Title: Preoperative Quadriceps Muscle Strength and Functional Ability Predict Performance-Based Outcomes 6 Months After Total Knee Arthroplasty: A Systematic Review

Running Title: Functionality Predictors After Knee Arthroplasty

TOC CATEGORY: Musculoskeletal

Article Type: Review

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KEYWORDS: Osteoarthritis, Knee Arthroplasty, Predictor, Stair Climbing, Walking Speed

ACCEPTED: May 23, 2018

SUBMITTED: December 2, 2017

Background. One-third of individuals report limitations in activities of daily living even 6 months after total knee arthroplasty (TKA). Moderate-quality evidence exists for several sociodemographic and clinical predictors of patient-reported outcome measures of perceived functionality. Objectively measured performance-based measures (PBMs) provide a less subjective approach to informing patient treatment after TKA; however, there is a dearth of information on predictors of functionally relevant PBMs.

Purpose. This systematic review synthesized the available research on preoperative predictors of PBMs after primary TKA for osteoarthritis.

Data Sources. In June 2016 and January 2017, Medline, Embase, and PsycINFO databases were searched.

Study Selection. Cohort studies exploring preoperative predictors of stair climbing, walking speed, and gait speed measured at least 6 months after primary TKA were included. Screening of abstracts and selection of full texts were undertaken by 2 independent reviewers.

Data Extraction. Information on study design, patient characteristics, analysis, and results was extracted using pilot-tested forms. Two independent reviewers assessed risk of bias using modified Quality in Prognostic Studies criteria.

Data Synthesis. Of the eligible 12 studies involving 6 prospective cohorts, 10 studies reported information on baseline predictors. Meta-analysis of predictors was not possible because of missing information on effect size or standard errors. Narrative synthesis of evidence of predictors was therefore performed.

Limitations. The quality of evidence was low because of the risk of bias and heterogeneity of included studies as well as nonreporting of

measures of effect.

Conclusions. Low-quality evidence exists for an association of preoperative functional ability and quadriceps muscle strength with functionality at 6 months after TKA. There is a need for improving the reporting of predictor analyses to enable evidence generation for clinical management.

Osteoarthritis of the knee is an age related degenerative condition leading to considerable disability.[1,2] Total knee arthroplasty (TKA) is a well-established procedure for end stage osteoarthritis[3] and has been shown to significantly improve pain, function, and quality of life.[4,5] Evidence from systematic reviews of observational studies of patients undergoing TKA have shown improvements in walking speed,[6] rates of return to work[7] or sports.[8] Since its inception in 1970, both the surgical procedure and the prosthesis have evolved over the years,[9] leading to early recovery, greater range of motion, and longer prosthesis survival. Consequently there has been an increase in the use of this procedure across developed and developing nations[10–12] with a demographic shift towards younger (less than 60 years) persons.[13]

From a patients' perspective, gain in function and relief from pain are the most important outcomes after TKA.[14] There is evidence to show that 10% to 30% of patients have suboptimal benefit in terms of relief from pain[15] and around 25% have limitations in activities of daily living.[16] This is also corroborated by objective measures like limitation in stair climbing, which can persist 2 years after TKA.[17] Such impairments and limitations contribute to dissatisfaction among patients.[18] Longitudinal studies with repeated measurements of walking ability have shown that while acute recovery occurs during the first 3 months of surgery, improvement continues to occur beyond this period, peaking at 6 months and plateauing thereafter.[19,20] Other studies[21–24] have shown that maximum benefit in other measures of recovery also follow a similar pattern.

Therefore, follow-up until at least 6 months will be required to gauge the extent of recovery and identify patients with suboptimal functional outcomes after TKA.

Functional recovery is measured using either subjective patient-reported outcome measures (PROMs)[25] or objective performance-based measures (PBMs).[26] Previous studies have shown PROMs fail to capture actual objectively measured change.[22,27,28] Use of PROMs alone has resulted in an overestimation of functional improvement, and a key reason for this discrepancy is confounding of perceived benefit by pain.[29] Hence, the current recommendation is to use both types of measurement tools to define extent of benefit after arthroplasty.[30,31] However, PROMs are not a substitute of PBMs or vice versa. Other advantages of PBMs over PROMs is the ease of interpretation across varying contexts, interpretable units and availability of minimally important change.[32] Despite, this the PROMs has dominated arthroplasty prognostic research, most likely because of its ease of use.

Several systematic reviews of cohort studies have identified predictors of suboptimal improvement in PROMs such as post-TKA persistent pain,[33,34] patient satisfaction,[35] and knee-specific quality of life.[34,36,37] However, the predictors of objective functional outcomes are comparatively less well understood. It is possible that the predictors of objective outcomes may differ from those of subjective outcomes because of poor agreement between them.[22,27,28,38] Hence, knowledge of predictors of suboptimal objective functional outcomes alongside the existing knowledge of predictors of PROMs will better inform the surgeon and physical therapist to identify individuals who may have persistent

functional impairment and to communicate this information to patients prior to TKA. Further, any modifiable preoperative predictor could also form the basis for preoperative interventions aiming to improve post-TKA outcomes. A previous systematic review[39] collated evidence on predictors of stair-climbing ability in post-TKA population and was inconclusive because of insufficient number of studies. This prior review also included cross-sectional studies which have limited value for identifying predictors. Moreover, the studies included in this prior review focused on a single outcome (stair climbing) only. Since this time, several newer cohort studies of varying follow-up periods have been published, which have reported on predictors of other standardized single activity PBMs such as walking speed and gait speed.

Therefore, we asked the following 2 research questions for this systematic review: What is the average change in PBMs from the preoperative state to at least 6 months after TKA? What are the preoperative predictors of objectively determined performance-based measures at 6 months after primary TKA for osteoarthritis?

[H1] Methods

[H2] Overall Approach

Search methods, eligibility criteria, methods for selection, and data extraction of eligible studies were prespecified in a protocol registered at PROSPERO 2016:CRD42016039872,[40] and we report this review as per requirement of the PRISMA statement.[41]

[H2] Data Sources and Searches

We searched MEDLINE (OVID interface, 1948 onwards), EMBASE (OVID interface, 1980 onwards), PsycINFO (from inception of the database in 1800) in June 2016 and updated the search in January 2017, using a combination of the search terms “Knee Arthroplasty”,

"Osteoarthritis", "Outcomes", and "Predictors". We restricted the search to human studies and to journal publications only. No study design or language restrictions were imposed in the search. The search strategy for MEDLINE is shown in the Appendix.

[H2] Study Inclusion Criteria

We included observational and experimental prospective cohorts, and retrospective cohort studies. Cross-sectional and case-control studies were not included.

Patients were undergoing primary unilateral or bilateral TKA for degenerative osteoarthritis. Studies including both knee and hip replacement surgery patients were excluded if data was not presented separately. We did not include studies focusing unicompartment knee arthroplasty or for those undergoing arthroplasty for knee injuries or rheumatoid arthritis.

[H3] Predictors.

Any patient-related predictor measured before undergoing TKA was included.

[H3] Outcomes.

Four objectively measured functional outcomes—stair-climbing (SC) ability, walking speed (WS), chair-rising test, and Timed "Up & Go" Test (TUG)—at a minimum follow-up period of 6 months were used. The prespecified definitions of the outcomes were as follows: WS—timed distance in meters (eg, 6-Minute Walk Test) or time taken to cover a fixed distance at self- or fast-paced walking; SC ability—total time in seconds needed to ascend and descend stairs (9 steps and 12 steps, respectively, with a height of 16–20 cm) with or without the use of a handrail or speed of ascending or descending stairs; TUG—total time in seconds needed to get up from a chair, walk up to 3 m, turn around, walk back,

and sit on the same chair; and chair-rising test—number of times a patient came to a full standing position from a chair (with a height of ~43 cm [17 in]) in 30 seconds without taking support from an arm of the chair or a walking aid.

[H3] Types of analysis.

We included studies that reported univariable or multivariable regression analysis irrespective of the phase of prognosis research.[42]

[H2] Selection of Studies

Two independent reviewers (N.D. and S.S.) performed nonmasked screening of title and abstract. Disagreements were resolved by discussion, and a third reviewer's opinion (R. Maddison) was sought only if agreement was not reached between N.D. and S.S. Full texts of potentially eligible articles were further screened for eligibility. An online systematic review data management system (COVIDENCE; www.covidence.org) was used for the screening and selection process. We did inverse searching of the reference lists of eligible articles and systematic reviews in this topic to identify further eligible studies.

[H2] Data Extraction and Quality Assessment

Two reviewers (N.D. and S.S.) independently extracted data from eligible full texts on patient characteristics, study design, sample size at baseline and follow-up visits, outcomes (mean and SD) along with their definitions, predictor information along with coefficients and 95% CI or standard error of estimate, and data related to quality assessment at the study level. When authors reported stepwise regression, change in R^2 was extracted for each predictor. If predictor analysis was provided for multiple time points then data were extracted for all time points that were equal to or more than 6 months.

The assessment of the risk of bias of individual studies was undertaken using the modified version of the Quality in Prognostic Studies criteria described by Hayden et al.[43] This approach uses information on selection of patients (convenience sample or consecutive/random patients), collection of predictor data (prospective or retrospective), selection criteria for predictors (statistical or clinical criteria or both), extent and method of handling missing data (above or below 5% of the sample size and whether a complete data set analysis was performed or whether robust imputation methods were used), overfitting (<10 participants per predictor for linear regression and <10 outcomes per predictor for logistic regression), testing for linearity of continuous predictors, and testing for model assumptions. Studies were categorized as high risk or low risk of bias on the basis of the criteria elaborated in eTable 1 (available at https://academic.oup.com/ptj). We planned to assess the quality of evidence of a predictor for a given outcome or related outcomes using principles of Grading of Recommendations Assessment, Development, and Evaluation system of rating quality of evidence.[44] The consistency of direction of effect, directness, risk of bias of included studies and imprecision around the effect estimate were assessed for each predictor that was included in at least 3 studies.

[H2] Data Synthesis and Analysis

For the first objective of this review, quantitative pooling of standardized mean differences (SMDs) between preoperative and postoperative PBMs was done with random-effects methods using Stata 14.2 (Stata Statistical Software: Release 14; StataCorp LP, College Station, Texas) whenever at least 2 studies with the same outcomes from unique cohorts reported preoperative and post-TKA sample size, mean, and SD or SE. If 2 studies from overlapping cohorts reported an outcome for the same time point, only the study with the largest sample size was included in this analysis.

Quantitative synthesis of effect of predictors was not possible because of inadequate reporting of statistical results (beta coefficients and SE or 95% CI), or variations in the way predictors were included in the prediction model across studies or availability of less than 3 unique cohorts per predictor. Therefore a narrative synthesis of the findings from the included studies structured around each predictor was undertaken in line with the guidance for narrative synthesis from the Centre for Reviews and Dissemination.[45] As an initial step to qualitative synthesis, we used a tabulation method for collating information on study characteristics; descriptive data for outcomes measured at various time points, along with the measure of variance; and predictor-wise results across studies for each of the outcomes, with information on type of analysis, adjusted or unadjusted, along with magnitude, direction of effect, and strength of association quantified by *P* value. The narrative synthesis is presented only for predictors that were evaluated in 3 or more unique cohorts. If 2 studies from same cohort reported a predictor for an outcome only the study with the largest sample size was included in this synthesis.

[H1] Results

[H2] Identification and Selection of Studies

Our search yielded 2412 articles (excluding duplicates) of which we reviewed 295 full texts in detail for eligibility. Twelve studies were included in this review, of which 4 were obtained from reverse search. Six[22,23,46–49] of these 12 studies were from a single cohort of a randomized controlled trial (RCT).[50] Hence, only reports from unique cohorts contributed to the qualitative synthesis of predictors and 2 of the longitudinal

studies[22,23] had performed only correlation analysis at each time point rather than a predictor analysis. The PRISMA flowchart (Fig. 1) shows the summary of the search and selection process and the reasons for the exclusion of full-text articles (eTab. 2).

[H2] Study Characteristics

We report the patient characteristics of each study in Table 1. Two unique cohorts[50,51] reported SC ability (n = 279 patients; mean age = 68.2 years; mean percent women = 47.5; mean body mass index [BMI] = 29.3 kg/m^2) and from these, 6 studies[46–51] reported various predictors for this outcome. Five unique cohorts [20,50–53] reported predictors for WS (n = 698 patients; mean age = 65.6 years; mean percent women = 53.7; mean BMI = 29.7 kg/m^2) and 2 cohorts[50,54] reported gait speed quantified by the TUG (n = 287 patients; mean age = 70.1 years; mean percent women = 68; mean BMI = 27.85 kg/m^2) and using these 2 cohort, 5 studies[46,47,49,50,54] reported predictors for gait speed. The maximum follow-up period after TKA was 24 months. No study reported predictors for chair-rising ability. None of the studies reported explicitly if their research was aimed at establishing etiological factors or was aimed at developing a prognostic model for poor functional outcomes after TKA.

[H2] Assessment of Risk of Bias

Of the 12 studies from 6 cohorts, 7 were classified as high risk of bias for method of selection of participants. The overlapping cohorts[22,23,46–49] did not clearly report how their sample was derived from the trial cohort.[50] Seven of 12 studies were classified as high risk for selection predictors as they used solely statistical criteria for retaining predictors in the model. Eight studies did not report to have assessed for testing the linearity assumption and test for model fit and hence were classified as high risk for each of these items. For the items on measurement of

predictors (n = 12 studies) and overfit of models (n = 11 studies) the risk of bias was low. For the item of missing data, 5 studies were considered as low risk of bias. The summary of risk of bias of each study across 7 items is presented in Table 2.

[H2] Outcome at 6 Months and Beyond

Nine[22,23,46–49,51,52,54] of the 12 studies reported at least 1 of the functional outcomes measured at baseline and at various time points after TKA. However, several of the eligible studies (eTab. 3) did not report measure of variance and hence could not be included in estimating the pooled SMD. Our attempts to contact authors to provide the information on SD or SE did not yield the missing information. Pooling was not possible for change in SC ability after TKA because of lack of more than 1 unique cohort reporting SCT using similar procedures. For WS, the pooled SMD was 0.66 (95% CI = 0.29 to 1.03) from 3 studies[47,51,52] (I^2 = 74.1%; *P* for heterogeneity = .021) (eFig. 1). The pooled SMD from 3 studies[47,52,54] for the TUG at 6 months was −0.73 (95% CI = −1.05 to −0.44) (I^2 = 68.2%; *P* = .043) (eFig. 2).

[H2] Predictors of Stair-Climbing Ability

Six studies[46–51] of 2 cohorts[50,51] reported predictors for SC ability(ie, sociodemographic characteristics age and sex), clinical characteristics (ie, BMI, comorbidity, preoperative functional ability, and impairment measures), knee or bodily pain, range of motion (ROM) (flexion and extension), and quadriceps muscle strength (ipsilateral and contralateral Of these, age, BMI, active flexion of knee, contralateral and ipsilateral quadriceps strength, and preoperative SC function predicted post-TKA SC ability in at least 1 study. None of the predictors were reported for more than 2 unique cohorts, and even in those, effect estimates and 95% CIs were not reported in most studies (Tab. 3).

Increasing age showed a statistically significant detrimental effect on SC ability in 1 study[49] and no effect in another.[51] Higher BMI was associated with poorer SC ability is 2 studies.[49,51] Preoperative knee flexion was a significant predictor in 1 study[50] and the direction of effect was not reported. Preoperative pain (knee or bodily pain) was not associated with post-TKA SC in 2 cohorts.[49–51]

[H2] Predictors of Walking Speed

Ten predictors were reported across 6 studies from 5 cohorts (Tab. 4).[20,50–53] Female sex, presence of comorbidity, higher ipsilateral quadriceps strength, preoperative WS, and shorter preoperative TUG time were statistically significantly associated with faster post-TKA WS in at least 1 study. Preoperative pain was reported in 3 cohorts[50,51,53] and it was not associated with WS. Higher preoperative WS was significantly associated with better post-TKA WS in 3 cohorts.[20,47,52]

[H2] Predictors of Timed "Up & Go" Test

Seven preoperative predictors (age, BMI, preoperative TUG, flexion and extension ROM, pain, and muscle strength), 4 early postoperative predictors (pain, flexion ROM, and ipsilateral and contralateral muscle strength) and 2 postoperative predictors (physical activity and change in sit-to-stand time) were explored in 5 studies[23,47,49,50,54] from 2 cohorts[50,54] (eTab. 4). The preoperative predictors (ie, increasing age, shorter preoperative TUG time, higher ipsilateral quadriceps muscle strength, and flexion ROM) were statistically associated with improved postoperative gait speed in at least 1 study. Shorter preoperative TUG time was significantly associated with better function in 2 cohorts.[49,54]

[H2] Consistency in Association of Predictors Across Outcomes and Quality of Evidence

Across outcomes preoperative functional status and ipsilateral quadriceps strength showed a positive association with postoperative function

(low-level evidence because of risk of bias of included studies and no measure of precision). Higher preoperative pain failed to show statistical significance in all studies, across outcomes. However, owing to serious risk of bias, heterogeneity in inclusion of predictors in the model, and lack of information on imprecision the level of evidence was low. Level of evidence for age and active flexion ROM was very low, because of inconsistency in results, serious risk of bias of included studies and lack of information on imprecision.

[H1] Discussion

[H2] Summary of Main Results

This systematic review included 5 prospective cohorts with a total of 701 patients undergoing primary TKA. There was a moderate to large improvement in functionality after 6 months compared to preoperative state for walking speed and gait speed. Ten studies from 5 cohorts reported preoperative predictors of objectively measured functional outcomes at least 6 months after TKA. Quantitative synthesis of predictors was not possible because of inadequate reporting of the included studies. Evidence from qualitative syntheses show that poor preoperative functional ability and poor preoperative ipsilateral quadriceps muscle strength are likely to have suboptimal objectively measured functional recovery at 6 months after TKA. Preoperative knee or bodily pain was not associated with poor objective functional outcomes. Association of age, sex, BMI, range of motion, and comorbidity with PBM was inconclusive. In general the overall quality of evidence was low to very low, mainly because of the poor methodological quality of the included studies.

[H2] Applicability of Evidence

Quadriceps muscle strength could be a promising modifiable preoperative predictor. On the basis of the proportion of variance (R^2) explained by this predictor on the outcomes, strength of evidence (*P* value), and consistency of association across studies and outcomes, we can conclude that higher ipsilateral quadriceps muscle strength was independently associated with better SC ability after TKA. However, the clinical meaningfulness of these findings is limited as the included studies did not report the magnitude of effect and the uncertainty around estimates. There are several prehabilitation (ie, preoperative rehabilitation) strategies for improving muscle strength during the waitlist period. A qualitative systematic review of prehabilitation physical therapist interventions aimed at improving preoperative quadriceps strength indicated lack of efficacy of such intervention strategies in improving post-TKA patient-reported subjective outcomes.[55] However, trials (sample size ranging from 22 to 120) evaluating effect of prehabilitation interventions on objectively measured functional outcomes at 3 months after TKA demonstrated significant benefits at 3 months in WS,[56–58] stair ascend and descend[57,58] and TUG.[59] The results of our systematic review and the findings from these RCTs suggest that prehabilitation interventions targeted at improving preoperative quadriceps strength may potentially improve objective outcomes after TKA. However, adequately sized RCTs with longer follow-up are needed to establish this link conclusively. Further, the independent role of contralateral quadriceps strength and other muscles like hip abductors on functional outcomes needs further evaluation in future studies.

Predictors of patient-reported functional outcomes, such as post-TKA pain, satisfaction, and perceived function, have been extensively researched. On the basis of previous studies, there is moderate-quality evidence on the role of preoperative pain in predicting persistent postoperative pain[33] and poor mental state[60] in predicting postoperative perceived functional recovery. In contrast, our review indicated that preoperative pain did not predict objective functional recovery. This discrepancy may relate to the poor agreement between perceived and objective outcomes.[22,27,28] It is plausible that other preoperative subjective measures (such as mental state and pain catastrophizing) may also similarly not correlate with objective functional recovery. Therefore, risk profiling of patients on the basis of preoperative pain and mental state may not be useful when measuring recovery objectively.

The pooled analysis of change scores after TKA from baseline showed a moderate to large effect at midterm for walking (SMD = 0.66; 95% CI = 0.29 to 1.03) and gait speed (−0.73; 95% CI = −1.05 to −0.44) expressed in terms of standardized mean difference (interpretation: small SMD = 0.2; medium SMD = 0.5; large SMD = 0.8). A previous systematic review[6] had reported short, mid and long term improvement in WS from 16 pre-TKA and post-TKA comparisons that included WS measured by various measurement methods. The 95% CI of the SMD between 6 and 12 months reported in this study[6] was 0.68 to 1. The earlier review[6] showed a large heterogeneity in WS between 0.5 and 5 months[6] because of varying recovery rates. Hence, studies aiming to evaluate predictors of functional measures should have a follow-up period of at least 6 months when functional recovery reaches its peak.

All studies included in this review were conducted in developed countries (United States, Canada, and Japan) indicating lack of representativeness for developing nations, where TKA is increasingly being performed.[61,62] There are limited published data on outcomes after

arthroplasty from developing countries. This is important because patients undergoing TKA in developing countries may differ in terms of preoperative activity levels, access to rehabilitation after surgery, and awareness about the recovery process. This is supported by evidence to suggest racial and ethnic disparities in arthroplasty outcomes within developed countries.[63] There is a need to establish registries and cohorts in developing countries to bridge this knowledge gap.

[H2] Strengths and Limitations of This Review

The key strength of our systematic review is its methodological rigor, since we followed the currently recommended guideline[45] that improves the objectivity of narrative synthesis. We rated the quality of evidence not only on the basis of the risk of bias of included studies but also on other elements—such as the consistency of results across studies, indirectness, and imprecision—as advocated by the Grading of Recommendations Assessment, Development, and Evaluation system of rating quality of evidence.[44]

The main limitation of this systematic review was the inability to perform a meta-analysis to quantify the predictors' effects. The key reason was that fewer cohorts were available for the synthesis. Six of the eligible studies[22,23,46–49] had derived their sample for predictor analyses from 1 randomized trial,[50] and there seemed to be considerable overlap in the study population. Hence, only the study with the largest sample size could be used per predictor per outcome. Missing information on the magnitude of the effect and confidence intervals was a greater concern than heterogeneity due to heterogeneity in outcome measurements. Multiple attempts to contact the original researchers did not yield the required information. The findings of this review are solely based on *P* values which on its own provides very limited information to clinicians as opposed to the effect estimate along with the confidence intervals.[64] Further, the measurement of predictors like muscle strength, ROM and

outcomes (SC, WS, and TUG) were quite similar across studies, but the predictors were variably included in the statistical models across studies (eg, as continuous or categorical variables). Preoperative pain intensity was measured using varying tools such as the Medical Outcomes Study 36-Item Health Survey Questionnaire Western Ontario and McMaster Universities Arthritis Index, Knee Outcomes Survey, and Oxford Knee Score. Hence, it is unclear whether this heterogeneity in measurement tools would have had any impact on its association with functional outcomes.

Finally, selectively reporting predictors that were only statistically significant could have biased the overall evidence. This review highlights the need for consistency and adherence in following reporting guidelines for cohort studies and RCTs. Clear identification of reports as primary or secondary analysis of the original cohort and any overlap in sample from previous published studies is crucial for unbiased evidence synthesis.

[H2] Implications for Clinical Practice

Patients with poor preoperative functionality and preoperative ipsilateral quadriceps strength may have suboptimal improvement in function. Severity of preoperative pain may not be mean poorer post-TKA functional ability. Further, predictors of objective functional outcomes need to be considered alongside of patient-reported outcomes for better clinical decision making and patient management.

[H2] Implications for Future Research

Despite the large body of research in the field of arthroplasty, generated primarily from developed nations, there is lack of high quality evidence regarding predictors of long term functional outcomes after TKA. This is primarily due to deficiencies in study methodology, incomplete reporting, and use of varied measurement tools leading to inability to pool evidence quantitatively. This review has identified specific gaps that

need to be addressed in future studies. We provide some suggestions outlined in Figure 2 to be considered at design stage and improvement in quality of reporting of predictor analyses[42] to enable evidence synthesis and in effective use of research findings in day to day practice. Establishing the role of other known predictors of PROMs like preoperative pain and mental state on objective functional recovery is required for risk profiling of patients who are likely to have poorer outcomes. There is a need for adequately powered RCTs to evaluate the efficacy of prehabilitation interventions that strengthen lower limb muscles on objective functional outcomes. Independent role of contralateral quadriceps and other muscle groups such as hamstrings and hip abductors on functional outcomes before and after TKA will guide future physical therapy rehabilitation regimens. Data is required from developing nations for better applicability of such research in patient management.

Author Contributions and Acknowledgments

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We acknowledge Ms Rachel West, Liaison Librarian at Deakin University, for assisting with the literature search.

Ethics Approval

This work was a systematic review of published studies; therefore, ethics approval was not required.

Funding

No funding was sought for this work. N. Devasenapathy is a PhD candidate at Deakin University, Melbourne, Victoria, Australia, and is supported by the Deakin India Research Initiative. This work is part of her PhD thesis.

Systematic Review Registration

This study was registered in PROSPERO (ref. no. PROSPERO2016:CRD42016039872).

Disclosure

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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Table 1.

Characteristics of Included Studies (n = 12)[a]

Study	Characteristics of Patients Undergoing TKA	Performance-Based Outcome(s)	Predictors Reported	Type of Analysis
Lamb and Frost,[51] 2003 (United Kingdom)	n = 79 Mean age = 71.2 (SD = 6.8) 49% women Mean BMI = 29.1 (SD = 3.81)	Fast-paced 5-m walking speed, 5-step ascent time	Age in years, sex, pain (OKS knee pain, 1–5), comorbidities, flexion ROM, BMI, total quadriceps power **(**Nottingham Leg Extensor Power Rig)	Multivariate repeated ANOVA
Mizner et al,[46,*b*] 2005 (United States)	n = 40 Mean age = 63 (SD = 8) 37% women Mean BMI = 29.4 (SD = 4.2)	TUG, SCT	Age in years, flexion ROM, bodily pain (SF-36 bodily pain, 0–100; 100 = no pain), quadriceps strength (electromechanical dynamometer)	Multivariable stepwise linear regression
Mizner et al,[23,*b*] 2005 (United States)	n = 40 Mean age = 64 (SD = 9) 45% women Mean BMI = 31.4 (SD = 3.7)	TUG, SCT	No baseline predictors reported	Only cross-sectional correlation analysis reported
Mizner et al,[22,*b*] 2011 (United States)	n = 100 Mean age = 65 (SD = 9) 48% women Mean BMI = 30.8 (SD = 4.5)	TUG, 6MW, SCT	No baseline predictors reported	Only cross-sectional correlation analysis reported
Kennedy et al, 2008[20] (Canada	44 women Median age = 60 (IQR = 64–71) Median BMI =29 (IQR = 32–34) 40men Median age = 61 (IQR = 67–74) Median BMI =27 (IQR = 29–32)	6MW	Preop walk speed stratified by sex	Nonlinear mixed-effects modeling with stepwise regression
Petterson et al,[50,*b*] 2009 (United States)	n = 200 Mean age = 65.2 (SD = 8.5) 46% women Mean BMI = 29.8 (SD = 4.9)	TUG, SCT, 6MW	Quadriceps strength (electromechanical dynamometer), extension ROM, pain (KOS pain	Multivariable hierarchical linear regression

			score, 0–6)	
Zeni and Snyder-Mackler,[48,b] 2010 (United States)	n = 105 Mean age = 65.8 (SD = 8.9) 45% women Mean BMI = 30.9 (SD = 5.2)	Use of handrail during stair ascent or descent	Age in years, preop handrail use, quadriceps index (electromechanical dynamometer)	Multivariable forward stepwise logistic regression
Zeni and Snyder-Mackler,[49,b] 2010 (United States)	n = 155 Mean age = 64.9 (SD = 8.7) 43% women Mean BMI = 30.2 (SD = 4.9)	TUG, SCT	Age in years, BMI, early postop SCT, TUG, ROM, pain (KOS pain score, 0–6), ipsilateral and contralateral quadriceps strength (electromechanical dynamometer)	Multivariable hierarchical linear regression
Stevens-Lapsley et al,[47,b] 2010 (United States)	n = 140 Mean age = 65.3 (SD = 9.2) 53.5% women Mean BMI = 30.8 (SD = 5.2)	TUG, SCT, 6MW	Preop function (TUG, SCT, 6MW), BMI	Multivariable hierarchical linear regression
Maxwell et al,[53] 2013 (United States)	n = 271 Mean age = 67 (SD = 7.5) 72.1% women Mean BMI = NR	Slow walking speed: (<1 m/s) in 20-m self-paced walk test	Contralateral limb pain quantified by WOMAC pain and categorized as 0, 1–4, 5–9, and 10–20	Multivariable logistic regression
Bade et al,[52] 2014 (United States)	n = 64 Mean age = 64.6 (SD = 8.5) 50.5% women Mean BMI = 30.6 (SD = 4.8)	6MW	Age in years, sex, preop TUG, preop ROM, acute TUG	Multivariable hierarchical linear regression
Taniguchi et al,[54] 2016 (Japan)	n = 87 Mean age = 72.1 (SD = 7) 90% women Mean BMI = 25.9 (SD = 4.1)	TUG	Physical activity at 6 mo after surgery, change in sit-to-stand time from baseline, preop TUG	Stepwise multivariable linear regression analysis

[a]ANOVA = analysis of variance; BMI = body mass index; IQR = interquartile range; KOS = Knee Outcomes Survey; OKS = Oxford Knee Score; NR = not reported; postop = after surgery; preop = before surgery; ROM = range of motion (active knee flexion and extension ROM measured in the supine position with a long-axis goniometer); SCT = stair-climbing test (time taken for ascent or descent of 12 steps); SF-36 = Medical Outcomes Study 36-Item Health Survey Questionnaire; TKA = total knee arthroplasty; TUG = Timed "Up & Go" Test (time to rise from a seated position in an armchair [seat height = 46 cm], walk for 3 min, turn around, and return to a seated position); WOMAC = Western Ontario and McMaster Universities Arthritis Index; 6MW = 6-Minute Walk Test (distance covered in meters in 6 minutes of self-paced walking).
[b]These studies had overlap of cohorts, and samples were derived from Petterson et al.[50]

Table 2.

Assessment of Risk of Bias (n = 12)[a]

Study	Year	Patient Sampling	Measurement of Predictors	Selection of Predictors	Missing Data	Linearity Assumption	Overfit	Model Assumptions
Lamb and Frost[51]	2003	Low	Low	High	High	Low	High	Low
Mizner et al[23]	2005	High	Low	High	Low	High	Low	High
Mizner et al[46]	2005	High	Low	Low	Low	Low	Low	Low
Mizner et al[22]	2011	High	Low	Low	High	Low	Low	Low
Kennedy et [20]	2008	Low	Low	Low	Low	High	Low	High
Petterson et al[50]	2009	Low	Low	Low	High	High	Low	High
Zeni and Snyder-Mackler[48]	2010	High	Low	High	High	High	Low	High
Zeni and Snyder-Mackler[49]	2010	High	Low	High	High	High	Low	High
Stevens-Lapsley et al[47]	2010	High	Low	High	High	High	Low	High
Maxwell et al[53]	2013	Low	Low	Low	Low	Low	Low	High
Bade et al[52]	2014	High	Low	High	Low	High	Low	High
Taniguchi et al[54]	2016	Low	Low	High	High	High	Low	Low

[a]High = high risk of bias; low = low risk of bias.

Table 3.

Predictors of Stair-Climbing Ability[a]

Predictors	No. of Studies	No. of Cohorts	Study	Sample Size	Magnitude of Effect	*P*	Covariates Adjusted[b]							
							Age	Sex	Comorbidity	BMI	Pain	Preop/ Postop SCT	ROM	Muscle Strength
Age in years (per unit increase)	4	2	Lamb and Frost,[51] 2003	79	NR	.388		•	•	•	•		•	• (TP)
			Mizner et al,[23] 2005[c]	40	Change in R^2, 0.019	.393								
			Zeni and Snyder-Mackler,[48] 2010[c]	105	OR = 1.089 (for use of handrail at 2 y)	.001						• (Pre)		•
			Zeni and Snyder-Mackler,[49] 2010[c]	155	Change in R^2, 0.051 at year 1	.01						• (Post)		
					Change in R^2, 0.036 at year 2	.006						• (Post)		
Sex	1	1	Lamb and Frost,[51] 2003	79	NR; unclear base category	.483	•		•	•	•		•	• (TP)
Comorbidity	1	1	Lamb and Frost,[51] 2003		NR	.462	•	•		•	•		•	• (TP)
BMI in kg/m^2 (per unit increase)	3	2	Lamb and Frost,[51] 2003		NR	.017	•	•	•		•		•	• (TP)
			Zeni and Snyder-Mackler,[49] 2010[c]		Change in R^2, 0.14 at year 1	.044	•					• (Pre)		
					Change in R^2, 0.14 at year 2	.078	•					• (Pre)		
			Stevens-Lapsley et al,[47] 2010[c]		Change in R^2, 0.0001	.698						• (Pre)		
Preop knee/bodily	3	2	Lamb and Frost,[51] 2003		NR (OKS knee pain, 1–5)	.393	•	•	•	•			•	• (TP)

Predictors	No. of Studies	No. of Cohorts	Study	Sample Size	Magnitude of Effect	*P*	Covariates Adjusted[b]							
							Age	Sex	Comorbidity	BMI	Pain	Preop/ Postop SCT	ROM	Muscle Strength
pain (per unit increase)			Mizner et al, 2005[46]		Change in R^2, 0.004 (SF-36 bodily pain, 0–100; 100 = no pain)	.7	•						•	
			Petterson et al,[50] 2009		Change in R^2, 0.014 (KOS pain score, 0–6)	.1							•	•
Early postop pain	1	1	Zeni and Snyder-Mackler,[49] 2010		Change in R^2, 0.004 at year 1	.251	•			•		• (Pre)		
					Change in R^2, 0.004 at year 2 (KOS pain score, 0–6)	.337	•			•		• (Pre)		
Preop knee active ROM (per unit increase)	3	2	Lamb and Frost,[51] 2003		NR (flexion)	.472	•	•	•	•	•			• (TP)
			Mizner et al, 2005[46]		Change in R^2, 0.044 (flexion)	.193	•							
			Petterson et al,[50] 2009		Change in R^2, 0.018 (flexion)	.007								•
			Petterson et al,[50] 2009		Change in R^2, 0.001 (extension)	.653					•		• (F)	•
Early postop active flexion ROM	1	1	Zeni and Synder-Mackler,[49] 2010		Change in R^2, 0.021 at year 1	.012	•			•	•	• (Pre)		
					Change in R^2, 0.012 at year 2	.113	•			•	•	• (Pre)		
Preop quadriceps muscle strength (per unit increase)	4	1	Lamb and Frost,[51] 2003		NR (total power of both quadriceps in watts)	.003	•	•	•	•	•		•	
			Mizner et al,[46] 2005		Change in R^2, 0.471, ipsilateral quadriceps	<.001	•				•		•	
			Petterson et al,[50] 2009		Change in R^2, 0.225, Ipsilateral quadriceps	<.001								
			Zeni and Snyder-Mackler,[48] 2010		Higher quadriceps index (ratio of power in limb that had surgery to power in limb that did not have surgery); less likelihood of handrail use	.024	•							•
			Zeni and Snyder-		Higher ipsilateral normalized quadriceps	.022	•					•		• (QI)

Predictors	No. of Studies	No. of Cohorts	Study	Sample Size	Magnitude of Effect	*P*	Covariates Adjusted[b]							
							Age	Sex	Comorbidity	BMI	Pain	Preop/ Postop SCT	ROM	Muscle Strength
			Mackler,[48] 2010		strength; less likelihood of handrail use									
Early postop quadriceps muscle strength	1	1	Zeni and Snyder-Mackler,[48] 2010		Change in R^2, 0.0 at year 1	.99	•			•	•	•	•	•
					Change in R^2, 0.03 at year 2	.422	•			•	•	•	•	•
					Unit increase in ipsilateral quadriceps strength									
			Zeni and Snyder-Mackler,[49] 2010		Change in R^2, 0.054 at year 1	.001	•			•	•	•	•	•
					Change in R^2, 0.064 at year 2	.001	•			•	•	•	•	•
					Unit increase in contralateral quadriceps strength									
Preop stair-climbing ability	2	1	Zeni and Snyder-Mackler,[48] 2010		Preop use of handrail associated with handrail use after surgery	.002	•					•		• (QI)
			Stevens-Lapsley et al,[47] 2010[c]		Change in R^2, 0.312	<.001				•				
Early postop stair-climbing ability	1	1	Zeni and Snyder-Mackler,[49] 2010		Change in R^2, 0.43 at year 1	.001								
					Change in R^2, 0.42 at year 2	.001								

[a]BMI = body mass index; F = flexion range of motion (ROM); KOS = Knee Outcomes Survey; NR = not reported; OKS = Oxford Knee Score; OR = odds ratio; post = acute postsurgery function; postop = after surgery; pre = baseline; preop = before surgery; QI = Quadriceps Index (ratio of quadriceps strength of ipsilateral limb to that of contralateral limb); R^2 = proportion of variance explained; SCT = stair-climbing test; SF-36 = Medical Outcomes Study 36-Item Health Survey Questionnaire; TP = total power of both quadriceps.

[b]Bullets indicate the factors adjusted for.

[c]These studies had an overlap of cohorts, and samples were derived from Petterson et al.[50]

Table 4.

Predictors of Walking Speed[a]

Predictors	No. of Studies	No. of Cohorts	Study	Magnitude	*P*	Covariates Adjusted[b]										
						Age	Sex	Race	Education	Mental State	Comorbidity	BMI	Pain	Preop/ Postop WS	Flexion/Extension	Muscle Strength
Age in years (per unit increase)	2	2	Bade et al,[52] 2014	MD, −1.3 m; SE, 0.98	.21		•							• (Pre)		
			Lamb and Frost,[51] 2003	NR	.847		•				•	•	•	• (Post)	•	• (TP)
Sex	2	2	Lamb and Frost,[51] 2003	NR; unclear base category	.266	•					•	•	•	• (Pre)	•	• (TP)
			Bade et al,[52] 2014	For men vs women: MD, 34.2 m; SE, 16.2	.04	•								• (Post)		
BMI (kg/m^2) unit increase	2	2	Lamb and Frost,[51] 2003	NR	.06	•	•				•		•		•	• (TP)
			Stevens-Lapsley et al,[47] 2010[c]	Change in R^2, 0.006, compared to null model	.247									• (Pre)		
Comorbidity (yes vs no)	1	1	Lamb and Frost,[51] 2003	NR	.02	•	•						•		•	• (TP)
Knee pain (unit increase in pain score)	3	2	Lamb and Frost,[51] 2003	NR (OKS pain score, 1–5)	.125	•	•				•	•			•	• (TP)

			Petterson et al,[50] 2009[c]	Change in R^2, 0.005 (KOS pain, 0–6)	.387										• (E)	
			Maxwell et al,[53] 2013	WOMAC pain in contralateral limb (RR [95% CI]): 1– 4 vs 0 (1.3 [0.5–2.9]); 5–9 vs 0 (1.3 [0.6–3.0]); 10+ vs 0 (1.9 [0.6–5.9])	>.05	•	•	•	•	•	•					
Quadriceps muscle strength	2	2	Lamb and Frost,[51] 2003	NR (total power in watts)	<.001	•	•				•	•	•		•	•
			Petterson et al,[50] 2009	Change in R^2, 0.352 (ipsilateral)	<.001											
Active knee flexion	2	2	Lamb and Frost,[51] 2003	NR	.497	•	•				•	•	•			• (TP)
			Petterson et al,[50] 2009[c]	Change in R^2, 0.003	.532								•		• (E)	
Active knee extension	1	1	Petterson et al,[50] 2009[c]	Change in R^2, 0.013	.16											•
Preop function	3	3	Bade et al,[52] 2014	For every 1% increase in preop TUG time, walk distance decreased by 2 m	<.001	•	•							• (Pre)		

			Kennedy et al,[20] 2008	MD in m: 0.6 (SE = 0.1) for women; 0.5 (SE = 0.1) for men	<.05 for women; <.05 for men											
			Stevens-Lapsley et al,[47] 2010[c]	Change in R^2, 0.545	<.001								•			
Early postop function	1	1	Bade et al,[52] 2014	For every 1% increase in acute TUG time, walk distance increased by 0.067 m	.65	•	•							• (Post)		

[a]BMI = body mass index; E = extension range of motion (ROM); KOS = Knee Outcomes Survey; MD = mean difference; NR = not reported; OKS = Oxford Knee Score; post = acute postsurgery function; postop = after surgery; pre = baseline; preop = before surgery; R^2 = proportion of variance explained; RR = relative risk; TP = total power of both quadriceps; TUG = Timed "Up & Go" Test; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; WS = walking speed.

[b]Bullets indicate the factors adjusted for.

[c]These studies had an overlap of cohorts, and samples were derived from Petterson et al.[50]

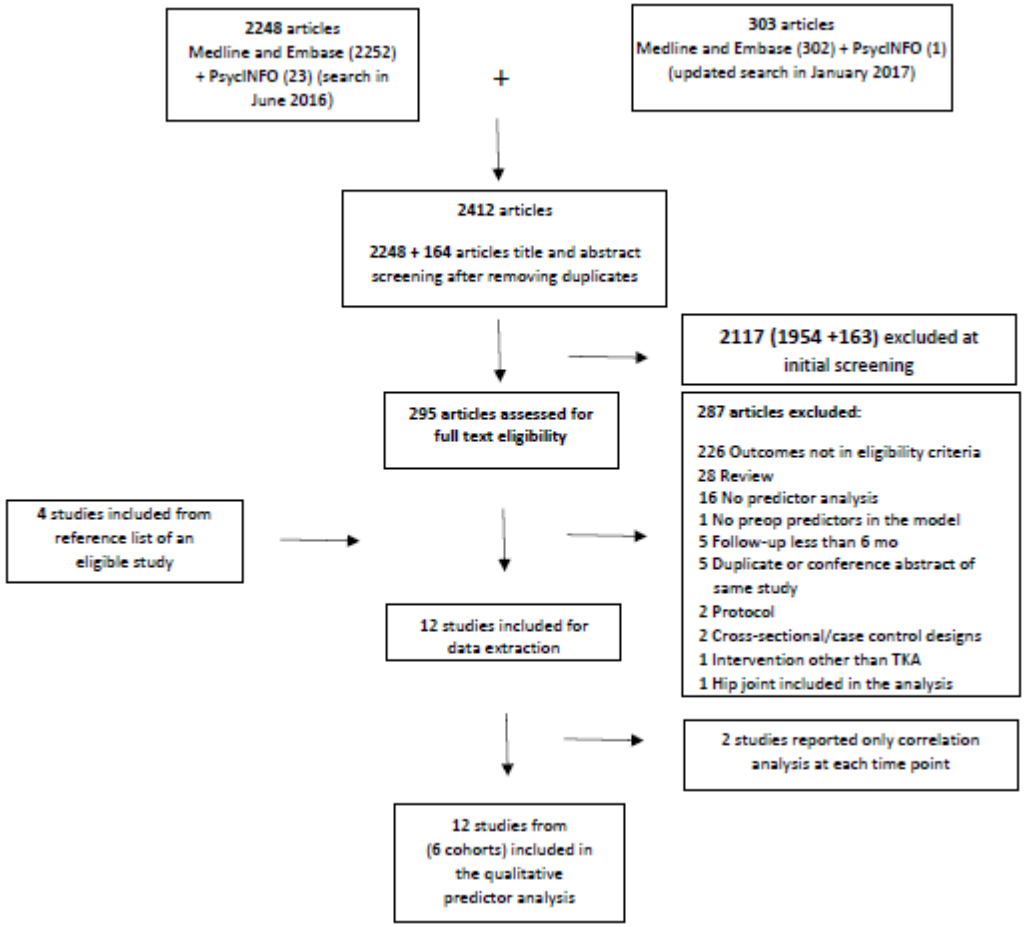

Figure 1.PRISMA flowchart. TKA = total knee arthroplasty.

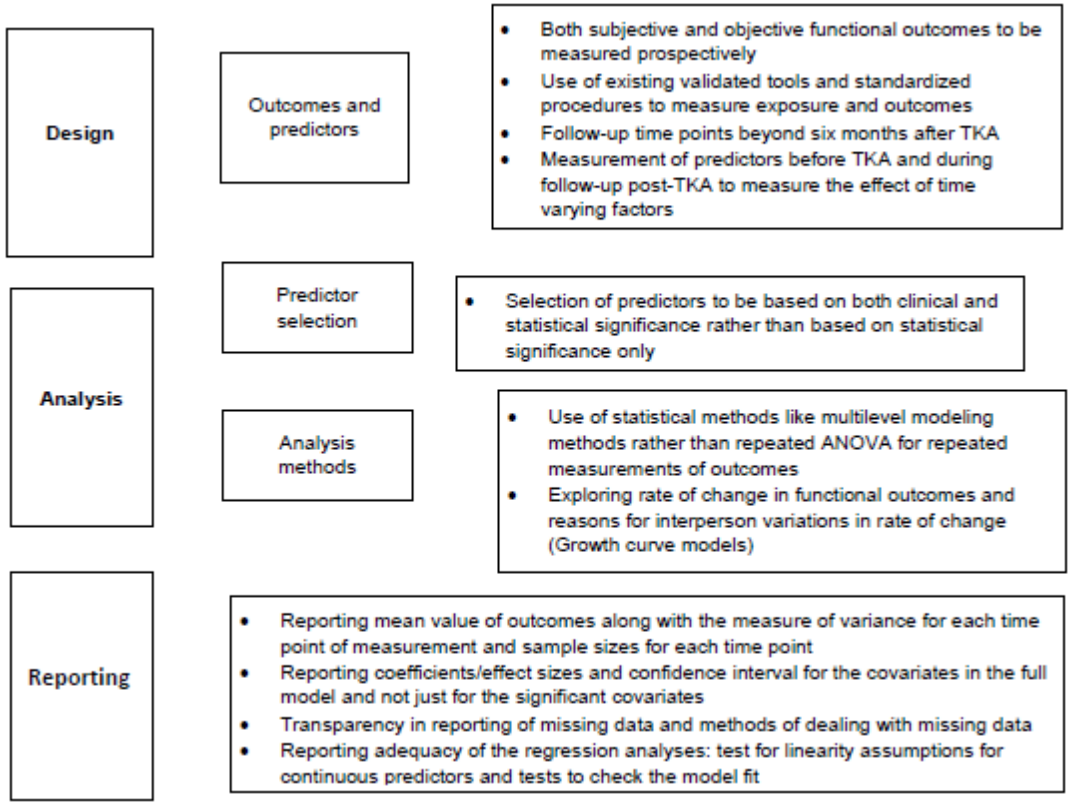

Figure 2. Suggestions for improving the design, analysis, and reporting of prospective studies that generate data for the prediction of functional outcomes after total knee arthroplasty (TKA). ANOVA = analysis of variance.

Appendix

Search Strategy

a. Dates of searches: June 1, 2016, and January 24, 2017
b. Databases: Medline, Embase, and PsycINFO
c. Search via: EBSCO host
d. Period of search: the initial search was from the conception of each database; the second searches were from May 2016 to February 2017 for PsycINFO and from January 2016 to January 2017 for Embase.
e. Search results: June for Embase (2252) and PsycINFO (23); January for Embase (302) and PsycINFO (1)
f. Limits: English and Human

1. “Knee Arthropla*”
2. TKA
3. TKR
4. “Knee Prosthesis”
5. 1 or 2 or 3 or 4
6. outcome*

7. stair*

8. climb*

9. walk*

10. “chair ris*”

11. “Up & Go”

12. TUG

13. SCT

14. CRT

15. activity

16. muscle*

17. exercis*

18. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17

19. risk*

20. predict*

21. predispo*

22. prognos*

23. caus*

24. determinant*

25. 19 or 20 or 21 or 22 or 23 or 24

26. osteoarthr*

27. arthrit*

28. 26 or 27

29. 5 and 18 and 25 and 28