Knee instability as the primary cause of failure following Total Knee Arthroplasty (TKA): A systematic review on the patient, surgical and implant characteristics of revised TKA patients

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Abstract

Background

The aim of this review was to systematically assess the current evidence available regarding knee instability after TKA to identify time to failure between primary and revision TKA. In addition, we considered the patient, surgical and implant characteristics of primary TKA patients revised for knee instability, and investigated methods used for knee instability diagnosis.

Methods

A systematic search of six databases and the unpublished literature was performed. Studies referring to instability in post-operative primary TKA patients, reporting on revision TKA due to instability, and published or available between 2005 to 30-Mar-2015 were eligible for inclusion. Quantitative data for continuous variables were pooled in statistical meta-analyses.

Results

A total of 1841 unique studies were identified, 42 of which met the selection criteria and a total of 22 studies included in the review. Time to failure between primary and revision TKA was 44.7 months (95% CI [33.8, 55.7]), and the weighted mean age at time of revision surgery was 67.6 years (95% CI [65.38, 69.75]). A gender distribution was identified, with approximately 16.4% more females revised for instability, however this was unable to be corrected for the baseline population. The majority of studies used a combination of radiographic and clinical testing to diagnose knee instability.

Conclusion

Research on knee instability following primary TKA reported early failure and subsequent revision knee surgery. The need for revision due to instability was frequently reported in a younger patient cohort and most commonly in female TKA patients. Early revision at a younger age highlights the severe implications of an unstable knee.

Key Words

Knee instability; total knee arthroplasty; revision; prosthetic failure; early failure.

1. Introduction

Revision Total Knee Arthroplasty (TKA) is a significant undertaking for patients with both higher morbidity and mortality in comparison to primary TKA [1]. In recent years, there has been an increase in patients reporting symptoms relating to knee instability; similarly, the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) has reported rising rates of revision for knee instability. In the 2008 AOANJRR report, instability was identified as the ninth most common reason for all revisions, at 2.9% [2]. In 2011, this increased to the seventh most common cause, at 3.4% [3], and more recently, the sixth most common reason for revision at 3.9% [4]. It is unclear whether this trend is due to an increasing incidence, or an increased awareness of the diagnosis. Recent work has also debated whether these failures are related to surgical techniques or knee implant design, with the issue remaining unclear [5].

Instability can arise from component loosening, component breakage, polyethylene wear, ligamentous instability or surgical error in relation to implant size or balancing of the knee [6]. In addition, some implant designs have features that predispose to development of 'mid flexion instability' where the ligaments appear balanced at 0° and 90° of flexion but become lax in the mid-range [7]. These patients can experience significant symptoms climbing steps or rising from a chair.

Discussion around clinical cases and presentations within the Arthroplasty Society of Australia has suggested that there is a growing awareness of instability as a mode of implant failure amongst surgeons. In addition to patients who are developing mid flexion instability, there may be a subgroup developing a form of 'acquired instability' after initially successful, knee arthroplasty surgery. With the limited evidence available, it is assumed that this is due to ligamentous failure months or years after the knee arthroplasty procedure. While other common modes of failure such as aseptic loosening and prosthetic infection have been studied extensively, there is a lack of evidence in relation to instability as a mechanism of failure.

A number of definitions of knee instability exist in the literature. Instability may refer to the whole knee or may be used interchangeably with the term 'loosening', which more appropriately refers to a specific component and its fixation to the bone. In addition, symptoms that present and appear to be caused by instability may also be due to a number of other factors

including patellofemoral articulation, muscular weakness, component loosening, and infection [8].

With instability increasing as a cause of revision TKA, a clear understanding of the factors contributing to instability and subsequent revision is imperative. Recent AOANJRR figures consistently confirm that revision surgery not only reports higher rates of complication, but also poses a greater risk for further surgery. Such evidence highlights the need to enhance our understanding of how to achieve the optimal outcome at the primary procedure, and reduce the patient's risk of entering a descending spiral of multiple surgeries.

An assessment of an unstable knee has been recently described by Petrie and Haidukewych [9] and Cottino and others [10]. The use of clinical and radiological assessment is considered in these papers to obtain the correct diagnosis. A combination of both assessments is required to accurately confirm the diagnosis of instability and to exclude other diagnoses, which may elicit a different treatment approach. In the present review we assessed whether the orthopaedic literature supported this recommendation, and considered how the results available could enhance our understanding of these diagnostic issues in clinical practice.

1.1 Time to Failure

The AOANJRR data suggests that a significant proportion of knees that fail and require revision surgery do so at an early stage [4]. TKA implants are expected to last more than ten years in the majority of cases, however most failures occur before this time [4]. The most common reasons for early revision were infection, instability and peri-prosthetic fracture. The AOANJRR is a powerful source of Australian data, providing yearly cumulative percentage revision rates in consideration of various factors, such as implant type. The present review explored the international literature on knee instability to investigate time to failure following primary TKA. Time to failure is an essential factor in our understanding of an unstable knee, as patients with early knee failure are at greater risk of higher complication rates and re-revision surgery prematurely in their surgical journey.

1.2 Patient Characteristics

Failure of primary knee arthroplasty has been more commonly reported in a younger patient cohort of ≤ 70 years of age [4]. A younger cohort is consequently more likely to require further

surgery over time, emphasising the need for further investigation of specific modes of failure. Evidence on patient characteristics such as age, gender and Body Mass Index (BMI) were investigated in this review to screen for potential correlation between patient characteristics and instability failure.

1.3 Surgical Technique

Chang et al. [11] described that prevention of knee instability through the use of appropriate prostheses and technique was paramount. Although current interest in the orthopaedic community is focused on failures of specific implants, Chang et al. [11] emphasised the importance of surgical technique and appropriate intraoperative gap balancing, over implant use, when attempting to reduce risk of failure. Given current evidence, this review considered literature on both surgical technique and implant type, to determine their influence of knee instability and TKA failure.

The aim of this review was to systematically assess the current evidence available regarding knee instability after TKA to identify the patient, surgical and implant characteristics of primary TKA patients revised for knee instability.

More specifically, the primary objectives were *to consider literature that describes knee instability as the primary cause of failure of primary TKA to determine:*

1. *time to failure between primary TKA and revision TKA;*
2. *patient characteristics, surgical technique or implant type used in patients revised due to knee instability.*

The secondary objective was to *identify the methods of diagnosis of knee instability.*

2. Materials and Methods

The Cochrane Library and PROSPERO were screened for published protocols or reviews related to the topic of interest, of which none were identified. Our review was then registered online with PROSPERO (Registration Number CRD42015019898) to prevent duplication of work by other centres. The review was performed on the basis of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12].

2.1 Search Strategy

We conducted a sensitive and comprehensive search for published and unpublished studies relevant to the review question. Searches were restricted to studies published in English within the past ten years.

Orthopaedic implant companies regularly update and modify their implants as advances in design and engineering lead to improvements in results and quality. Following an initial screen of the literature it was apparent that older articles referred to knee implants no longer in use in the current market. Furthermore, surgical techniques have developed significantly over the last ten years compared to previous methods. As a result it was essential to impose a search date limit to ensure studies identified and reviewed would be relevant to current clinical practice.

Before developing the final search strategy, a preliminary scoping search of Ovid Medline was conducted to identify relevant Medical Subject Headings (MeSH) and a wide range of synonymous text-words. A detailed, sensitive search strategy was then developed in this database before accurate translation for other databases. These databases were: *PubMed; Cochrane Database of Systematic Reviews, Central Register of Controlled Trials, EMBASE (OvidSP), CINAHL, Scopus,* and *Web of Science.* A database search strategy is available in Appendix A.

A simplified version of the database search strategy was used to find unpublished (‘grey’) literature. This search included web search engines Google (Advanced) and Google Scholar (Advanced), clinical trial registries, major theses catalogues, grey literature repositories (e.g. Open-Grey), and the websites of significant conferences and organisations.

Authors endeavoured to contact authors wherever additional data or clarification was required.

2.2 Eligibility/Selection Criteria

Systematic search results were merged in the reference management software program (EndNote X7, Thomson Reuters, New York, USA), and duplicate articles removed. Titles and abstracts were screened for eligibility based on the inclusion and exclusion selection criteria by a single author. Full-text articles were then retrieved for titles and abstracts that were deemed relevant, or where eligibility was unclear. Eligibility of the full-text articles was reviewed by two authors independently, and any disagreement between authors was further deliberated until consensus was reached.

Articles were selected in accordance with the following inclusion criteria: (1) Any articles referring to instability in post-operative primary TKA patients; (2) Articles reporting on revision TKA due to instability; (3) Articles published or available between 2005 to 30th March 2015.

Articles were excluded in accordance with the following exclusion criteria: (1) The term 'instability' was identified by review authors to define other pathologies such as aseptic implant loosening or loosening/dislocation failure of mobile bearing knees; (2) Articles reported on atypical knee implants (i.e. Unicompartmental or Partial Knee Arthroplasties); (3) Articles described historical implants no longer in use in Australia or globally; (4) Articles which refer to revision of components previously revised; (5) No data relevant to knee instability as a cause of revision in title or abstract.

2.3 Critical Appraisal

The Methodological Index for Non-Randomised Studies (MINORS) instrument was used to assess the methodological quality and risk of bias of non-randomised surgical studies included in the review. MINORS is a validated, 12 – item critical appraisal tool for assessment of quality of comparative or non-comparative non-randomised surgical studies [13]. Items are scored as *0 (not reported)*, *1 (reported but inadequate)* and *2 (reported and adequate)*, with an ideal score of 16 for non-comparative and 24 for comparative studies [13]. Case reports were not critically appraised.

2.4 Data Extraction

Two authors independently extracted the data from all eligible studies. Data extraction was piloted on three studies before use independently. Data extracted included *age, gender, BMI, primary implant design and surgical technique, time to revision, revision type and prosthesis, diagnostic testing for instability, cause for instability (traumatic or non-traumatic), instability type (chronic or acute) and reported dislocation.*

Disparities in data extraction were discussed, reviewed and resolved.

2.5 Data Analysis

Quantitative data for continuous variables including *time to failure* and *age* were pooled in a statistical meta-analysis using the Comprehensive Meta Analysis (Version 3.3.070). Effect sizes were expressed as weighted mean differences with 95% confidence intervals, and a random effects model was used. As included studies reported mean *time to revision* with the variance measure of range, ranges were converted to standard deviations to allow for meta-analysis calculation, using, "Standard Deviation Estimator" implemented in PASS 14 Power Analysis and Sample Size Software (2015) [14]. A patient-level weighted mean was calculated for the remaining continuous variable, BMI. Dichotomous data was analysed descriptively using percentages and ratio.

3. Results

3.1 Systematic Search

The database and grey literature searches identified a total of 1841 unique studies. Following initial abstract screening, 252 studies were retrieved for full-text assessment, of which 42 met the selection criteria. A number of included studies did not report sufficient information relevant to the primary objective of this review. As such, corresponding authors or institutions of 25 selected studies were attempted to be contacted for further data. Despite efforts, the authors of three studies were uncontactable. Data was deemed unattainable if a response was not received within six weeks following initial contact, and 17 studies were consequently withdrawn. A total of 22 studies were included in the qualitative synthesis, a breakdown of study selection can be found in Fig. 1 [15-36]. A description of the characteristics of included studies is also provided in Table 1.

3.2 Methodological Quality of Included Studies

Studies were assessed for quality, however there was no quality restrictions imposed for inclusion in the review. The majority of the 22 studies included were of a case series study design (15) and a retrospective nature (19). Further study designs included a single case-control study (1), retrospective comparative studies (2) and case reports (4).

For the 15 non-comparative studies the MINORS mean score was 8.2 (Min-Max: 6 – 12, out of 16) and 13.7 (Min-Max: 10 – 18, out of 24) for the 3 comparative studies.

3.3 Time to Failure

Time to failure between primary TKA and revision TKA was described in 16 of the 22 included studies, of which reported on a total of 374 knees revised for instability. Of these 16 studies, 5 were unable to be included in the meta-analysis as 4 were case reports and 1 did not report a time to failure range. The remaining 11 studies reported on a total of 218 knees, and demonstrated a weighted mean time to failure of 44.7 months (95% CI [33.8, 55.7]) (Fig. 2).

3.4 Patient Characteristics

Of the 22 studies included, 19 reported a gender distribution, with approximately 16.4% more females revised for instability than males (Table 2). It must be noted that some studies reported the number of knees revised for instability and the gender distribution, without specifying the gender of bilateral patients, causing a discrepancy between the total number of knees and total number of males and females reported in this review. Furthermore, gender distribution was unable to be corrected for baseline populations, most commonly due to the design of included studies. Of the 19 studies, 9 used revision for knee instability as a study inclusion criterion, and consequently, no data on the gender ratio of the primary TKA cohort was reported. Four studies solely considered a revised TKA study cohort, and a further 4 were of case report study designs. A mere 2 studies reported the gender ratio of the primary TKA cohort from which the revised instability subgroup was collected, of which the vast majority were female (88.8%).

The mean age at time of revision surgery was reported in 16 of 22 included studies. Of these 16, 2 were unable to be included in the meta-analysis as they were of a case report study design. The remaining 14 studies reported on a total of 378 knees, and demonstrated a mean age of 67.6 years at time of revision surgery (95% CI [65.38, 69.75]) (Table 2). A total of 88 revised knees reported BMI, with only 1 patient identified with a BMI $\geq$ 40 kg/m^2. The patient-level weighted mean BMI was 30.4 kg/m^2 (Min-Max: 19 – 61), however range was not reported for 1 study included in the calculation of the weighted mean.

3.5 Surgical Technique and Implant Type

3.5.1 Primary TKA

Osteoarthritis was the principle indication leading to primary TKA in patients that later required revision for instability. The conventional surgical technique was the main technique employed for the primary TKA, however this was only reported in 4 of the included studies (15 knees). None of the included studies provided specific data regarding the effect of Computer – Assisted Surgery (CAS) or Patient Specific Instrumentation (PSI) surgery.

In comparison to the Posterior Stabilised (PS) implant design; the Cruciate Retaining (CR) implant was used in greater than double of the primary TKA procedures subsequently revised for instability (Table 3).

3.5.2 Revision TKA

A total of 10 studies reported the type of revision, with the majority of patients requiring a complete revision (77.4%). A constrained or semi-constrained revision prosthesis was more commonly used in patients revised for instability, in comparison to unconstrained (Table 3).

3.6 Knee Instability: Diagnosis, Cause and Type

Of the 22 included studies, 15 reported the diagnostic approach used to determine instability. The majority of studies (12) used a combination of both radiographic and clinical testing, while only 3 used clinical assessment. A number of studies (6) also reported the cause of instability, with 9 categorised as traumatic and 58 non-traumatic, reported in a total of 67 revised knees. Authors also categorised the type of instability as either chronic or acute. A mere 3 studies reported the type of instability, with 23 chronic and 3 acute cases identified. Dislocation rate across included studies was unable to be appropriately investigated given the complication had been used as part of the selection criteria in some studies.

4. Discussion

The aim of this review was to systematically assess the current evidence available regarding knee instability after TKA to identify time to failure between primary and revision TKA. In addition, we considered the patient characteristics, surgical technique and implant type used in patients revised due to knee instability.

Not only has instability been identified as a significant cause of revision knee arthroplasty but also a leading cause for early revision. Our findings of the relevant literature identified that on average, patients underwent revision for instability at 44.7 months (95% CI [33.8, 55.7]) following primary TKA. With over 90.0% of primary knees surviving for more than ten years in Australia [4], patients and surgeons expect greater longevity from TKA surgery than ever before. Our results highlight that current evidence reports knee instability as a cause of early failure and subsequent revision knee surgery. Early revision has shown the potential to instigate a downward spiral for the patient, with high risks of re-revision surgery over the following five years [4], demonstrating the severe clinical implications of an unstable knee.

4.1 Patient Characteristics: Age, BMI and Gender

In regards to gender distribution, a greater number of females were identified as undergoing revision for instability in included studies. This finding is consistent with AOANJRR figures which report greater revision rates for females across all causes [37]. However, it must be emphasised that the data could not be corrected for the gender distribution of the baseline, primary TKA population. This information was omitted from the majority of included articles, and consequently limits plausible inferences regarding gender. Of the two studies which did report the gender distribution of the primary TKA population from which the instability subgroup was obtained, the vast majority were female (88.8%). This is comparable to AOANJRR findings, which highlight a consistently higher proportion of females undergoing primary TKA (56.1%) [4].

Average age at revision TKA was low, with patients undergoing the procedure in their mid-to-late sixties. This result is consistent with Australian national data, which suggests revision rates are higher in patients who are less than 70 years of age when the primary knee surgery was performed [4]. Furthermore, a third (34.8%) of all knee arthroplasty revisions reported by the AOANJRR occurred in the 65 to 74 age bracket [37]. Correspondingly, The Swedish Knee

Arthroplasty Register also reported the highest incidence of revision for TKA in osteoarthritic patients aged 65 to 74 years [38]. A recent epidemiological study of revision TKA in the United States also identified that patients aged 65 to 74 years underwent the largest number of revisions (30.1%) [39]. Interestingly, Meehan, et al. 2014 [40] reported that patients younger than 50 years had a higher risk for periprosthetic joint infection and aseptic mechanical failure at one year post TKA. Finally our data suggests that BMI was not a relevant patient characteristic with regards to revision, however this was reported in a very few number of articles and inferences cannot be concluded.

4.2 Surgical Technique and Primary Implant Design

Of the four studies commenting on surgical technique, only one study was performed using a MIS technique, while all other revised knees were performed using conventional instruments. Of the two implant designs, the majority of revised knees had received a CR design, however, this may simply be due to greater use of this implant type. When reviewing the ten most common knee implants used in Australia in 2014, 76% were CR designs while 24% were PS [4].

An outstanding majority (77.4%) of cases reported were performed with a total revision of all original components. A variety of minor revisions were reported with exchange of, for example, just the polyethylene insert of the tibial component. The use of polyethylene exchange is common as surgeons are concerned about the need for further revisions, especially in younger patients. This practice is supported by AOANJRR results who suggest the risk of re-revision in patients who undergo their first revision in five years is almost 30.0% for major revision surgery in comparison to approximately 20.0% in patients who undergo minor revision such as a poly-insert exchange. As most revisions for knee instability occur in the first five years, a more conservative approach may be more supported given the greater risks of re-revision.

4.3 Diagnostic Approach for TKA Instability

A combination of clinical assessment and radiological assessments were most commonly used to diagnose instability, highlighting adherence to recommended practice [10, 41]. The most important diagnostic factor is the clinical history. Patients with symptomatic instability, particularly in flexion, report a common series of symptoms including a feeling of insecurity

in the knee without frank giving way, difficulty with stairs, recurrent knee swelling and anterior knee pain [10].

The primary strength of this review was that a large body of literature was systematically assessed against predefined criteria to critically review and summaries knee instability as a mechanism of failure. A limitation of review methodology was that the initial screening of citations was performed by a single reviewer. Further limitations were a reflection of the limited data available from eligible studies, resulting in an inability to include such studies in review results. Furthermore, demographic data was unable to be corrected for the baseline primary TKA population due to limited data reported in included studies, restricting plausible inferences. In addition, vague definitions and/or inconsistent terminology was used when describing the type and cause of instability across included studies, emphasising the need for uniformity, and detailed reporting in the literature in the future. Appendix B provides a summary of the descriptions used when discussing type of instability across included studies.

4.4 Conclusions

Research on knee instability following primary TKA reported early failure and subsequent revision knee surgery. The need for revision due to instability was frequently reported in a younger patient cohort and most commonly in female TKA patients. Early revision at a younger age highlights the severe implications of an unstable knee.

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Figure Legend

Figure 1. PRISMA Flow Diagram for Study Selection

Figure 2. Forest plot of time to failure between primary TKA and revision TKA in months; CI: Confidence Interval

References

[1] Nichols CI, Vose JG. Clinical Outcomes and Costs Within 90 Days of Primary or Revision Total Joint Arthroplasty. J Arthroplasty. 2016;31: 1400-06 e3.

[2] Australian Orthopaedic Association National Joint Replacement Registry. Annual Report. Adelaide:AOA. 2008.

[3] Australian Orthopaedic Association National Joint Replacement Registry. Annual Report. Adelaide:AOA. 2011.

[4] Australian Orthopaedic Association National Joint Replacement Registry. Annual Report. Adelaide:AOA. 2015.

[5] Stoddard JE, Deehan DJ, Bull AM, McCaskie AW, Amis AA. The kinematics and stability of single-radius versus multi-radius femoral components related to mid-range instability after TKA. J Orthop Res. 2013;31: 53-8.

[6] Vince KG, Abdeen A, Sugimori T. The unstable total knee arthroplasty: causes and cures. J Arthroplasty. 2006;21: 44-9.

[7] Athwal KK, Hunt NC, Davies AJ, Deehan DJ, Amis AA. Clinical biomechanics of instability related to total knee arthroplasty. Clin Biomech (Bristol, Avon). 2014;29: 119-28.

[8] Del Gaizo DJ, Della Valle CJ. Instability in primary total knee arthroplasty. Orthopedics. 2011;34: e519-21.

[9] Petrie JR, Haidukewych GJ. Instability in total knee arthroplasty : assessment and solutions. Bone Joint J. 2016;98-B: 116-9.

[10] Cottino U, Sculco PK, Sierra RJ, Abdel MP. Instability After Total Knee Arthroplasty. Orthop Clin North Am. 2016;47: 311-6.

[11] Chang MJ, Lim H, Lee NR, Moon YW. Diagnosis, causes and treatments of instability following total knee arthroplasty. Knee Surg Relat Res. 2014;26: 61-7.

[12] Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151: 264-9, W64.

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

[14] PASS 14 Power Analysis and Sample Size Software (2015). NCSS, LLC. Kaysville, Utah, USA, https://ncss-wpengine.netdna-ssl.com/wp-content/themes/ncss/pdf/Procedures/PASS/Standard_Deviation_Estimator.pdf.

[15] Abdel MP, Pulido L, Severson EP, Hanssen AD. Stepwise surgical correction of instability in flexion after total knee replacement. Bone Joint J. 2014;96-B: 1644-8.

[16] Arnout N, Vandenneucker H, Bellemans J. Posterior dislocation in total knee replacement: a price for deep flexion? Knee Surg Sports Traumatol Arthrosc. 2011;19: 911-3.

[17] Bieger R, Kappe T, Fraitzl CR, Reichel H. The aetiology of total knee arthroplasty failure influences the improvement in knee function. Arch Orthop Trauma Surg. 2013;133: 237-41.

[18] DePuy Synthes Institute. DePuy Synthes Joint Reconstruction Knee Revision Solutions X-Ray Case Book. DePuy International Ltd. and DePuy Orthopaedics, Inc. 2014.

[19] Firestone TP, Eberle RW. Surgical management of symptomatic instability following failed primary total knee replacement. J Bone Joint Surg Am. 2006;88 Suppl 4: 80-4.

[20] Flierl MA, Bravman JT, Eckhoff DG. Successful LCL reconstruction and PCL repair for LCL tear and PCL avulsion following total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2014;22: 2783-7.

[21] Girard J, Amzallag M, Pasquier G, Mulliez A, Brosset T, Gougeon F, et al. Total knee arthroplasty in valgus knees: predictive preoperative parameters influencing a constrained design selection. Orthop Traumatol Surg Res. 2009;95: 260-6.

[22] Hamilton DF, Burnett R, Patton JT, Howie CR, Simpson AH. The identification and quantification of instability in a primary total knee replacement prior to revision. Bone Joint J. 2014;96-B: 1339-43.

[23] Hosaka K, Saito S, Ishii T, Mori S, Sumino T, Tokuhashi Y. Asian-specific total knee system: 5-14 year follow-up study. BMC Musculoskelet Disord. 2011;12: 251.

[24] Kannan A, O'Connell RS, Kalore N, Curtin BM, Hull JR, Jiranek WA. Revision TKA for Flexion Instability Improves Patient Reported Outcomes. J Arthroplasty. 2014.

[25] Kasahara Y, Majima T, Kimura S, Nishiike O, Uchida J. What are the causes of revision total knee arthroplasty in Japan? . Clin Orthop Relat Res. 2013;471: 1533-38.

[26] Koskinen E, Remes V, Paavolainen P, Harilainen A, Sandelin J, Tallroth K, et al. Results of total knee replacement with a cruciate-retaining model for severe valgus deformity-A study of 48 patients followed for an average of 9 years. Knee. 2011;18: 145-50.

[27] Mayle RE, Jr., Graw BP, Huddleston HG, Woolson ST, Goodman SB, Huddleston JI. MI TKA: a risk factor for early revision surgery. J Knee Surg. 2012;25: 423-7.

[28] Raab GE, Fehring TK, Odum SM, Mason JB, Griffin WL. Aspiration as an aid to the diagnosis of prosthetic knee instability. Orthopedics. 2009;32: 318.

[29] Schwab JH, Haidukewych GJ, Hanssen AD, Jacofsky DJ, Pagnano MW. Flexion instability without dislocation after posterior stabilized total knees. Clin Orthop Relat Res. 2005;440: 96-100.

[30] Scott RD. Reoperation after total knee arthroplasty. Revision Total Knee Arthroplasty, 2005: p. 3-9.

[31] Song IS, Sun DH, Chon JG, Jang SW, Sun DH. Results of revision surgery and causes of unstable total knee arthroplasty. Clin Orthop Surg. 2014;6: 165-72.

[32] Springer BD, Curtin BM. Chapter 13 Revision Total Knee Arthroplasty: Management of Ligamentous Instability. Complex Primary and Revision Total Knee Arthroplasty: A Clinical Casebook. Switzerland: Springer International Publishing 2015.

[33] Tay KS, Lo NN, Yeo SJ, Chia SL, Tay DK, Chin PL. Revision total knee arthroplasty: causes and outcomes. Ann Acad Med Singapore. 2013;42: 178-83.

[34] Unnanuntana A, Murphy JE, Petersilge WJ. Management of chronic lateral instability due to lateral collateral ligament deficiency after total knee arthroplasty: A case report. J Med Case Rep. 2010;4.

[35] Van Kempen RW, Schimmel JJ, van Hellemondt GG, Vandenneucker H, Wymenga AB. Reason for revision TKA predicts clinical outcome: prospective evaluation of 150 consecutive patients with 2-years followup. Clin Orthop. 2013;471: 2296-302.

[36] Villanueva M, Rios-Luna A, Pereiro J, Fahandez-Saddi H, Perez-Caballer A. Dislocation following total knee arthroplasty: A report of six cases. Indian j. 2010;44: 438-43.

[37] Australian Orthopaedic Association National Joint Replacement Registry. Revision Hip and Knee Arthroplasty Supplementary Report; AOA; Adelaide 2015.

[38] Swedish Knee Arthroplasty Register. Annual Report 2016. http://www.myknee.se/en/; 2016 [accessed 14.06.17].

[39] Delanois RE, Mistry JB, Gwam CU, Mohamed NS, Choksi US, Mont MA. Current Epidemiology of Revision Total Knee Arthroplasty in the United States. J Arthroplasty. 2017.

[40] Meehan JP, Danielsen B, Kim SH, Jamali AA, White RH. Younger age is associated with a higher risk of early periprosthetic joint infection and aseptic mechanical failure after total knee arthroplasty. J Bone Joint Surg Am. 2014;96: 529-35.

[41] Abdel MP, Haas SB. The unstable knee: wobble and buckle. Bone Joint J. 2014;96-B: 112-4.

Tables

Table 2. Time to Failure and Characteristics of patients revised for Instability

	Units	*Results*
Time to Failure *(n_k= 218; n_a= 11)*	Weighted Mean 95% CI	44.7 months 95% CI [33.8, 55.7]
Gender *(n_k=386; n_a= 19)*	M : F	158 : 220
BMI *(n_k=88; n_a=5)*	BMI < 40 : ≥ 40	87 : 1
	Weighted Mean*	30.4 kg/m^2
	Min – Max*	19 – 61
Age at Time of Revision Surgery *(n_k=378; n_a=14)*	Weighted Mean 95% CI	67.6 years 95% CI [65.38, 69.75]

n_k = number of knees revised for instability reported for each parameter

n_a = number of articles that reported the parameter

BMI = Body Mass Index; Min = Minimum; Max = Maximum; CI = Confidence Interval

**BMI range not reported for one study included in the calculation of the BMI weighted mean.*

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Table 3. Characteristics of Surgical Technique and Implant

Primary TKA		*N*	
Indication for Primary TKA	Osteoarthritis	118	
(n_k =120; n_a= 8)	Rheumatoid Arthritis	2	
Surgical Technique	Conventional	14	
(n_k =15; n_a=4)	Minimal Invasive Surgery	1	
Implant Design	Posterior Stabilised	86	
(n_k =294; n_a=14)	Cruciate Retaining	208	
Revision TKA		*N*	*(%)*
Type of Revision	Complete Revision (T+F)	106	*(77.4)*
(n_k =137; n_a=10)	Femoral Only	6	*(4.4)*
	Tibial Only	4	*(3.8)*
	PE Insert Only	18	*(13.1)*
	Femoral and PE Insert	1	*(0.7)*
	Patella and PE Insert	2	*(1.5)*
Revision Prosthesis	Constrained	35	*(35.0)*
(n_k =100; n_a=7)	Semi – Constrained	44	*(44.0)*
	Standard/Unconstrained	21	*(21.0)*

N = number; PE = Polyethylene

n_k = number of knees revised for instability reported for each parameter

n_a = number of articles that reported the parameter

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Appendix A: Search Strategy

Ovid MEDLINE Search Strategy
MeSH Terms
Arthroplasty, Replacement, Knee/ Knee prosthesis/ Causality/ or Precipitating factors/ or Risk factors/ Joint instability/ (Knee joint/ or Knee/) and Arthroplasty/
Free Text Terms
(TKA? or TKR?).tw. (Knee* adj4 (replacement* or arthroplast* or prosthe*)).tw. (Stable or stabili* or instabili* or unstable or destabili* or constrain* or balanc* or imbalanc* or unbalanc*).tw. (Etiology or Adverse effects).fs. (Causalit* or causati* or cause* or ?etiolog* or risk* or precipitat* or predispos* or multifactor* or multi-factor*).tw
/ MeSH/Subheading combination; * Search Term Truncation

Appendix B: Type of instability descriptions provided in included studies

First Author, Year	Number of knees revised for instability	Instability Description
Schwab, J. H., 2005[1]	10	Isolated symptomatic flexion instability in the AP plane
Scott, R. D., 2005[2]	6	Late-onset knee instability: ▪ 3 knees: Trauma due to fall; ▪ 2 knees: Status post patellectomy with persistent quadriceps weakness and episodes of giving way; ▪ 1 knee: Muscle weakness and imbalance due to a syringomyelia
Firestone, T. P., 2006[3]	109	*'Patients were found to be at risk for symptomatic instability if they demonstrated one or more of the following findings: laxity in mid-flexion, substantial anteroposterior translation, discomfort with medial-lateral stress, and/or a "ballottable" flexion gap.'* *'Radiographic evidence of instability following primary total knee replacement includes excessive posterior condyle resection, inadequate distal femoral resection, nonweight- bearing component gapping, and bearing surface eccentricity.'*
Girard J., 2009[4]	2	Frontal instability
Raab, G. E., 2009[5]	42	Subtle instability patterns, for example normal-appearing radiographs and multiple subjective symptoms.
Unnanuntana, A., 2010[6]	1	Chronic lateral instability due to lateral collateral ligament deficiency after primary total knee arthroplasty.
Villanueva, M., 2010[7]	6	Residual instability (5 knees: Posterior dislocation; 1 knee: Anterior dislocation).

Arnout, N., 2011[8]	4	Posterior dislocation
Hosaka, K., 2011[9]	2	Instability
Koskinen, E., 2011[10]	10	▪ 8 Knees: Medial collateral instability; ▪ 1 Knee: Lateral collateral instability; ▪ 1 Knee: Instability with subluxation.
Mayle, R. E., 2012[11]	1	Instability
Bieger, R., 2013[12]	13	*'Patients with instability had to report pain and swelling related to activity, the finding of instability upon clinical examination, as well as sterile joint aspiration.' 'In one patient the medial collateral ligament was re-fixated during revision TKA.'*
Kasahara, Y., 2013[13]	13	*'Instability was evaluated using varus/valgus and anterior/posterior drawer stress radiograph.'*
Tay, K. S., 2013[14]	3	Instability
Van Kempen, R. W., 2013[15]	23	*'Instability was defined as a clinical diagnosis with pain and instability experienced by the patient caused by a collateral ligament laxity or PCL insufficiency without any sign of component malpositioning.'*
Abdel, M. P., 2014[16]	60	Symptomatic instability in flexion in the AP plane.
Hamilton, D. F., 2014[17]	25	*'Knee instability was diagnosed clinically by the surgical team on the basis of the patient's symptoms and an assessment of the laxity of the knee in all planes and in both flexion and extension.'*
Kannan, A., 2014[18]	37	Flexion instability *'A clinical diagnosis of flexion instability was made in patients with painful TKA based on the presence of coronal*

		plane instability with or without sagittal plane instability at 90 degrees of flexion, but without instability in extension.'
Song, I. S., 2014[19]	24	▪ 13 Knees: Coronal instability with posteromedial polyethylene wear and lateral laxity; ▪ 6 Knees: Coronal instability with posteromedial polyethylene wear; ▪ 3 Knees: Sagittal instability (including post breakage); ▪ 1 Knee: Global instability; ▪ 1 Knee: Flexion instability.
Flierl, M. A., 2014[20]	1	Posterior instability
DePuy Synthes, 2014[21]	4	▪ 1 Knee: Excessive constraint, in an unbalanced knee; ▪ 1 Knee: Medial collateral ligament insufficiency; ▪ 1 Knee: The knee presented problems of balance, bone loss and fixation at revision surgery; ▪ 1 Knee: 25 degrees hyperextension and global instability.
Springer, B. D., 2015[22]	1	Ligamentous Instability

References

1. Schwab JH, Haidukewych GJ, Hanssen AD, Jacofsky DJ, Pagnano MW. Flexion instability without dislocation after posterior stabilized total knees. *Clin Orthop Relat Res 2005;440:96-100.*

2. Scott RD. Reoperation after total knee arthroplasty. Revision Total Knee Arthroplasty, 2005: p. 3-9.

3. Firestone TP, Eberle RW. Surgical management of symptomatic instability following failed primary total knee replacement. *Journal of Bone & Joint Surgery - American Volume 2006;88 Suppl 4:80-4.*

4. Girard J, Amzallag M, Pasquier G, Mulliez A, Brosset T, Gougeon F, Duhamel A, Migaud H. Total knee arthroplasty in valgus knees: predictive preoperative parameters influencing a constrained design selection. *Orthopaedics & traumatology, surgery & research 2009;95-4:260-6.*

5. Raab GE, Fehring TK, Odum SM, Mason JB, Griffin WL. Aspiration as an aid to the diagnosis of prosthetic knee instability. *Orthopedics 2009;32-5:318.*

6. Unnanuntana A, Murphy JE, Petersilge WJ. Management of chronic lateral instability due to lateral collateral ligament deficiency after total knee arthroplasty: A case report. *Journal of Medical Case Reports 2010;4-144.*

7. Villanueva M, Rios-Luna A, Pereiro J, Fahandez-Saddi H, Perez-Caballer A. Dislocation following total knee arthroplasty: A report of six cases. *Indian Journal of Orthopaedics 2010;44-4:438-43.*

8. Arnout N, Vandenneucker H, Bellemans J. Posterior dislocation in total knee replacement: a price for deep flexion? *Knee Surgery, Sports Traumatology, Arthroscopy 2011;19-6:911-3.*

9. Hosaka K, Saito S, Ishii T, Mori S, Sumino T, Tokuhashi Y. Asian-specific total knee system: 5-14 year follow-up study. *BMC Musculoskeletal Disorders 2011;12:251.*

10. Koskinen E, Remes V, Paavolainen P, Harilainen A, Sandelin J, Tallroth K, Kettunen J, Ylinen P. Results of total knee replacement with a cruciate-retaining model for severe valgus deformity-A study of 48 patients followed for an average of 9years. *Knee 2011;18-3:145-50.*

11. Mayle RE, Jr., Graw BP, Huddleston HG, Woolson ST, Goodman SB, Huddleston JI. MI TKA: a risk factor for early revision surgery. *The Journal of Knee Surgery 2012;25-5:423-7.*

12. Bieger R, Kappe T, Fraitzl CR, Reichel H. The aetiology of total knee arthroplasty failure influences the improvement in knee function. *Archives of Orthopaedic & Trauma Surgery 2013;133-2:237-41.*

13. Kasahara Y, Majima T, Kimura S, Nishiike O, Uchida J. What are the causes of revision total knee arthroplasty in Japan? Knee. *Clinical Orthopaedics and Related Research 2013;471-5:1533-8.*

14. Tay KS, Lo NN, Yeo SJ, Chia SL, Tay DK, Chin PL. Revision total knee arthroplasty: causes and outcomes. *Annals of the Academy of Medicine, Singapore 2013;42-4:178-83.*

15. Van Kempen RW, Schimmel JJ, van Hellemondt GG, Vandenneucker H, Wymenga AB. Reason for revision TKA predicts clinical outcome: prospective evaluation of 150 consecutive patients with 2-years followup. *Clinical Orthopaedics & Related Research 2013;471-7:2296-302.*

16. Abdel MP, Pulido L, Severson EP, Hanssen AD. Stepwise surgical correction of instability in flexion after total knee replacement. *Bone & Joint Journal 2014;96-B-12:1644-8.*

17. Hamilton DF, Burnett R, Patton JT, Howie CR, Simpson AH. The identification and quantification of instability in a primary total knee replacement prior to revision. *Bone & Joint Journal 2014;96-B-10:1339-43.*

18. Kannan A, O'Connell RS, Kalore N, Curtin BM, Hull JR, Jiranek WA. Revision TKA for Flexion Instability Improves Patient Reported Outcomes. *J Arthroplasty 2014.*

19. Song IS, Sun DH, Chon JG, Jang SW, Sun DH. Results of revision surgery and causes of unstable total knee arthroplasty. *Clinics in Orthopedic Surgery 2014;6-2:165-72.*

20. Flierl MA, Bravman JT, Eckhoff DG. Successful LCL reconstruction and PCL repair for LCL tear and PCL avulsion following total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy 2014;22-11:2783-7.*

21. DePuy Synthes Institute. DePuy Synthes Joint Reconstruction Knee Revision Solutions X-Ray Case Book. DePuy International Ltd. and DePuy Orthopaedics, Inc. 2014.

22. Springer BD, Curtin BM. Chapter 13 Revision Total Knee Arthroplasty: Management of Ligamentous Instability. *Complex Primary and Revision Total Knee Arthroplasty: A Clinical Casebook.* Switzerland: Springer International Publishing 2015

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