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Cerebrovascular Disease Is Associated with Outcomes after Total Knee Arthroplasty: A U.S. Total Joint Registry Study

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Abstract

We assessed the association of cerebrovascular disease with patient-reported outcomes (PROs) of moderate-severe activity limitation and moderate-severe pain at 2- and 5-years after primary total knee arthroplasty (TKA) using multivariable-adjusted logistic regression. 7,139 primary and 4,234 revision TKAs were included. Compared to the patients without cerebrovascular disease, those with cerebrovascular disease had a higher odds ratio (OR) of moderate-severe limitation at 2-years and 5-years, 1.32 (95% confidence interval [CI]: 1.02, 1.72; P=0.04) and 1.83 (95% CI: 1.32, 2.55; P<0.001). No significant associations were noted with moderate-severe pain at 2-years or 5-years. In conclusion, we found that cerebrovascular disease is independently associated with pain and function outcomes after primary TKA. This should be taken into consideration when discussing expected outcomes of TKA with patients.

Keywords

Pain; Activity limitation; cerebrovascular disease; Total knee replacement; arthroplasty; joint replacement; outcomes; Patient-Reported Outcomes; Activities of Daily Living; ADLs; Function; functional limitation

Introduction

Total Knee Arthroplasty (TKA) is the commonest elective orthopedic procedure [1-3], performed mostly for patients with refractory chronic knee joint pain due to arthritis and other causes. TKA provides long-lasting improvements for 10-15 years or even longer. The longevity of the implant has led to a great amount of interest in identifying risk factors for undesirable outcomes. For example, studies have examined the predictors of early revision

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surgery and periprosthetic fractures after TKA [4-9]. This has led to a better understanding of these outcomes after TKA and improved longevity of implants.

Recent years have witnessed an increasing interest related to the patient-reported outcomes (PROs) such as pain, function as assessed by limitation in activities of daily living (ADLs), quality of life and patient satisfaction. This should not be surprising. While revision and fractures are very important events/complications in patients who have undergone TKA, one must not forget that the main reasons why patients undergo these elective procedures are refractory pain, functional impairment and poor quality of life. These outcomes improve dramatically after TKA [10]. Recently, outcomes research has identified that patient demographics, implant factors and comorbidities are associated with these important PROs after TKA [11-19]. A better understanding of predictors of PROs after TKA will not lead to a more informed patient, but also help to identify potentially modifiable factors that can lead to further improvement in these outcomes. Cardiovascular and cerebrovascular diseases are common among the elderly, who often undergo TKA [20]. The effect of cardiovascular disease on TKA outcomes has been recently assessed [21]. To our knowledge, there are no studies that have assessed the impact of cerebrovascular disease on TKA outcomes. Therefore, our study objective was to assess the association of cerebrovascular disease with pain and function outcomes after primary TKA. We hypothesized that cerebrovascular disease will be independently associated with higher odds of worse pain and function after primary TKA and these associations will be no longer significant after adjusting for preoperative pain and function.

Materials and Methods

Methods and results are described as recommended in the Strengthening of Reporting in Observational studies in Epidemiology (STROBE) statement [22]. We used prospectively collected data from the Mayo Clinic Total Joint Registry. Patients were included in this study if they had undergone primary TKA at the Mayo Clinic during 1993-2005 and completed the patient questionnaire at 2- or 5-years post-TKA. We wanted a large enough sample to study outcomes controlling for multiple important covariates. Therefore we included eligible patients from 1993 to 2005, for whom data were captured electronically in the joint registry.

The Mayo Clinic Total Joint Registry captures data for all patients undergoing TKA using a validated standardized questionnaire including questions assessing pain and function that has construct validity and reproducibility [23], with questions similar to KSS. The questionnaire was administered to patients during an in-person clinic visit, by mail or phone call by trained, dedicated registry staff, at 2- and 5-year time-points post-arthroplasty. Data on demographics (age, gender), body mass index (BMI), operative diagnosis, limitation in ADLs, pain severity and distance from the medical center were obtained from the Mayo Total Joint Registry, captured for every patient. American Society of Anesthesiologists (ASA) class was retrieved from Department of Anesthesiology database. ICD-9 codes for the Deyo-Charlson index were obtained from linked Mayo Clinic electronic databases. The Mayo Clinic Institutional Review Board approved the study.

Patients answered the following pain question at 2- and 5-years post-TKA: "Do you have pain in the knee in which the joint was replaced?" The responses were: no pain, mild (occasional), stairs only, walking and stairs (all combined into reference category); moderate (occasional), moderate (continuous) and severe categories - combined into outcome variable, moderate-severe pain, based on an *a priori* decision and as in previous studies [16, 24, 25]. This question is same as the pain question in the Knee Society Scale (KSS), a validated outcome instrument [26] that is most commonly used for patients with TKA.

Patient-reported limitations in three key ADLs, specific for knee function, i.e., walking, climbing stairs and rising from chair. The limitations were classified *a priori* as follows, as previously [15]: (1) distance walked: “unlimited” or “more than 10 blocks” = none; “5 to 10 blocks” = mild; “less than 5 blocks” = moderate; and “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; and “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; and “unable” = severe. Moderate-severe ADL limitation was defined as moderate or severe limitation in 2 ADLs, to allow an easier interpretation of the study findings [15].

Presence of cerebrovascular disease at the time of TKA surgery was the main predictor of interest. This was assessed based on the presence of any International Classification of Diseases-ninth revision (ICD-9) codes 430-438 for cerebrovascular disease preoperatively in patients’ medical records. ICD codes for cerebrovascular disease have been shown to have high validity [27-29]. Codes for hemiplegia or paraplegia were not included, since these are often considered in separate category due to their severity.

We adjusted the multivariable models for following covariates/potential confounders: (1) demographics: age, categorized as <60, >60-70, >70-80, >80; gender; and body mass index categorized as <25, overweight, 25-29.9, obese, 30-34.9, very obese, 35-39.9, or extremely obese, ≥40 as per WHO classification [30], as previously [25]; (2) American Society of Anesthesiology (ASA) Physical Status score, categorized as class I-II vs. III-IV [31], a validated measure of peri-operative mortality and immediate post-operative morbidity [31, 32]; (3) operative diagnosis: osteoarthritis, rheumatoid arthritis (RA)/inflammatory arthritis, or other (avascular necrosis, fracture etc.); (4) implant fixation: cemented or uncemented/hybrid; and (5) distance from medical center: 0-100 miles, >100-500 miles, >500 miles, calculated by using zip codes and country codes from the patients’ records at the time of surgery (if available) or at present. Confounders/covariates were chosen based on their known association with post-TKA outcomes, including demographics [24, 25], underlying diagnosis [7], implant fixation [33] and ASA score [34, 35]. Distance from the medical center was included, since Mayo Clinic is a tertiary referral center providing care to local as well as referred patients, who are likely to differ in complexity and thus, the risk for poorer outcome.

We anticipated some non-response at both 2- and 5-years for this prospective registry of all-comers, higher at 5- than 2-years. We minimized confounding bias by including factors previously known or suspected to be associated with use of pain and ADL limitation after THA, but recognize that residual confounding is a limitation of the study design.

Statistical Analyses

We performed univariate and multivariable logistic regressions using a generalized estimating equations (GEE) approach to adjust the standard errors for the correlation between observations on the same subject due to both knees having been replaced. We assessed the association of cerebrovascular disease with the odds of moderate-severe ADL limitation and moderate-severe pain at both 2- and 5-years post-primary TKA. The multivariable model included age, gender, BMI, ASA class, implant fixation, income category, distance from the medical center and Deyo-Charlson index. We reported odds ratios (ORs) with 95% confidence intervals (CIs). A p-value < 0.05 was considered statistically significant. Sensitivity analyses were planned for the ADL limitation outcome, by adjusting the main multivariable-adjusted model additionally for preoperative limitation in ADLs.

Results

The mean age of the 2-year cohort was 68 years, 56% were women, 8% were older than 80 years, 9% had BMI of 40 or higher, 42% had ASA class III or IV and mean Deyo-Charlson score was 1.2 (Table 1). Clinical and demographic characteristics of 5-year cohort were similar and are shown in Table 1.

Univariate association of cerebrovascular disease with outcomes

There was no significant association of cerebrovascular disease with moderate-severe pain 2- or 5-years, even though odds were higher than 1.0 for both (Table 2). At 2- and 5-years, patients with cerebrovascular disease had significantly higher odds of moderate-severe ADL limitation with OR of 1.79 and 2.50, respectively.

Multivariable-adjusted association of cerebrovascular disease with outcomes

At 2-years, a trend towards significance was noted between cerebrovascular disease with moderate-severe pain with OR of 1.41 ($p=0.06$), but not at 5-years (OR, 1.13; $p=0.61$; Table 3). At 2- and 5-years, presence of cerebrovascular disease was associated with higher odds of moderate-severe ADL limitation of 1.32 and 1.83 ($p=0.04$ and $p<0.001$), respectively (Table 3).

Results were similar, when the main multivariable model was additionally adjusted for preoperative ADL limitation. Cerebrovascular disease was associated with higher odds of moderate-severe ADL limitation with OR (95% CI) at 5-years, 1.89 (1.23, 2.90), ($p=0.003$). At 2-years, OR did not change much, 1.21 (0.87, 1.69) ($p=0.263$), but it was not statistically significant.

Discussion

In our study, we found that the presence of cerebrovascular disease was associated with higher odds of moderate-severe ADL limitation as 2- and 5-years after primary TKA. In contrast, it was not associated with higher odds of moderate-severe pain. These findings merit further discussion.

Our finding of association of cerebrovascular disease with higher odds of moderate-severe ADL limitation at both 2- and 5-years was confirmed in multivariable-adjusted analyses that were adjusted for several important known predictors of functional outcomes. We excluded hemiplegia and paraplegia (a separate diagnostic category). Functional decline is well known in the elderly and increases with age [36-39]. However, it is unlikely to explain the association we noted since both patients with and without cerebrovascular disease are aging and our multivariable analyses were adjusted for age. In addition, the adjustment for pre-operative ADL limitation led to minimal attenuation of the association, implying that the pre-existing ADL limitation contributed only to some degree to poorer ADL limitation in these patients, but did not explain it completely. Instead, the poorer ADL outcomes at 2- and 5-years after primary TKA are indicative of postoperative impact of cerebrovascular disease on ADL outcomes. Several hypotheses can explain these observations. A higher risk of stroke and acute myocardial infarction has been reported within the first few weeks in patients undergoing total hip or knee arthroplasty compared to matched populations not undergoing these procedures [40, 41], and this risk would be expected to be even higher in those with pre-existing cerebrovascular disease. These events can interfere with timely recovery and rehabilitation of patients with a recent TKA and thus impact ADL outcomes. It is also possible that medications used for the treatment of cerebrovascular disease and associated cardiovascular disease may impact the ADL outcomes, however, we weren't able to examine this due to lack of availability of medication use in our electronic databases.

Cerebrovascular disease was not associated with moderate-severe pain at 2- or 5-years. This finding is important since it indicates, that the effect of cerebrovascular disease on ADL function and pain are not synchronous. A similar finding of uncoupling of effect on body mass index on pain and function had been previously noted, namely that BMI negatively impacted function, but not pain after TKA [25, 42].

So what implications do these findings have for patients undergoing primary TKA? The findings from our study should be shared with patients with cerebrovascular disease undergoing primary TKA regarding their relative and absolute risk of poor function outcomes after primary TKA. They can be reassured of similar pain outcomes compared to patients without cerebrovascular disease. In addition, our findings should trigger future studies investigating the underlying mechanism of poor functional outcomes in patients with cerebrovascular disease undergoing primary TKA.

Although the study was not randomized, our study included prospectively collected data from an institutional total joint registry with dedicated, trained registry staff, included every patient who underwent primary TKA and responded to survey over a 12-year period, used multivariable-adjusted analyses and provided robust estimates, that should be strongly considered when interpreting study results. Our study has several limitations. Non-response biased our findings, and therefore the 5-year findings were more likely to be potentially biased. On the other hand, response rates in this 12-year study met/exceeded the average response rates of 61% for large surveys of this size [43]. Our study was from a large medical center and therefore it is unclear whether the results could be generalized to other settings. However, characteristics of our study cohort are similar to those reported from other settings in the published literature.

In conclusion, we found that presence of cerebrovascular disease is associated with poorer function, but not pain outcomes 2- and 5-years after primary TKA. These associations were independent of other important predictors of these patient-reported outcomes. Future studies should examine as to what aspect of cerebrovascular disease (disease, medications, complications) impacts TKA outcomes. Better insights into mechanism of this association might allow us to improve ADL outcomes in patients with cerebrovascular disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic and clinical characteristics

	Primary TKA	
	2-year (n=7,139)	5-year (n=4,234)
Mean Age ($\pm$ standard deviation)	68 $\pm$ 10	68 $\pm$ 10
Men/Women (%)	44%/56%	45%/55%
Age groups (%)		
60 yrs	18%	18%
>60-70 yrs	35%	37%
>70-80 yrs	38%	38%
>80 yrs	8%	7%
Body Mass index (%)		
<25 kg/m ²	13%	13%
25-29.9 kg/m ²	35%	36%
30-34.9 kg/m ²	29%	43%
35-39.9 kg/m ²	14%	7%
40 kg/m ²	9%	7%
American Society of Anesthesiologists (ASA) Class		
Class I-II	58%	58%
Class III-IV	42%	41%
Deyo-Charlson Index, mean ($\pm$ standard deviation)	1.2 $\pm$ 1.9	1.1 $\pm$ 1.9
Psychological Comorbidity (%)		
Anxiety	6%	5%
Depression	11%	8%

Table 2
Univariate association of cerebrovascular disease with post-primary TKA outcomes

		Moderate-severe Pain			Moderate-severe ADL limitation		
		Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
		2-years					
Cerebrovascular disease							
No	1.0 (ref)				1.0 (ref)		
Yes	1.27	0.90, 1.79	0.18		1.79	1.44, 2.23	<0.001
		5-years					
Cerebrovascular disease							
No	1.0 (ref)				1.0 (ref)		
Yes	1.19	0.77, 1.84	0.42		2.50	1.88, 3.32	<0.001

ADL, activities of daily living; CI, confidence interval

Table 3
Multivariable-adjusted* association of cerebrovascular disease with post-primary TKA outcomes

Moderate-severe Pain				Moderate-severe ADL limitation		
	OR	95% CI	p-value	OR	95% CI	p-value
2-years						
Cerebrovascular disease						
No	1.0 (ref)			1.0 (ref)		
Yes	1.41	0.98, 2.05	0.06	1.32	1.02, 1.72	0.04
5-years						
Cerebrovascular disease						
No	1.0 (ref)			1.0 (ref)		
Yes	1.13	0.70, 1.81	0.61	1.83	1.32, 2.55	<0.001

Adjusted for age, gender, BMI, ASA class, operative diagnosis, implant fixation, income category, distance from the medical center and Deyo-Charlson index ADL, activities of daily living; CI, confidence interval