungskonzepte nach Knie-TEP multimodal und nutzen neben lokalen oder regionalen Analgesieverfahren auch Co-Analgetika, die über eine Reduktion der Inflammationsreaktion bzw. der neuralen Sensitivierung ihre Wirkung entfalten. Das chirurgische Gewebetrauma führt zu einer lokalen peripheren sowie zu einer zentralen Entzündungsreaktion. Beide Inflammationsreaktionen spielen eine zentrale Rolle in der Vermittlung des Schmerzes. Daher stellen Glucokortikoide mit ihrem antiinflammatorischen Wirkungspotential eine Gruppe der Co-Analgetika dar.

Das Antikonvulsivum Gabapentin, das an die alpha-2-delta Untereinheit N-Typ spannungsabhängiger Calcium-Kanäle bindet wird primär in der Behandlung von Epilepsie und chronischem neuropathischem Schmerz eingesetzt. Es hat jedoch auch einen antinozizeptiven Effekt, der auf einem Einfluss auf die neurale Sensitivierung nach Nerven- oder Gewebetrauma beruht.

Sowohl für Dexamethason als auch für Gabapentin ist der perioperative Einsatz zwar etabliert, die optimale Dosierung und Anwendungsdauer jedoch noch nicht ausreichend untersucht ist.

Um zu evaluieren, ob eine Steigerung der postoperativ verabreichten Dosen an Dexamethason und Gabapentin in einem etablierten multimodalen Schmerzprotokoll zu einem geringeren Opioid-Verbrauch nach Knie-TEP führt, wurden in dieser Arbeit die Daten jeweils einer Patientengruppe vor und nach einer erfolgten Medikationsumstellung retrospektiv untersucht.

Bei ansonsten unveränderter Medikation erhielten Patienten nach der Umstellung postoperativ 900mg statt zuvor 600mg Gabapentin täglich sowie 10mg statt zuvor 4mg Dexamethason an den ersten beiden postoperativen Tagen. Es wurde die Hypothese aufgestellt, dass sich hierdurch die eingenommene Opioid-Gesamtdosis reduzieren ließe. An der Basismedikation, bestehend aus 400 mg Celecoxib (Celebrex) und 975 mg Acetaminophen (Tylenol) 1-3 Stunden präoperativ sowie 975 mg Acetaminophen (Tylenol) dreimal täglich, 500 mg Naproxen (Naprosyn) zweimal täglich sowie der Opioid-Basismedikation, welche üblicherweise aus 100mg Tramadol (Ultram) alle 8 Stunden oder 1-2 mg Hydromorphon (Dilaudid) bestand, wurde nichts verändert. Gegen Durchbruchschmerzen wurden Ketorolac, Hydromorphon oder Oxycodon in Abhängigkeit des Schmerzniveaus verabreicht.

Ein Screening der Knie-TEP Patienten eines einzelnen Operateurs vor- bzw. rückwärts vom Zeitpunkt der Änderung des Schmerzschemas ausgehend erfolgte, bis in beiden Gruppen 80 Patienten rekrutiert waren. Ausgeschlossen wurden Patienten die eine simultane beidseitige Versorgung erhielten, unter Opioid-Dauermedikation standen oder eine mit einer separaten Opioid-Gabe verbundene Allgemeinanästhesie erhielten. Da mehrere verschiedene Opioide verabreicht wurden, erfolgte eine Umrechnung der Applikationen in Morphinäquivalente.

Insgesamt wurden 186 Patienten gescreent. Sechs Patienten die eine Allgemeinanästhesie erhalten hatten, vier Patienten die eine einzeitige beidseitige OP erhalten hatten und 16 Patienten mit einer laufenden Dauer-Opioid-Medikation wurden von der Analyse ausgeschlossen.

Sowohl innerhalb von 24h, 48h, 72h als auch während des gesamten stationären Aufenthalts war die Opioid-Einnahme in der Gruppe mit gesteigerter Dexamethason und Gabapentin Dosierung nach neuem Schmerzschema signifikant geringer (Abbildung 5). Innerhalb der ersten beiden Tage nach einer Knie-TEP waren diese Patienten auf etwa 25% weniger Opioide angewiesen.

Weiterhin erfolgte eine „treated per protocol“ Analyse in der die Patienten nach der erhaltenen Co-Analgetika Medikation und nicht nach Zugehörigkeit zur ursprünglichen Gruppe anlysiert wurden, um möglichen Fehlmedikationen in der Übergangsphase nach Umstellung der Basismedikation Rechnung zu tragen. Auch hier war die Opioid Einnahme der Patienten mit gesteigerter Dexamethason und Gabapentin Dosierung innerhalb von 48 und 72h signifikant geringer.

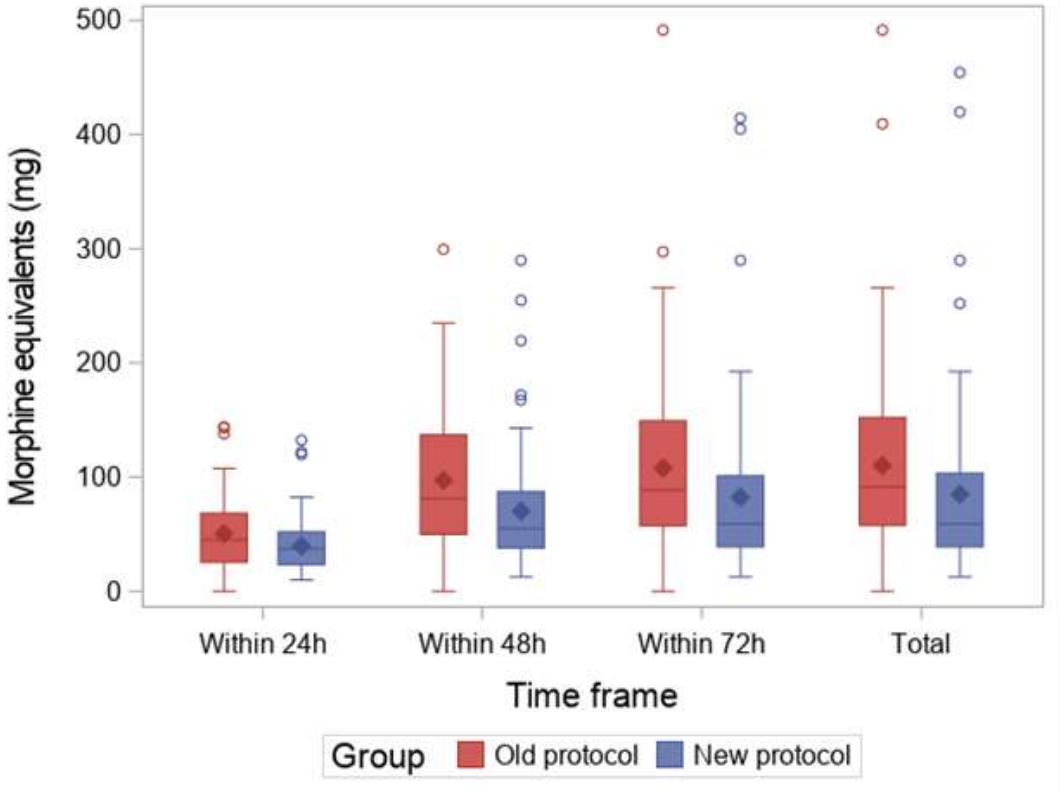

Abbildung 5: Boxplot des Opioidverbrauchs in Morphinequivalenten

Erstmals konnte in dieser Studie also gezeigt werden, dass die über den direkt perioperativen Zeitraum hinaus verlängerte und zudem gesteigerte Gabe der untersuchten Co-Analgetika zu einem verringerten Opioid-Bedarf führt.

Auch andere Autoren beobachteten positive Effekte durch den Einsatz gesteigerter Dexamethason-Dosen nach Knietotalendoprothesenoperationen. Jules-Elysee et al. etwa demonstrierten niedrigere Interleukin-6 Spiegel sowie niedrigere Schmerzangaben auf der visuellen Analogskala nach gesteigerten Dexamethason-Dosierungen, was eine

Schmerzreduktion aufgrund des antiinflammatorischen Effektes von Dexamethason nahelegt.

Auch diese Studie hat Limitationen. Bedingt durch das retrospektive Design ist eine unvollständige oder inkorrekte Dokumentation der verabreichten Medikation möglich, wobei sich etwaige Verzerrungen hierdurch aufgrund der großen Kohortengröße nivellieren sollten. Weiterhin erfolgten zwei Umstellungen der Medikation gleichzeitig. Ob die beobachteten Effekte zum reduzierten Opioidbedarf also mit der geänderten Dexamethason- oder Gabapentin-Dosierung zusammenhängen kann mit den vorliegenden Daten nicht geklärt werden.

Wann immer die Dosierung einer Medikation verändert wird, gilt es auch die potentiell damit verbundenen unerwünschten Wirkungen zu beleuchten. Da Dexamethason die inflammatorische Antwort des Körpers limitiert, ist ein mit einer gesteigerten Dosierung verbundenes Risiko einer erhöhten Rate an periprothetischen Infektionen sowie Wundheilungsstörungen denkbar. Daten zu diesen Komplikationen wurden aufgrund des retrospektiven Designs der Studie nicht erhoben. Zahlreiche vorherige Studien zum Einsatz von Dexamethason in der Orthopädie fanden jedoch in der Vergangenheit keinen Zusammenhang mit höheren Raten an Wundinfektionen.

Die häufigsten Nebenwirkungen verbunden mit der Einnahme von Gabapentin sind Sedation und Schwindel. Dieser Aspekt sollte in künftigen Studien, insbesondere in Anbetracht der postoperativ bestehenden Gefahr von Stürzen bei noch unsicherem Gang, weiter untersucht werden.

Zusammenfassend konnte in dieser Studie gezeigt werden, dass durch gesteigerte Dosen an Dexamethason und Gabapentin in den ersten 48 Stunden nach Knie-TEP der Bedarf an Opioiden um 25% gesenkt werden konnte.

3.4 Die KOOS-12 Kurzfassung zeigt keinen ceiling effect, gute Änderungssensitivität und Konstruktvalidität verglichen mit etablierten Messinstrumenten patientenberichteter Ergebnisse nach Knie-Totalendoprothetik

Eckhard L et al., Knee Surg Sports Traumatol Arthrosc. 2021

In der Bewertung des Therapieerfolges nach medizinischen Behandlungen rückt neben objektiven, vom Untersucher erfassten Kriterien immer mehr das vom Patienten empfundene und berichtete Outcome in den Fokus. Gerade in der Endoprothetik, welche das Ziel hat durch eine Verbesserung der Gelenkfunktion und Linderung der arthrosebedingten Schmerzen die Lebensqualität des Patienten zu verbessern, entscheidet maßgeblich die Einschätzung des Patienten darüber, ob die Behandlung erfolgreich war. Anhand von „patient reported outcome measures“ (PROMs) wird die Patientenzufriedenheit erfasst.

Der Knee Injury and Osteoarthritis Outcome Score (KOOS) ist ein etabliertes und häufig zur Bestimmung der Patientenzufriedenheit nach Knie-TEP eingesetztes PROM. Er wurde in seiner Ursprungsversion 1998 von Roos et al. publiziert und seitdem um verschiedene spezielle Subskalen wie etwa für Endoprothesen (KOOS-JR, „joint replacement“), funktionell ambitioniertere Kohorten (KOOS-PS, „physical function short form“) oder das Patellofemoralgelenk (KOOS-PF, „patellofemoral subscale“) ergänzt.

Um den Bearbeitungsaufwand auf Seiten des Patienten zu reduzieren wurde von Gandek et al. eine 12-Fragen Kurzversion des ursprünglich 42 Fragen umfassenden Fragebogens entwickelt– der KOOS-12. Anhand von „computer adaptive test (CAT)“ Simulationen wurden Fragen basierend auf Inhalt, Abdeckung einer breiten Meßbreite, hoher Einzelfrageninformation und qualitativer Informationen ausgewählt.

Vor der Veröffentlichung der hier zusammengefassten Studie war keine externe Validierung des KOOS-12 publiziert worden, sodass dies Ziel dieser Studie war. Hierzu wurden die Daten einer unabhängigen Multi-Center-Studie zur Untersuchung des Saiph Knie-TEP Systems (MatOrtho, Leatherhead, United Kingdom) im Rahmen welcher die Patienten die KOOS, KOOS-Joint Replacement Kurzversion (KOOS-JR), KOOS Physical Function Kurzversion (KOOS-PS), Western Ontario and McMaster

Universities Osteoarthritis Index (WOMAC), Oxford Knee Score (OKS) und University of California, Los Angeles (UCLA) Aktivitätsskala Fragebögen präoperativ sowie bei der follow-up Untersuchung 12 Monate postoperativ ausgefüllt hatten, verwendet. Die KOOS-12 Schmerz-, Funktions- und Lebensqualitäts-Subskalen sowie der Gesamtscore wurden wie von den Entwicklern des PROMs beschrieben aus der Langversion des KOOS errechnet.

Patienten wurden von 13 verschiedenen Chirurgen an 16 Standorten eingeschlossen. Teilnahmeberechtigt waren Patienten, die eine primäre Knie-Totalendoprothese aufgrund einer Osteoarthrose durch einen der an der Studie beteiligten Chirurgen erhielten. Für die hier dargestellte Analyse wurden zudem Patienten ausgeschlossen, die eine einzeitige beidseitige Operation erhielten oder bei denen präoperative oder postoperative Fragebögen unvollständig waren.

Aufgrund unterschiedlicher verwendeter Scoring Algorithmen der einzelnen Fragebögen wurden Scores gegebenenfalls so invertiert, dass hohe Scores jeweils das gute Ende und niedrige Scores das schlechte Ende der Skala repräsentierten. Zudem erfolgte eine Normalisierung der Ergebnisse hin zu einer 0-100 Punkte Skala wann immer Scores miteinander verglichen wurden.

Die Konstruktvalidität wurde anhand einer Spearmans Korrelations-Analyse zur Untersuchung der Assoziation zwischen KOOS, KOOS-JR, KOOS-PS, KOOS-12, WOMAC, OKS und UCLA untersucht. Dies erfolgte jeweils sowohl für die Gesamtscores, als auch für die einzelnen Subskalen, sofern vorhanden. Eine Korrelation mit $r > 0{,}70$ wurde als hoch angesehen, $0{,}50 < r < 0{,}70$ wurde als moderat bewertet, $0{,}30 < r < 0{,}50$ wurde als niedrig angesehen und $r < 0{,}30$ wurde als vernachlässigbar gewertet.

Ein Deckeneffekt (ceiling effect) wurde als vorhanden angesehen, wenn mehr als 15% der Teilnehmer die bestmögliche Punktzahl eines Scores erreichten. Die Änderungssensitivität (responsiveness) aller Subskalen und Gesamtscores wurde mittels gepaarter t-Tests der Veränderungen der Score-Ergebnisse zwischen den Untersuchten Zeitpunkten und die Berechnung von Cohen's *d* ermittelt. Werte von 0,2 und darunter zeigten kleine Effektgrößen an, Werte um 0,5 moderate Effektgrößen und Werte von 0,8 und höher große Effektgrößen.

Eine post-hoc Poweranalyse wurde anhand folgender Parameter gerechnet: Effektgröße (p=2,5), alpha (α = 0,05) und Stichprobenumfang (n = 527 und n = 327). Es wurde so eine Power von 0,99 berechnet.

Die Korrelation der untersuchten PROMs mit dem KOOS-12 sind in Tabelle 1 dargestellt. Die KOOS Symptome, KOOS Funktion, Sport und Freizeitaktivitäten sowie die WOMAC Steifigkeits-Subskalen zeigten eine moderate Korrelation mit dem KOOS-12, während die Korrelationen mit dem UCLA durchweg niedrig waren. Alle anderen Korrelationen waren hoch.

	Preop Correlations				1 year Correlations			
	KOOS-12 Total	KOOS-12 Pain	KOOS-12 Function	KOOS-12 QoL	KOOS 12 Total	KOOS-12 Pain	KOOS-12 Function	KOOS-12 QoL
KOOS Symptoms	0.55**	0.48**	0.48**	0.46	0.69**	0.65**	0.54**	0.62**
KOOS Pain	0.85**	0.89**	0.78**	0.59**	0.84**	0.93**	0.69**	0.67**
KOOS ADL	0.88**	0.78**	0.90**	0.63**	0.84**	0.74**	0.81**	0.69**
KOOS Sports	0.69**	0.50**	0.71**	0.57**	0.59**	0.39**	0.69**	0.46**
KOOS QoL	0.85**	0.57*	0.60**	1.00**	0.90**	0.64**	0.62**	1.00**
KOOS PS	0.86**	0.71**	0.89**	0.64**	0.75**	0.58**	0.82**	0.60**
KOOS JR	0.87**	0.79**	0.85**	0.62**	0.86**	0.81**	0.79**	0.70**
WOMAC Pain	0.84**	0.93**	0.76**	0.54*	0.80**	0.90**	0.66**	0.62**
WOMAC Stiffness	0.62**	0.57**	0.60**	0.45	0.64**	0.60**	0.54**	0.55**
WOMAC Function	0.89**	0.78**	0.90**	0.63**	0.83**	0.73**	0.81**	0.68**
WOMAC Total	0.91**	0.84**	0.90**	0.63**	0.85**	0.79**	0.79**	0.69**
Oxford-12 normalized	0.85**	0.74**	0.78**	0.68**	0.81**	0.74**	0.71**	0.70**
UCLA normalized	0.44**	0.35**	0.40**	0.39*	0.30**	0.23**	0.33**	0.24**

*Tabelle 1: Spearman's Korrelationskoeffizienten (r) zwischen den einzelnen Funktionsscores (** zeigt eine Signifikanz auf dem Niveau 0.01 an, *zeigt eine Signifikanz auf dem Niveau 0.05 an). Präoperative und 1-Jahres Korrelationen wurden mit den entsprechend korrespondierenden Zeitpunkten durchgeführt. Niedrige Korrelationen (0,30 < r < 0,50) sind rot unterlegt, moderate Korrelationen in gelb (0,50 < r < 0,70) und hohe Korrelationen in grün (r > 0,70).*

Ein ceiling Effekt fand sich ein Jahr postoperativ bei den KOOS Schmerz-, Aktivitäten des täglichen Lebens- und Lebensqualitäts-Subskalen sowie im KOOS-JR.

Die nur moderate Korrelation der KOOS-12 Funktionsskala mit der KOOS Funktion, Sport und Freizeitaktivitäten Skala kann dadurch erklärt werden, dass nur eine Frage dieser Subskala aus der Langversion in die Kurzversion übernommen wurde. Während die in dieser Skala abgefragten, schwierigeren Aktivitäten für den typischen Knie-TEP Patienten weniger relevant sind, wird daher für die Untersuchung jüngerer, aktiverer Kohorten der Einsatz der KOOS Funktion, Sport und Freizeitaktivitäten Skala aus der Langversion empfohlen.

Die Korrelation der KOOS-12 Schmerz Subskala mit der KOOS Schmerz Subskala war hoch, was anzeigt, dass die in der Kohorte vorhandene Varianz auch durch die verkürzte Version des Fragebogens suffizient abgebildet wurde. Das Konstrukt Lebensqualität wurde in der Lang- wie in der Kurzversion mit denselben vier Fragen untersucht, weshalb die Korrelation natürlicherweise bei 1,0 lag.

Der WOMAC und der OKS sind Scores die häufig für die externe Validierung Knie-spezifischer Fragebögen eingesetzt werden. Beide zeigten eine hohe Korrelation mit dem KOOS-12, was zeigt, dass der KOOS-12 zur Evaluation Knie-spezifischer Fragestellungen zur Patientenzufriedenheit gut geeignet ist.

Die responsiveness aller PROMs wurde untersucht, indem der mittlere Unterschied zwischen präoperativem Ergebnis und dem Ergebnis zum Zeitpunkt des 12 Monate follow ups berechnet und anschließend die Effektgröße anhand von Cohens *d* ermittelt wurde. Die Effektgröße des UCLA war moderat, wohingegen alle weiteren PROMs große Effektgrößen aufwiesen. In der Analyse der Änderungssensitivität zeigten alle untersuchten Skalen eine signifikante Veränderung von präoperativ zu einem Jahr postoperativ. Die Änderungssensitivität des KOOS-12 zeigte sich mit einem Cohens *d* von 2,4 als im Vergleich im Vergleich zu den anderen untersuchten Fragebögen besonders hoch.

Zusammengefasst war dies somit die erste Studie, die den KOOS-12 in Relation zu anderen Knie-spezifischen Scores evaluierte und hierbei zeigen konnte, dass der KOOS-12 eine gute Konstruktvalidität hat, keinen relevanten ceiling effect aufweist und eine gute Sensitivität gegenüber Veränderungen von Schmerz, Funktion und Lebensqualität besitzt.

3.5 Der ceiling effect von Messinstrumenten patientenberichteter Ergebnisse für die Knie-Totalendoprothetik

Eckhard L et al., Orthop Traumatol Surg Res. 2021

Gerade bei der Untersuchung von Patientenkollektiven nach endoprothetischem Gelenkersatz an Hüfte und Knie haben es Kliniker und Wissenschaftler gleichermaßen mit einer generell eher hohen Patientenzufriedenheit zu tun. Werden in diesem Fall PROMs eingesetzt, deren Diskriminationsfähigkeit am oberen Ende der Skala gering ist, kommt es zu einer Cluster-Bildung. Der Deckeneffekt (ceiling effect) beschreibt die Ansammlung von Patienten mit hohen Punktzahlen am oberen Ende der Skala eines PROMs und ist somit ein Maß für dessen Diskriminationsfähigkeit.

Ist ein ceiling effect vorhanden wird die in einer Patientenkohorte vorhandene Varianz im Outcome insuffizient abgebildet. Zudem können dann Verbesserungen von einem Untersuchungszeitpunkt zum anderen oder Unterschiede zwischen untersuchten Gruppen nicht erfasst werden. Folglich sind bei der Bestimmung der Patientenzufriedenheit nach Möglichkeit PROMs ohne einen für die betreffende Kohorte relevanten ceiling effect einzusetzen.

Für die Berechnung des ceiling effects werden in der Literatur unterschiedliche Methoden herangezogen. Thomsen et al. betrachteten einen ceiling effect als vorhanden, wenn Befragte einen Score innerhalb von 15% des Maximalpunktwertes erzielten. Jenny et al. hingegen berechneten den Anteil der Befragten innerhalb einer Standardabweichung vom Maximalpunktwert und gaben hierüber das Ausmaß des ceiling effects an. In der Absicht Qualitätskriterien für die Messeigenschaften von Fragebögen zu definieren empfahlen Terwee et al., einen ceiling effect als vorhanden anzusehen, wenn 15% oder mehr der Befragten die höchste mögliche Punktzahl erzielten, wie in einer Arbeit von McHorney et al. beschrieben. Diese Methode ist zum einen validiert und zum anderen weit verbreitet, weshalb sie in der vorliegenden Arbeit ebenfalls angewendet wurde.

Es wurde bereits für die meisten der häufig verwendeten patient reported outcome measures untersucht, ob sie einen ceiling effect aufweisen. Jedoch ist das Auftreten eines ceiling effects abhängig vom untersuchten Patientenkollektiv sowie dem Untersuchungszeitpunkt. Absolute Unterschiede in der Anzahl zum Beispiel besonders

zufriedener Patienten können einer untersuchten Behandlungsmethode oder einem bestimmten Implantat inhärent sein. In der Literatur vorhandene Ergebnisse zum ceiling effect verschiedener PROMs können also nicht zwischen mehreren Publikationen verglichen werden.

Um einen direkten Vergleich des ceiling effects zu ermöglichen wurde er in dieser Arbeit parallel am selben Patientenkollektiv für einige der am häufigsten nach Knie-TEP eingesetzten patient reported outcome measures bestimmt. Ein Jahr nach Knie-TEP wurden der Knee Injury and Osteoarthritis Outcome Score (KOOS), die KOOS 12-Fragen Kurzversion (KOOS-12), die KOOS-Joint Replacement Kurzversion (KOOS-JR), die KOOS Physical Function Kurzversion (KOOS-PS), der Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), der Oxford Knee Score (OKS) sowie der Forgotten Joint Score (FJS) bestimmt. Genutzt wurden die Daten von 563 Patienten einer unabhängigen Multi-Center-Studie zur Untersuchung des Saiph Knie-TEP Systems (MatOrtho, Leatherhead, United Kingdom) mit medialer Stabilisierung durch ein sogenanntes „Ball-in-socket“ Design. Die Generalisierbarkeit der Daten war durch die Beteiligung von 13 Operateuren an 16 Standorten gut. Entsprechend aktueller Empfehlungen zur Definition von Qualitätskriterien von Fragebögen zum Gesundheitszustand wurde ein ceiling effect als vorhanden angesehen, wenn 15% oder mehr der Teilnehmer das bestmögliche Ergebnis eines PROMs erreichten.

In die Analyse wurden die Daten von 279 Männern (49,6%) und 284 Frauen (50,4%) eingeschlossen. Für den Body-Mass-Index sowie das Alter zeigten sich für Endoprothetik-Kohorten typische Mittelwerte (BMI 32,2kg/m^2; Alter 68,0 Jahre).

Ein Jahr nach Knie-TEP zeigte sich ein ceiling effect für die Schmerz- und Aktivitäten des täglichen Lebens (ADL)- Subskalen des KOOS sowie für den KOOS JR. Die KOOS Schmerz, Symptome, ADL und Lebensqualität (QoL) Subskalen sowie der Gesamt-WOMAC und der KOOS JR zeigten zwei Jahre nach Knie-TEP einen ceiling effect (Abbildung 6).

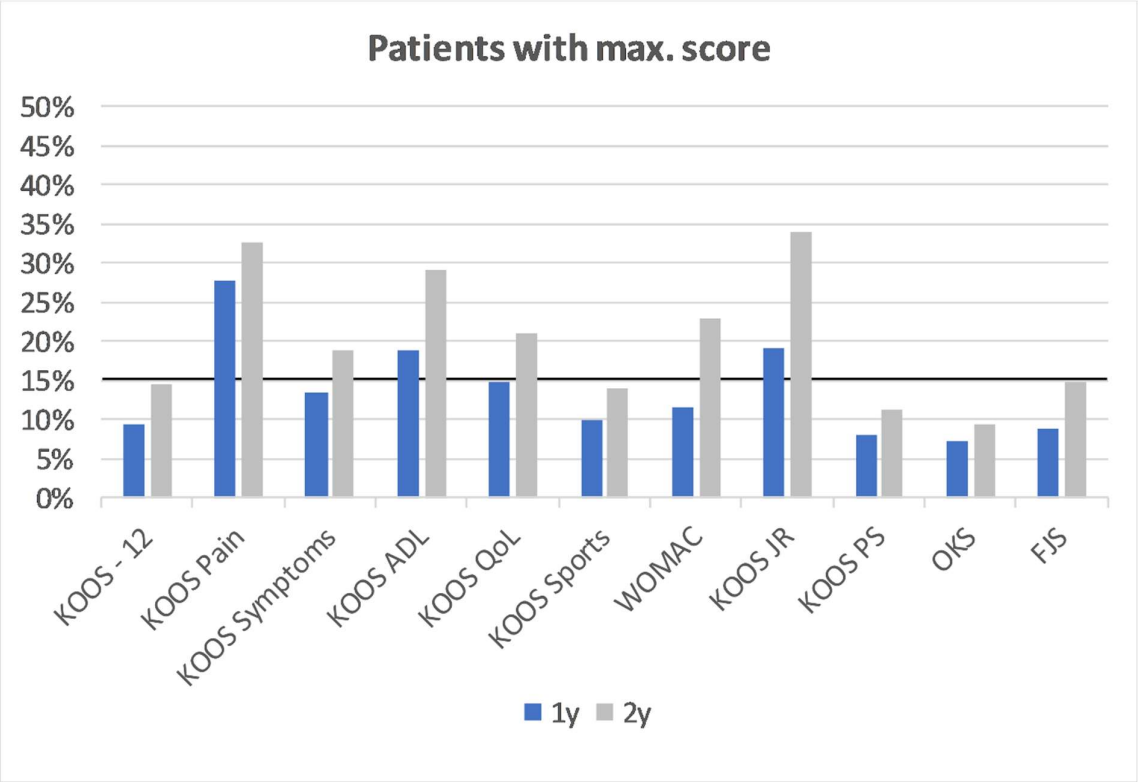

Abbildung 6: Balkendiagramm des Anteils der Patienten mit dem bestmöglichen Ergebnis in den untersuchten PROMs ein bzw. zwei Jahre nach Knie-TEP

Auch die Verteilung der erreichten Ergebnisse der verschiedenen PROMs wurde analysiert. Während der KOOS-12 und der FJS eine gleichmäßige Verteilung der Punktzahlen zeigten, fand sich für die KOOS Subskalen, WOMAC, KOOS JR, KOOS PS und OKS eine Verdichtung von Ergebnissen am oberen Skalenende (Abbildung 7).

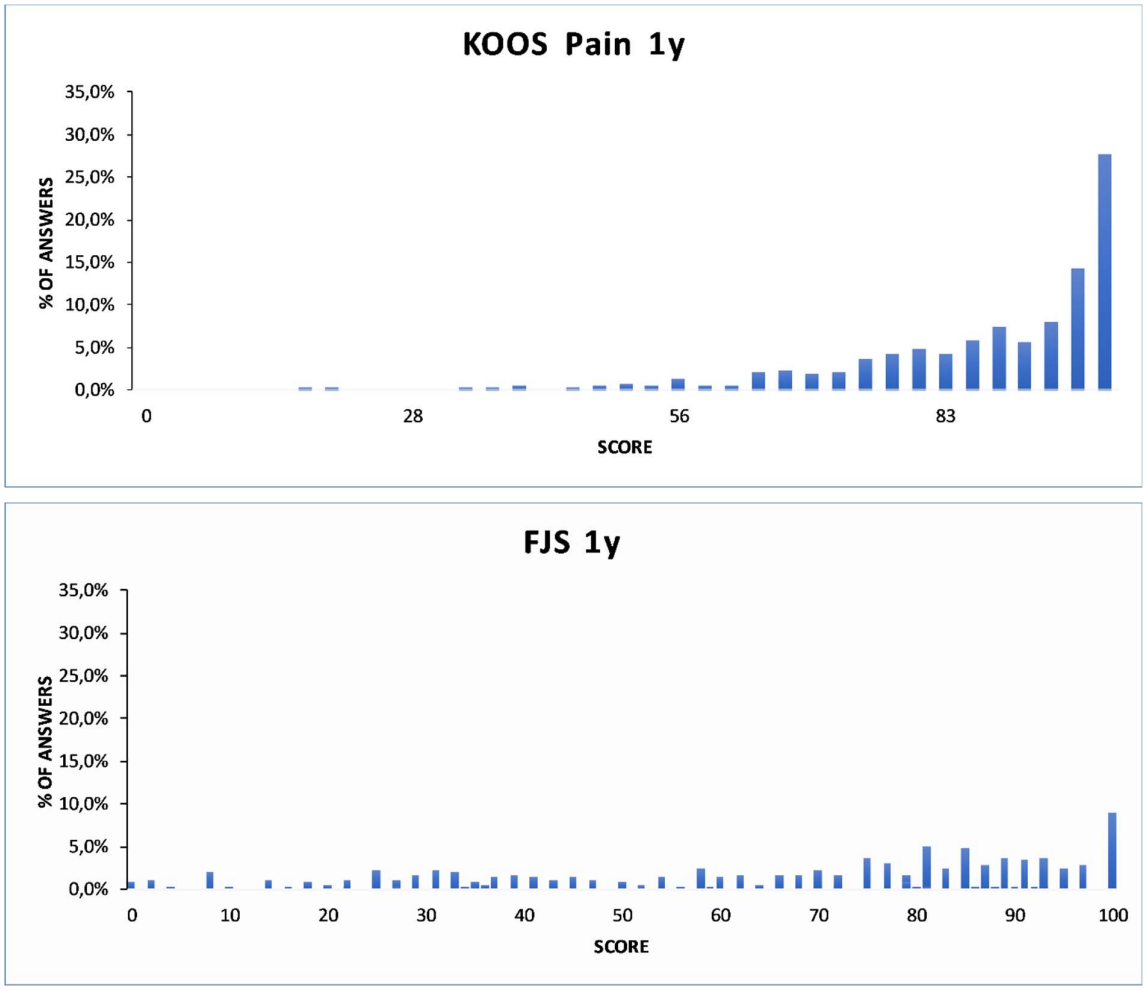

Abbildung 7: Beispielhafte Darstellung der Punktzahlverteilung in der KOOS Schmerz Subskala sowie im FJS. In der KOOS Schmerz Subskala ist eine deutliche Ansammlung bei hohen Punktzahlen zu beobachten, während im FJS eine gleichmäßige Verteilung vorherrscht.

In der Darstellung der erreichten Punktzahlen fiel beim Oxford Knee Score eine Häufung von Ergebnissen direkt unterhalb der maximal erreichbaren Punktzahl auf. Daher wurde eine separate Analyse der erreichten Ergebnisse der Einzelfragen von Oxford Knee Score und Forgotten Joint Score durchgeführt. Hier zeigte sich für den FJS eine gleichmäßige Verteilung der erreichten Höchstpunktzahlen in den einzelnen Fragen, beim OKS jedoch zeigte sich für die Frage nach der Fähigkeit sich Hinzuknien ein deutlich geringerer Anteil an Patienten, der die mögliche Höchstpunktzahl erreichte. Diese einzelne Frage führte folglich bei der oben genannten, angewendeten Methode zur Bestimmung des ceiling effects zu einem scheinbar niedrigeren Effekt. Hierdurch wird erneut die Bedeutsamkeit der Methodenauswahl unterstrichen. Die in Abbildung 7 gezeigte graphische Darstellung ist weniger anfällig für solche Artefakte und daher nach

Meinung der Autoren der vorliegenden Arbeit eine wichtige Ergänzung zur reinen numerischen Nennung des ceiling effects. Ein clustering von Ergebnissen am oberen Skalenende wird hier leicht erkannt und eine mathematische Methode diesen Effekt in Zahlen, die zwischen Publikationen vergleichen werden können, auszudrücken sollte in zukünftigen Studien entwickelt werden.

In dieser bisher umfangreichsten Analyse des ceiling effects von PROMs im Einsatz nach Knie-TEP konnte also gezeigt werden, dass erhebliche Unterschiede hinsichtlich der Diskriminationsfähigkeit am oberen Skalenende der am häufigsten eingesetzten Messinstrumente zur Bestimmung der Patientenzufriedenheit bestehen.

Über alle PROMs hinweg zeigte sich, dass insbesondere Subskalen zur Bestimmung der Patientenzufriedenheit hinsichtlich des Schmerzes einen ausgeprägten ceiling effect aufweisen. Dies lässt sich am ehesten damit erklären, dass bei dem gemessenen Konstrukt Schmerz eine natürliche Obergrenze besteht. Mit anderen Worten, weniger Schmerz als kein Schmerz kann von den Patienten nicht empfunden werden, weshalb es hier besonders häufig zur Auswahl der bestmöglichen Antworten kommt.

Zurückkehrend zur Ausgangsfrage, welche der untersuchten PROMs sich für den Einsatz in mutmaßlich gut abschneidenden Kohorten besonders eignen, lässt sich anhand der in dieser Studie gewonnenen Erkenntnisse eine Kombination aus FJS und KOOS-12 empfehlen. Beide Instrumente weisen keinen signifikanten ceiling effect auf, zeigen eine gleichmäßige Verteilung der Ergebnisse und bedienen sich jeweils nur 12 Fragen. Insbesondere die Kombination der beiden Fragebögen erscheint sinnvoll. Während der FJS misst inwiefern das als ultimative Ziel der Endoprothetik proklamierte „vergessene Gelenk“ erreicht wurde, stellt der KOOS-12 neben dem Gesamtergebnis Subskalen zu Schmerz, Funktion und Lebensqualität zur Verfügung.

3.6 „Minimal important change“ und „minimum clinically important difference“ Werte des KOOS-12 Fragebogens nach Knie-Totalendoprothetik

Eckhard L et al., Knee. 2021

In der Interpretation von Ergebnissen von patient reported outcome measurements ist es entscheidend statistisch signifikante von klinisch relevanten Unterschieden zwischen Gruppen oder Veränderungen über die Zeit zu unterscheiden. Zur besseren Einschätzung der klinischen Bedeutung von PROM-Ergebnissen wurden die Maßzahlen „minimal important change“ (MIC) und „minimum clinically important difference“ (MCID) definiert. Der MIC beschreibt die geringste Änderung im Ergebnis eines PROM im Vergleich zum Ausgangswert, die ein Patient als klinisch relevant einschätzt. Die MCID wiederum repräsentiert den geringsten Unterschied zwischen zwei Messpunkten, der von Patienten bemerkt wird.

Ist beispielsweise die Veränderung von präoperativ zu postoperativ nach Implantation einer Knie-TEP bei einem Patienten kleiner als der MIC, fühlt sich der Patient nicht relevant verbessert. Der MIC ist also anzuwenden, wenn die Veränderungen innerhalb einer Kohorte zwischen zwei Zeitpunkten verglichen werden. Wenn hingegen die Unterschiede zwischen zwei verschiedenen Gruppen, zum Beispiel beim Vergleich zweier Endoprothesen unterschiedlicher Bauart, bewertet werden sollen, ist der MCID zu verwenden.

Nachdem die vorangegangenen und unter 3.4 und 3.5 zusammengefassten Arbeiten eine gute Performance des KOOS-12 hinsichtlich Validität, Reliabilität, Responsiveness und ceiling effect gezeigt hatten war es anschließend Ziel der hier zusammengefassten Studie, MIC und MCID erstmals für den KOOS-12 zu bestimmen. Hierzu beantworteten Patienten im Rahmen einer Multicenter-Studie zur Untersuchung des Saiph Knie-Systems (MatOrtho, Leatherhead, United Kingdom) neben dem KOOS-12 ein Jahr postoperativ auch die Anker-Frage, wie sie ihre Probleme nun insgesamt im Vergleich zu präoperativ bewerten. Anhand der Antworten auf einer 5-Punkt Likert-Skala von „viel besser“ bis „viel schlechter“ wurden die Patienten entsprechend des Anker-basierten Vorgehens zur Bestimmung von MIC und MCID in klinisch relevant

gebesserte und nicht klinisch relevant gebesserte gruppiert. Tabelle 2 stellt diese Gruppierung samt prozentualem Anteil der Teilnehmer dar.

Importantly Improved	Patients much better	92.3%	97.1%
	Patients a little better	4.8%	
Not Importantly improved	Patients about the same	1.1%	2.8%
	Patients a little worse	1.1%	
	Patients much worse	0.6%	

Tabelle 2: Darstellung der Gruppierung in relevant verbesserte und nicht relevant verbesserte Patienten anhand der Anker-Frage samt prozentualem Anteil der Antworten und Gruppen.

Die Bestimmung erfolgte sowohl für den KOOS-12 Gesamtscore als auch für die Subskalen Schmerz, Lebensqualität und Funktion. Die MIC-Werte wurden mittels des „predictive modeling approaches“ (MIC_{pred}), wie von Terluin et al. beschrieben, berechnet. Diese Methode wurde aufgrund ihrer überlegenen Präzision und der geringeren Abhängigkeit von der Korrelation zwischen PROM und Ankerfrage im Vergleich zur receiver operating characteristics Methode (MIC_{ROC}) ausgewählt.

Zur Bestimmung des MCID wurde die Differenz im mean change score zwischen Patienten die angegeben hatten eine „leichte Besserung“ und Patienten die angegeben hatten „keine Besserung“ erfahren zu haben errechnet und mittels linearer Regressionsanalyse für potentielle Confounder adjustiert. Abbildung 8 zeigt die mean change scores für die drei Subskalen und den Gesamtscore, jeweils unterteilt nach relevant verbesserten und nicht relevant verbesserten Patienten.

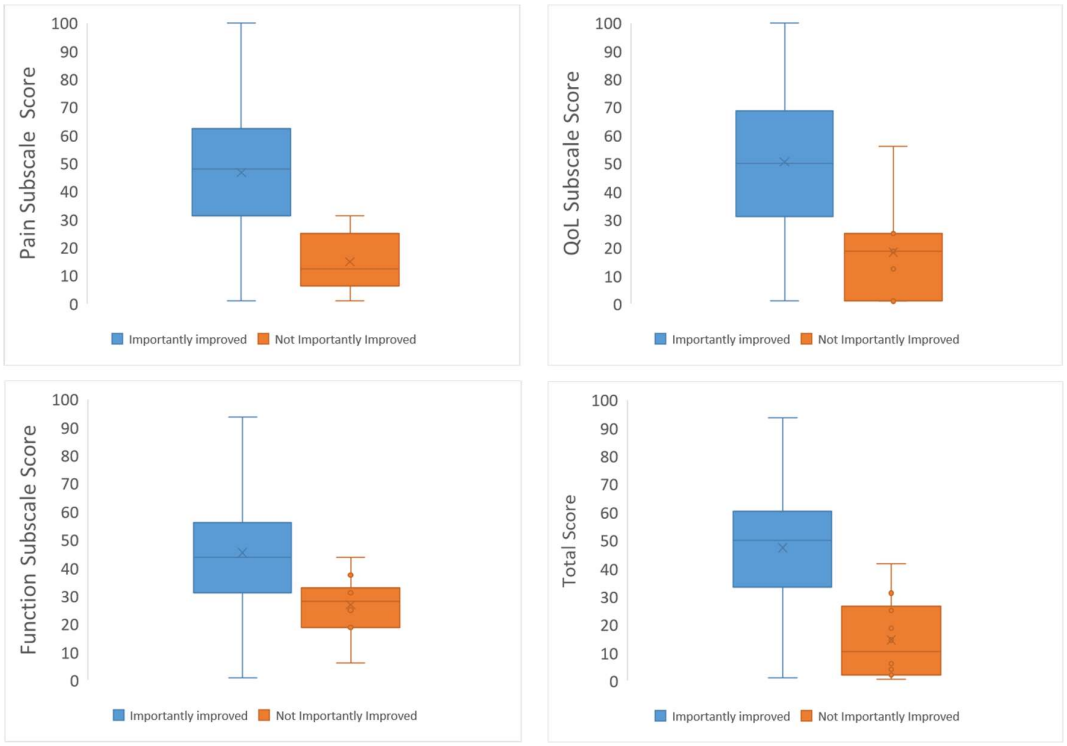

Abbildung 8: Box-Plots zur Darstellung der Verteilung der Change-Scores (präoperativ zu ein Jahr postoperativ) für relevant verbesserte (blau) und nicht relevant verbesserte Patienten (orange) nach Knie-TEP

Vom Grunddatensatz der Multicenter-Studie wurden Patienten mit unvollständigen Datensätzen von der vorliegenden Analyse ausgeschlossen. Die Einschlusskriterien wurden von 352 Patienten erfüllt. Die Studienpopulation bestand aus 161 Männern (45,7%) und 191 Frauen (54,3%). Für BMI und Alter fanden sich typische Werte einer Endoprothesenkohorte (BMI 31,4kg/m^2; Alter 67,9 Jahre). Zum Ausschluss einer möglichen selection bias wurden die demographischen Daten auch für die Gruppe der von der Analyse ausgeschlossenen Patienten bestimmt. Hier zeigte sich kein signifikanter Unterschied hinsichtlich Alter oder BMI der Patienten, jedoch befanden sich in der von der Analyse ausgeschlossenen Gruppe mehr Frauen.

Der MIC des Gesamtscores wurde mit 14,9 Punkten bestimmt, der für Schmerz betrug 11,5, Funktion 13,7 und Lebensqualität 5,5. Die MCID des Gesamtscores wurde auf 11,1 errechnet, die für Schmerz auf 13,5, für Funktion auf 15,2 und für Lebensqualität auf 8,0.

In wissenschaftlichen Publikationen angegebene p-Werte geben dem Leser eine Aussage darüber, mit welcher Wahrscheinlichkeit der Zufall für ein beobachtetes

Resultat verantwortlich ist. Patienten bemerken jedoch keine statistischen Differenzen. Während die Angabe von p-Werten in wissenschaftlichen Publikationen Standard ist, fehlen Einordnungen der Ergebnisse mittels MIC oder MCID weiterhin häufig. Die in dieser Studie erhobenen Werte können daher Wissenschaftlern und Klinikern bei der Interpretation von Studiendaten unter Berücksichtigung der Patientenebene helfen. Weiterhin ist insbesondere die MCID zur Planung von Studien wertvoll. Neben der gewünschten Power einer zu planenden Studie und dem Signifikanzniveau das erreicht werden soll, ist sie der entscheidende Parameter in der Berechnung der benötigten Fallzahlen.

Die in der aktuellen Studie errechnete MCID besagt, dass eine Differenz von mindestens 11,1 Punkten im KOOS-12 von Patienten als klinisch relevant empfunden wird und kennzeichnet den Unterschied zwischen den Gruppen mit geringer Besserung und keiner Besserung. Studien mit einer ausreichend hohen Fallzahl könnten zwar einen Unterschied von z.B. 7 Punkten als statistisch signifikant feststellen. Jedoch würde dies entsprechend der hier vorgelegten Daten durch Patienten nicht als klinisch bedeutsam bewertet werden.

Es ist wichtig zu vermerken, dass die berichteten Ergebnisse nur für eine Verbesserung im KOOS-12 gelten. MIC- und MCID-Werte für eine Zustandsverschlechterung müssten im Rahmen einer zukünftigen Studie mit einer ausreichend hohen Anzahl an verschlechterten Patienten bestimmt werden. Dies war aufgrund der wenigen verschlechterten Patienten in der untersuchten Kohorte in dieser Studie nicht möglich. Weiterhin können MIC und MCID in verschiedenen Populationen unterschiedlich ausfallen, weshalb die Ergebnisse primär nur auf Knie-TEP Patienten anwendbar sind wenngleich der KOOS-12 für Kniepathologien generell eingesetzt werden kann.

4 Zusammenfassung und Ausblick

Ziel dieser Habilitationsarbeit war es, die Auswirkung moderner Methoden in der Endoprothetik von Hüft- und Kniegelenk auf die Patientenzufriedenheit zu untersuchen und gleichzeitig durch Fortschritte auf dem Gebiet der „patient reported outcome measures“ zur besseren Bestimmung und Bewertung der durch diese Methoden erzielten Therapieerfolge beizutragen.

Zunächst wurden mit der Computer-Navigation in der Hüft-Endoprothetik, patientenindividuellen Implantaten in der Knie-Endoprothetik und einem multimodalen Schmerzkonzept drei Ansätze der vielfältigen Innovationen zur Steigerung der Patientenzufriedenheit nach endoprothetischem Gelenkersatz untersucht. Hierbei konnte anhand einer Auswertung von Daten des australischen Endoprothesenregisters gezeigt werden, dass der Einsatz von Navigation bei der Hüft-TEP Implantation zu einer geringeren Rate an Revisionen aufgrund von Luxationen führte. Die Untersuchung der coronaren Beinachse nach Knie-TEP zeigte keinen Vorteil beim Einsatz patientenindividueller Implantate und Instrumente im Vergleich zur etablierten Standardmethode. Erhöhte Dosierungen der Co-Analgetika Dexamethason und Gabapentin führten schließlich zu einer Verringerung des Opioid-Bedarfs um etwa 25% während des stationären Aufenthalts nach der Implantation einer Knie-TEP.

Nach der Evaluation der genannten modernen Methoden sollte dann in einem nächsten Schritt die Messbarkeit der damit erzielten Veränderungen der Patientenzufriedenheit verbessert werden. Mit dem KOOS-12 war ein PROM kurz genug für den routinemäßigen klinischen Einsatz publiziert worden, dessen externe Validierung und Einordnung gegenüber bisherigen Standard-PROMs jedoch noch ausstand. Die im Rahmen dieser Habilitationsarbeit vorgenommene externe Validierung sowie der Vergleich des ceiling effects gegenüber etablierten Knie-spezifischen Outcome-Messinstrumenten bestätigten die psychometrische Qualität des KOOS-12. Daher wurden anschließend mit der Berechnung von MIC und MCID zwei wichtige Maßzahlen zu Einordnung der klinischen Relevanz von Änderungen im KOOS-12 über die Zeit als auch von Unterschieden zwischen Gruppen etabliert.

Basierend auf den Ergebnissen dieser Arbeit kann ein zukünftiger Einsatz des KOOS-12 zur Evaluation von Behandlungsergebnissen nach Knie-TEP also empfohlen werden.

Hinsichtlich der oben genannten Innovationen in der endoprothetischen Versorgung tun sich für die nahe Zukunft weitere interessante Fragen auf. Da der klinische Nutzen der Computer-Navigation in der Hüftendoprothetik immer deutlicher wird, gilt es nun die Vor- und Nachteile verschiedener Navigationssysteme herauszuarbeiten und insbesondere die bisher oft aufwändigen perioperativen Vorbereitungen und Anforderungen an das Personal zu reduzieren. Im Bereich der patientenindividuellen Knieendoprothetik sind Ergebnisse randomisiert-kontrollierter Studien samt PROMs dringend erforderlich, um die Mehrkosten dieser Systeme wissenschaftlich fundiert begründen zu können. Multimodale Schmerzbehandlungsprotokolle sind aus der Endoprothetik nicht mehr wegzudenken. Die Übertragung der hier gemachten Erfahrungen auf andere Entitäten der Orthopädie und Unfallchirurgie ist im Gange und sollte weiter wissenschaftlich begleitet werden.

5 Originalarbeiten

The Use of Computer Navigation in Total Hip Arthroplasty Is Associated with a Reduced Rate of Revision for Dislocation

A Study of 6,912 Navigated THA Procedures from the Australian Orthopaedic Association National Joint Replacement Registry

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Background: The use of computer navigation has been shown to produce more accurate cup positioning when compared with non-navigated total hip arthroplasty (THA), but so far there is only limited evidence to show its effect on clinical outcomes. The present study analyzed data from the Australian Orthopaedic Association National Joint Replacement Registry to assess the impact of computer navigation on the rates of all-cause revision and revision for dislocation following THA.

Methods: Data for all non-navigated and navigated primary THAs performed for osteoarthritis in Australia from January 1, 2009, to December 31, 2019, were examined to assess the rate of revision. We analyzed the effects of navigation on rate, reason, and type of revision. Hazard ratios (HRs) from Cox proportional hazard models, adjusted for age, sex, and head size, were utilized. Because of known prosthesis-specific differences in outcomes, we performed a further analysis of the 5 acetabular and femoral component combinations most commonly used with navigation.

Results: Computer navigation was utilized in 6,912 primary THAs for osteoarthritis, with the use of navigation increasing from 1.9% in 2009 to 4.4% of all primary THAs performed in 2019. There was no difference in the rate of all-cause revision between navigated and non-navigated THAs looking at the entire group. There was a lower rate of revision for dislocation in the navigation THA cohort. The cumulative percent revision for dislocation at 10 years was 0.4% (95% confidence interval [CI], 0.2% to 0.6%) for navigated compared with 0.8% (95% CI, 0.8% to 0.9%) for non-navigated THAs (HR adjusted for age, sex, and head size, 0.46; 95% CI, 0.29 to 0.74; $p = 0.002$). In the 5 component combinations most commonly used with navigation, the rate of all-cause revision was significantly lower when these components were navigated compared with non-navigated. The cumulative percent revision at 10 years for these 5 prostheses combined was 2.4% (95% CI, 1.6% to 3.4%) for navigated compared with 4.2% (95% CI, 4.0% to 4.5%) for non-navigated THAs (HR, 0.64; 95% CI, 0.48 to 0.86; $p = 0.003$).

Conclusions: This study showed that the use of computer navigation was associated with a reduced rate of revision for dislocation following THA. Furthermore, in the component combinations most commonly used with navigation there was also a reduction in the rate of all-cause revision.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Total hip arthroplasty (THA) is an established method of surgical treatment for advanced, symptomatic hip arthritis and has been named as one of the most successful operations of the last century[1]. However, THA comes with a small but meaningful burden of revision, and prothesis dislocation has been identified as one of the most common reasons for revision[2,3]. Malpositioning of the acetabular component in THA has been identified as a major risk factor for dislocation[4-8]. About 50% of early revisions are deemed avoidable, and suboptimal positioning of the acetabular component is the most common reason, accounting for 48% of avoidable revisions in 1 study[9]. The use of computer navigation in primary

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THA commenced in the 1990s and has constantly evolved[10]. It has been shown to improve the reproducibility of acetabular cup positioning, but there are limited studies to demonstrate that this effect is translated into the clinical benefit of improved prosthesis survival[11-15].

The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) began collecting data on the use of computer-navigated arthroplasty in 2003. The use of navigation has increased in total knee arthroplasty (TKA), with approximately a quarter of TKAs being navigated in 2012[16] and a third in 2018. However, the AOAJJRR shows that <2% of THAs overall have utilized navigation. The reason for this discrepancy could be that THAs most frequently use image-based navigation, which is associated with increased cost, planning time, and radiation, whereas TKAs most commonly involve the use of imageless navigation. Imageless navigation for THA overcomes many of the disadvantages associated with image-based navigation and is being increasingly used[17].

The aim of this study was to determine if there were differences in the rates of all-cause revision and revision for dislocation between navigated and non-navigated THA, utilizing data from a large national registry. We also performed a subanalysis of the 5 most commonly implanted prosthesis combinations with and without computer navigation.

Materials and Methods

The AOANJRR began data collection on September 1, 1999, and includes data for almost 100% of the arthroplasty procedures performed in Australia since 2002.

Registry data are validated against patient-level data provided by each of the state and territory health departments in Australia with use of a sequential, multilevel matching process. In order to link each revision to its respective primary procedure, a monthly matching of procedures involving the same side and joint of a patient recorded in the registry is performed. Twice a year, data are also matched with the Department of Health and Aging National Death Index to check for deceased patients. Since 2003, information on the use and type of navigation is collected with an addition to the form for THA and TKA marked "computer-assisted."

The present study included all THA procedures recorded in the registry from January 1, 2009, to December 31, 2019, that were performed for osteoarthritis. We included only procedures with modern bearing surfaces, defined as ceramic-on-ceramic or metal- or ceramic-on-polyethylene. We excluded all metal-on-metal bearing surfaces because of their known high rate of revision, as well as all dual-mobility and constrained liners. The AOANJRR records the reason for and type of revision of THA. To address concerns regarding the hospital and surgeon cluster effect, a frailty model with hospital and surgeon frailties was utilized. Included in the model were computer navigation (computer navigated versus non-navigated), head size, age, and sex.

The cumulative percent revision rate was compared between the non-navigated and navigated THAs over the same time period, and the impact of head size, surgical approach, surgical experience, reason for revision, and type of revision were assessed. Furthermore, a subanalysis restricted to the 5 most commonly used acetabular and femoral component combinations, inserted with and without navigation, was performed.

Statistical Analysis

The AOANJRR uses Kaplan-Meier estimates of survivorship to describe the time to the first revision of an arthroplasty, with censoring at the time of death or closure of the database at the time of analysis. The unadjusted cumulative percent revision at 10 years after the index primary arthroplasty, with an accompanying 95% confidence interval (CI), was calculated with the use of unadjusted pointwise Greenwood estimates in order to allow for the same-time-matched comparison of navigated and non-navigated THAs, as the former had a shorter follow-up in the registry. The unadjusted cumulative-incidence functions of the reasons for revision of navigated and non-navigated THA were also calculated. The hazard ratio (HR) was calculated with use of Cox proportional hazard models adjusted for age, sex, and head size, and was utilized to make statistical comparisons of the revision rates between the 2 groups. The assumption of proportional hazards was checked analytically for each model; if the interaction between the predictor and the log of the postoperative time was significant in the standard Cox model, then a time-varying model was used. For this study, the reported HRs pertain to the entire follow-up period. To address concerns regarding hospital and surgeon cluster effect, a frailty model was utilized with crossed random effects of hospital and surgeon. All tests were 2-tailed with significance set at 0.05. Statistical analysis was performed with the use of SAS (version 9.3; SAS Institute).

Source of Funding

The AOANJRR is funded by the Commonwealth of Australia's Department of Health and Aging.

Results

There were 269,848 THAs performed for the treatment of osteoarthritis. Of these, 6,912 were performed with use of computer navigation (2.6%) and 262,936 were non-navigated (97.4%). Age and sex were similar in both groups. A summary of patient demographic data and follow-up time is displayed in Table I.

The use of navigation has increased from 1.9% of all THAs in 2009 to 4.4% in 2019. There were more patients in the navigation group that had femoral head sizes of >32 mm (Fig. 1). The AOANJRR recorded 228 surgeons who performed navigation over this period of time, and the use of navigation was recorded in 181 hospitals (of 318 hospitals in Australia performing arthroplasty). There were 16 surgeons who had performed >100 navigated THAs.

A total of 160 of 6,912 computer-navigated THAs were revised. When adjusted for age, sex, and femoral head size, there was no difference in the rate of all-cause revision between navigated and non-navigated THA in either the Cox or frailty model. The cumulative percent revision at 10 years was 4.0% (95% CI, 3.2% to 4.9%) for navigated compared with 4.6%

TABLE I Patient Age, Sex, and Follow-up Duration*

	Computer-Navigated THA (N = 6,912)	Non-Navigated THA (N = 262,936)
Sex		
Male	3,184 (46.1%)	123,224 (46.9%)
Female	3,728 (53.9%)	139,712 (53.1%)
Age *(yr)*	68.3 ± 10.7	67.6 ± 10.7
Follow-up *(yr)*	3.76 ± 2.98	4.44 ± 2.96

*Values are given as either the count with the percentage in parentheses or the mean ± standard deviation.

(95% CI, 4.4% to 4.7%) for non-navigated THAs (HR, 0.89; 95% CI, 0.76 to 1.04; p = 0.138) (Fig. 2).

There was a lower rate of revision for dislocation among navigated THAs. The cumulative percent revision for dislocation at 10 years was 0.4% (95% CI, 0.2% to 0.6%) for navigated compared with 0.8% (95% CI, 0.8% to 0.9%) for non-navigated THAs (HR, 0.46; 95% CI, 0.29 to 0.74; p = 0.002) (Fig. 3). There was no difference in the rate of revision for the diagnosis of fracture, loosening, or infection between navigated and non-navigated THAs.

The AOANJRR has collected data on 3 surgical approaches—posterior, lateral, and anterior—since 2015, and there were 4,209 THAs performed with navigation and 140,582 without over this time period. There was no difference in the rate of revision between navigated and non-navigated for any of the 3 approaches.

Because of known prosthesis-specific differences in outcomes, we performed an analysis of devices used with and without navigation. The 5 acetabular and femoral component combinations most commonly used with navigation were Trident and Exeter V40 (Stryker), Pinnacle and Corail (DePuy Synthes), Trident and Accolade II (Stryker), Continuum and M/L Taper Kinectiv (Zimmer Biomet), and Fitmore and CLS (Zimmer Biomet). The rate of all-cause revision was significantly lower for navigated compared with non-navigated THAs. The cumulative percent revision at 10 years for these 5 prostheses combined was 2.4% (95% CI, 1.6% to 3.4%) for navigated compared with 4.2% (95% CI, 4.0% to 4.5%) for non-navigated THAs (HR, 0.64; 95% CI, 0.48 to 0.86; p = 0.003).

The rate of revision for dislocation, adjusted for age, sex, and head size of the 5 most commonly used component combinations, was significantly lower among navigated THAs in both the Cox and frailty models. The cumulative percent revision at 10 years was 0.3% (95% CI. 0.1% to 0.8%) for navigated compared with 0.9% (95% CI, 0.8% to 1.0%) for non-navigated THAs (HR, 0.37; 95% CI, 0.16 to 0.82; p = 0.014).

To control for surgeon experience, an analysis was performed that was restricted to surgeons who performed both navigated and non-navigated THAs. There was no difference in the rate of all-cause revision between navigated and non-navigated THAs in this analysis, but there was a lower rate of revision for dislocation for navigated THAs. The cumulative percent revision at 10 years, adjusted for age, sex, and head size, was 0.4% (95% CI, 0.2% to 0.6%) for navigated compared with 0.8 (95% CI, 0.7% to 0.9%) for non-navigated THAs (HR, 0.49; 95% CI, 0.30 to 0.79; p = 0.004).

Discussion

This study, which included patient data from an entire nation, demonstrated no difference in the rate of all-cause revision but a lower rate of revision for dislocation in navigated compared with non-navigated THA. To our knowledge, the present study is the second largest on computer navigation in primary THA and has the longest follow-up compared with similar studies, with a mean follow-up of 3.8 years in the navigated cohort and 4.4 years in the non-navigated cohort.

The position of the acetabular component is considered to be crucial in order to gain a good postoperative range of motion. Malposition can cause impingement and instability, edge-loading (and associated complications such as accelerated wear of polyethylene, squeaking and catastrophic failure in hard bearings)[6-8,18]. "Safe zones" for cup placement have been described by Lewinnek et al. and are widely followed by hip arthroplasty surgeons[19]. Cup placement outside the Lewinnek safe zone has been associated with higher rates of revision and dislocation[20,21], underlining the importance of optimum cup positioning. Although it has been shown that the use of navigation improves accuracy and precision of cup placement[11,12,14,22-24], few studies have assessed the impact of navigation in THA on clinical outcomes[13,15,25]. Lass et al. performed a follow-up to a randomized controlled trial comparing THA implanted with imageless computer-assisted navigation or conventionally[25,26]. Although the initial trial showed more accurate positioning of the acetabular component in the navigated THA group, there was no difference in clinical outcomes or revision rate at 2-year follow-up. With a group size of 65 patients each, that study was not powered to investigate differences in revision rate, and no dislocations were observed in either group.

In a randomized controlled study with a 10-year follow-up, Parratte et al. reported no difference between navigated and

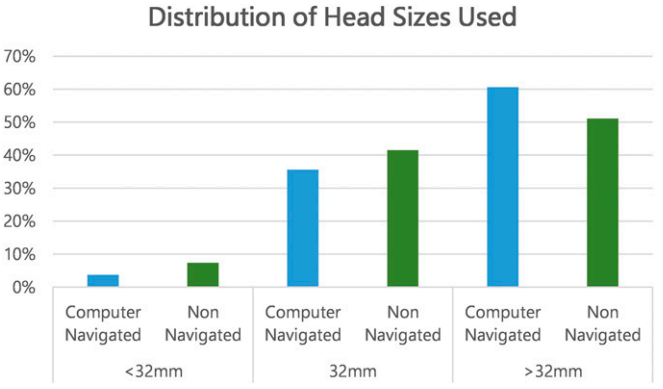

Fig. 1

Bar graph showing the distribution of head sizes used in computer-navigated and non-navigated THA.

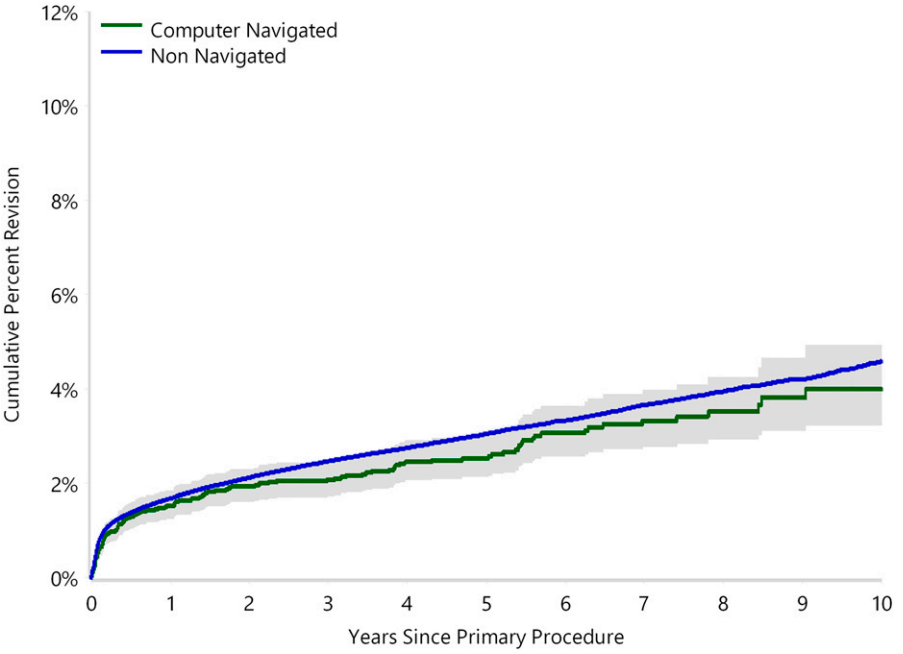

Fig. 2

Graph showing the all-cause cumulative percent revision. Gray areas indicate 95% confidence intervals.

non-navigated THA with regard to Harris hip score, acetabular liner wear, or survivorship, despite having demonstrated improved cup positioning with the use of navigation[27,28]. However, these results do not contradict the finding in the present study of a lower rate of revision for dislocation in navigated THA because the study by Parratte et al. included only 30 patients and was not powered to find differences in rates of revision.

Sugano et al. compared the results of 60 cementless ceramic-on-ceramic THAs performed with computed tomography navigation and 120 non-navigated THAs[13]. Survival at 13 years was 100% among navigated THAs and 95.6% (95% CI,

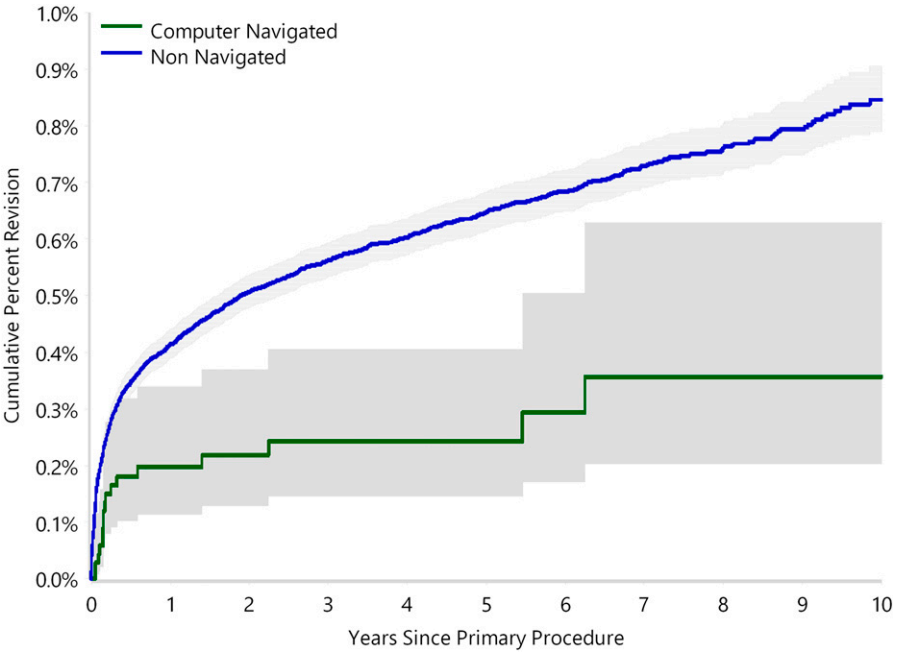

Fig. 3

Graph showing the cumulative percent revision for dislocation. Gray areas indicate 95% confidence intervals.

88.4% to 98.4%) among non-navigated THAs. Similar to the present study, the dislocation rate was higher in non-navigated (8%) compared with navigated THAs (0%), although only 1 acetabular component was revised for dislocation. Revision was performed in 4 non-navigated THAs, all of which showed evidence of neck impingement on the ceramic liner. Moreover, 7 other non-navigated THAs showed posterior neck erosion on radiographs while there were no cases of neck erosion among navigated THAs. These 11 impingement-related mechanical complications were correlated with cup malorientation.

In another recent study, Bohl et al. analyzed U.S. Medicare claims data for >800,000 primary THAs[15]. The use of navigation in THA (1.8% of cases) was only slightly less than that of the present study (2.6% of cases). The authors showed a reduced risk of dislocation among navigated (1.0%) compared with non-navigated THAs (1.7%; HR, 0.69; 95% CI, 0.58 to 0.82; $p < 0.001$).

Similar to the above, the present study showed a significantly lower cumulative percent revision for dislocation (HR, 0.46; 95% CI, 0.29 to 0.74; $p = 0.002$) among navigated THAs. Although 10-year revision rates were low in both treatment cohorts, the difference was significant over the whole period studied. However, there were differences between studies in terms of the registry and administrative data sets. The study by Bohl et al.[15] only included patients ≥65 years old, did not have laterality information, and may have missed data on head and/or liner revisions. In contrast, the present study captured all age groups undergoing navigated THA, and we are confident that all revisions were linked to the primary procedure. We were also able to adjust for femoral head size, an important variable when analyzing the revision of primary THA. In the present study, there were more patients in the navigated THA cohort with femoral head sizes of >32 mm than in the non-navigated cohort.

The registry is also aware of prosthesis-specific variation in revision rates and, by choosing the 5 devices most commonly used with and without navigation, we were able to eliminate revision rate variation among different implants while still capturing a large enough data set for comparative analysis of navigated versus non-navigated THA. When analyzing the 5 most commonly used THA combinations for navigated and non-navigated THA recorded in the registry, there was a reduced rate of revision for dislocation in the navigation group.

There were several limitations to the present study. We did not account for surgeon or hospital volume of THAs performed. Surgeons currently using navigation systems are likely to be doing a high volume of hip replacements, and therefore there may be a bias leading toward a lower rate of revision in the navigated group. However, the AOANJRR shows that navigation is utilized in THA in more than half the hospitals performing arthroplasty in Australia, and therefore its use is not confined to larger academic or tertiary referral hospitals. Both surgeons who have just started using navigation and those who have used navigation for some time were included in the analyses. In a study utilizing AOANJRR data to assess the use of navigation in TKA, de Steiger et al. found no difference in the rate of revision between navigated and non-navigated procedures across 4 subgroups stratified by surgeon volume[16]. We were unable to perform similar volume-based analyses for THA because of the much smaller numbers involved. Furthermore, an analysis was performed that was restricted to THAs performed by surgeons who performed both navigated and non-navigated THAs in order to control for surgeon experience. Like the unrestricted analysis, this subanalysis showed the same outcome of a lower rate of revision for dislocation among navigated THAs.

With the study period being from 2009 to 2019, only about 4% of patients had a 10-year follow-up; however, all HRs reflect the entire study period because they all met the proportional hazard assumption.

The data utilized in this analysis do not account for surgical decision-making. Therefore, it is possible that navigation was used in more complex cases or in patients with spinal-pelvic concerns. However, if anything, this possibility makes the reduction in revision for dislocation even more clinically relevant.

The AOANJRR only records revisions for dislocation, and therefore there are dislocations treated with closed reduction that the registry may not have captured. As improved acetabular cup position has been shown to reduce dislocation[4-8], there may have been fewer dislocations among navigated THAs, but we could not be certain of this.

The posterior surgical approach has been linked with a higher rate of revision for dislocation. In our analysis, we did not find a difference in the overall rate of revision when comparing different approaches and had too small a sample to determine an interaction between navigation and revision for dislocation according to surgical approach.

The AOANJRR also does not have radiographic data regarding implant position. Therefore, we cannot comment on whether navigation led to better cup alignment, and a direct correlation cannot be made between improved acetabular cup position through the use of computer navigation and a reduced rate of revision for dislocation. Although the AOANJRR is confident that all procedures reported as navigated were navigated, it is possible that a small number of cases were navigated and not recorded as such. We believe that this would be unlikely to alter the results of this study. Additionally, complications such as pin-track infections or fractures that did not result in revision would not be recorded by the registry. Furthermore, we were also unable to perform an analysis of the different navigation systems available in the Australian market. The confounding variables of different prostheses and different navigation systems made it difficult to draw any firm conclusion regarding the benefit of a certain brand of navigation.

In conclusion, this study demonstrated a reduced rate of revision for dislocation among computer-navigated THAs but no reduction in all-cause revision compared with non-navigated THAs. However, although this study has the strength of a national registry representing a national population, we cannot infer causation. Larger randomized clinical trials are necessary to answer this

question, but the present results suggest that navigation is beneficial, particularly with regard to avoiding revision for dislocation. ■

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Article

Comparison of Postoperative Coronal Leg Alignment in Customized Individually Made and Conventional Total Knee Arthroplasty

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Abstract: Neutral coronal leg alignment is known to be important for postoperative outcome in total knee arthroplasty (TKA). Customized individually made implants (CIM) instrumented with patient-specific cutting guides are an innovation aiming to increase the precision and reliability of implant positioning and reconstruction of leg alignment. We aimed to compare reconstruction of the hip–knee–ankle angle (HKA) of the novel CIM system iTotal™ CR G2 (ConforMIS Inc.) to a matched cohort of the off-the-shelf (OTS) knee replacement system Vanguard™ CR (Zimmer Biomet). Retrospective analysis of postoperative coronal full-leg weight-bearing radiographs of 562 TKA (283 CIM TKA, 279 OTS TKA) was conducted. Via a medical planning software, HKA and rotation of the leg were measured in postoperative radiographs. HKA was then adjusted for rotational error, and 180° ± 3° varus/valgus was defined as the target zone HKA. Corrected postoperative HKA in the CIM group was 179.0° ± 2.8° and 179.2° ± 3.1° in the OTS group (p = 0.34). The rate of outliers, outside of the ±3° target zone, was equal in both groups (32.9%). Our analysis showed that TKA using patient-specific cutting guides and implants and OTS TKA implanted with conventional instrumentation resulted in equally satisfying restoration of the coronal leg alignment with less scattering in the CIM group.

Keywords: total knee arthroplasty; leg alignment; patient-specific instruments; custom-made implant; rotational correction

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1. Introduction

Total knee arthroplasty is a common and reliable procedure for successfully treating end-stage osteoarthritis (OA) of the knee. Although continued development of implant design, surgical technique, and postoperative follow-up treatment has improved the overall outcome of the procedure, there is still a noticeable number of patients who remain partially unsatisfied after TKA [1]. Amongst other factors, correct fitting and position of the TKA components with consecutive restoration of the axial alignment and mechanical axis of the limb lead to a good postoperative outcome and longer implant survival [2–5]. To maximize the capabilities of TKA regarding these factors, patient-specific customized implants have been developed in the recent past [6,7]. One of these implants is the patient-specific cruciate retaining knee replacement system iTotal™ CR G2 with custom-made implants and instruments, using computer-aided design and manufacturing (CAD/CAM) based on computed tomography (CT) scans of the patients' leg. The goal of this implant is to restore

a neutral postoperative mechanical axis, reduce bone resection, and optimize component fit. Previously published results are promising [8,9], although studies comparing CIM TKA to off-the-shelf implants implanted using conventional instrumentation are scarce, while most existing studies focus on patient-specific instrumentation rather than patient-specific implants. We therefore aimed to compare restoration of the hip–knee–ankle angle of the novel patient-specific knee replacement system iTotal CR G2 (ConforMIS Inc.; Burlington, MA, USA) to a matched cohort of the traditional knee replacement system Vanguard™ CR (Zimmer Biomet; Warsaw, IN, USA).

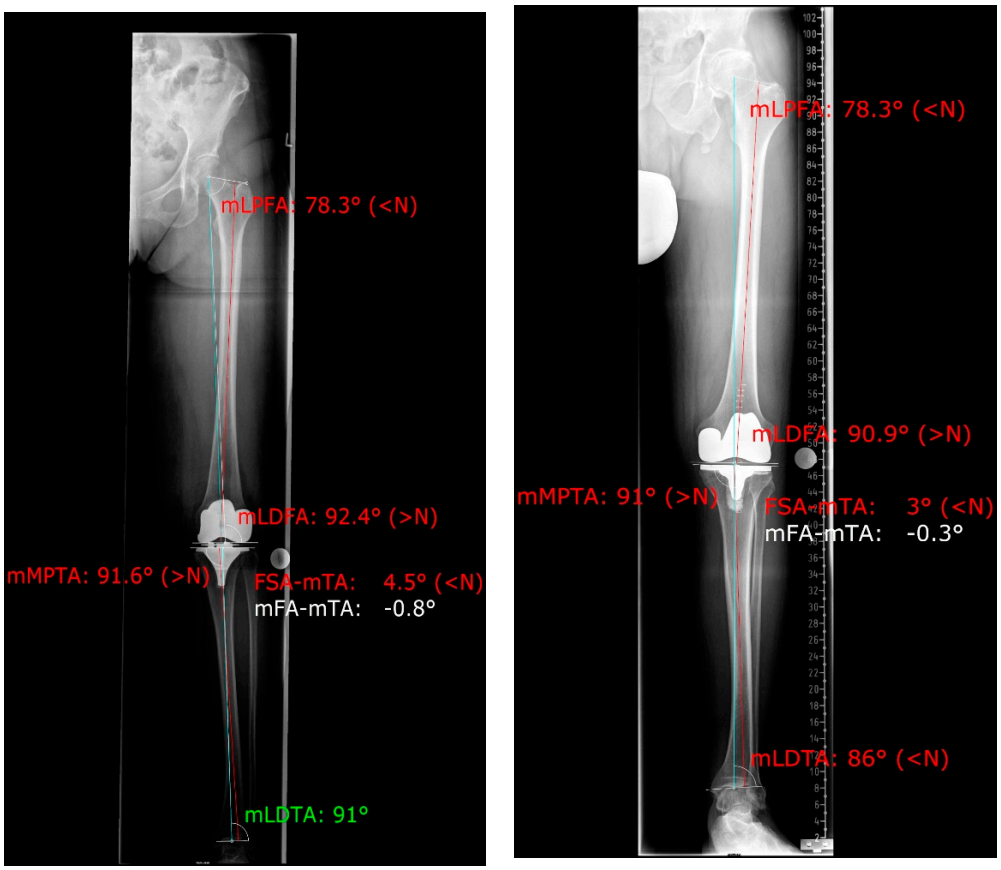
2. Materials and Methods

In total, 562 patients undergoing TKA (right: 235; left: 205; bilateral: 122) were included in the retrospective analysis with a distribution of 283 patient-specific knee replacement systems, iTotal™ CR G2, and a matched cohort of 279 traditional knee replacement systems, Vanguard™ CR. Both products match the country product clearances for Germany and are approved by the United States Food and Drug Administration (FDA).

All surgeries were conducted from 2015 to 2020 by the endoprosthetics team of the Department of Orthopedics and Traumatology of the University Medical Center of the Johannes Gutenberg University, containing four primary surgeons. Indication for TKA was end-stage primary or posttraumatic OA of the knee with no signs of ligamentous instability. Patients with varus or valgus deformity >15° were excluded due to eligibility criteria of the implants. For preoperative planning, all patients received coronal full-leg weight-bearing radiographs as well as antero-posterior lateral, and patella tangential conventional radiographs of the affected knee. Planning of the OTS Vanguard™ CR system was conducted via the mediCAD 2D Knee planning software (mediCAD Hectec GmbH, Altdorf, BY, Germany). In the case of a planned implantation of the iTotal™ CR G2 system, a CT-scan of the affected leg was conducted with a standard protocol and the CIM was designed and manufactured using the iFit software algorithm and 3D CAD/CAM technology as previously described by Arnholdt et al. [8]. We used a standard midline incision and medial parapatellar capsulotomy in all patients, adding local infiltration analgesia containing ropivacaine and adrenalin as well as i.v. and intraarticular tranexamic acid at the end of each surgery. No tourniquet or drainage was used. Postoperative radiological control of implant fit and leg axis was conducted via ap and lateral knee radiographs and coronal full-leg weight-bearing radiographs as soon as the patient was able to walk stairs and a full extension of the operated knee was possible.

Radiographic analysis of the postoperative coronal leg alignment was executed using the mediCAD 2D planning software on postoperative coronal full-leg weight-bearing radiographs. The radiographs were first checked for eligibility according to the following quality criteria: missing postoperative pictures, minor quality with incomplete imaging of the operated leg or poor image quality, and excessive rotational error. For determination of the leg axis, the HKA was measured using the angle between the mechanical axis of the femur (FMA) and tibia (TMA) (Figure 1). The operation aimed to restore a neutral mechanical alignment (180° ± 3° varus/valgus). For further improvement of the measurement accuracy, we calculated rotational correction for the measured HKA using the formula published by Maderbacher et al. in 2014 and 2021 [10,11], which is based on the proximal tibio-fibular overlap in long leg radiographs measured via the mediCAD 2D planning software (Figure 2).

Microsoft Excel 2007 (Microsoft Corporation, Redmond, USA) was used for descriptive analysis (mean ± standard deviation). R version 4.0.2 with ggplot2 version 3.3.3 was used to create histograms and for all hypothesis tests. Group mean angles were compared with two-sided Welch two-sample t-tests for equality of means, and group proportions were compared using chi-squared tests for equal proportions. For all statistical analyses, single knees were treated as independent observations.



(**a**) (**b**)

Figure 1. Measuring the HKA angle in mediCAD 2D planning software (**a**) iTotal CR G2 patient specific implant; (**b**) Vanguard CR conventional implant.

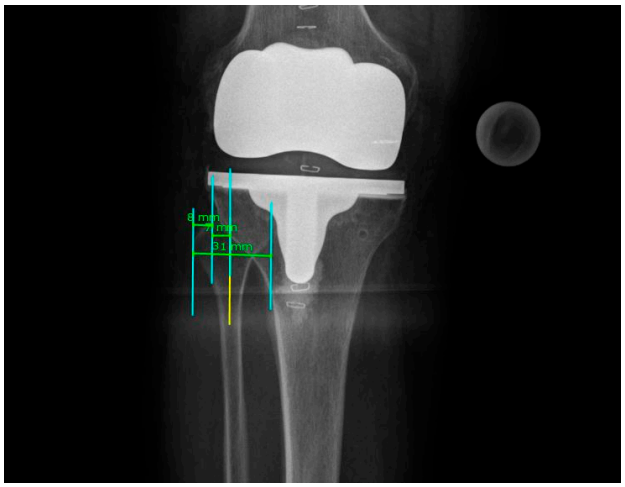


Figure 2. Detail of rotational analysis of a full-leg weight-bearing radiograph using the proximal tibio-fibular overlap.

3. Results

All 562 postoperative full-leg weight-bearing radiographs could be included in the analysis according to the above-mentioned quality criteria. Mean age at time of surgery in the CIM group was 69.4 ± 10.31 years (range 24–89 years) with a gender distribution of 149 male and 134 female patients. Mean age at time of surgery in the OTS group

was 71.7 ± 10.43 years (range 35–92 years) with a gender distribution of 105 male and 174 female patients. In all, 8.5% (24/283) and 5.3% (15/279) of patients had prior surgery on the affected knee in the CIM and OTS group, respectively. Baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics.

Variable	CIM (iTotal CR G2)	OTS (Vanguard CR)
Age (years) (mean (SD))	69.5 (10.3)	71.7 (10.4)
Gender		
male	149	105
female	134	174
Side of Surgery		
left	90	115
right	108	127
both	85	37
Previous operation on affected leg (%)	24 (8.5%)	15 (5.3%)

3.1. Rotational Correction

Calculated rotation in coronal full-leg weight-bearing radiographs in the CIM group ranged from −32.05° internal to 22.57° external rotation of the leg (mean −3.56°, SD 9.65°). Rotation in the OTS group ranged from −1.51° to 23.49° (mean −5.29°, SD 9.10°). Derived correctional factors for HKA ranged from −2.23° varus to 1.57° valgus correction (mean −0.25°, SD 0.67°) in the CIM, and −2.20° to 1.64° correction (mean −0.37°, SD 0.63°) in the OTS group, respectively.

3.2. Coronal Alignment

The postoperative radiologically measured corrected and uncorrected HKAs with SD in all 562 patients who underwent TKA are displayed in Table 2.

Table 2. Postoperative uncorrected and corrected mean HKA ± SD after iTotal™ CR G2 and Vanguard™ CR implantation.

	iTotal™ CR G2 (*n* = 283)	Vanguard™ CR (*n* = 279)
HKA uncorrected	179.2° ± 2.9°	179.6° ± 3.1°
HKA corrected	179.0° ± 2.8°	179.2° ± 3.1°

Maximum varus and valgus HKAs were 171.2° (171.2° corrected) and 190.1° (189.2° corrected) in the OTS group and 168.6° (169.3° corrected) and 187.7° (188.21° corrected) in the CIM group, respectively. The distribution of corrected HKAs in both groups is shown in Figure 3. Outliers, outside the 180° ± 3° target zone, were 32.9% in both implant groups (93/283 CIM group; 92/279 OTS group) with a trend toward varus alignment in both groups (CIM group: 71/283 varus; OTS group: 62/279 varus).

The Welch two-sample test for mean corrected HKA between both groups showed no significance, with $p = 0.34$. Further analysis for corrected HKA range +/−1° and +/−3° degrees showed no significant differences between the OTS and CIM group, with p-values $p = 0.56$ and $p = 1.00$, respectively.

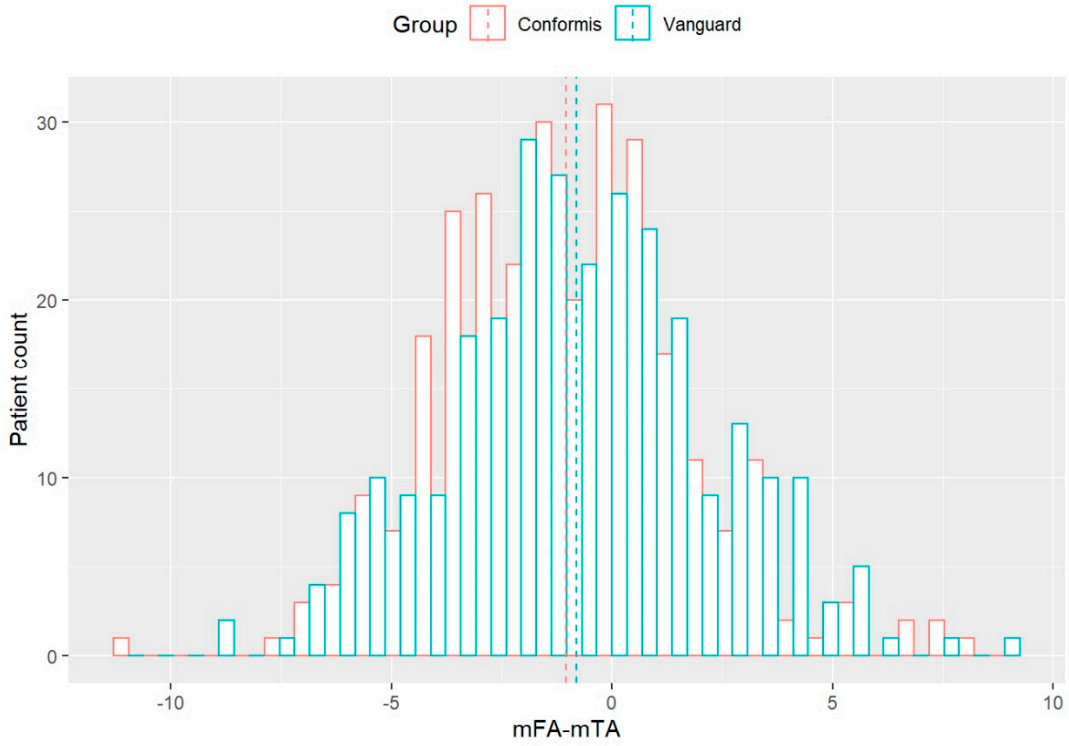


Figure 3. Distribution of corrected postoperative HKA angle in CIM (ConforMIS) and OTS (Vanguard) groups (0 on x-axis corresponds to 180°, dotted lines indicate group mean).

4. Discussion

In this study, analysis of the up-to-now largest cohort of postoperative coronal leg alignment after implantation of CIM TKA using patient-specific cutting guides and OTS TKA implanted with conventional instrumentation showed equally satisfying results in restoring the HKA angle toward neutral alignment.

To improve surgical technique toward better postoperative leg alignment, computer-aided surgery as well as patient-specific instruments and implants have been developed, especially while conventional techniques using intramedullary guides show high liability to failure due to anatomic variability or surgical error [12]. Although there were no significant differences between leg alignments in both of our groups, we noticed a lower scattering range of leg axis in the CIM group. The rate of outliers in both groups (32.9% with more than $\pm$ 3° deviation) was in line with the rates described in other studies [13–16]. As postoperative leg malalignment and malpositioning of the implant are known to have a high impact on overall outcome and survivorship of TKA [3,13], it is of paramount interest to restore these entities precisely. Whilst computer-aided surgery proved to be superior in restoring leg axis than conventional techniques [17], patient-specific instruments such as cutting guides showed no improvement [18]. Even though patient-specific surgery in TKA is relatively well studied, comparison of CIM and OTS implants and their restoration of leg axis is scarce. Arbab et al. [9] showed no significant difference in pre- and postoperative leg axis change between conventional and patient-specific implants but noticed a trend toward fewer outliers in their CIM group. Steinert et al. [8] detected proper fitting and positioning of the patient-specific implant and a good restoration of leg axis toward neutral alignment. In both studies, coronal full-leg weight-bearing radiographs were used to determine the postoperative leg axis. Because of its complex provision and high liability to failure especially in malrotation [19,20], this radiograph shows a high variability in its reproducibility and therefore in determination of the leg axis. Further, weight-bearing full-leg radiographs are costly and expose the patient's pelvis to ionizing radiation, which makes correct analysis of the radiographs even more important to reduce recurrent imaging.

Various studies have shown alternatives for measuring the long leg axis, but long limb radiographs remain the gold standard [9,20,21]. To further exceed the analyzability of these radiographs, Maderbacher et al. [10,11] published a formula to predict knee rotation via tibio-fibular overlap and to calculate the influence of rotation on the measured alignment parameters. However, this method is limited by the uncertainty of knee flexion during the radiograph, which is common in the early postoperative long-leg radiograph due to painful or mechanical extension deficits. Nevertheless, surgeons should be aware of this method when regularly assessing postoperative long leg radiographs after TKA to prevent incorrect measurement.

The strengths of this study are that it is the largest analysis of custom TKA implants on leg axis and that it considers the rotation in all radiographs as well as its influence on coronal leg alignment. However, we did not take a possible extension deficit after surgery into account. Although full extension of the operated knee was a benchmark for postoperative long leg radiograph in our setting, a bias due to flexion of the knee during X-ray cannot be excluded. Furthermore, due to the retrospective nature of this comparative analysis, a bias for implant selection cannot be excluded. Lastly, we only assessed the ConforMIS iTotal™ CR G2 CIM, and our findings might not be transferable to other patient-specific customized implants.

5. Conclusions

TKA using patient-specific cutting guides and implants and OTS TKA implanted with conventional instrumentation resulted in equally satisfying restoration of the coronal leg alignment. When using coronal full-leg weight-bearing radiographs to assess the postoperative leg axis, the modifiers through rotational correction should be taken into account.

Author Contributions: All authors contributed to the study conception and design. F.W., M.A., R.W., P.B. and L.E. performed data collection, radiographic analysis, graphics production, and statistical analysis. The first draft of the manuscript was written by F.W., and all authors commented on previous versions of the manuscript. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

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KNEE

Increased postoperative dexamethasone and gabapentin reduces opioid consumption after total knee arthroplasty

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Abstract

Purpose Dexamethasone and gabapentin are used in multimodal pain management protocols to reduce postoperative pain after total knee arthroplasty. For both analgesic adjuvants, the optimal dose regimen to reduce opioid usage is still unclear.

Methods The opioid consumption of patients undergoing primary TKA before and after a change of the analgesic adjuvant medication in our protocol (old protocol: 4 mg of dexamethasone daily for 2 days, 600 mg gabapentin daily for 1 week; new protocol: 10 mg dexamethasone daily for 2 days, 300 mg gabapentin every 8 h for 1 week) were retrospectively compared. All surgeries were performed under spinal anesthesia. Peri- and postoperative pain medication remained unchanged.

Results A total of 186 patients who received TKA between 11/29/2016 and 06/09/2017 were screened. Six patients who received general anesthesia, 4 patients who underwent simultaneous bilateral TKA, and 16 patients with ongoing opioid consumption at the time of surgery were excluded, leaving 80 patients in each group. Opioid consumption within 24 h [morphine equivalents in mg: mean 50.5, standard deviation (SD) 30.0 (old) vs. 39.8, SD 24.2 (new); $P = 0.0470$], cumulative consumption over 48 h (97.3, SD 64.4 vs. 70.4, SD 51.2; $P = 0.0040$) and cumulative consumption over 72 h (108.1, SD 79.5 vs. 82.5, SD 72.6; $P = 0.0080$), were all significantly lower in the new protocol.

Conclusion Increased postoperative administration of dexamethasone and gabapentin after TKA is associated with lower opioid consumption. Within the first 48 h, up to about 25% of opioids can be spared, comparing high-dose to low-dose protocols.

Level of evidence Therapeutic Level III.

Keywords TKA · Pain · Opioids · Glucocorticoids · Gabapentin

Abbreviations

BMI	Body mass index
DOS	Date of surgery
PCA	Patient-controlled anesthesia
PONV	Postoperative nausea and vomiting
PPSP	Persistent post-surgical pain
SD	Standard deviation
TKA	Total knee arthroplasty
TPP	Treated per protocol

Introduction

Total knee arthroplasty (TKA), while being an efficacious procedure to treat osteoarthritis of the knee, is one of the most painful orthopedic surgeries [1]. Postoperative pain impedes early recovery after surgery, leads to poor patient satisfaction, and is a major risk factor for the development of persistent post-surgical pain (PPSP) [2]. Opioid analgesics are routinely used in perioperative pain management protocols but have substantial side effects such as nausea, vomiting, constipation, and sedation, besides a relevant addiction potential. Thus, reducing patients' perioperative opioid consumption, while maintaining adequate pain relief, is an essential goal driving the improvement of pain management protocols.

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Contemporary multimodal pain management protocols use varied mechanisms to reduce pain. Multiple medications are given pre-, intra-, and post-operatively to control central nervous system sensitization and prevent the development of PPSP [3].

The surgical tissue trauma of TKA causes both local peripheral and central inflammatory reaction. These reactions have an additive effect and contribute to the severity of acute postoperative pain [4]. Because inflammation plays a major role in mediating local and central pain responses, glucocorticoids, with their anti-inflammatory potency, are proven analgesic adjuvants. Earlier studies have shown the potential of glucocorticoids in the perioperative setting; they reduce postoperative nausea and vomiting (PONV), as well as postoperative pain, after hip and knee surgery [5–7].

Gabapentin, an anticonvulsant that binds to the alpha-2-delta subunit of N-type voltage-gated calcium channels, is primarily used for the treatment of epilepsy and chronic neuropathic pain. However, it also has an antinociceptive effect in the setting of neural sensitization after nerve or tissue damage [8]. Thus, it is not surprising that gabapentin decreases pain and reduces opioid usage in acute postoperative pain management following TKA [9, 10].

For both analgesic adjuvant agents, glucocorticoids and gabapentin, the optimal dose regimen and length of treatment are unclear for patients undergoing TKA. In an effort to further reduce the use of opioids after TKA surgery, recognizing promising results in the literature [11, 12], the dosages of gabapentin and dexamethasone within the multimodal pain regimen used in our practice were increased.

The aim of this study was to investigate the impact of changes in our multimodal treatment protocol on patients' opioid consumption during their hospital stay after TKA. It was hypothesized, that increasing postoperative dexamethasone from 4 to 10 mg daily, and gabapentin from 600 to 900 mg daily, would reduce postoperative opioid consumption.

Materials and methods

400 mg celecoxib (Celebrex), 975 mg acetaminophen (Tylenol), and 600 mg gabapentin 1–3 h prior to surgery were included in our preoperative treatment protocol. Since patients undergoing general anesthesia received an oral opioid as well, only patients undergoing spinal anesthesia were included. Patients were given either 0 mg, 4 mg or 8 mg dexamethasone during surgery, per the judgment of the treating anesthesiologist.

The following postoperative treatment protocol was administered: 975 mg acetaminophen (Tylenol) at 8:00 a.m., 12:00 p.m. and 4:00 p.m., 500 mg of naproxen (Naprosyn) every 12 h, and a baseline opioid medication: usually 100 mg tramadol (Ultram) every 8 h, or occasionally 1–2 mg hydromorphone (Dilaudid) every 4 h.

For breakthrough pain, patients received first 7.5 mg ketorolac (Toradol) intravenously, and then either 1–2 mg hydromorphone or 5–10 mg oxycodone every 4 h, depending on their level of pain and preference. Rarely, fentanyl, intravenous hydromorphone, or intravenous morphine was given in recovery for breakthrough pain at the discretion of the treating anesthesiologist.

To compare the two regimens, a sample of patients who received TKA under the old protocol (before March 20, 2017) and a sample who received TKA under the new protocol (after March 24, 2017) were taken. Under the old protocol, patients received 600 mg gabapentin before surgery and a daily morning dose of 600 mg after surgery for 1 week. For patients over 75, gabapentin doses were reduced to 300 mg. Patients also received 4 mg dexamethasone daily for 2 days. Under the new protocol, patients received 600 mg gabapentin before surgery and 300 mg gabapentin every 8 h throughout their hospital admission. For patients over 75, each 600 mg dose was changed to 300 mg, and each 300 mg dose to 100 mg. Patients were also given 10 mg dexamethasone daily for 2 days. No changes were made to preoperative or intraoperative analgesia, baseline or breakthrough pain medications. All opioid administrations were documented in our longitudinal medical record system and utilized for analysis.

It was hypothesized that our protocol changes would decrease total postoperative opioid consumption during patients' hospital stay.

The study was performed at a high-volume arthroplasty center using fast-track surgery principles. All surgeries were performed by a single surgeon (WF). Patients undergoing primary TKA for all indications were included. Patients were excluded if they underwent simultaneous bilateral TKA, received general anesthesia, or were not opioid naïve at the time of surgery. Patients in our old protocol were screened backwards from March 20, 2017 until 80 eligible subjects were enrolled; patients in our new protocol were screened consecutively from March 24 onwards.

A total of 186 patients who received TKA between 11/29/2016 and 06/09/2017 were screened. Six patients who received general anesthesia, 4 patients who underwent simultaneous bilateral TKA, and 16 patients with ongoing opioid consumption at the time of surgery were excluded, leaving 80 patients in each group (Fig. 1). There were no statistically significant differences in patient characteristics between the two groups (Table 1). Preoperative dexamethasone administration was equally distributed amongst the two groups (Table 2).

For the identified eligible patients, routine demographics such as age, gender, BMI, date of surgery (DOS), surgery end time, and type of anesthesia were collected from our

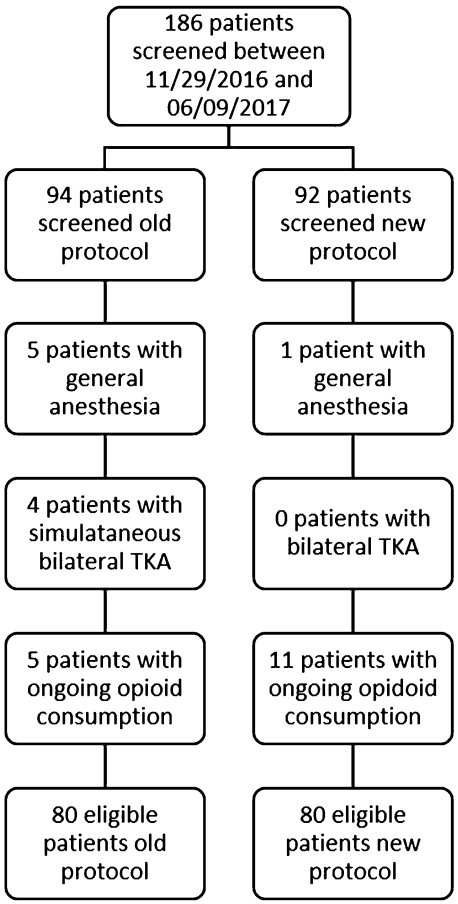

Fig. 1 Patient screening flow chart

Table 1 Patient characteristics

Demographics	Old protocol $n=80$	New protocol $n=80$	P value
Age (years)	67.0	68.1	n.s.
Gender (M/F)	41%/59%	39%/61%	n.s.
Height (cm)	1.68	1.76	n.s.
Weight (kg)	89.10	88.16	n.s.
BMI (kg/m^2)	31.29	30.53	n.s.

n.s. not significant

Table 2 Preoperative dexamethasone administration

Preoperative dexamethasone	Old protocol $n=80$	New protocol $n=80$
None	53 (66%)	52 (65%)
4 mg	11 (14%)	11 (14%)
8 mg	16 (20%)	17 (21%)

medical records database. All pain medications administered during the patient's hospital stay were recorded in 8-h increments, starting at the end of surgery for each patient. Morphine equivalents were calculated according to internationally accepted oral morphine milligram equivalent conversion factors [13].

The study was approved by Partners Human Research Committee review board (ID 2017P002756/PHS) and informed consent was waived.

Statistical analysis

Based on pilot data showing mean postoperative opioid consumption of 50 mg and standard deviation 30 mg, we powered for a reduction of 30% (mean opioid consumption after the protocol change of 35 mg). To achieve 80% power with an alpha of 0.05, we needed to enroll 64 per group. To adjust for possible missing data, the data for 80 consecutive eligible patients who received TKA under each regimen were collected.

All data analyses were performed using SAS version 9.4 (Copyright 2002–2012 by SAS Institute Inc., Cary, NC, USA). The level of significance was set at 0.05. The mean and standard deviation were calculated for continuous variables, while numbers and percentages were calculated for categorial variables. A Wilcoxon rank sum test was used to compare results for continuous variables, while a Chi-squared test was used to compare results for categorical variables.

Results

Opioid consumption

Opioid consumption for both groups are shown in Tables 3 and 5 as well as in Fig. 2. Opioid consumption within 24 h [morphine equivalents in mg: mean 50.5, standard deviation (SD) 30.0 (old) vs. 39.8, SD 24.2 (new); $P=0.0470$], cumulative consumption over 48 h (97.3, SD 64.4 vs. 70.4, SD 51.2; $P=0.0040$) and cumulative consumption over 72 h (108.1, SD 79.5 vs. 82.5, SD 72.6; $P=0.0080$), were all significantly lower in the new protocol group. When only analyzing patients who were treated per protocol (TPP), opioid consumption in the new protocol group was again significantly lower at 48 h (90.1, SD 57.3 vs. 69.8, SD 55.5; $P=0.0179$) and 72 h after surgery (98.4, SD 62.2 vs. 82.8, SD 80.3; $P=0.0261$) but did not reach significance at 24 h (46.5, SD 29.9 vs. 40.5, 26.1; $P=$n.s.). The percentages of patients who were treated and not treated per protocol are displayed in Table 4.

Since gabapentin dosage was reduced for patients older than 75 years, a separate analysis of opioid consumption was

Table 3 Opioid consumption in mean morphine equivalents in mg

Group	Old protocol *n*; mean (SD); median	New protocol *n*; mean (SD); median	*P* value
Opioid consumption within 24 h	80; 50.5 (33) 45	80; 39.8 (24.2) 37.3	0.0470
Opioid consumption within 48 h	80; 97.3 (64.4) 81.3	80; 70.4 (51.2) 55	0.0040
Opioid consumption within 72 h	80; 108.1 (79.5) 88.8	80; 82.5 (72.6) 59	0.0080
Total opioid consumption	80; 110.2 (83.7) 91.5	80; 85.1 (77.8) 59	0.0091

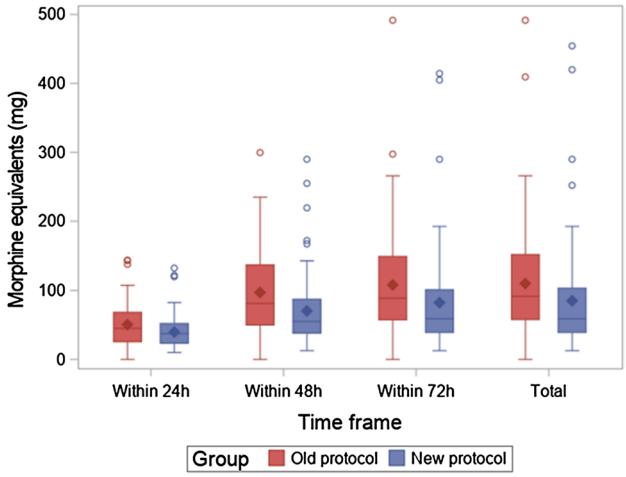

Fig. 2 Boxplot of opioid consumption in mean morphine equivalents for patients treated per protocol

Table 4 Percentages of patients treated and not treated per protocol

Group	Old protocol	New protocol
TPP—dexamethasone		
No	5 (6%)	11 (14%)
Yes	75 (94%)	69 (86%)
TPP—gabapentin		
No	10 (13%)	13 (16%)
Yes	70 (88%)	67 (84%)
TPP—dexamethasone and gabapentin		
No	14 (18%)	20 (25%)
Yes	66 (83%)	60 (75%)

performed for patients older and younger than 75. When only looking at patients younger than 75, opioid consumption within 24 h [56.4, SD 33.8 (old) vs. 43.4, SD 25.8 (new); $P=0.0231$], cumulative consumption within 48 h [108.1, SD 66.7 (old) vs. 77.9, SD 55.9 (new); $P=0.0062$], 72 h [118.5, SD 84.0 (old) vs. 91.4, SD 80.7 (new); $P=0.0160$] and total opioid consumption [120.3, SD 88.8 (old) vs. 94.8, SD 86.8 (new); $P=0.0238$] were all significantly lower in the new protocol. Patients 75 and older, in general, consumed fewer opioids. No significant differences between old and new protocol were found for opioid consumption within 24 h [27.1, SD 14.0 (old) vs. 29.8, SD 15.3 (new); $P=$ n.s.], 48 h [54.0, SD 26.4 (old) vs. 49.1, SD 25.6 (new); $P=$ n.s.] or 72 h [66.3, SD 36.7 (old) vs. 57.4, SD 31.9 (new); $P=$ n.s.], but the study was not powered to investigate this due to the small number of patients older than 75 (old protocol $n=16$, new protocol $n=21$).

Discussion

The most important finding of this study was that patients undergoing TKA, treated according to the new multimodal pain management protocol with increased dosage of gabapentin and dexamethasone, demonstrated a decreased opioid consumption throughout their hospital stay. Therefore, the hypothesis of this study has been proven. To our knowledge, this study is the first to assess the effect of a prolonged and increased administration of these analgesic adjuvant medications on opioid consumption.

The efficacy of preoperative gabapentin in reducing opioid consumption has been demonstrated by several meta-analyses, including analyses for total knee and total hip

Table 5 Opioid consumption in mean morphine equivalents in mg, only including patients treated per protocol

Group	Before guideline change *n*; mean (SD); median	After guideline change *n*; mean (SD); median	*P* value
Opioid consumption within 24 h	66; 46.5 (29.9) 37.8	60; 40.5 (26.1) 37.5	n.s.
Opioid consumption within 48 h	66; 90.1 (57.3) 75.4	60; 69.8 (55.5) 54	0.0179
Opioid consumption within 72 h	66; 98.4 (62.2) 84.3	60; 82.8 (80.3) 56.8	0.0261
Total opioid consumption	66; 99.3 (62.3) 85.1	60; 85.6 (86.5) 56.8	0.0264

n.s. not significant

arthroplasty [9, 14, 15]. In a dose–response study by Pandey et al. [16] the optimal preoperative dose of gabapentin in patients undergoing lumbar discectomy was 600 mg, with higher doses causing more side effects without any additional pain reduction. The evidence regarding postoperative gabapentin dosages, on the other hand, is limited. In the present study, the prolonged administration of analgesic adjuvants dexamethasone and gabapentin in high doses correlated with an opioid-sparing effect up to 72 h post-surgery. These findings are consistent with the results of Clarke et al. [11] who found that patients receiving gabapentin (versus placebo) for 4 days after TKA used significantly less PCA morphine at 24 h, 36 h, and 48 h post-surgery. When testing different postoperative doses (100 mg, 200 mg and 300 mg each administered three times per day), due to small numbers of patients recruited in each group, Clarke et al. [11] pooled these three groups in the analysis and compared them against patients not receiving postoperative gabapentin.

Dexamethasone has been widely used as a perioperative analgesic adjuvant medication in orthopedic surgery patients, and its efficacy in reducing opioid consumption and PONV has been demonstrated by several meta-analyses [7, 17–19]. While its pre- and intraoperative significance is well established, the benefit of a prolonged postoperative dexamethasone administration has yet to be determined. Jules-Elysee et al. [12] found that 100 mg hydrocortisone, given over three doses 8 h apart, decreased IL-6 levels and lowered visual analog pain scores after bilateral TKA. Converting this study's dose of hydrocortisone to the dexamethasone used in our study, the hydrocortisone equivalent dosages used were similar. While Jules-Elysee et al. [12] did not report opioid usage, our results suggest that increased postoperative cortisone doses do reduce opioid consumption after unilateral TKA with only one dose, instead of three as in their study. Additionally, we were able to show a beneficial effect of prolonged dexamethasone treatment given over 2 days.

In a meta-analysis of RCTs investigating perioperative single-dose systemic dexamethasone, De Oliveira et al. [20] also conducted a dose-dependency analysis, revealing opioid-sparing effects of intermediate-dose (0.11–0.2 mg/kg) and high-dose (more than 0.2 mg/kg), but not of low-dose (less than 0.1 mg/kg), perioperative systemic dexamethasone administrations. With our old protocol's dexamethasone dosage fitting into the low-dose group and our new protocol's dosage fitting into the intermediate group, our observation of a significant difference between these protocols in regard to the opioid-sparing effect are consistent with De Olivera's findings.

This study has several limitations. Due to the study's retrospective nature, lost or incorrect recording and retrieval of information may have occurred. However, this effect should be minimized by the large cohort size in both groups and the double abstraction we performed to ensure data quality. Another limitation was the fact that our protocol increased the administration of two adjuvant medications at once, making it hard to attribute the observed effects to either one of them conclusively. For patients treated per protocol, opioid consumption within 24 h after the surgery was not significantly different, whereas after 48 h and 72 h patients in the new protocol group used significantly fewer opioids. This difference might be explained by the fact that oral dexamethasone was first administered on the morning of the first postoperative day, and therefore had no impact on opioid consumption within the first 24 h post-surgery. Future studies should include parallel groups receiving placebo, dexamethasone, or gabapentin, along with a group of patients receiving both, to determine more conclusively how much the opioid-sparing effect can be attributed to each medication.

As it limits patients' inflammatory response, dexamethasone has been claimed to potentially increase the risk of surgical site infections and wound healing problems. Due to the retrospective nature of our study, we could not access information about early wound healing complications, nor could we compare those between high-dose and low-dose groups. However, numerous studies have found no increase in infectious complications [19, 21, 22].

Gabapentin is generally believed to have little side effects. Sedation and dizziness are the most common ones, but usually well tolerated. It has also been claimed, that gabapentin might be used alongside methadone by substance misusers to achieve the so-called 'high effect' [23]. In healthy patients with no history of substance abuse, however, a controlled trial did not find abusive usage of gabapentinoids [24]. Future studies are needed to evaluate this effect in orthopedic patients.

One of the strengths of this study is its large cohort size of patients operated by one single surgeon. Furthermore, despite the large cohort size, data were only retrieved from patients operated within a very short time frame, approximately 3 months before and 3 months after the change in our pain management protocol. Therefore, other potential influencing factors could be minimized.

Conclusion

Increased postoperative administration of dexamethasone and gabapentin after TKA is associated with lower opioid consumption. Within the first 48 h after TKA, up to about 25% of opioids can be spared when comparing high-dose to low-dose protocols.

Author contributions LE participated in the design of the study, carried out data abstraction and drafted the manuscript. TJ participated in the design of the study, carried out data abstraction and helped to draft the manuscript. JEC and SS performed the statistical analysis. WF conceived the study and participated in its design and coordination, and helped to draft the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was conducted after approval from the IRB at Brigham and Women's Hospital.

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KNEE

The KOOS-12 shortform shows no ceiling effect, good responsiveness and construct validity compared to standard outcome measures after total knee arthroplasty

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Abstract

Purpose To investigate the validity, responsiveness and ceiling effect of the recently introduced KOOS-12 and compare its performance to the KOOS, OKS, WOMAC and UCLA activity scales.

Methods Patients from an independent multicentre study examining a medially stabilized knee system prospectively completed the KOOS, OKS, WOMAC and UCLA preoperatively and at 1 year postoperatively. KOOS-12 scores were calculated from the full length KOOS data. Construct validity was assessed using Spearman's correlation analysis. The ceiling effect was evaluated by calculating the percentage of patients with a maximum score. If the percentage exceeded 15%, a ceiling effect was considered to be present. Responsiveness was evaluated by performing paired *t* tests on the changes in measures and calculation of Cohen's *d*.

Results A ceiling effect was present for the KOOS Pain, ADL and QoL subscales and the KOOS-JR at 1 year postoperatively. No ceiling effect was observed for the KOOS-12. Correlation of the KOOS-12 was low ($0.3 < r < 0.5$) with the UCLA, moderate ($0.5 < r < 0.7$) with the KOOS symptoms, sports and WOMAC stiffness subscales and high ($r > 0.7$) with all other scores and subscales. Effect size of the UCLA activity scale was moderate (Cohen's *d* 0.2–0.8) whereas effect sizes of all other outcome measures were large ($d > 0.8$).

Conclusion The KOOS-12 does not exhibit a ceiling effect, has good convergent construct validity and is responsive to changes in pain, function, QoL and knee impact between preoperatively and 1 year postoperatively.

Level of evidence Diagnostic level III.

Keywords KOOS · KOOS-12 · Osteoarthritis · Patient reported outcome measures · TKA

Abbreviations

TKA	Total knee arthroplasty
PROM	Patient reported outcome measure
ROM	Range of motion
KOOS	Knee injury and osteoarthritis outcome score
KOOS-12	Knee injury and osteoarthritis outcome score-12
KOOS-JR	Knee injury and osteoarthritis outcome score joint replacement
KOOS-PS	Knee injury and osteoarthritis outcome score physical function short form
OKS	Oxford knee score

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WOMAC	Western Ontario and McMaster Universities osteoarthritis index
UCLA	University of California, Los Angeles (UCLA) activity scale

Introduction

In recent years success of total joint arthroplasty surgery has increasingly been defined through the assessment of patient reported outcomes [1, 6, 9, 10, 14, 15, 17]. Such subjective outcomes are measures of patient satisfaction, the ability to perform activities of daily living and the patient's overall quality of life [10]. Patient reported outcome measures (PROMs) are clinical instruments that can collect and quantify these constructs [15].

The knee injury and osteoarthritis outcome score (KOOS) is one of the most widely used PROMs with regard to total knee arthroplasty (TKA) [16]. However, completing the 42-item questionnaire presents a significant burden for patients and it is, therefore, often regarded as being too time-consuming for routine clinical use. The length of time and level of burden on patients has led to the development of shorter questionnaires to achieve a higher compliance rate which will ultimately be reflected in more complete data capture [3].

The new 12-item short form KOOS-12 derived from the original KOOS is an example of the newer shorter questionnaires [4]. The KOOS-12 provides an overall knee impact score in addition to domain-specific scores for pain, function and knee-specific quality of life (QoL). While reliability, validity and responsiveness of the KOOS-12 have been evaluated and its psychometric properties have been compared to the full length KOOS, the originators underlined the necessity to study its performance in other TKA samples. Furthermore, comparison of its performance to other commonly used knee-specific scores are needed to aid decision-making for clinicians and researchers alike to choose the right score for their intended study population. The aim of this study was to provide this comparison and to externally validate the KOOS-12.

This study was designed to investigate (1) the correlation of the KOOS-12 with the Oxford knee score (OKS), Western Ontario and McMaster Universities osteoarthritis index (WOMAC), KOOS and its short forms (KOOS-JR & KOOS-PS), and University of California, Los Angeles (UCLA) activity scale, (2) the responsiveness and (3) the ceiling effect of the KOOS-12 compared to these scores. It was hypothesized that the KOOS-12 shows equal psychometric properties with regard to responsiveness and the ceiling effect compared to the standard scores while reducing the respondent's burden.

Materials and methods

The data used in this analysis were collected from an ongoing independent multicentre study prospectively examining patient reported outcome after TKA with a unique medially stabilized knee system. Informed consent was obtained from all patients prior to inclusion in the study. Eligible for inclusion was any patient undergoing a primary TKA for osteoarthritis by one of the study surgeons. Thirteen different surgeons treated patients at 16 sites using the Saiph total knee replacement system (MatOrtho, Leatherhead, United Kingdom). The surgical technique was standardized throughout all the 16 sites according to the manufacturer's instructions, using a medial parapatellar approach. For the present study, patients who underwent a primary unilateral TKA and completed preoperative and postoperative questionnaires were included in the analysis. All other patients were excluded.

Patients completed the KOOS, KOOS-PS, KOOS-JR, the WOMAC, OKS, and UCLA preoperatively and postoperatively at a 12-month follow-up period. KOOS-12 pain, function, QoL and summary scores were calculated from the full length KOOS data as described by Gandek et al. [3]. Table 1 shows the overlap in questions between the full length KOOS, KOOS-12, KOOS-JR, KOOS-PS and WOMAC scores. The selection of timepoints was identified from the already collected data, where 12-month follow-up had the largest number of patients available. The study was approved by the St Vincent's ethics committee (Reference number 151/15) and was carried out in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Data were analysed using SPSS, version 11. Statistical significance was set at <0.05. Descriptive statistics was used to calculate the mean and standard deviation of each score and subscale. Due to different scoring algorithms used to evaluate a final score amongst the questionnaires, commonality was established between the grading systems, by taking a high score as good and low score as bad. Whenever scores were compared with each other, they were normalized to a 0–100 point scale before proceeding with the analysis to achieve a common reference. Construct validity was assessed using Spearman's correlation analysis to examine the association between the KOOS, KOOS-JR, KOOS-PS, KOOS-12, WOMAC, OKS, and UCLA. This was calculated for overall scores and for subscales where applicable. A correlation of $r>0.70$ was considered high, $0.50<r<0.70$ was considered moderate, $0.30<r<0.50$ was considered low and $r<0.30$ was negligible [7]. The ceiling effect was evaluated by calculating the percentage of patients with a maximum score. When more than 15% of respondents received the highest possible score, a ceiling effect was considered to be present

Table 1 The overlap in the questions between the full length KOOS, KOOS-12, KOOS-JR, KOOS-PS and WOMAC scores

KOOS	Question	KOOS-12	KOOS-JR	KOOS-PS	WOMAC
Symptoms					
S1	Do you have swelling in your knee?				✓
S2	Do you feel grinding, hear clicking or any other type of noise when your knee moves?				✓
S3	Does your knee catch or hang up when moving?				✓
S4	Can you straighten your knee fully?				✓
S5	Can you bend your knee fully?				✓
Stiffness					
S6	How severe is your knee joint stiffness after first wakening in the morning?		✓		✓
S7	How severe is your knee stiffness after sitting, lying or resting later in the day?				✓
Pain					
P1	How often do you experience knee pain?	✓			✓
P2	Twisting/pivoting on your knee		✓	✓	✓
P3	Straightening knee fully		✓		✓
P4	Bending knee fully				✓
P5	Walking on flat surface	✓			✓
P6	Going up or down stairs	✓	✓		✓
P7	At night while in bed				✓
P8	Sitting or lying	✓			✓
P9	Standing upright		✓		✓
ADL					
Degree of difficulty experienced in the last week					
A1	Descending stairs				✓
A2	Ascending stairs				✓
A3	Rising from sitting	✓	✓	✓	✓
A4	Standing	✓			✓
A5	Bending to floor/pick up an object		✓	✓	✓
A6	Walking on flat surface				✓
A7	Getting in/out of car	✓			✓
A8	Going shopping			✓	✓
A9	Putting on socks/stockings			✓	✓
A10	Rising from bed				✓
A11	Taking off socks/stockings				✓
A12	Lying in bed (turning over, maintaining knee position)				✓
A13	Getting in/out of bath				✓
A14	Sitting				✓
A15	Getting on/off toilet				✓
A16	Heavy domestic duties (moving heavy boxes, scrubbing floors, etc.)				✓
A17	Light domestic duties (cooking, dusting, etc.)				✓
Function/sports					
Degree of difficulty experienced in the last week					
SP1	Squatting			✓	
SP2	Running				
SP3	Jumping				
SP4	Twisting/pivoting on your injured knee	✓			
SP5	Kneeling			✓	
Quality of life					
Q1	How often are you aware of your knee problem?	✓			
Q2	Have you modified your life style to avoid potentially damaging activities	✓			
Q3	How much are you troubled with lack of confidence in your knee?	✓			

Table 1 (continued)

KOOS	Question	KOOS-12	KOOS-JR	KOOS-PS	WOMAC
Q4	In general, how much difficulty do you have with your knee?	✓			

[11]. Responsiveness of all knee-specific scales and summary measures were evaluated by performing paired *t* tests on the changes in the measures between timepoints and calculation of Cohen's *d*. Values of 0.2 or less represent small effect sizes, values near 0.5 represent moderate effect sizes and values of 0.8 or higher represent large effect sizes [8]. The study sample size was chosen based on the availability of data collected. A post hoc analysis was conducted to determine the power of the study. The input parameters for the power analysis were the effect size ($p=2.5$), alpha ($\alpha=0.05$) and sample size ($N=527$ and $N=327$), which resulted in a power of 0.99.

Results

For a total of 563 patients who underwent surgery between December 2015 and November 2017 preoperative data were available. Mean patient age was 68.0 years (range 38–92, SD 8.5) and the mean BMI was 31.3 kg/m^2 (16.0–59.3, 6.6). 279 female and 284 male patients receiving 247 left and 316 right TKAs were included. Follow-up data at 1 year postoperatively were available for 381 patients with a mean age of 68.0 (46–91, 8.0) and a mean BMI of 31.2 kg/m^2 (15.4–59.3, 6.3) including 202 female and 179 male patients with 168 left and 213 right knees. Table 2 shows the mean score and standard deviation of all knee questionnaires assessed preoperatively and at 1 year follow-up.

Table 3 Percentage of patients achieving the maximum possible score in the KOOS-12, KOOS, WOMAC, KOOS-JR, KOOS-PS and OKS

Questionnaire	Subscale	Patients. with max score	
		Preoperative (%)	1 year (%)
KOOS-12	Total	0.0	9.5
KOOS	Pain	0.2	27.7
	Symptoms	0.0	13.4
	ADL	0.2	18.9
	QoL	0.0	14.9
	Sports	2.0	10.1
WOMAC	Total	0.0	11.5
KOOS-JR	Total	0.2	19.2
KOOS-PS	Total	0.2	8.0
Oxford-12	Total	0.0	7.3

The percentage of patients achieving the maximum possible result in the different scores is displayed in Table 3. A ceiling effect was present for the KOOS Pain, ADL and QoL subscales as well as the KOOS-JR at 1 year postoperatively (Fig. 1).

Table 2 Mean score and standard deviation of all knee questionnaires assessed preoperatively and at 1 year follow-up

Preoperative					1 year		
Questionnaire	Subscale	*n*	Mean	SD	*n*	Mean	SD
KOOS-12	Total	560	35.5	15.4	378	86.2	16.8
	Pain	560	40.8	16.1	378	84.3	16.4
	Function	560	40.9	18.6	378	74.6	20.8
	QoL	560	25.0	18.2	378	81.7	16.0
KOOS	Pain	563	44.7	16.7	379	87.6	14.6
	Symptoms	563	45.7	19.1	380	82.0	15.4
	ADL	562	50.2	18.9	376	89.3	12.3
	QoL	563	25.1	18.2	379	74.7	20.8
	Sports	554	18.2	21.4	336	61.1	29.0
Normalized WOMAC	Total	563	50.4	18.7	375	92.6	11.2
	Pain	563	51.1	18.9	378	93.5	11.6
	Stiffness	563	44.1	21.7	379	86.8	17.4
	Function	563	51.0	19.7	378	92.9	11.2
KOOS-JR	Total	527	46.8	13.9	364	82.2	14.0
KOOS-PS	Total	527	49.4	15.9	327	78.1	12.5
Oxford-12	Total	563	35.5	15.4	381	85.4	6.48
Normalised UCLA	Total	561	42.9	16.7	380	58.9	17.4

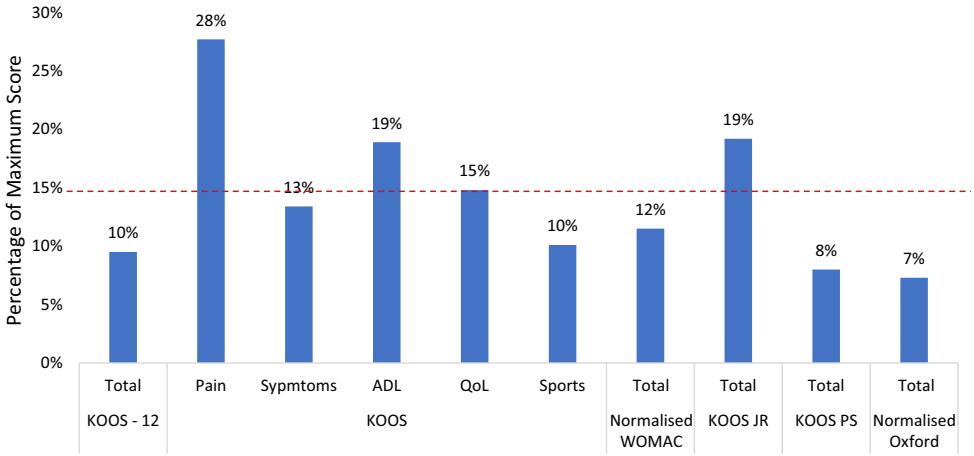

Fig. 1 Graph displaying the percentage of patients achieving the maximum possible score in the KOOS-12, KOOS, WOMAC, KOOS-JR, KOOS-PS and OKS at 1 year postoperatively

Table 4 Spearman's correlation coefficients between functional scores. (**Indicates significance at the 0.01 level, *indicates significance at the 0.05 level. Preoperative and 1 year correlations of the KOOS-12 and subscales were performed using their respective time-point counterparts. Low correlations are highlighted in red, moderate correlations are highlighted in yellow and high correlations are highlighted in green.)

	Preop Correlations				1 year Correlations			
	KOOS-12 Total	KOOS-12 Pain	KOOS-12 Function	KOOS-12 QoL	KOOS 12 Total	KOOS-12 Pain	KOOS-12 Function	KOOS-12 QoL
KOOS Symptoms	0.55**	0.48**	0.48**	0.46	0.69**	0.65**	0.54**	0.62**
KOOS Pain	0.85**	0.89**	0.78**	0.59**	0.84**	0.93**	0.69**	0.67**
KOOS ADL	0.88**	0.78**	0.90**	0.63**	0.84**	0.74**	0.81**	0.69**
KOOS Sports	0.69**	0.50**	0.71**	0.57**	0.59**	0.39**	0.69**	0.46**
KOOS QoL	0.85**	0.57*	0.60**	1.00**	0.90**	0.64**	0.62**	1.00**
KOOS PS	0.86**	0.71**	0.89**	0.64**	0.75**	0.58**	0.82**	0.60**
KOOS JR	0.87**	0.79**	0.85**	0.62**	0.86**	0.81**	0.79**	0.70**
WOMAC Pain	0.84**	0.93**	0.76**	0.54*	0.80**	0.90**	0.66**	0.62**
WOMAC Stiffness	0.62**	0.57**	0.60**	0.45	0.64**	0.60**	0.54**	0.55**
WOMAC Function	0.89**	0.78**	0.90**	0.63**	0.83**	0.73**	0.81**	0.68**
WOMAC Total	0.91**	0.84**	0.90**	0.63**	0.85**	0.79**	0.79**	0.69**
Oxford-12 normalized	0.85**	0.74**	0.78**	0.68**	0.81**	0.74**	0.71**	0.70**
UCLA normalized	0.44**	0.35**	0.40**	0.39*	0.30**	0.23**	0.33**	0.24**

Correlations of the assessed outcome measures with KOOS-12 and its subscales are presented in Table 4. Low correlation ($0.30 < r < 0.50$) was observed between the UCLA and KOOS-12. The KOOS symptoms, KOOS function, sports and recreational activities and WOMAC stiffness subscales showed a moderate correlation ($0.5 < r < 0.70$) with the KOOS-12. All other scores and subscales showed a high ($r > 0.70$) correlation with the KOOS-12.

Internal responsiveness for each outcome measure was assessed by calculating the mean change between

Table 5 Internal responsiveness for each outcome measure at preoperative and 1 year follow-up

Questionnaire	Subscale	Mean change	*P*	Cohen *d*
KOOS-12	Total	45.7	< 0.001	2.4
	Pain	44.9	< 0.001	2.2
	Function	43.6	< 0.001	2.1
	QoL	48.7	n.s	2.1
KOOS	Pain	43.2	< 0.001	2.2
	Symptoms	37.0	< 0.001	1.7
	ADL	39.4	< 0.001	2.0
	QoL	48.7	< 0.001	2.1
	Sports	42.9	< 0.001	1.5
Normalized WOMAC	Total	38.9	< 0.001	2.0
KOOS-JR	Total	35.2	< 0.001	2.0
KOOS-PS	Total	28.5	< 0.001	1.6
Normalized UCLA	Total	15.9	< 0.001	0.8
Normalized Oxford-12	Total	40.9	< 0.001	2.1

preoperative and 1 year as well as testing the effect size using Cohen's *d* (Table 5). All investigated outcome measures showed significant changes ($p < 0.001$) between preoperative and 1 year. Effect size of the UCLA activity scale was moderate (Cohen's *d* 0.2–0.8) whereas all other outcome measures showed effect sizes that were large ($d > 0.8$).

Discussion

The most important findings of this study were that the KOOS-12 does not exhibit a ceiling effect, has good convergent construct validity and is responsive to changes in pain, function, QoL and overall knee impact between preoperative and 1 year. This was the first study to evaluate the performance of the newly established KOOS-12 in relation to other disease-specific measures in addition to the full length KOOS from which it was derived.

In this study, the KOOS-12 did not show a ceiling effect preoperatively (0.0%) or at 1 year (9.5%) follow-up. The absence of a ceiling effect in the KOOS-12 is indicative of it having a suitable design for TKA patients. This study was in agreeance with Gandek et al. who reported 6.6% of participants with the highest possible score at 1 year postoperatively in the initial validation study [3]. Compared to the full length KOOS subscales, KOOS-JR and WOMAC total at 1 year postoperatively, fewer patients reached the maximum score in the KOOS-12. In turn, a smaller number of patients scored the maximum outcome in the KOOS-PS and the OKS than in the KOOS-12. This is most likely to be explained by the composition of these scores. The KOOS-PS asks for the patient's difficulty in performing high demand activities like twisting/pivoting the knee, kneeling or squatting and the OKS asks for the patient's ability to kneel down and get up again, which are the activities not sampled by the KOOS-12. In these questions the subjects scored significantly lower compared to the average over all the questions (data not shown). The KOOS-PS is designed for high activity patients and does not reflect the general patient population following a TKA; therefore TKA patients would not generally be expected to score high in the KOOS-PS.

Correlation of the KOOS-12 pain with KOOS pain ($r = 0.89$ resp. $r = 0.93$) and WOMAC pain ($r = 0.93$ resp. $r = 0.90$) subscales in the present study was high, indicating that the variance in the KOOS/WOMAC pain scales was sufficiently captured by the four shared questions in the KOOS-12 Pain scale. Likewise, in the original validation study of the KOOS-12, a high correlation with $r = 0.93$ was observed [3]. The correlation of the KOOS-12 function scale with KOOS ADL ($r = 0.81$) and WOMAC function ($r = 0.81$) scales was high, whereas it was only moderate, just missing the criteria of high correlation with the KOOS sport/recreation scale ($r = 0.69$) at 1 year postoperatively. The only moderate correlation of the KOOS-12 function with the KOOS sport/recreation can be explained by the fact that the KOOS-12 contains only one of the KOOS sport/recreation subscale's items. The authors of the KOOS-12 acknowledged the fact that the KOOS-12 only measures more difficult functions to a limited extent. Because these functions may be important to younger and more active patients, administering the full length KOOS sport/recreation scale along with the KOOS-12 when investigating these populations was recommended [3]. Since the KOOS-12 QoL and the KOOS QoL share the exact same four questions, their correlation coefficient naturally was 1.0.

Gandek et al. did not compare the KOOS-12 to other knee-specific measures. In the present study, the KOOS-12 summary score correlated highly with the WOMAC total preoperatively and at 1 year postoperatively ($r = 0.91$ resp. $r = 0.85$). It also correlated highly with the OKS ($r = 0.85$ resp. $r = 0.81$). Both these scores are regularly used to externally validate new knee-specific scoring systems [2, 5, 18, 19] and the high correlation of the KOOS-12 with them indicates its good convergent construct validity. The KOOS-12 highly correlated with the KOOS, WOMAC and Oxford-12 preoperatively, whilst it correlated moderately with the KOOS sport and poorly correlated with the UCLA. The 1-year postoperative results showed a similar finding with the KOOS-12 highly correlating with the KOOS, WOMAC and Oxford-12. Providing a high correlation for both preoperative and postoperative timepoints is a strong indication that the KOOS-12 can be used in settings where KOOS, WOMAC and Oxford-12 questionnaires are considered. The moderate and poor correlation with KOOS sport and UCLA indicate that the KOOS-12 does not emphasize symptoms, stiffness, and high-level activity.

The UCLA measures a patient's physical activity along a spectrum ranging from being wholly inactive to participating in impact sports whereas the KOOS-12 assesses a different construct by measuring the impact of a patient's knee in the categories of pain, function and QoL. Therefore, it is no surprise that the correlation between KOOS-12 and the UCLA was low ($r = 0.30$). In the past, correlation of the UCLA with other disease-specific PROMs namely OKS and WOMAC was reported to be moderate ($r = 0.55$ resp. $r = 0.50$), which was also observed in this study cohort (data not shown). This underlines that these knee- or disease-specific tools assess inherently different outcomes compared to the UCLA after TKA.

In assessing the internal responsiveness of the KOOS-12, KOOS, WOMAC, UCLA and OKS, a significant change after treatment was observed in all of these scores. The effect size of change in the KOOS-12 between preoperative and 1 year was the largest ($d = 2.4$), in comparison to the effect sizes observed in the WOMAC ($d = 2.0$), OKS ($d = 2.1$) or the KOOS subscales ($d = 1.51$–2.2). Gandek et al. found the KOOS-12's effect size (2.7) to be greater than the KOOS subscale's (1.6–2.2), but they did not investigate the WOMAC or OKS [3]. This study has shown that the KOOS-12 is the best PROM with the ability to detect change in comparison to the OKS, WOMAC and KOOS-JR.

This study has several limitations. First, the results only reflect patients' situations preoperatively and at 1 year follow-up and, therefore, this study cannot draw any conclusion on the KOOS-12's ability to assess early-postoperative or long-term results. However, this interval was chosen since it is commonly used in orthopaedic literature and most of a patient's functional gains are made within the first year [12, 13]. Second, the data used in this analysis were initially acquired for a different study of prospectively examining patient reported outcome after TKA performed with a medially stabilized knee system. While this study, therefore, was designed retrospectively, the dataset used is representative of TKA populations and the retroactive use of existing KOOS data to assess KOOS-12 performance was encouraged by its originators [3].

Lastly, since this study only involved patients who underwent TKA the findings are not generalizable to other knee conditions or treatments. Further studies involving patients undergoing treatments other than TKA are, therefore, needed to more fully evaluate the KOOS-12. Lastly, despite the strength of the study having the availability of multiple knee questionnaire to provide a comparison, it also presented a potential limitation as participants would have completed a minimum of 89 items of similar wording for each item. The concern raised is potential response fatigue and the potential influence of repetitive items influencing scores of other items within the multiple measures.

Conclusion

The KOOS-12 showed good convergent construct validity, does not exhibit a ceiling effect and is responsive to changes in pain, function, QoL and knee impact between preoperatively and 1 year postoperatively. In combination with its lower respondent's burden it can, therefore, be recommended for routine use in the evaluation of patient reported outcome after TKA. The KOOS-12 can be used as an alternative PROM to the WOMAC, Oxford, and 3 sub sections of the KOOS (QoL, Function, and Pain). The shorter design of the questionnaire is less demanding on respondents, which is likely to result in higher compliance. However, based on this study's findings it might not be suitable for high demand cohorts and, therefore, it is suggested to add the KOOS sports subscale to the KOOS-12 when studying these populations.

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Author contributions All authors have contributed to the conception and design of the study, interpretation of the data, and revising it critically. LE and SM assembled the data and performed the data analysis, developed the study concept and design, and wrote the manuscript. All authors have read and approved the final manuscript and have taken responsibility for the integrity of the work as a whole.

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Compliance with ethical standards

Conflict of interest The authors have conflicts of interest to declare. SM reports payment to the Australian Institute of Musculo-Skeletal Research (AIMS) from MatOrtho, for manuscript preparation. SM is employed by AIMS Research. WLW reports personal fees from MatOrtho, outside the submitted work and discloses being a design surgeon for the SAIPH knee. JB, DW, ST and RB report sponsored travel to conferences from MatOrtho, outside the submitted work. LE has no conflicts of interest to declare.

Ethical approval The study was approved by the St Vincent's ethics committee (Reference number 151/15) and was carried out in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Informed consent Informed consent was obtained from all patients prior to inclusion in the study.

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Original article

The ceiling effects of patient reported outcome measures for total knee arthroplasty

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ABSTRACT

Background: Patient reported outcome measurements (PROMs) that exhibit a substantial ceiling effect show clustering of participant's scores towards the upper limit of a scale and consequently have low discriminatory power among high end scores. This study aimed to compare ceiling effects at 1 and 2 years postoperatively across commonly usedPROMs for TKA.
Hypothesis: We hypothesized, that the analyzed PROMs differ substantially in regards to their ceiling effect.
Patients and methods: Patients that underwent a primary unilateral TKA and completed pre-operative and post-operative questionnaires were included in the analysis. Participants completed the KOOS, KOOS-12, KOOS-JR, KOOS-PS, WOMAC and OKS preoperatively, and completed the KOOS, KOOS-12, KOOS-JR, KOOS-PS, WOMAC,OKS and FJS postoperatively at 1 and 2 years.
Results: 1-year and 2-year follow-up data was available for 380 and 193 patients, respectively. The pre-operative mean age was 68.0 (8.5) and mean BMI was 31.4 kg/m^2 (6.6), with a male to female ratio of 49.6% to 50.4%. At 1 year postoperatively, a ceiling effect was seen for the Pain and ADL subscales of the KOOS and the KOOS JR. The KOOS Pain, Symptoms, ADL and QoL subscales, the WOMAC Total and KOOS JR exhibited a ceiling effect at 2 years postoperatively. We found 9.0% and 14.8% of patients achieving a maximum score in the FJS at 1 and 2 years, respectively, indicating the absence of a substantial ceiling effect.
Conclusion: The PROMs studied differ substantially with regards to their ceiling effect and consequently their ability to detect differences between well performing groups. The KOOS Pain, Symptoms, ADL and QoL subscales, the WOMAC Total and KOOS JR exhibited a substantial ceiling effect at 2 years postoperatively. We recommend using PROMs like the FJS and KOOS-12 with a more evenly distribution of scores across the scale when studying well performing cohorts.
Level of evidence: III.

1. Introduction

Patient reported outcomes have been a common tool used in the assessment of patient improvement following a total knee arthroplasty (TKA) [1,2]. Because patients after TKA generally perform well, it is important that the measurement tools used have the ability to detect small differences among high achieving individuals in order to assess the effect of different treatments or implants.

The ceiling effect is a statistical construct that describes clustering of participant's scores towards the upper limit of a scale.

Abbreviations: ADL, Activities of daily living; FJS, Forgotten Joint Score; KOOS, Knee Injury and Osteoarthritis Outcome Score; KOOS-12, KOOS 12-item shortform; KOOS-JR, KOOS-Joint Replacement shortform; KOOS-PS, KOOS Physical Function shortform; OKS, Oxford Knee Score; PROMs, Patient reported outcome measurements; QoL, Quality of life; TKA, Total knee arthroplasty; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

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If a ceiling effect is present, variance in outcome is insufficiently measured above a certain level [3,4]. Therefore, the instrument's discriminatory power among high-end scores is low. Additionally, the inability to appropriately measure the improvement of patients in a ceiling cluster, limits the instrument's responsiveness.

In an effort to define quality criteria for the measurement properties of health status questionnaires for the use in systematic reviews of these tools, Terwee et al. recommended to consider a ceiling effect being present if 15% or more of respondents achieved the highest possible score, as described by McHorney et al. [5,6]. Yet, varying other methods to calculate the ceiling effect are being used when patients undergoing TKA are studied, necessitating caution when comparing ceiling effects between studies [7–9].

While PROMs typically used for the assessment of TKA cohorts have been examined for their ceiling effects in the past, values are not directly comparable between different study cohorts due to possible differences in patient satisfaction. Therefore, a comparative analysis of ceiling effects of TKA PROMs should be done within the same study cohort. To date, we are unaware of a study examining a wide range of PROMs at once.

This study aimed to compare ceiling effects at 1 and 2 years postoperatively across commonly used patient reported outcome measurements (PROMs) for TKA, namely the Knee Injury and Osteoarthritis Outcome Score (KOOS), KOOS 12-item shortform (KOOS-12), KOOS-Joint Replacement shortform (KOOS-JR), KOOS Physical Function shortform (KOOS-PS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Knee Score (OKS) and Forgotten Joint Score (FJS). The goal was to identify PROMs with no substantial ceiling effect that are thus suitable for the use in well performing TKA cohorts. It was hypothesized, that the analyzed PROMs differ substantially in regards to their ceiling effect.

2. Material and Methods

2.1. Study design and participants

The data used in this analysis was collected from an ongoing independent multicenter study examining a unique medially stabilized knee system. The study was approved by the institutional research ethics committee and was carried out in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients prior to inclusion in the study. Eligible for inclusion was any patient undergoing a primary TKA for osteoarthritis by one of the study surgeons. 13 different surgeons treated patients at 16 sites using the Saiph total knee replacement system (MatOrtho, Leatherhead, United Kingdom). The surgical technique was standardized throughout all 16 sites according to the manufacturer's instructions, using a medial parapatellar approach. For the present study, patients that underwent a primary unilateral TKA and completed pre-operative and post-operative questionnaires were included in the analysis. Patients with incomplete questionnaires were excluded.

2.2. Outcome Measures

Participants completed the full-length KOOS, and OKS preoperatively, and completed the KOOS, OKS and FJS postoperatively during in person visits at 1 and 2 years [10,11]. The KOOS-12, KOOS-JR, KOOS-PS and WOMAC were calculated from the full-length KOOS at preop., 1 year and 2 years [12–15]. The KOOS-12 is a recently developed and validated 12-item short form of the original KOOS that provides an overall knee impact score in addition to domain-specific scores for pain, function and knee-specific quality of life (QoL) [16–18].

2.3. Statistical analysis

Data was analyzed using Microsoft Excel 2016. Descriptive statistics was used to calculate the mean and standard deviation (SD) for patient demographics. Ceiling effects for the measurement tools were calculated as the percentage of patients achieving the maximum score of the respective PROMs. A ceiling effect was considered to be present when 15% or more of patients obtained the maximum score of a PROM [5]. The distribution of all the scores were shown graphically at 1 year postoperatively.

To provide further insight into the reason for the distinct differences in ceiling effects found when using different calculation methods, an exemplary calculation on the percentage of best answers per individual questions was performed for the FJS and OKS.

3. Results

3.1. Patient demographics

For a total of 563 patients who underwent surgery between December 2015 and November 2017, 1-year and 2-year follow-up data was available for 380 (67.5%) and 193 (34.3%), respectively. The preoperative mean age was 68.0 (standard deviation (SD) 8.5; 38–92) and mean BMI was 31.4 kg/m^2 (6.6; 15.4–61.0), with a male to female ratio of 49.6% to 50.4% (279 males, 284 females). The mean age at 1-year follow-up was 68.0 (8.0) and mean BMI was 31.2 (6.3). The percentage of male to female patients was 46.8% and 53.2% (178 males, 202 females) respectively. The 2-year mean patient age and BMI were 67.6 (8.0) and 30.6 (6.1), with 47.7% of subjects being male (92 males, 101 females).

3.2. Ceiling effects

The maximum scores calculated for all the outcome measures assessed are shown as percentages in Table 1. The percentage of patients with a maximum score increased from 1 year to 2 years for all scores and subscales.

Fig. 1 shows the percentage of maximum scores for all the analyzed questionnaires at both 1 year and 2 year follow up. A line set at 15% marks the threshold for a substantial ceiling effect. At 1 year postoperatively, a ceiling effect was seen for the Pain and ADL subscales of the KOOS and the KOOS JR (Fig. 1). The KOOS Pain, Symptoms, ADL and QoL subscales, the WOMAC Total and KOOS JR exhibited a ceiling effect at 2 years postoperatively (Fig. 1).

The distribution of achieved scores in the KOOS-12, KOOS subscales, WOMAC, KOOS JR, KOOS PS, OKS and FJS at 1 year are shown in Fig. 2a–k. The KOOS-12 and the FJS show an even distribution across the score (Fig. 2a and k). In contrast, the other questionnaires assessed show clustering in the higher score range (Fig. 2b–j).

3.3. Percentage of best answers by individual questions

The percentage of best answers chosen partitioned by individual questions for the FJS and OKS at 1- and 2-year follow up are shown in Fig. 3a and b. At 1 year postoperative, the percentage of best answers in the FJS ranged from 24.3 to 65.2% (SD 10.9%) and at 2 years postop. it ranged from 35.4% to 71.6% (SD 10.5%). For the OKS, the percentage of best answers at 1 year postoperative ranged from 14.4% to 84.7% (SD 19.1%) and at 2 years from 15.7% to 90.6% (SD 20.4%).

Table 1
Percentage of patients with a maximum possible score.

Questionnaire	Category	Pts. with max. score		
		Preoperative	1y	2y
KOOS – 12	Total	0.0%	9.5%	14.7%
KOOS	Pain	0.2%	27.7%	32.6%
	Symptoms	0.0%	13.4%	18.8%
	ADL	0.2%	18.9%	29.2%
	QoL	0.0%	14.8%	21.1%
	Sports	2.0%	10.1%	13.9%
WOMAC	Total	0.0%	11.5%	22.9%
KOOS JR	Total	0.2%	19.2%	34.0%
KOOS PS	Total	0.2%	8.0%	11.3%
OKS	Total	0.0%	7.3%	9.4%
FJS	Total	–	9.0%	14.8%

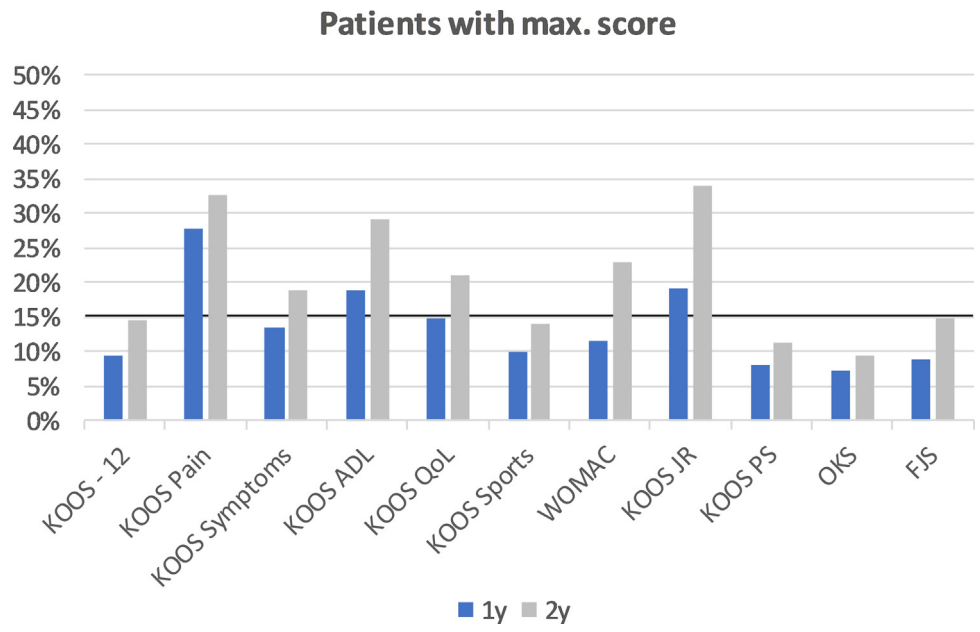

Fig. 1. Diagram of patients with a maximum possible score at 1 and 2 years postoperatively.

4. Discussion

To date, this is the most comprehensive comparative analysis of the ceiling effect across commonly used PROMs following TKA. It is also the first non-developer study to report on the ceiling effect for the recently developed KOOS-12. It was demonstrated that the PROMs studied differ substantially with regards to their ceiling effect. As a result their ability to detect changes over time and to discriminate differences between well performing groups are variable.

Substantial ceiling effects were found for the KOOS Pain, ADL and QoL subscales as well as the KOOS JR at 1 and 2 years, the KOOS Symptoms subscale and the WOMAC Total only at 2 years. Steinhoff et al. found similar percentages of patients scoring the maximum score for the subscales of Symptoms, Pain, QoL and ADL subscales compared to our results [9]. However, the findings in regards to the Sports/Recreation subscale differed (Steinhoff et al., 18%, present study 10.1%).

The initial introductory publication of the KOOS JR by Lyman et al. compared the ceiling effects of the five KOOS subscales, three WOMAC subscales, KOOS JR and KOOS PS at 2 years postoperatively [13]. While the absolute values varied, the order of magnitude of the observed ceiling effect across the subscales agreed with this study (Pain > ADL > QoL > Symptoms > Sports). The consistent order of the subscales demonstrates what categories of outcome are generally more likely affected by a ceiling effect, whereas the differences in percentages of maximum scores achieved might be potentially explained by the different patient demographics and implant designs studied.

A study conducted by Roos et al. also demonstrated the same order of subscales in regards to their ceiling effect at 1 year follow up compared to the current study, simultaneously Roos et al. reported similar absolute ceiling effects [19]. Commonly across all studies mentioned above, the most substantial ceiling effects were found for the Pain subscale of the KOOS, KOOS-12 and WOMAC. While this might indicate impaired discriminatory power and responsiveness, it has been argued that some individuals truly feel further improvement is not possible [20]. Certain constructs such as pain may have an inherent ceiling, in the sense that there is no less pain than no pain.

Our study additionally assessed the ceiling effect of the KOOS-12, OKS and FJS. Only one other study assessed the ceiling effect of the KOOS-12 and reported 7% of participants with the highest possible score at 1 year, which is comparable to 9.5% found in our study [16]. These findings indicate, that the KOOS-12 does not exhibit a substantial ceiling effect.

The FJS has previously been reported to have a particularly low ceiling effect, making it a suitable measurement tool for well

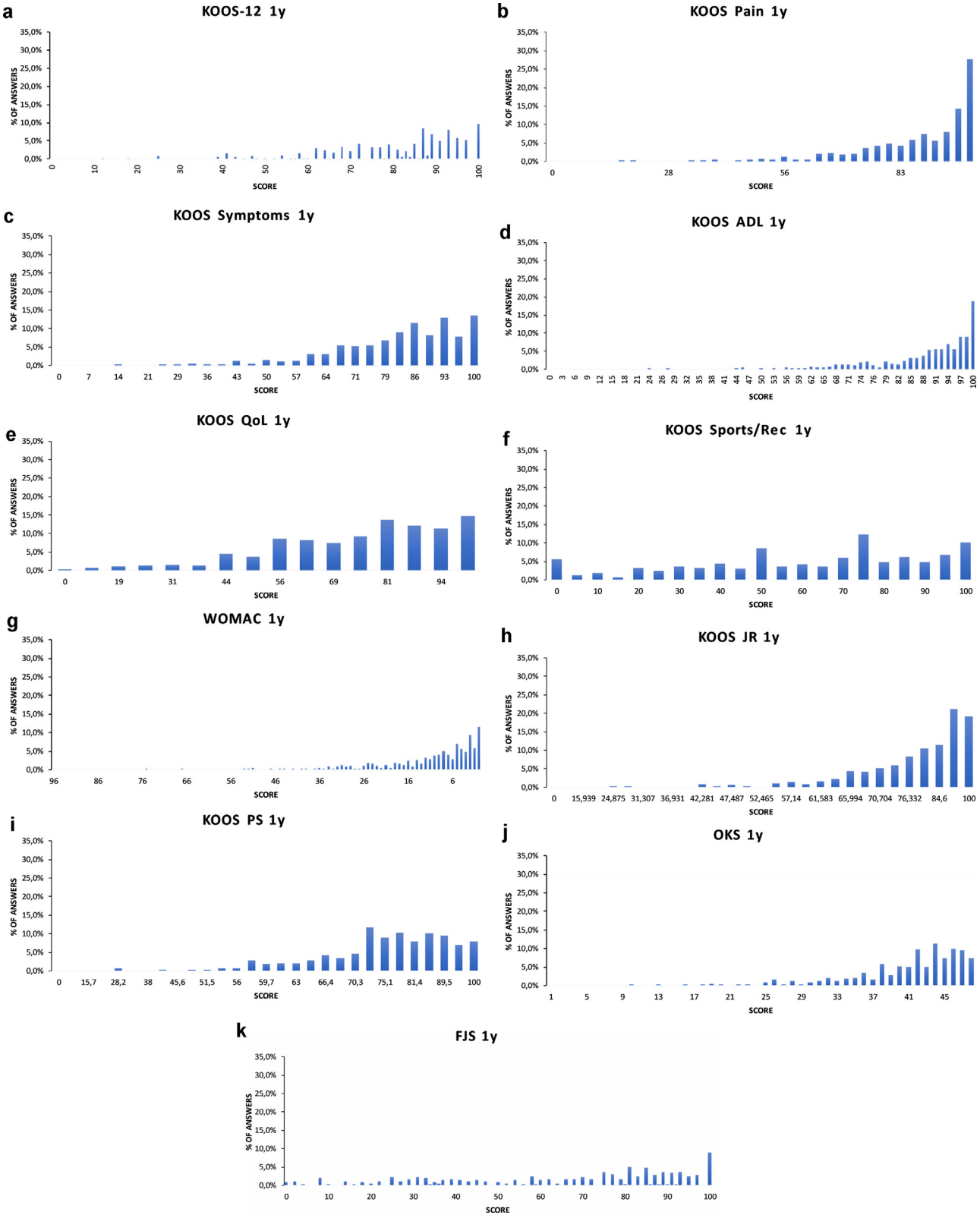

Fig. 2. Distribution of achieved scores for the (a) KOOS-12, (b) KOOS Pain subscale, (c) KOOS Symptoms subscale, (d) KOOS Activities of Daily Living subscale, (e) KOOS Quality of Life, (f) KOOS Sports and Recreation subscale, (g) WOMAC, (h) KOOS Joint Replacement shortform, (i) KOOS Physical Function shortform, (j) Oxford Knee Score and (k) Forgotten Joint Score at 1 year postoperatively.

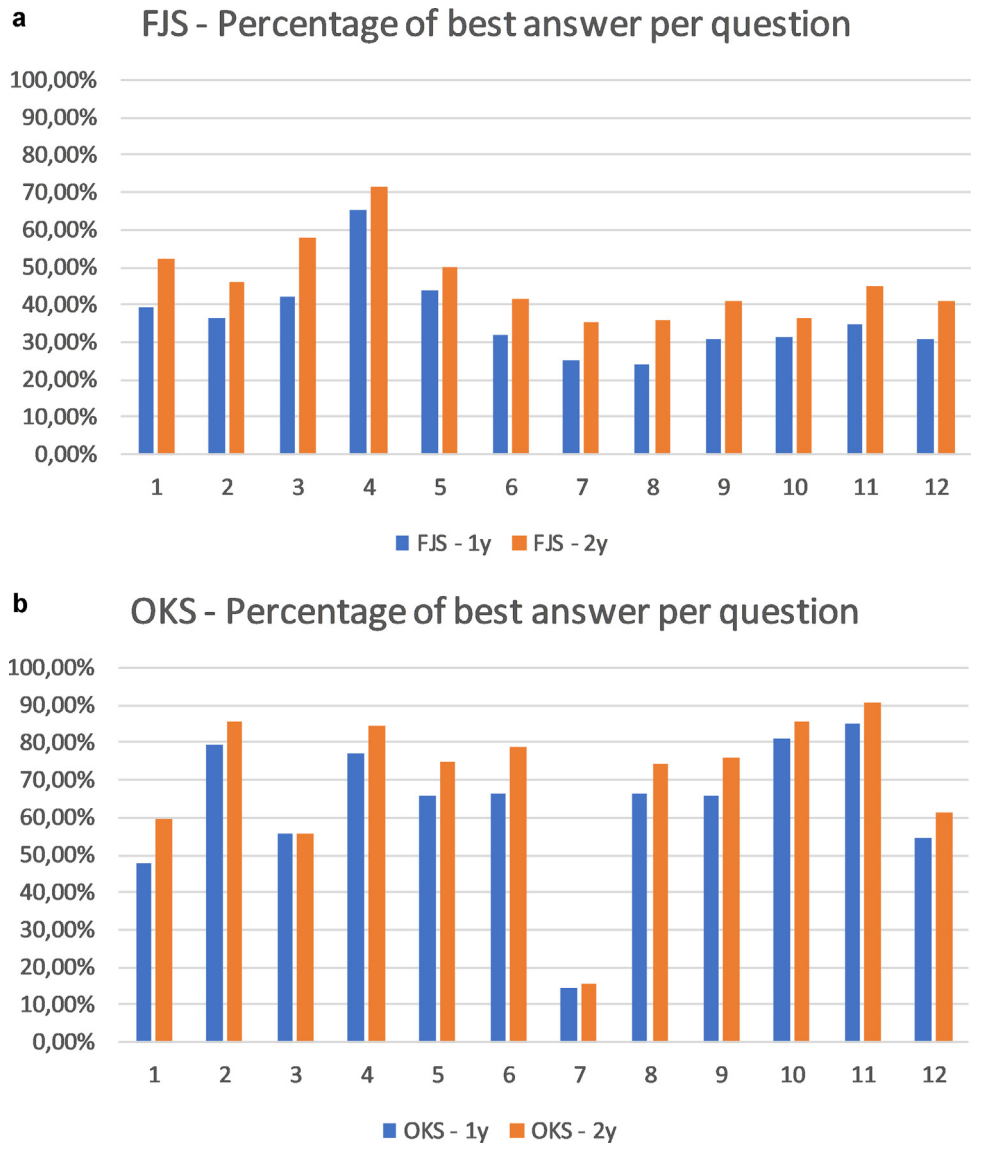

Fig. 3. a: the percentage of best answers for the FJS at 1 year (blue) and 2 year (orange) follow up; b: the percentage of best answers for the OKS at 1 year (blue) and 2 year (orange) follow up.

performing cohorts [21]. We found 9.0% and 14.8% of patients achieving a maximum score in the FJS at 1 and 2 years, respectively, indicating the absence of a substantial ceiling effect. Previously reported ceiling effect values at 1 year were similar to that found in our study and ranged from 3% to 9% at 1 year [21–23]. Giesinger et al. observed a substantial ceiling effect at 2 years (33%), demonstrating that patients generally are more likely to be able to 'forget' their joint over time after their surgery, while the magnitude achieving this goal might be different across different populations studied [23].

Previous studies have reported a substantial ceiling effect of 33% to 37% for the OKS, which seemingly contradicts our findings of 7.3% and 9.4% of patients with a maximum score at 1 and 2 years, respectively [7,8,24]. However, it is important to consider the method used to assess the ceiling effect. Thomsen et al. defined the ceiling effect as the percentage of patients within 15% of the maximum possible score, whilst Jenny et al. considered all patients within one SD of the best possible score for the calculation of the ceiling effect in both their studies. These definitions inherently increase the percentage of patients at the 'ceiling' of a score. Furthermore, they might skew the comparative rating of scoring systems.

Hamilton et al. found a ceiling effect of 3.9% for the FJS and 0.9% for the OKS at 1 year including only patients with a maximum result as advocated by Terwee et al. [5,21]. When they considered the top 10% of scores for the calculation, a ceiling effect was present in the OKS compared to the FJS (25.5% vs. 12.6%), inverting the interpretation of which score performs better regarding the ceiling effect [21]. In order to compare our results to Hamilton's, we performed an additional analysis considering all scores within the top 10% instead of just the maximum scores. Likewise, this increased the respective ceiling effects to 45.4% (OKS) and 22.3% (FJS) at 1 year and thus again inverting the judgement of which score performed better. First, this highlights the importance of noting the method used in order to achieve comparable results for the assessment of the ceiling effect. Second, it emphasizes that the statistical construct of the ceiling effect highly depends on the method used to assess it. Therefore, when assessing the discriminatory power of a PROM among high-end scores, researchers should not solely rely on the construct of the ceiling effect.

The calculation performed on the percentage of best answers per individual questions provides further insight into the reason for the distinct difference between the two methods compared above.

The percentage of best possible answers was relatively evenly distributed across the twelve questions of the FJS, whereas markedly fewer participants chose the best possible answer to question 7 (Could you kneel down and get up again afterwards?) compared to the other 11 questions in the OKS. This single question therefore acts as a threshold inhibiting the OKS from exhibiting a substantial ceiling effect when calculated based on the percentage of maximum scores, but not when calculated using any of the methods which define the ceiling effect by a range at the top end of the scale.

While it does not accurately measure the ceiling effect as defined by McHorney [6], the idea behind calculating the percentage of subjects within a certain range remains interesting as it addresses the problem of patients clustering at the top end of a scale. In an effort to depict the different score's susceptibility to clustering we rather chose to present distribution graphs of scores achieved as did others [24–26]. At 1 year clustering of patients at the top end of the scale was evident in the KOOS Pain, Symptoms and ADL subscales, KOOS JR, WOMAC Total and OKS. In contrast, the FJS presents a much more even spread of scores throughout the scoring scale. The KOOS-12 presents a distribution somewhat in between with a more even spread but slight shift to the top half of the scale. Therefore, the FJS and KOOS-12 may be more sensitive when evaluating small changes over time and better able to discriminate differences between well performing groups.

As both these observations are important descriptives of an outcome measurement's performance we propose using the term 'clustering effect' for the accumulation of scores achieved at a certain end of a measurement scale in distinction to the ceiling effect. Because description of the distribution of scores observed in a graph are subjective and not comparable across studies, we believe it is necessary to implement a mathematical method to describe this clustering through future studies.

A potential limitation of this study is the percentage of patients with missing follow-up data at 1 and 2 years, which may limit this data in terms of absolute clinical outcome scores. Though, patient demographics and preoperative outcome scores were similar among those with and those without follow-up data.

5. Conclusion

The PROMs assessed in this study differ substantially with regards to their ceiling effect and consequently their ability to detect differences between well performing groups. At 1 year postoperatively, a substantial ceiling effect was seen for the Pain and ADL subscales of the KOOS and the KOOS JR. The KOOS Pain, Symptoms, ADL and QoL subscales, the WOMAC Total and KOOS JR exhibited a substantial ceiling effect at 2 years postoperatively. We therefore recommend using PROMs like the FJS and KOOS-12 with a more evenly distribution of scores across the scale when studying well performing cohorts.

Disclosure of interest

The authors declare that they have no competing interest. SM reports payment to the Australian Institute of Musculo-Skeletal Research (AIMS) from MatOrtho, for manuscript preparation. SM is employed by AIMS Research. WLW reports personal fees from MatOrtho, outside the submitted work and discloses being a design surgeon for the SAIPH knee. JB, DW, ST and RB report sponsored travel to conferences from MatOrtho, outside the submitted work. LE has no conflicts of interest to declare.

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Author contributions

LE and SM designed the study, analysed the data, interpreted the data and wrote the manuscript.

JB, DW, RB, BW and ST were responsible for the acquisition of data and revised the manuscript critically.

All authors approve of the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Minimal important change and minimum clinically important difference values of the KOOS-12 after total knee arthroplasty

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ABSTRACT

Purpose: The minimal important change (minimal amount of change vs. baseline that a patient recognizes as a clinical change) and minimum clinically important difference (smallest difference between two measurements that are deemed important by patients) are important values to evaluate the clinical relevance of changes over time and differences between groups. This study aims to establish these values for the KOOS-12 at 1 year post-operatively.

Methods: KOOS-12 scores were calculated from the full-length KOOS completed by patients undergoing primary TKA preoperatively and at 1 year follow up. Minimal important change (MIC) values were estimated using the anchor-based predictive modeling approach and adjustment for the large proportion of improved patients in the study cohort was performed. The MCID was defined as the difference in the mean change in the KOOS-12 between the 'no improvement' and 'little improvement' groups.

Results: A total of 352 patients (161 male:191 female) with an overall mean age of 67.9 years (standard deviation (SD) 8.2) and a mean body mass index of 31.4 kg/m^2 (SD 6.3) were included: 97.1% of patients reported an important improvement, 1.1% reported being about the same and 1.7% reported being importantly worse. The MIC improvement values were 11.5 for Pain, 13.7 for Function, 5.5 for Quality of Life (QoL) and 14.9 for the total KOOS-12 score. MCID values were 13.5 for Pain, 15.2 for Function, 8.0 for QoL and 11.1 for the total KOOS-12 score.

Conclusion: MIC of 14.9 and MCID of 11.1 established in this study can assist clinicians and researchers in the interpretation of within-group changes (MIC) and differences between groups (MCID) at 1 year after TKA.

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1. Introduction

The Knee Injury and Osteoarthritis Outcome Score (KOOS) is a commonly used patient-reported outcome measure (PROM) for the assessment of patients undergoing total knee arthroplasty (TKA). In an effort to reduce respondent burden, a 12-item short-form (KOOS-12) of the original 42-item KOOS has recently been developed and its reliability and validity have been demonstrated [1,2]. In addition, it performs well compared with established PROMs after TKA [3].

In order to properly interpret changes in the KOOS-12 it has to be differentiated between statistically significant and clinically meaningful differences. The 'minimal important change' (MIC) and 'minimum clinically important difference' (MCID) are two values often used for this differentiation. To avoid confusion caused by the similarity of these terms, the reader's focus should be on the 'change' in MIC and the 'difference' in MCID.

The MIC represents the smallest change in a PROM score (vs. baseline) that a patient recognizes as a clinical change [4]. For example, if a patient change score is lower than the MIC, then their clinical outcome is not perceivably different to baseline for the patient. The MIC needs to be used when changes within a cohort (e.g., preoperative to postoperative) are assessed.

When differences between groups (e.g., study group implant A vs. control group implant B) are studied, the MCID of a PROM needs to be used for the interpretation of results. The MCID represents the smallest difference between two measurements that is deemed important by patients.

For every particular PROM the MIC and MCID may vary depending on the population, intervention and context studied [5]. Therefore, specific MIC and MCID threshold values need to be established for commonly investigated scenarios to enable researchers and clinicians to assess the clinical relevance of their PROM results.

Neither MIC nor MCID values for the KOOS-12 have been reported in previous studies. We therefore aimed to determine (1) the MIC value and (2) the MCID value for the KOOS-12 at 1 year post primary TKA using predictive modeling.

2. Material and methods

2.1. Patient demographics

The data used in this analysis was collected from a prospective independent multicenter study examining a unique medially stabilized TKA. Eligible for inclusion was any patient undergoing primary TKA for osteoarthritis by one of the 13 study surgeons between December 2015 and November 2017. For this analysis, patients were excluded if they did not complete both pre-operative and postoperative questionnaires and the anchor question, had secondary osteoarthritis, or had undergone a bilateral procedure.

2.2. Outcome measures

Patients completed the full-length KOOS preoperatively and at 1 year postoperatively. KOOS-12 scores were calculated from the full-length KOOS using the method described by Gandek et al. [1]. The KOOS-12 is a validated short-form of the KOOS that consists of 12 items rated on a five-point Likert scale. It provides an overall knee impact score in addition to domain-specific scores for pain, function and knee-specific quality of life (QoL). A total score ranging from 0 to 100 is calculated, with higher scores indicative of superior outcomes.

Additionally, at 1 year follow up the amount and importance of change perceived by the patient was assessed by the anchor question: "Overall, how are your problems now, compared with before your joint replacement?" A five-point Likert scale was used with possible answers ranging from "much better" to "much worse" (Table 1). Patients answering "much better" or "a little better" were classified as being importantly improved.

2.3. Statistics

Patient demographics were presented as means (standard deviation (SD)) for continuous variables and numbers (percentage) for categorical variables. KOOS-12 change score distribution across the anchor response categories was investigated with boxplots. The anchor's validity was evaluated with Spearman's correlation coefficients between the KOOS-12 change scores and the anchor responses. Data was analyzed using SPSS, version 11. A post hoc analysis was conducted to determine the power of the study. The input parameters for the power analysis were the effect size ($P = 2.9$), alpha ($\alpha = 0.05$) and sample size ($n = 352$), which resulted in a power of 0.98.

2.4. MIC

The MIC values were estimated using an anchor-based approach. Anchor-based methods relate changes in the score to a clinically meaningful reference measure, which are usually responses to a global transition item (much better, a little better, about the same, etc.) [6]. Due to its superior precision and lesser dependency on the correlation between the PROM and the anchor responses compared with the receiver operating characteristics (MIC_{ROC}) method, the 'predictive modeling approach'

Table 1
Minimal important change anchor question response options and classification into importantly improved or not.

Classification of importance/response options
Importantly improved
• Much better
• A little better
Not importantly improved
• About the same
• A little worse
• Much worse

(MIC_{pred}) to calculate the MIC introduced by Terluin et al. was the chosen method for estimating MIC values [4]. A detailed description on how to calculate the MIC_{pred} has previously been published [7]. Adjustment for the large proportion of improved patients in the study cohort was performed according to the adjustment method proposed by Terluin et al. [8].

2.5. MCID

Patients were grouped into those with 'no' improvement and those with 'little' improvement according to their answers in the anchor question. The MCID was defined as the difference in the mean change in the KOOS-12 between these two groups, in which the no improvement group represented the baseline and the little improvement group the next available in the anchor question. To calculate the MCID for the KOOS-12 score linear regression analysis was used to adjust for potential preoperative confounding variables (age, gender, body mass index (BMI) and preoperative KOOS-12 score).

3. Results

3.1. Study population

Eight patients were excluded because of missing preoperative questionnaires and 211 were excluded because they were not due for their 1-year follow up. A total of 352 patients met the inclusion and exclusion criteria and were used in the final analysis. The study group consisted of 161 (45.7%) males and 191 (54.3%) females with an overall mean age of 67.9 years (SD 8.2) and a mean BMI of 31.4 kg/m^2 (SD 6.3). The differences between the included and excluded patients were assessed (Table 2), showing no significant difference between the two groups, with the exception of gender. The incomplete group had a lower number of females.

3.2. Patient outcomes

Table 3 shows the mean score for the total and subscales of the KOOS-12 questionnaire assessed preoperatively and at 1 year postoperatively. Table 4 shows the mean change of scores between the two time-points for both the KOOS-12 total and subscales.

3.3. Box plots

Figure 1 shows the KOOS-12 change score distribution for both the 'importantly improved' and 'not importantly improved' categories defined earlier.

3.4. Descriptive data

The percentage of patients reporting an important improvement was 97.1%, while 1.1% reported being about the same and 1.7% of patients reported being importantly worse (Table 5).

3.5. MIC

The correlations between the anchor questions and the KOOS-12 change scores were 0.223 for QoL, 0.158 for Function, 0.263 for Pain and 0.285 for Total. The MIC pre-improvement values were 11.5 for Pain, 13.7 for Function, 5.5 for QoL and 14.9 for the total score.

3.6. MCID

The MCID was defined as the difference in the mean change in the KOOS-12 between patients with 'no improvement' and those with 'little improvement'. MCID values calculated for the KOOS-12 total and subscales are presented in Table 6.

4. Discussion

P-values reported in scientific publications help the reader to evaluate the likelihood of chance being involved in obtaining an observed result. While they are valuable to clinicians when assessing presented data, patients do not recognize statistical differences. They rather perceive change caused by a certain treatment which is described by the effect size. The MIC describes the smallest change in health status perceivable for patients (compared with a baseline), whereas the smallest difference deemed beneficial enough by a patient when comparing between two groups to be clinically important is the MCID. Therefore, it has been advocated that authors present differences found in clinical studies in relation to the respective MICs/MCIDs [9]. To our knowledge, the present study is the first to define the MIC and MCID for the KOOS-12. The MIC and MCID for the KOOS-12 total found in this study was 14.9 and 11.1, respectively. These values may provide a reference for investigators studying outcomes following TKA.

The MIC is the smallest change from baseline clinically perceived by a patient in a cohort. In this study it was defined as the change in KOOS-12 to baseline of patients who reported little improvement in their health status. Using the MIC of 14.9 found in this study, clinicians could assess the clinical relevance of a study cohort's improvement from before to after a TKA procedure. The predictive modeling approach was used to calculate the MIC values in this study [4]. In order to facilitate comparison of our findings to other study groups we additionally calculated the $MIC_{ROC,}$ as this was a commonly used method (results not shown). However, due to this method's inability to adjust for the large proportion of improved patients, these results were considered unreliable and were therefore not presented.

The defined MCID states that a difference of at least 11.1 points in the KOOS-12 between the two groups (no improvement and a little improvement) is perceived as clinically important by patients. Even though a study with a large enough sample size might find a difference of, for example seven points, between two study groups statistically significant, our study's findings suggest this would not be clinically important to patients. Furthermore, the MCID can be used in order to calculate sample sizes for clinical trials with the KOOS-12 as a primary outcome. TKA cohorts commonly have high improvement rates, with only a small number of patients within a study cohort reporting no change. This study reflects the lower numbers observed with only 1.1% of patients reporting no difference. A larger multicenter study could potentially gain higher numbers in the no change group, and hence could be used to further confirm our findings. The small number of patients in the no change group irrespective of our sample size, is a possible limitation in the strength of our results.

A limitation of our study is the risk of selection bias due to 1 year follow up data being only available for 67% of patients, therefore a comparison between complete and incomplete data is shown in Table 2. Males were more likely to be lost to follow up. No difference was found with regard to age, BMI or preoperative KOOS-12 score when comparing individuals lost to follow up to individuals with complete data. Therefore, we do not expect our values do be different if a higher follow up rate was obtained. Because MIC and MCID may vary depending on the population studied it is important to relate patients' demographics of a study establishing these values to any future study cohort demographics. Demographic characteristics observed in our study were similar to those of the overall Australian population undergoing primary TKA, which supports the representativeness of our cohort [10]. A future international multi-center trial could produce more generalizable MIC and MCID values due to the larger variation in patient demographics across a larger, more diverse study cohort.

It should be noted, that the MIC was calculated for improvement in the KOOS-12 and cannot be equated with that for deterioration in knee impact [11]. Because only 1.7% of patients reported being importantly worsened, the absolute numbers for a separate calculation of a MIC value for deterioration were too low.

Table 2
Comparison between included and excluded data.

	Patients with		
	Complete data *n* = 352	Incomplete data *n* = 219	*P*
Age	67.9 (8.2)	68.2 (8.9)	0.775
Female, *n* (%)	191 (54.3%)	96 (45.5%)	0.015
BMI (kg/m^2)	31.4 (6.3)	31.3 (6.9)	0.840
Pre-operative KOOS-12	35.5 (14.8)	35.6 (16.4)	0.943

BMI, body mass index; KOOS-12, 12-item short-form of the Knee Injury and Osteoarthritis Outcome Score (KOOS-12).

Table 3
Mean 12-item short-form of the Knee Injury and Osteoarthritis Outcome Score (KOOS-12) total and subscale scores preoperatively and at 1 year.

	Mean	Standard deviation	Standard error of the mean	95% Confidence interval of the difference	
				Lower	Upper
Pain – preoperative	40.78	16.05	0.85	39.10	42.46
Function – preoperative	43.57	37.15	1.96	39.71	47.43
QOL – preoperative	25.60	17.46	0.92	23.79	27.42
Total – preoperative	35.24	14.82	0.78	33.69	36.78
Pain – 1 year	89.05	32.67	1.73	85.66	92.45
Function – 1 year	84.07	16.35	0.86	82.37	85.77
QOL – 1 year	73.93	21.38	1.13	71.71	76.16
Total – 1 year	81.58	16.08	0.85	79.90	83.26

QoL, quality of life.

Table 4
Mean change scores between preoperative and 1 year for 12-item short-form of the Knee Injury and Osteoarthritis Outcome Score (KOOS-12) total and subscales.

Categories	n	Mean difference	Standard deviation	Standard error of the mean	95% Confidence interval of the difference	
					Lower	Upper
Total	352	46.49	19.15	1.02	44.48	48.51
Pain	352	45.97	20.22	1.08	43.85	48.09
Function	352	45	19.67	1.05	42.94	47.06
QoL	352	49.82	24.09	1.28	47.29	52.34

QoL, quality of life.

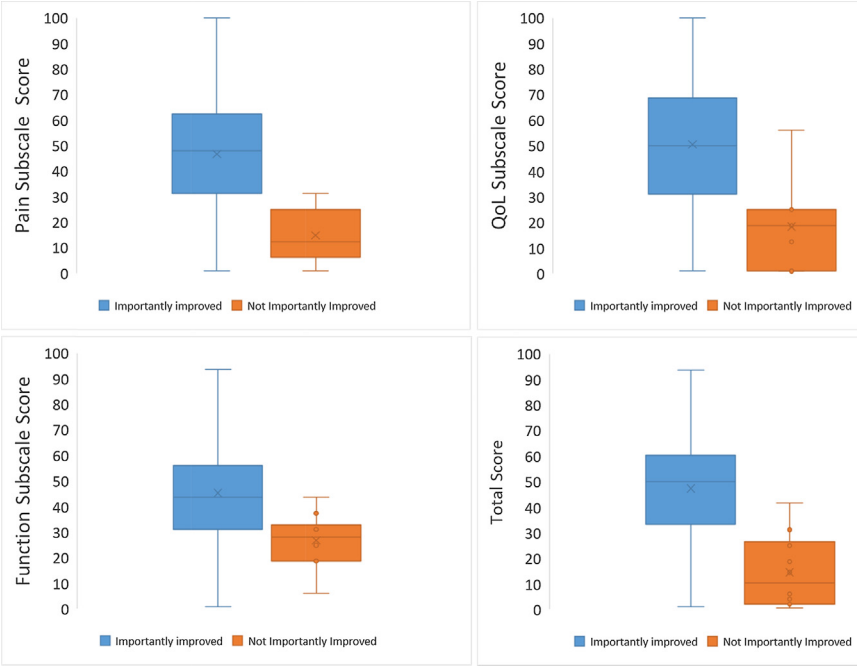

Figure 1. KOOS-12 change score distribution for patients in the "importantly improved" and "not importantly improved" categories.

5. Conclusion

The MIC and MCID for improvement values of 14.9 and 11.1, respectively, found in this study, can assist clinicians and researchers in the interpretation of within-group changes (MIC) and differences between groups (MCID) at 1 year after TKA.

Table 5
Percentages of patients per anchor question answer.

Importantly Improved	Patients much better	92.3%	97.1%
	Patients a little better	4.8%	
Not Importantly improved	Patients about the same	1.1%	2.8%
	Patients a little worse	1.1%	
	Patients much worse	0.6%	

Table 6
Minimum clinically important difference (MCID) values for 12-item short-form of the Knee Injury and Osteoarthritis Outcome Score (KOOS-12) total and subscales.

Category	MCID	Standard error of the mean	95% Confidence interval of the difference		Significance
			Lower	Upper	
KOOS 12 – Pain	13.5	3.5	7.9	22.5	<0.001
KOOS 12 – Function	15.2	4.5	5.2	23.8	0.004
KOOS 12 – QoL	8.0	4.0	6.9	23.5	0.001
KOOS 12 – Total	11.1	3.0	9.9	22.2	<0.001

QoL, quality of life.

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Declaration of Competing Interest

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

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