Research Article

Outcomes After Total Knee Arthroplasty in Patients With Autism: A Retrospective Database Study

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ABSTRACT

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder associated with osteoarthritis for which total knee arthroplasty (TKA) may be considered. The safety and efficacy of TKA in patients with ASD had been poorly characterized.

Methods: Total knee arthroplasty patients were identified using the M157 PearlDiver database. Patients with autism spectrum disorder were matched 1:4 with control TKA patients based on age, sex, and Elixhauser Comorbidity Index (ECI). 90-day adverse events were compared by multivariable regression, controlling for age, sex, and ECI. 5-year rates of revision were compared using Kaplan-Meier survival analyses.

Results: Of 1,194,063 TKA patients, ASD was identified in 352 (0.02%). Patients with autism spectrum disorder were younger (60.0 vs. 65.8 years, $P < 0.001$) with higher ECIs (7.8 vs. 4.2, $P < 0.001$) than control patients. Patients with autism spectrum disorder had higher odds of aggregated adverse events driven by sepsis (odds ratio [OR] 3.11), pneumonia (OR 3.55), and urinary tract infection (OR 3.02) ($P < 0.0036$ for each). 5-year revision rates were not significantly different for the matched cohorts ($P = 0.8000$).

Conclusion: Total knee arthroplasty patients with ASD had elevated odds of several infectious adverse events and may warrant additional perioperative precautions. No notable differences were observed in most adverse outcomes investigated, nor in 5-year implant survival, suggesting that patients with ASD can safely be considered for TKA.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by repetitive behaviors and deficits in social interaction and communication.[1] In the United States, an estimated 2.2% of adults have ASD and the overall prevalence across age groups has been steadily increasing, from 1.1% in 2008 to 2.3% in 2018.[2,3] As the prevalence of autism has increased, the population of older adults with the condition has increased, leading to an increased amount of recent research attention.[4]

It is notable that patients with ASD are at risk of many comorbidities and premature mortality.[5–7] A cross-sectional study of Medicare patients in 2016 to 2017 found that older adult patients with ASD had higher odds of health conditions that included osteoarthritis.[8] While the specific reason for this greater risk is unknown, other studies have found that autistic traits were associated with a faster pace of aging and subsequently age-related conditions including osteoarthritis, osteoporosis, heart disease, and cancer.[9]

Total knee arthroplasty (TKA) is the definitive treatment of knee osteoarthritis refractory to other treatments.[10] One epidemiological study found that the volume of TKA procedures in the United States increased by 156% between 2000 and 2019 and is projected to have a continued annual growth rate of over 4% by year.[11] With the increasing prevalence of diagnoses of ASD and the increased risk of osteoarthritis with age, more and more of those affected by ASD are expected to present as candidates for TKA.

Given the risk of multiple comorbidities and premature mortality in patients with ASD, it is important to understand condition-specific risks of undergoing TKA. However, there is a lack of knowledge surrounding surgical outcomes in patients with ASD. Thus, using a large, national database, this study evaluated postoperative outcomes among a cohort of patients with and without ASD undergoing TKA for osteoarthritis with the aim of understanding the postoperative adverse event profile and implant survival associated with ASD.

Methods

Database and Cohort

A retrospective study was conducted with data using the M157 PearlDiver Mariner Patient Claims Database (PearlDiver Technologies), a large national, administrative database containing over 157 million patients, from January 1, 2010, to October 31, 2021. The use of this database has been well established in total joint arthroplasty research.[12–16] Because PearlDiver data are output in a deidentified/aggregated form, our institutional review board deemed studies using this database as exempt from review.

Adult patients undergoing primary TKA were identified based on Current Procedural Terminology code 27447. Exclusion criteria included age younger than 18 years; a lack of osteoarthritis diagnosis; a diagnosis of trauma, infection, or neoplasm within 90 days before surgery; and not being active in the database for at least 90 days after surgery.

Patients with ASD were identified with the International Classification of Diseases 9th and 10th revision (ICD-9 and ICD-10) codes ICD-9-D-29900 and ICD-10-D-F840 and matched with control patients 1:4 based on age, sex, and Elixhauser Comorbidity Index (ECI).[11]

Postoperative Outcomes

The incidence of adverse events within 90 days of surgery was then abstracted from the database using ICD coding. Severe adverse events were defined as the occurrence of one of the following: cardiac events (myocardial infarction and cardiac arrest), sepsis, pulmonary embolism, surgical site infection, and deep vein thrombosis. Minor adverse events were defined as the occurrence of one of the following: pneumonia, urinary tract infection (UTI), acute kidney injury, wound complications (hematoma and wound dehiscence), and transfusion. The occurrence of any adverse event was defined as the occurrence of a severe or minor adverse event.

The incidence of hospital readmissions within 90 days was also abstracted from the database. 5-year revisions were identified based on Current Procedural Terminology codes 27134, 27137, and 27138.

Data Analyses

Differences in patient characteristics among the matched and unmatched control and ASD cohorts were determined in the univariable analysis through the Student t-tests and chi-square tests where appropriate. These tests were repeated after matching.

Multivariable regressions, controlling for age, sex, and ECI, were conducted to calculate odds ratios (ORs) and 95% confidence intervals for each of the 90-day postoperative complications.

Kaplan-Meier survival analyses were conducted for 5-year revision rates. Cumulative incidence at the end of 5 years was compared using log-rank tests.

All statistical analyses were conducted using PearlDiver software. Figures and tables were created using Microsoft PowerPoint (Microsoft Corporation) or GraphPad Prism version 9 (GraphPad Software). Significance was defined with a baseline of $P < 0.05$, with a Bonferroni correction applied to each set of analyses.

Results

Study Population

A total of 1,194,063 patients undergoing TKA for osteoarthritis were identified, who met the inclusion

criteria. Of this population, ASD was noted in 352 (0.03%). The ASD cohort was, on average, younger (60.0 vs. 65.8 years, $P < 0.001$) and had a higher ECI (7.8 vs. 4.2, $P < 0.001$). No notable difference was observed in gender distribution.

Matching the ASD to control cohorts 1:4 eliminated these demographic differences. The number of patients in the final study cohort was 1708. The number of control patients in this matched population was 1,365, and the number of patients with ASD was 343. Patient characteristics for the matched and unmatched cohorts are summarized in Table 1.

90-Day Outcomes

Overall, 90-day any adverse events were noted for 17.4% of the control cohort and 27.4% of the ASD cohort ($P < 0.0001$) (Table 2). Hospital readmissions within 90 days were found for 5.8% and 6.4% of the populations, respectively (not statistically significantly different).

Multivariable logistic regression analyses are summarized in Table 2 and Figure 1. On application of the Bonferroni correction, where $P < 0.0036$ was deemed significant, patients with ASD were found to have significantly increased odds of sepsis (OR 3.11), pneumonia (OR 3.55), and UTI (OR 3.02) and increased odds of the composite groups of minor adverse events (OR 2.16) and all adverse events (1.86).

5-Year Revisions

At 5 years postoperatively, Kaplan-Meier survival analysis found that in the ASD cohort, the proportion of patients without revision TKA was 95.1% while this proportion in the matched control cohort was 95.5%. A log-rank test showed this not to be statistically significantly different ($P = 0.800$, Figure 2).

Discussion

With increasing incidence of TKA and an aging ASD population,[3,17] more patients with ASD will be considered for TKA. However, the complication profile of such patients relative to those without ASD has not previously been described in the literature.

Patients with ASD comprised a small proportion of the overall TKA cohort (0.03%). The unmatched ASD cohort was markedly younger and had a higher comorbidity burden than the control cohort. A recent cross-sectional study of Medicare patients found that osteoarthritis was more common in patients with ASD.[8] The higher comorbidity burden is consistent with previous literature showing greater multiorgan comorbidities in patients with ASD.[5–8]

Matched patients with ASD were at independently elevated odds of sepsis, pneumonia, and UTI relative to patients without ASD, also driving elevated overall odds of all or minor adverse events. There is a known association between ASD and immunological conditions, including allergic, inflammatory, and autoimmune conditions, and immune dysregulation including adverse reactions to benign factors such as common illness, vaccinations, and environmental challenges.[18,19] Furthermore, previous literature has shown that adult patients with ASD are more likely to be discharged to skilled nursing facilities after hospital encounters for trauma.[20] Given the high incidence of nosocomial infection in skilled nursing facilities,[21–23] discharge location could also be contributing to elevated odds of infectious adverse events in patients with ASD.

Of note, no differences were found for the noninfectious medical complications or other infectious medical complications, including surgical site infection. It is further noted that 5-year survival to revision was not markedly different among patients with versus without ASD.

Table 1. Descriptive Characteristics of Adult Total Knee Arthroplasty Patients With and Without Autism

| Factor or Variable | Nonmatched TKA Groups | | | Matched TKA Groups (4:1) | | |
	Nonautism	Autism	P	Nonautism	Autism	P
Total	1,193,711	352		1365	343	
Age (mean ± SD)	65.8 ± 8.7	60.0 ± 11.5	<0.001	60.6 ± 10.7	60.4 ± 10.79	0.804
Sex			0.176			1.000
Female	749,121 (62.8%)	204 (58.0%)		801 (58.7%)	201 (58.6%)	
Male	444,587 (37.2%)	148 (42.0%)		564 (41.3%)	142 (41.4%)	
ECI (mean ± SD)	4.3 ± 3.2	7.8 ± 4.1	<0.001	7.6 ± 3.9	7.6 ± 3.9	0.992

ECI, Elixhauser Comorbidity Index; SD, standard deviation; TKA, total knee arthroplasty
A 4:1 match controlling for age, sex, and ECI is shown.

Table 2. Univariable and Multivariable Comparisons of 90-Day Adverse Events After Total Knee Arthroplasty in Patients With and Without Autism

Factor or Variable	Univariable			Multivariable, Controlling for Age, Sex, and ECI	
	No Autism (n = 1365)	Autism (n = 343)	*P*	OR (95% CI) (n = 1708)	*P*
90-day outcomes					
All adverse events	237 (17.4%)	94 (27.4%)	<**0.0001**	1.86 (1.40-2.48)	<**0.0001**
Severe events	111 (8.1%)	41 (12.0%)	0.034	1.56 (1.06-2.29)	0.025
Cardiac events	11 (0.8%)	<11	1	3.97 (0.25-63.95)	0.331
Sepsis	19 (1.4%)	14 (4.1%)	**0.0026**	3.11 (1.53-6.34)	**0.002**
Pulmonary embolism	22 (1.6%)	<11	0.303	1.66 (0.75-3.64)	0.209
Surgical site infection	25 (1.8%)	<11	0.467	1.45 (0.67-3.13)	0.350
Deep vein thrombosis	44 (1.9%)	11 (3.2%)	1	1.00 (0.51-1.95)	0.992
Minor events	168 (12.3%)	77 (22.4%)	<**0.0001**	2.16 (1.58-2.95)	<**0.0001**
Pneumonia	19 (1.4%)	16 (4.7%)	**0.0003**	3.55 (1.79-7.02)	**0.0002**
Urinary tract infection	65 (4.8%)	44 (12.8%)	<**0.0001**	3.02 (2.01-4.54)	<**0.0001**
Acute kidney injury	52 (3.8%)	24 (7.0%)	0.0158	2.01 (1.19-3.40)	0.009
Wound complication	32 (2.3%)	11 (3.2%)	0.472	1.39 (0.69-2.81)	0.358
Transfusion	34 (2.5%)	<11	0.800	1.18 (0.57-2.41)	0.657
90-day readmissions	79 (5.8%)	22 (6.4%)	0.755	1.12 (0.68-1.83)	0.661

CI, confidence interval; ECI, Elixhauser Comorbidity Index; OR, odds ratio; TKA, total knee arthroplasty
Bonferroni correction applied: $P < 0.0036$ deemed significant and bolded.
Wound complication: hematoma and wound dehiscence.
Cardiac events: cardiac arrest and myocardial infarction.

Like all administrative database studies, this study is limited by the accuracy and completeness of administrative coding. Additional knee-specific measures were not able to be assessed. We were also not able to investigate discharge location to assess whether differences in recovery location affected rates of adverse events.

Figure 1
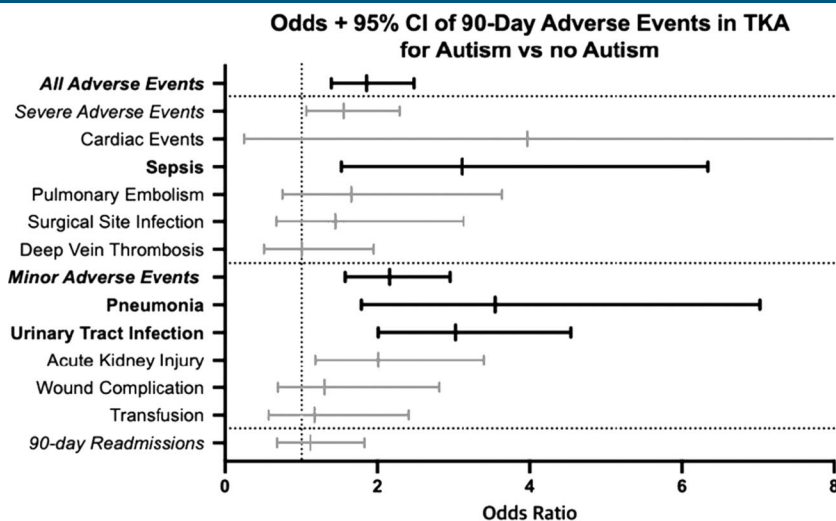
Forest plot of OR and 95% confidence interval for multivariable analysis of 90-day outcomes after TKA for patients with and without autism spectrum disorder. CI, confidence interval; OR, odds ratio; TKA, total knee arthroplasty

Figure 2

Impact of Autism on 5 Year Survival to Revision Following Total Knee Arthroplasty
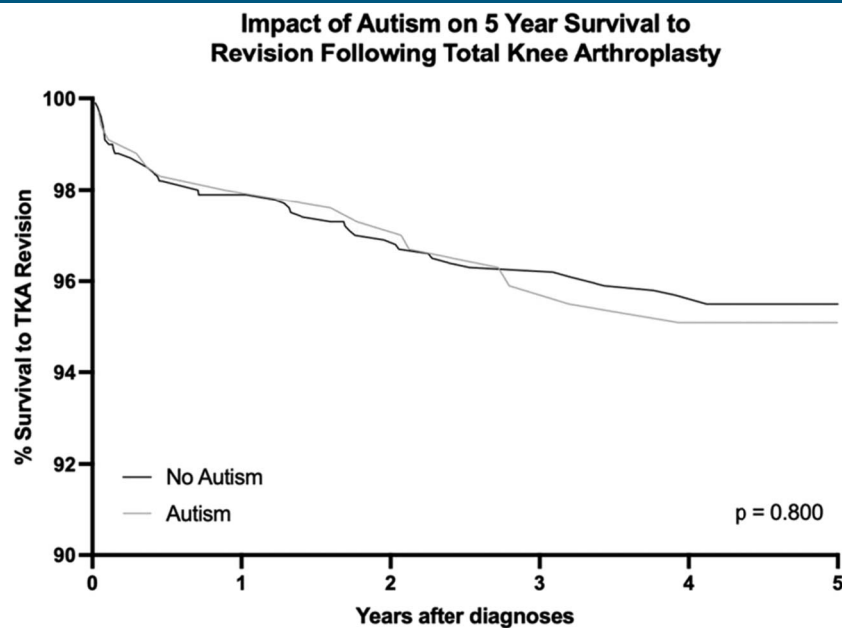
5-year Kaplan-Meier curve of implant survival until revision TKA for patients with and without autism spectrum disorder. TKA, total knee arthroplasty

Overall, these findings suggest that, with appropriate perioperative considerations and monitoring, patients with ASD may safely be considered for TKA. Several 90-day infectious complications should be noted, and additional attention/preventive measures may be warranted. These findings should be helpful for surgical planning and patient/family counseling.

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