Predictors of moderate–severe functional limitation after primary Total Knee Arthroplasty (TKA): 4701 TKAs at 2-years and 2935 TKAs at 5-years

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Objective: Investigate whether body mass index (BMI), comorbidity, gender and age predict patient-reported functional limitation 2- and 5-years after primary Total Knee Arthroplasty (TKA).

Methods: Overall moderate–severe activity limitation was defined as ≥2 activities (walking, stairs, rising from chair) with moderate–severe limitation. Complete dependence on walking aids or inability to walk was assessed (reference, no dependence). Multivariable logistic regression models were adjusted additionally for income, diagnosis, distance from medical center, American Society of Anesthesiologists (ASA) score and implant type.

Results: Overall moderate–severe activity limitation was reported by 20.7% at 2-years and 27.1% at 5-years. Significantly predictors of overall moderate–severe activity limitation 2-years post-TKA (odds ratio (95% confidence interval)) were: BMI 30–34.9, 1.5 (1.0, 2.0), 35–39.9, 1.8 (1.3, 2.7) and ≥40, 3.0 (2.0, 4.5) vs BMI <25; higher Deyo–Charlson index, 1.7 (1.4, 2.2) per 5-point increase; female gender, 2.0 (1.7, 2.5); age 71–80, 2.1 (1.5, 2.8) and age >80, 4.1 (2.7, 6.1) vs age <60. At 5-years post-TKA, significant predictors of overall moderate–severe activity limitation were: BMI 35–39.9, 2.1 (1.4, 3.3) and ≥40, 3.9 (2.3, 6.5); higher Deyo–Charlson index, 1.4 (1.0, 1.8); female gender, 2.2 (1.7, 2.7); age 71–80, 2.4 (1.7, 3.5) and age >80, 4.7 (2.8, 7.9). Complete dependence on walking aids was significantly higher at 2- and 5-years, respectively, in patients with: higher comorbidity, 2.3 (1.5, 3.3) and 2.1 (1.4, 3.2); female gender, 2.4 (1.5, 3.9) and 1.7 (1.1, 2.6); age 71–80, 1.4 (0.8, 2.6) and 1.5 (0.8, 2.8); and age >80, 3.2 (1.6, 6.7) and 5.1 (2.3, 11.0).

Conclusions: Modifiable (BMI, comorbidity) and non-modifiable predictors (age, gender) increased the risk of functional limitation and walking-aid dependence after primary TKA. Interventions targeting comorbidity and BMI pre-operatively may positively impact function post-TKA.

Introduction

The 2003 NIH consensus statement1 and a recent systematic review of Total Knee Arthroplasty (TKA) outcomes2 concluded that age, gender and body mass index (BMI) do not seem to significantly impact short-term outcomes following TKA. However, most studies that examined these relationships consisted of small sample sizes. Since poor outcomes after knee arthroplasty occur in <10% of patients, sample sizes of 500 patients or less provide only 50 patients with outcomes of interest, which may not allow adjustment for important covariates/confounders. Examination of associations of these modifiable (BMI and comorbidity) and unmodifiable (gender and age) factors with functional outcome after TKA should be done with well-designed studies of large cohorts that can control for important covariates. This is important, since: (1) TKA is a common procedure – half a million procedures were performed in 2005 in the US3; (2) The increase in proportion of older adults4 and those with obesity5 in the US will have a major impact on volume of knee arthroplasty, which is projected to grow by 673% to 3.48 million by 20303; and (3) Sub-optimal TKA outcomes can have a significant impact on patient satisfaction, medical costs and health care utilization. Knowing whether these
factors are associated with functional outcomes can inform patients, surgeons and policy makers alike.

Published literature in this area can be summed up being contradictory and consisting of small sized studies that did not adjust for important covariates and confounders. Higher BMI was significantly associated with worse function outcomes in some studies, while other studies found no association or association with stairs, but not walking distance. BMI is of special interest, since it is modifiable and is a significant risk factor for osteoarthritis and for undergoing TKA. Higher medical comorbidity was associated with poorer function in some studies, but not in others. Age was associated with function in one study, but not in others. Women were reported to have significantly worse function outcomes in this population. Possible reasons for variation include using different outcome measures (Knee Society Scale vs Western Ontario McMaster Arthritis Index (WOMAC) vs other measures), follow-up duration, sample sizes and controlling for different confounders. Due to contradictory results of previous results, more research is needed to examine if these factors are associated with functional outcomes.

We recently reported that female gender and younger age are significantly associated with more knee pain 2-years after primary TKA in a large cohort of patients. In this study, using the same prospectively collected function data during clinical follow-up, we aimed at assessing impact of patient factors on 2- and 5-year function outcomes after primary TKA. We hypothesized that: (1) higher pre-operative BMI and comorbidity will be independently associated with poorer function outcomes 2- and 5-years after primary TKA; (2) female gender and older age will be independently associated with worse function outcomes in this population.

Methods

Data sources and study cohort

The Mayo Clinic Total Joint registry, that has prospectively captured pain and function data from every patient who underwent a primary TKA at the Mayo Clinic since 1993, was used for this study. A validated knee questionnaire that included knee function questions is mailed to the patients, administered during the clinic visit or by telephone at 2- and 5-year time-points after the TKA. The questions are similar to those in the Knee Society Score, the most widely used outcome instrument used in studies of TKA follow-up. For this study, a patient was included in the analyses if they had undergone a primary TKA between 1993 and 2005 (to allow for the 2-year questionnaire response) and had responded to at least one of the questionnaires at 2- or 5-year follow-up. We obtained additional variables of interest such as zip code and comorbidity using other institutional research databases.

Predictor variables of interest

BMI, comorbidity, gender and age were the four variables of interest. BMI was categorized as <25, 25–29.9, 30–34.9, 35–39.9, ≥40; categories <18.5 and 18.5–24.9 were collapsed into single category due to small numbers in <18.5 category. Comorbidity was assessed using validated Deyo–Charlson index, and treated as a continuous variable. The Deyo–Charlson index is the most commonly used comorbidity measure consisting of a weighted scale of 17 comorbidities (including cardiac, pulmonary, renal, hepatic disease, diabetes, cancer, Human Immunodeficiency Virus (HIV) etc.), expressed as a summative score. Age was categorized as <60, 61–70, 71–80, >80, based on an a priori clinical decision by an experienced orthopedic surgeon (DL), similar to previous studies. The reference categories were, BMI <25, male gender and age ≤60, respectively. To test the robustness of our estimates, we also considered BMI and age as continuous variables in separate multivariable regression models.

Functional outcomes

The outcomes of interest were function outcomes in patients with primary TKA at 2- and 5-years. We assessed this by:

(a) limitations of three key activities of daily living, including, distance walked, using stairs and rising from chair classified as follows:

(1) Distance walked: ‘Unlimited’ or ‘>10 blocks’ = None; ‘5–10 blocks’ = Mild; ‘<5 blocks’ = Moderate; ‘Housebound’, ‘Indoors only’ or ‘Unable’ = Severe;

(2) Stairs: ‘Normal Up and Down’ = None; ‘Normal Up, Down with Rail’ = Mild; ‘Up and Down with Rail’ = Moderate; ‘Up with Rail, Down Unable’ OR ‘Unable’ = Severe; and

(3) Rise from Chair: ‘Able, no arms’ = None; ‘Able, with Arms’ = Mild; ‘Able with difficulty’ = Moderate; ‘Unable’ = Severe.

(b) overall limitation of activities: overall limitation was defined as moderate/severe, if a patient had ≥2 activities (walking, stairs, rising chair) with moderate or severe limitation (reference, ≤2 limitations).

(c) use of walking aids: the use of walking aids was categorized clinically as follows: ‘no aid’, ‘cane occasionally’ = no dependence; ‘cane full time’ = some dependence; ‘crutch’ ‘two canes’, ‘two crutches’, ‘walker’ or ‘unable to walk’ = complete dependence/unable.

We examined the association of predictors of interest with presence of moderate–severe limitation in overall activity (reference, ≤2 activities with limitation), walking, climbing stairs and rising from chair. For use of walking aids, the outcomes were some dependence (reference, no dependence) or complete dependence/unable (reference, no dependence). It is important to realize that medical comorbidity can impact these measures of function far more than TKA, which was one of the reasons to simultaneously adjust all models for comorbidity.

Covariates/confounders

The following variables were included in the multivariable regression analyses: (1) demographic: median annual household income (<$35K, <$35K–$45K or ≥$45K (reference category)) determined based on zip code and the median household income for geographical area using the census data for the respective year of survey; (2) American Society of Anesthesiologists (ASA) Physical Status score, a validated measure of peri- and post-operative outcomes, categorized as class I–II vs III–IV; (3) operative diagnosis: osteoarthritis, rheumatoid/inflammatory arthritis, or other (avascular necrosis, fracture etc.) for primary TKA; (4) distance from medical center (0–100 miles, >100–500 miles, >500 miles); (5) implant type: cemented or uncemented/hybrid; and (6) pre-operative limitation in walking, climbing stairs and rising from a chair.

Statistical analyses

Summary statistics (mean, standard deviation (SD) and percents) are presented for demographic and clinical characteristics of primary TKA cohorts at 2- and 5-years. The prevalence of moderate–severe overall functional limitation was compared between primary TKA at 2- and 5-years using chi-square tests. All univariate and multivariable analyses were performed with logistic regression using a generalized estimating equations (GEE)
approach to adjust the standard errors for the correlation between observations on the same subject due to replacement of both knees. The primary variables of interest (BMI, comorbidity, gender and age) were assessed for association with moderate–severe limitation in the three activities (walking, climbing, and rising from a chair) moderate–severe overall limitation (defined as having a moderate–severe limitation in at least two of the three activities).

Univariate and multivariable association of these same variables of interest with the outcome of use of aids (categorized as some dependence, complete dependence, and no dependence) were assessed using polychotomous logistic regression. Separate regression analyses were performed for primary TKA cohorts at 2- and 5-years. Each multivariable regression included BMI, comorbidity, gender, age, operative diagnosis, distance from medical center, income category, implant design (cemented vs uncemented/hybrid), pre-operative functional limitation and ASA score; odds ratios with 95% confidence intervals are presented. A \( P \leq 0.05 \) was considered significant. Detailed univariate and multivariable-adjusted associations are presented in a tabular form in Appendix 1 and 2 (supplementary material) for the interested readers.

Since the outcomes may have changed over a 12-year period, due to changes in prostheses, peri-operative management and rehabilitation regimens, we performed sensitivity analyses by adjusting the main models for the year of surgery. Responder bias was examined with logistic regression, assessing the associations of demographic and clinical characteristics with completion of a follow-up questionnaire at 2- and 5-years post-TKA.

Results

Cohort characteristics

The baseline demographic and clinical characteristics of the cohort are described in Table 1. 7139 primary TKA patients responded to the survey at 2-years and 4234 primary TKA patients at 5-years. The main analytic cohort consisted of patients who provided both pre- and 2-year data (\( n = 4701 \)) and pre- and 5-year data (\( n = 2935 \)). There were no clinically meaningful differences in characteristics of responders at follow-up (2- or 5-years) and those that had both pre-operative and follow-up data (Table 1). The cohorts had a mean age of 68 years and consisted of nearly equal proportions of men and women; osteoarthritis was the commonest diagnosis for primary TKAs. The majority of patients (>87%) were overweight or obese, i.e., had BMI > 25.

Survey responders and non-responders

Of the 11,294 primary TKAs, 10,957 were eligible for 2-year follow-up, i.e., they were alive at 2-years post-surgery. Of these, 7139 (65%) had completed a 2-year questionnaire, with 4701 (66%) of these having completed both pre-operative and 2-year questionnaires. 7404 were eligible for 5-year follow-up, with 4234 (57%) having completed 5-year questionnaires, with 2935 (69%) having both pre-operative and 5-year questionnaires.

Non-responders were slightly more likely to be younger, have higher ASA class, higher Charlson index, live more than 500 miles away from the medical center or have diagnoses other than osteoarthritis for primary TKA.

Prevalence of moderate–severe overall functional limitation

The prevalence of overall moderate–severe limitations in walking, climbing stairs, rising from a chair and overall functional limitation (≥2 activities) decreased significantly from pre-operative to the 2-year and 5-year follow-up post-primary TKA (Table II).
After multivariable adjustment, the significant predictors of overall moderate–severe activity limitation 2-years post-primary TKA included the following: BMI 30–34.9, 35–39.9, and ≥40 (reference, BMI < 25); higher Deyo–Charlson index; age 71–80 and age > 80 (reference, age ≤ 60); and female gender (Fig. 1).

Moderate–severe limitation in stair climbing was significantly higher in the same groups as described for the overall activity limitation. Moderate–severe limitation in walking was significantly higher in BMI ≥ 35, higher Deyo–Charlson index, age 71–80 and age > 80 and female gender. Moderate–severe limitation in stair climbing was significantly higher in the same groups as described for the overall activity limitation. None of the predictors of interest was significantly associated with moderate–severe limitation in rising from a chair (Fig. 1).

Sensitivity analyses that adjusted for the year of surgery for analyses of outcomes at 2-years showed that all the factors found to be significant in the main analyses for three key activities and overall activity were still significant.

After multivariable adjustment, the significant predictors of overall moderate–severe activity limitation 5-years post-primary TKA included the following: BMI 35–39.9, and ≥40 (reference, BMI < 25); higher Deyo–Charlson index; age 71–80 and age > 80 (reference, age ≤ 60); and female gender (Fig. 2).

Moderate–severe limitation in walking was significantly higher in the same groups as described for the overall activity limitation. Moderate–severe limitation in stair climbing was also significantly higher in same groups as for the overall activity limitation, except that Deyo–Charlson index was not significantly associated (Fig. 2). Moderate–severe limitation in rising from a chair was significantly higher in patients aged > 80 years (Fig. 2).

Sensitivity analyses adjusting for the year of surgery showed that all the predictors significant in the main analyses at 5-years were still significant in this new model with one exception – the association of age > 80 with stair climbing was no longer significant.

**Use of walking aids**

In a polychotomous regression model, BMI was not associated with higher odds of dependence on walking aids at 2- or 5-years (Table III). Higher comorbidity, as indicated by higher Deyo–Charlson index, was associated with significantly higher odds for some dependence and complete dependence on walking aids at 2-years, (OR, 1.6 and 2.3, respectively) and higher odds of complete dependence at 5-years. Female gender was associated with increased odds for complete dependence on walking-aids compared to men at 2- and 5-years (OR, 2.4 and 4). Age 61–70 was associated with higher odds of some dependence on walking aids at

![Fig. 1. 2-year outcomes: Each figure shows the odds ratio of moderate–severe limitation in each activity (walking, stairs, chair) and for overall limitation for each category of variable as compared to the respective reference category. Each logistic regression analysis for walking, stairs, chair and overall limitation was adjusted for age, gender, BMI, comorbidity, income, distance from medical center, ASA class, operative diagnosis and the type of implant fixation. The dotted line represents an odds ratio of 1. Point estimates of odds ratios are represented by the solid circles; the whiskers represent the upper and lower 95% confidence interval estimates. Variables are significantly associated with the outcome in instances where the 95% confidence interval for the odds ratio does not cross one. For example, 5-point increase in Charlson index, female gender, age 71–80 and > 80 and BMI, 30–34.9, 35–39.9 and ≥ 40 were associated with significantly increased odds of overall moderate–severe activity limitation.](image-url)
2-years, age 71–80 with higher odds of some dependence on walking aids at 2- and 5-years and age > 80 with higher odds of walking-aid dependence, both some and complete at both 2- and 5-years.

Discussion

Our study, that included the largest US cohort of primary TKA patients to-date, found that BMI, comorbidity, female gender and older age significantly impact functional outcomes at 2- and 5-years after primary TKA, even after adjustment for pre-operative function and several other patient and surgical risk factors. We noted that at both 2- and 5-years post-primary TKA, several patient-level factors were consistently associated with higher risk of moderate–severe limitation in walking, climbing stairs and overall activity (no significant associations noted for rising from chair). These included BMI > 40, higher Deyo–Charlson index, age > 70 and female gender. Sensitivity analyses that adjusted for the year of surgery did not change any of these associations significantly, confirming the robustness of our findings. Dependence on walking aids was also significantly higher in women, older patients and in those with higher comorbidity, as indicated by a higher Deyo–Charlson index. The observation that almost same factors predict moderate–severe activity limitation at 2-year and 5-year follow-up and walking-aids dependence is important and adds to the literature.

Strengths and limitations

Our study analyzed functional limitation in one of the largest US cohort of primary TKA patients, adjusted for multiple confounders (socio-demographic, clinical and implant) and provided robust estimates as evident from the similarity of 2- and 5-year odds ratios and sensitivity analyses. There are several limitations to our study. Residual confounding due to variables not measured in this study such as depression, involvement of other joints and quadriceps weakness is possible. These and other non-TKA conditions can impact the functional outcomes assessed in our study, since these

Table III
Multivariable-adjusted association of BMI, comorbidity, gender and age with dependence on walking aids

<table>
<thead>
<tr>
<th>BMI (Ref, &lt;25 kg/m²)</th>
<th>2-year primary TKA</th>
<th>5-year primary TKA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Some dependence</td>
<td>Complete dependence</td>
</tr>
<tr>
<td></td>
<td>(n = 161/3063) P-value</td>
<td>unable (n = 113/3063)</td>
</tr>
<tr>
<td>25–29.9</td>
<td>0.8 (0.5,1.1)</td>
<td>0.38</td>
</tr>
<tr>
<td>30–34.9</td>
<td>1.2 (0.7,2.0)</td>
<td>0.59</td>
</tr>
<tr>
<td>35–39.9</td>
<td>1.2 (0.6,2.2)</td>
<td>0.62</td>
</tr>
<tr>
<td>≥40</td>
<td>1.9 (0.9,3.8)</td>
<td>0.07</td>
</tr>
<tr>
<td>Deyo–Charlson index</td>
<td>1.6 (1.1,2.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>(5-point change)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female Gender (Ref, Male)</td>
<td>1.3 (0.9,1.9)</td>
<td>0.11</td>
</tr>
<tr>
<td>Age (Ref, ≤60 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>61–70</td>
<td>2.8 (1.3,5.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>71–80</td>
<td>4.3 (2.0,9.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>&gt;80</td>
<td>13.2 (5.7,30.3)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Significant odds ratios and p-values are in bold. *Multivariable model adjusted for: gender, age, Deyo–Charlson index, BMI, ASA score, distance from medical center, operative diagnosis, type of implant (cemented, uncemented, hybrid), income category and pre-operative overall limitations.
limitation are not unique/specific to TKA. Non-response bias, referral bias and single-center study limits the generalizability to other populations. The non-responders were more likely to have higher comorbidity which would bias our results towards null, but the younger age of non-responders would bias our results away from the null. Therefore the exact direction of bias is unclear. A 100% follow-up is desirable, but we doubt that a response rate greater than 65% (reported in this study) is practically possible for a 13-year cohort study that included every patient operated upon in a large practice. Our response rate is higher than the average 60% response rate reported for mailed surveys of this size. We adjusted for pre-operative functional limitation, since it is one of the most important predictor of post-operative function outcomes, that could not be included in multivariable models due to risk of further bias. We think that a prospective multi-center cohort is needed to avoid many study limitations. Such a study can also provide data on longer-term outcomes.

BMI and functional limitation

The positive association of BMI > 40 kg/m² with limitations in walking, stair climbing and overall activity is an important finding of this study (BMI 30–35 was associated with some limitations). We studied not only the limitation of three key activities, but also overall activity and use of walking aids. Major limitations of previous studies were small sample size and dichotomization of BMI with two exceptions – one small study examined >2 BMI categories and one study had <200 patients. Previous studies showed a positive association of higher BMI with worse outcomes or no association. Our study findings support the hypothesis that only very high BMI (>40, or in some cases 35–40) is a risk factor for poor functional outcomes after primary TKA. By providing estimates of functional limitation for all BMI categories, our study adds significantly to the literature.

Based on these findings, the surgeons can inform patients with BMI higher than 35 and 40 regarding their risk of sub-optimal functional outcomes. This will allow patients to have realistic expectations regarding their outcomes. Second, a weight reduction program before undergoing TKA may improve the outcomes in those with very high BMI, an important hypothesis that needs to be tested. These findings are important, since obesity is a modifiable known risk factor for TKA and its prevalence is increasing in the US.

Higher comorbidity and function

Higher comorbidity was associated with poorer function outcomes and walking-aids dependency at 2- and 5-years post-primary TKA. Our findings confirm previous similar findings in patients with primary TKA, but are in contrast to other studies. Findings that diabetes and hypertension are associated with higher post-arthroplasty complication rates indicates that at least some functional limitation associated with comorbidity may result from higher post-operative complication rates in patients with higher comorbidity load. Further studies are needed, to examine if optimizing comorbidity treatment prior to TKA can improve function outcomes.

Gender and age associations

Women had poorer function and higher dependence on walking aids at both 2- and 5-years post-primary TKA, even after adjustment for pre-operative functional limitation, demographics and comorbidity compared to men. Our study raises the awareness of the association of gender with functional outcomes. However, our study was not designed to address the debate as to whether use of gender-specific implants impacts functional outcomes in female patients. Our findings of higher functional limitation in patients older than 70 years (relative to <60) undergoing primary TKA are similar to significantly greater functional decline in the ability of adults >75 years in performing basic activities of daily living in a national sample. These age and gender associations add to our recent findings of associations of age and gender with moderate–severe pain 2- and 5-years post-TKA.

In conclusion, we found that higher BMI, comorbidity, older age and female gender were independently associated with functional outcomes 2- and 5-year after primary TKA. These factors are also significantly associated with dependence on walking aids. It is possible that strategies focused at reducing obesity and treating comorbid conditions more effectively prior to TKA may improve functional outcomes following TKA. Surgeons can risk-stratify patients based on these characteristics and better inform patients about expected outcomes, thus reducing the gap between patient expectations and outcomes.

Conflict of interest

One of the authors (DL) has received royalties/speaker fees from Zimmer, has been a paid consultant to Zimmer and has received institutional research funds from DePuy, Stryker and Zimmer. Each author certifies that his or her institution has approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research. J.A.S. has received speaker honoraria from Abbott; research and travel grants from Allergan, Takeda, Savient, Wyeth and Amgen; and consultant fees from Savient and URL pharmaceuticals.

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Supplementary material

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References


