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Total Joint Arthroplasty in Patients With Achondroplasia: Comparison of 90-Day Adverse Events and 5-Year Implant Survival

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ABSTRACT

Background: Achondroplasia is the most common skeletal dysplasia, and total joint arthroplasty of the hip and/or knee in this patient population may present unique challenges.
Methods: All patients undergoing primary total hip or total knee arthroplasty (THA or TKA) for osteoarthritis in the 2010-2019 PearlDiver Mariner administrative database with least 90 days of postoperative follow-up were identified. Those with achondroplasia were matched 1:10 to patients without achondroplasia based on age, sex, and medical comorbidities. Ninety-day adverse events were assessed and compared using multivariate logistic regression. Five-year implant survival was determined and compared with Kaplan-Meier implant survival curves. Significance was set at $P < .05$.
Results: For THA, 150 patients with achondroplasia were matched to 1484 patients without and had significantly higher 90 days odds of surgical site infection (odds ratio [OR] = 3.49, $P = .005$) and readmission (OR = 2.35, $P = .016$). For TKA, 285 patients with achondroplasia were matched to 2828 without and had higher odds of aggregated any adverse event (OR = 1.52, $P = .006$) and transfusion (OR = 2.31, $P < .001$). Rates of the other studied adverse events were not significant for either set of the analyses. At 5 years, implant survival for those with and without achondroplasia was not different for those undergoing THA ($P = .321$) or TKA ($P = .910$).
Conclusions: The present study represents the largest cohort of patients with achondroplasia undergoing total joint arthroplasty to date. Although several short-term adverse events had greater odds for those with achondroplasia, 5-year survival was not different for those with or without achondroplasia after THA or TKA, supporting confidence in longer term implant success.

Introduction

Achondroplasia is the most common hereditary skeletal dysplasia and is characterized by an autosomal dominant, activating mutation in the fibroblast grown factor receptor-3 gene [1]. The mutation causes abnormal endochondral ossification leading to rhizomelic dwarfism with shortened proximal limb bones, normal or enlarged trunk size, frontal bossing, and midface hypoplasia [2].

Patients with achondroplasia experience altered osseous growth and present with increased metaphyseal flaring and angulation, creating altered loading through their hip and knee joints [3,4]. Moreover, these findings can be associated with ligamentous laxity that further alters to joint mechanics [5,6]. Together,

IRB: Our institutional review board (IRB) granted an exemption for studies using the PearlDiver Mariner data set.

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these factors lead to altered gait kinematics of the hip and knee that can contribute to degenerative changes [7,8].

Patients with achondroplasia present a unique challenge to arthroplasty surgeons, especially regarding implant sizing, positioning, and soft-tissue balancing. To date, the literature examining total joint arthroplasty (TJA) in achondroplasia consists of limited case series and case reports with the revision rate after THA in patients with dwarfism reported as high as 30% [9-14]. The only large-scale study examining outcomes across musculoskeletal dysplasias (MSDs) used the National Inpatient Sample data set and found that, despite a lower comorbidity burden and significantly younger average age at the time of surgery, the rate of in-hospital surgical site infection and postoperative hemorrhage was significantly greater in patients with MSD [15]. However, as an inpatient database, postdischarge and intermediate-term outcomes after TJA could not be assessed in this referenced study.

Based on the aforementioned limitations in characterizing short- and intermediate-term outcomes for those with achondroplasia undergoing TJA, the present study used a large United States administrative insurance data set to conduct an age- and comorbidity-matched comparison of 90-day postoperative outcomes and 5-year implant survival for over 400 primary total hip arthroplasty (THA)/total knee arthroplasty (TKA) procedures in patients with achondroplasia compared to those without.

Material and methods

Data set/patient population

The present study used data from the Mariner PearlDiver administrative insurance data set from 2010 through 2019. Mariner is a large, anonymized for-pay insurance data set encompassing billing data for a total of over 121 million patient lives in the United States. Mariner includes all payor types and maintains continuity as patients switch between different insurance carriers, including those patients who move from private insurance to Medicare when they are age-eligible. Studies using data from the PearlDiver database were granted exemption from approval from the institution's review board, as the data are deidentified and exact numbers are not reported for patient cohorts numbering ten or less.

Patients undergoing THA and TKA for a primary indication of osteoarthritis with least 90 days of postoperative follow-up in the database were identified using current procedural terminology, International Classification of Diseases (ICD)-9, and ICD-10 procedural codes. Those with ICD-9 or ICD-10 diagnoses of achondroplasia were identified based on code 956.5 or Q77.4. Patients with concurrent contralateral THA or TKA were excluded. Separate analyses were performed for THA and TKA cohorts.

Patient variables assessed included age, sex, region of country (Midwest, Northeast, South, West), preoperative ICD-9 or ICD-10 diagnoses of diabetes, chronic kidney disease, obesity, coronary artery disease, tobacco use, and congestive heart failure, as well as Elixhauser Comorbidity Index. For both THA and TKA, those with achondroplasia were matched (1:10) to a comparison population of patients without achondroplasia based on these variables.

Postoperative complications and implant survival

Ninety-day incidence of ICD-9 or ICD-10 diagnostic codes for urinary tract infection, transfusion, pneumonia, pulmonary embolism, deep vein thrombosis, cardiac complication, acute kidney injury, surgical site infection, periprosthetic fracture, prosthetic dislocation (THA only), and all-cause hospital readmissions was identified and compared.

Five-year implant survival was also assessed and compared based on a current procedural terminology, ICD-9, or ICD-10 procedural code for revision of one or both components of THA or TKA including liner exchange.

Statistical analysis

Chi-squared tests were used to compare categorical variables while unpaired two-tailed Student's t-test was used to compare quantitative variables. Kaplan-Meier curves were generated for both THA and TKA to evaluate implant survival and were statistically compared using a log-rank test. Significance was set at $P < .05$ for all analyses.

Results

Study cohort

In total, 150 of 171 total patients with achondroplasia undergoing THA in the PearlDiver database were matched 1:10 to 1484 patients out of 632,900 total patients in the PearlDiver database without achondroplasia undergoing THA, and 285 patients out of 309 total patients with achondroplasia undergoing TKA were matched to 2828 out of 1,040,425 total patients without achondroplasia. After matching, no difference in demographics or comorbidity burden was noted between groups for either THA or TKA cohorts, and several differences in the prevalence of certain comorbidities, overall comorbidity, and mean age were evident between the matched and unmatched cohorts, although these differences were not analyzed statistically (Tables 1 and 2).

Postoperative complications — univariate

For THA, univariate analysis did not show patients with achondroplasia to experience an increase rate of aggregated 90-day adverse events ($P = .065$; Table 3). When complications were examined individually, patients with achondroplasia had a higher rate of infection within 90 days of THA ($P = .003$). All-cause readmission was also significantly higher in patients with achondroplasia (7.3% vs 3.2%, $P = .009$).

For TKA, univariate analysis again did not show patients with achondroplasia to experience an overall increase in the rate of aggregated 90-day adverse events ($P = .067$; Table 4). When complications were examined individually, patients with achondroplasia had a higher rate of transfusion within 90 days of TKA ($P = .012$), but, unlike THA, they had a similar rate of all-cause readmission within the 90-day postoperative period compared to matched controls ($P = .945$).

Postoperative complications — multivariate

For THA, a logistic regression model controlling for any remaining differences in baseline characteristics between groups as well as other adverse events showed patients with achondroplasia to have higher odds of 90-day surgical site infection after THA (odds ratio [OR] = 3.49, $P = .005$) and readmission (OR = 2.35, $P = .016$; Table 5). Of note, rates of periprosthetic fracture and prosthetic dislocation were not significantly different between cohorts.

For TKA, a logistic regression model controlling for any remaining differences in baseline characteristics between groups as well as other adverse events showed patients with achondroplasia to have higher odds of 90-day any adverse event (OR = 1.52, $P = .006$), a result likely driven by the significantly higher odds of postoperative blood product transfusion (OR = 2.31, $P = .001$;

Table 1
Demographic characteristics for matched control and achondroplasia patients undergoing THA.

Demographic characteristics	Unmatched control N = 632,900		Matched control[mc] N = 1484		Matched achondroplasia N = 150		Unmatched achondroplasia N = 171		Matched *P* value
Age (mean ± SD)	64.7 ± 9.8		57.4 ± 13.1		55.6 ± 13.7		54.7 ± 14.2		0.111
Female	359,481	56.8%	848	57.1%	86	57.3%	102	59.6%	0.964
Region									0.859
Midwest	180,306	28.5%	437	29.4%	49	32.7%	54	31.6%	
Northeast	141,844	22.4%	359	24.2%	32	21.3%	36	21.1%	
South	209,070	33.0%	474	31.9%	46	30.7%	53	31.0%	
West	101,065	16.0%	212	14.3%	23	15.3%	28	16.4%	
Asthma	78,045	12.3%	157	10.6%	16	10.7%	34	19.9%	1.000
CKD	123,582	19.5%	139	9.4%	14	9.3%	31	18.1%	1.000
CHF	72,629	11.5%	54	3.6%	a	a%	a	%	1.000
COPD	218,303	34.4%	465	31.3%	49	32.7%	67	39.2%	0.808
CAD	210,879	33.3%	311	21.0%	31	20.7%	38	22.2%	1.000
Diabetes	256,149	40.4%	454	30.6%	45	30.0%	56	32.7%	0.954
Hypertension	517,896	81.8%	1082	72.9%	114	76.0%	132	77.2%	0.473
Obesity	257,335	40.7%	741	49.9%	76	50.7%	90	52.6%	0.932
Tobacco use	172,244	27.2%	375	25.3%	38	25.3%	47	27.5%	1.000
ECI mean ± SD	4.0 ± 3.0		5.4 ± 3.1		5.4 ± 3.1		4.6 ± 3.0		1.000

CKD, chronic kidney disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; SD, standard deviation.
[mc]Patients were matched (1:10 achondroplasia:control) by age, gender, Elixhauser Comorbidity Index (ECI), diabetes, chronic kidney disease, and obesity, coronary artery disease, and congestive heart failure. Nonmatched cohorts are indicated in gray.
[a] Sample size ≤10.

Table 6). As with THA, most complications studied after TKA were not significantly different between groups.

Implant survival

For THA, when evaluating the incidence of revision procedures at up to 5 years after the index THA, the mean postoperative follow-up was 4.33 ± 1.96 years for those with achondroplasia and 5.04 ± 2.43 years for those without achondroplasia. At 5 years after THA, 95.0% of the achondroplasia cohort and 96.6% of the matched controls without achondroplasia remained unrevised. A Kaplan-Meier comparison of implant survival was not significantly different ($P = .321$) (Fig. 1).

For TKA, the mean postoperative follow-up duration was 6.01 ± 2.01 years for patients with achondroplasia and 6.04 ± 2.14 years for patients without achondroplasia. At 5 years after THA, 95.1% of the achondroplasia cohort and 95.5% of the matched controls without achondroplasia remained unrevised after TKA. A Kaplan-Meier comparison of implant survival was also not significantly different ($P = .910$) (Fig. 2).

Discussion

Achondroplasia is the most common skeletal dysplasia in the United States, and patients with this condition may become candidates for total hip or total knee replacement. The smaller anatomy, varus deformity, and ligamentous laxity associated with the condition collectively contribute to unique reconstruction challenges for THA and TKA procedures in this patient population. The present study used a large national insurance claims data set to examine short-term complications and intermediate-term implant survival after total joint replacement in patients with achondroplasia as

Table 2
Demographic characteristics for matched control and achondroplasia patients undergoing TKA.

Demographic characteristics	Unmatched control N = 1,040,425		Matched control[mc] N = 2828		Matched achondroplasia N = 285		Unmatched achondroplasia N = 309		Matched *P* value
Age (mean ± SD)	65.3 ± 8.4		61.3 ± 9.4		61.1 ± 9.4		59.8 ± 11.2		0.731
Female	660,502	63.5%	1971	69.7%	199	69.8%	213	68.9%	0.964
Region									0.376
Midwest	305,706	29.4%	874	30.9%	80	28.1%	89	28.8%	
Northeast	198,036	19.0%	583	20.6%	52	18.2%	60	19.4%	
South	378,049	36.3%	968	34.2%	105	36.8%	108	35.0%	
West	157,251	15.1%	403	14.2%	48	16.8%	52	16.8%	
Asthma	149,614	14.4%	396	14.0%	42	14.7%	59	19.1%	0.802
CKD	233,402	22.4%	473	16.7%	47	16.5%	58	18.8%	0.996
CHF	139,105	13.4%	289	10.2%	30	10.5%	35	11.3%	0.952
COPD	395,038	38.0%	1071	37.9%	119	41.8%	137	44.3%	0.222
CAD	383,643	36.9%	934	33.0%	94	33.0%	107	34.6%	1.000
Diabetes	518,758	49.9%	1354	47.9%	136	47.7%	147	47.6%	1.000
Hypertension	916,401	88.1%	2448	86.6%	243	85.3%	261	84.5%	0.603
Obesity	529,860	50.9%	1551	54.8%	156	54.7%	174	56.3%	1.000
Tobacco use	263,435	25.3%	805	28.5%	81	28.4%	94	30.4%	1.000
ECI mean ± SD	4.0 ± 2.8		6.9 ± 3.7		6.9 ± 3.7		4.2 ± 3.0		0.930

[mc]Patients were matched (1:10 achondroplasia:control) by age, gender, Elixhauser Comorbidity Index (ECI), diabetes, chronic kidney disease, and obesity, coronary artery disease, and congestive heart failure.
CKD, chronic kidney disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; SD, standard deviation.

Table 3
Univariate comparison of complications within 90 days after THA for matched cohorts.

Complication	Matched control N = 1484		Achondroplasia, N = 150		Matched *P* value
Any adverse event	171	11.5%	25	16.7%	0.065
Urinary tract infection	48	3.2%	a	a%	0.354
Transfusion	42	2.8%	a	a%	0.209
Pneumonia	21	1.4%	a	a%	0.448
Cardiac complication	a	a%	a	a%	0.147
Thromboembolic event[b]	22	1.5%	a	a%	0.885
Acute kidney injury	17	1.1%	a	a%	0.364
Surgical site infection	**21**	**1.4%**	**a**	**a%**	**0.003**
Wound dehiscence	19	1.3%	a	a%	0.956
Periprosthetic fracture	17	1.1%	a	a%	0.364
Prosthetic dislocation	27	1.8%	a	a%	0.300
Readmission	**47**	**3.2%**	**11**	**7.3%**	**0.009**

PE, pulmonary embolism.
Bold rows indicate statistical significance.
[a] Sample size ≤10.
[b] Thromboembolic event includes cerebrovascular accident, deep vein thrombosis, and PE.

compared to patients without achondroplasia matched by age, sex, and comorbidities.

For THA, patients with achondroplasia were found to have a three plus higher odds of 90-day postoperative infection (OR = 3.49). Increased infection risk has been noted for patients with achondroplasia undergoing a variety of orthopedic and neurosurgical procedures [16,17]. In TJA specifically, a recent study by Patel et al. examining over one thousand patients with MSDs found in-hospital postoperative surgical site infections occurred at four times the rate of patients without MSD [15]. This increased infection might be contributed by longer and more complex procedures, possibly in the setting of prior limb procedures [18-21]. However, the large study by Patel et al. encompassed all MSDs, only queried in-hospital complications, and did not use a matched comparison cohort, all of which have been addressed in the present study's methodology [15].

For TKA, patients with achondroplasia were found to have a greater than two-fold increased odds of transfusion (OR = 2.31). This finding is consistent with observations by Patel et al. who found patients with achondroplasia undergoing TJA had over twice the odds of perioperative bleeding issues, although Patel et al. was unable to distinguish which TJA (THA or TKA) was the driver of this association [15]. There are several possible explanations for this finding. Smaller body habitus for those with achondroplasia can result in lower average circulating blood volume [22] and greater need for transfusion. In addition, a larger degree of initial deformity on average in patients with achondroplasia may lead to more difficult, complex, and ultimately prolonged surgery and increase in blood loss [23].

The postoperative complications observed after THA and TKA, when compared to one other, are somewhat counterintuitive. TKA in several national joint registries is associated with, on average, higher postoperative infection rates than THA, yet THA carried significantly higher odds of infection while TKA did not [24]. Similarly, it remains unclear why transfusion was significantly higher in the TKA group and not in the THA group despite historically greater blood loss during THA than during TKA [25]. Interestingly, the present study did not observe increased rates of implant failure at up to 5 years after surgery. Previous literature has suggested that bony healing could be impaired in MSDs, leading to higher rates of loosening or periprosthetic fracture [26]. Moreover, previous case reports observed that soft-tissue laxity might necessitate greater soft-tissue release or larger bony resection intraoperatively, thus increasing the risk of instability and implant failure [23,27]. Moreover, the increased laxity may result in prosthetic dislocation of the hip or instability in cruciate-retaining, unconstrained TKAs. Another factor that may raise concern for increased wear-related complications in a previous study of patients with small stature, [28] although not in achondroplasia specifically, is the smaller sizing of components. Head size may be limited by the smaller native hip anatomy in achondroplasia, and smaller head sizes result in decreased contact area as well as increased risk of impingement and dislocation [29,30].

Table 4
Univariate comparison of complications within 90 days after TKA for matched cohorts.

Complication	Matched control, N = 2828		Achondroplasia, N = 285		*P* value
Any adverse event	465	16.4%	59	20.7%	0.067
Urinary tract infection	135	4.8%	14	4.9%	0.917
Transfusion	**89**	**3.1%**	**17**	**6.0%**	**0.012**
Pneumonia	24	0.8%	a	a%	0.344
Cardiac complication	20	0.7%	a	a%	0.484
Thromboembolic event[b]	58	2.1%	a	a%	0.951
Acute kidney injury	49	1.7%	a	a%	0.682
Surgical site infection	46	1.6%	a	a%	0.548
Wound dehiscence	31	1.1%	a	a%	0.946
Periprosthetic fracture	0	0.0%	0	0.0%	1.000
Manipulation under anesthesia	108	3.8%	14	4.9%	0.365
Readmission	156	5.5%	16	5.6%	0.945

Bold row indicates statistical significance.
[a] Sample size ≤10.
[b] Thromboembolic event includes stroke, deep vein thrombosis, and pulmonary embolism.

Table 5
Multivariate odds of complications within 90 days after THA for matched cohorts.

Complication	Matched achondroplasia vs matched controls		*P* value
	OR	95% CI	
Any adverse event	1.51	0.93-2.36	.083
Urinary tract infection	1.25	0.47-2.77	.615
Transfusion	1.63	0.66-3.52	.245
Pneumonia	0.98	0.15-3.46	.978
Thromboembolic event	0.42	0.02-2.07	.405
Cardiac complication	6.35	0.68-48.15	.072
Acute kidney injury	1.17	0.18-4.33	.836
Surgical site infection	**3.49**	**1.34-8.08**	**.005**
Wound dehiscence	1.91	0.55-5.14	.242
Periprosthetic fracture	1.68	0.39-5.19	.415
Prosthetic dislocation	0.35	0.02-1.69	.308
Readmission	**2.35**	**1.12-5.47**	**.016**

CI, confidence interval; ECI, Elixhauser Comorbidity Index.
Multivariate controlled for age, gender, region, ECI, and all comorbidities listed in Table 1.
Bold rows indicate statistical significance.

Strengths of this study include a large number of patients with achondroplasia undergoing TJA over an 8-year period, the duration of mid-term follow-up for implant survival, and the inclusion of a matched comparison cohort without achondroplasia. Limitations include a reliance on insurance billing data, the accuracy of which is susceptible to coding errors, inaccuracies, or upcoding. In addition, we were unable to assess radiologic features of the joints including degree of varus or valgus deformity or spinopelvic parameters, type of surgical implant used (cemented vs noncemented, constrained vs unconstrained), or the surgical approach used.

In conclusion, TJA in patients with achondroplasia is associated with higher odds of infection and transfusion in the immediate postoperative period. However, despite the unique reconstruction challenges during TJA presented by bony anatomy, joint deformity, and ligamentous laxity in this patient population, surgeons should have a high degree of confidence in the durability of both THA and TKA at up to 5 years when compared to matched controls.

Conflicts of interest

G.G.P. received royalties from, is in the speakers' bureau of, and is a paid consultant for DJO Global and is a board member for American Association of Hip and Knee Surgeons. J.N.G. is a paid consultant for TIDI products, is in the editorial or governing board of North American Spine Society, and is a board member of Lumbar Spine Research Society. L.E.R. is a paid consultant for DePuy Synthes and Thompson Surgical Instruments, has stock or stock options in 3D Surgical Inc, receives royalties from SLACK Inc and Johns Hopkins University press, is in the editorial or governing board of *Journal of Arthroplasty*, *Arthroplasty Today*, and Reconstructive Review, and is a board member of the American Academy of Orthopaedic Surgeons and the American Association of Hip and Knee Surgeons/American Board of Orthopaedic Surgery.

Table 6
Multivariate odds of complications within 90 days after TKA in achondroplasia vs matched controls.

Complication	Achondroplasia vs matched controls		*P* value
	OR	95% CI	
Any adverse event	**1.52**	**1.12-2.04**	**.006**
Urinary tract infection	1.28	0.73-2.11	.246
Transfusion	**2.31**	**1.35-3.77**	**.001**
Pneumonia	2.14	0.71-5.29	.130
Thromboembolic event	1.04	0.39-2.25	.936
Cardiac complication	1.09	0.17-3.86	.908
Acute kidney injury	0.83	0.25-2.08	.722
Surgical site infection	1.94	0.87-3.86	.076
Wound dehiscence	1.95	0.73-4.44	.139
Manipulation under anesthesia	1.42	0.77-2.43	.230
Readmission	1.02	0.58-1.69	.933

CI, confidence interval; ECI, Elixhauser Comorbidity Index.
Multivariate controlled for age, gender, region, ECI, and all comorbidities listed in Table 2.
Bold rows indicate statistical significance.

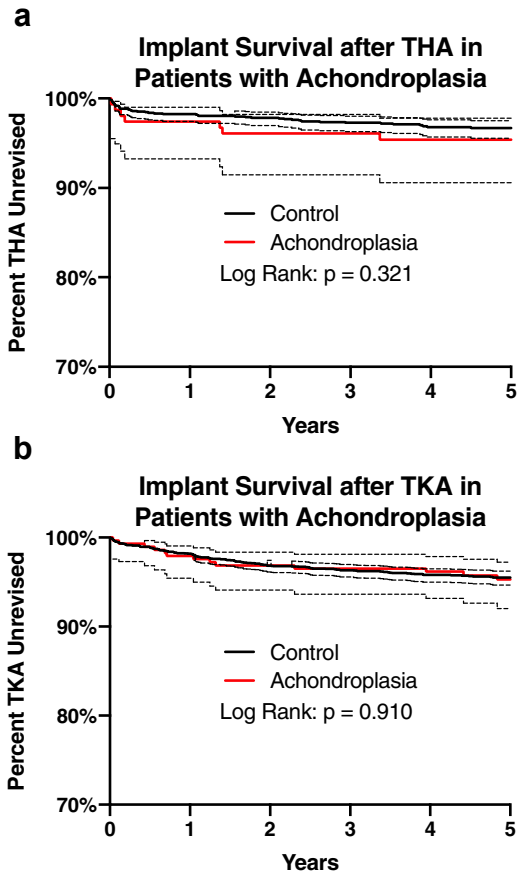

Figure 1. (a) Implant survival with single or dual component revision of total hip arthroplasty, including liner exchange, defined as the failure event for patients with achondroplasia and matched controls at up to 5 years. (b) Implant survival with single or dual component revision of a total knee arthroplasty defined as the failure event for patients with achondroplasia and matched controls at up to 5 years.

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