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Original article

Patients with musculoskeletal dysplasia undergoing total joint arthroplasty are at increased risk of surgical site Infection

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ABSTRACT

Introduction: Musculoskeletal dysplasias (MSD) are inherited conditions of abnormal cartilage and bone development and remodeling which include, amongst others, multiple epiphyseal dysplasia (MED), spondyloepiphyseal dysplasia (SED), achondroplasia, and hypochondroplasia. The aim of this study was to compare patient characteristics and in-hospital complications between MSD and non-MSD patients undergoing total joint arthroplasty (TJA).
Hypothesis: MSD patients undergoing TJA are at increased risk of in-hospital post-operative complications and mortality compared to non-MSD patients.
Materials and methods: The Nationwide Inpatient Sample (NIS) from the years 2005 to 2014 was used for this retrospective cohort study. International Classification of Diseases, Clinical Modifications (ICD-9-CM) procedure codes identified primary total knee arthroplasty (TKA) and total hip arthroplasty (THA) procedures and were used to separate MSD and non-MSD patients. Patients with trauma or malignancy as primary diagnoses, non-elective procedures, revision procedures, and concurrent bilateral surgeries were excluded. Patients were compared using linear regression or multivariate logistic regression analysis to control for confounders. All statistical analyses were performed taking into account the NIS sampling scheme and associated sampling weights.
Results: A total of 1,255 patients comprised the MSD group and 8,027,181 patients the non-MSD group. MSD patients were younger than non-MSD patients (50.9 vs. 65.8 years, $p < 0.001$), with less comorbidities including: hypertension (40.2% vs. 64.5%, $p < 0.001$), coronary artery disease (5.5% vs. 12.9%, $p < 0.001$), diabetes mellitus (9.4% vs. 19.0%, $p < 0.001$), and hypothyroidism (7.8% vs. 14.7%, $p = 0.002$). MSD patients had higher risks of surgical site infection (0.8% vs. 0.2%; OR, 4.16; 95% CI, 1.03–16.75; $p = 0.044$), and perioperative hemorrhage (2.1% vs. 0.7%; OR, 3.20; 95% CI, 1.32–7.76; $p = 0.010$).
Discussion: MSD patients undergoing TJA were younger with less co-morbidity compared to non-MSD patients, and had no significant difference in overall perioperative medical and surgical complication rates. However, they are at increased risk for surgical site infection and perioperative hemorrhage possibly due to the anatomical complexity encountered.
Level of Evidence: III, Retrospective Cohort.

1. Introduction

Musculoskeletal dysplasias (MSD) are inherited conditions of abnormal cartilage and bone development and remodeling [1] which include, amongst others, multiple epiphyseal dysplasia (MED), spondyloepiphyseal dysplasia (SED), achondroplasia, and hypochondroplasia [2]. Although each individual type of skeletal dysplasia is relatively rare, collectively the incidence of these disorders is 2.3 to 7.6 in 10,000 births [3]. Congenital osteochondrodysplsias lead to arrested epiphyseal development and delayed endochondral ossification, resulting in a lack of support for the cartilaginous surface and consequently, obliteration of the loaded joint [4]. Incongruent and restricted joints lead to severe pain and contracture, as well as ligament laxity around joint [4–6]. Ultimately, this results in premature osteoarthritis [7,8].

Previous studies have shown total hip and knee arthroplasty (THA/TKA) to be reasonable treatment options for MSD patients,

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resulting in substantial pain relief and marked improvement in quality of life with a relatively low rate of complications [7–17]. A few studies have reported good results for mid- to long-term implant survival following total joint arthroplasty (TJA) [8,9,11]. However, these studies are mostly small case series or case reports with specific focus on implant survival and mechanical complications.

To our knowledge, there are no large studies evaluating patient characteristics and in-hospital complications in patients with MSD undergoing TJA. The main impetus of our study was to compare patient characteristics and in-hospital complications between MSD and non-MSD patients undergoing TJA using a national inpatient database. We hypothesized that MSD patients undergoing TJA are at increased risk of in-hospital post-operative complications and mortality compared to non-MSD patients. We focused on the most common MSD diagnoses affecting the hip and knee joint including MED, SED, achondroplasia and hypochondroplasia.

2. Materials and methods

2.1. Data source

The Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP-NIS) was used as the data source for this study. The HCUP-NIS, developed by the Agency for Healthcare and Research and Quality (AHRQ), is the largest all-payer inpatient care database in the United States [18]. This database randomly samples 20-percent of inpatient admissions from the State Inpatient Databases from 1000 hospitals annually since 1988. As the largest source of inpatient hospitalization data, it is a valuable tool to study uncommon diseases and/or uncommon procedures in special patient populations. The NIS uses the International Classification of Diseases, ninth edition, Clinical Modifications (ICD-9-CM) to classify diagnosis and procedures [19]. It contains de-identified clinical and non-clinical patient information. Therefore, this study was considered exempt from review by the local Institutional Board Review (IRB).

2.2. Sample Selection

The HCUP-NIS database from 2005 to 2014 was queried using ICD-9 CM procedure codes for primary TKA (81.54) and THA (81.51). Patients were divided into those with MSD (ICD-9 CM 756.56 and 756.4) and those without. Exclusion criteria included those with trauma or malignancy as primary diagnoses, non-elective procedures, revision procedures, and concurrent bilateral surgeries were excluded to reduce selection bias.

2.3. Variables of Interest

Three groups of variables were compared between the MSD and non-MSD patients:

- Demographic and comorbidities;
- Hospital characteristics; and
- Postoperative complications.

Demographic variables included sex, race/ethnicity, age, primary diagnosis, household income based on zip code analysis and insurance status. Comorbidities included diabetes mellitus, hypertension, congestive heart failure, peripheral vascular diseases, deficiency anemia, chronic obstructive pulmonary disease, obesity, hypothyroidism, liver disease, renal failure and depression. Overall comorbidities of both groups were evaluated utilizing the Charlson comorbidity index. Hospital characteristics group included hospital teaching status and hospital geographic region. Postoperative complications were categorized as medical, including acute myocardial infarction, acute renal failure, pneumonia, pulmonary embolism, and surgical, including perioperative hemorrhage/hematoma, acute postoperative anemia, and surgical site infection.

2.4. Statistical analysis

The MSD and non-MSD patients were compared using the Rao-Scott chi-square test and t-tests, for categorical and continuous variables, respectively. Multivariate logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) comparing MSD and non-MSD patients, looking at specific outcomes of interest: medical or surgical complications, in-hospital mortality, and total complications. We controlled for potential confounders including: age, gender, payer status, hospital characteristics, primary diagnosis, procedure type and comorbidities. Linear regression was used to calculate differences in LOS, hospital days prior to surgery, and mean total hospital charges. All of the statistical analyses were performed taking into account the NIS sampling scheme and the associated sampling weights. P-values of less than 0.05 (two-tailed) were considered statistically significant.

3. Results

A total of 8,028,436 patients were identified as undergoing TKA or THA during the study period, with 1,255 patients in the MSD group and 8,027,181 patients in non-MSD group. Among the MSD patients 19.9% patients had MED and remaining 80.1% patients had achondroplasia, hypochondroplasia and SED. MSD patients were younger, requiring on average TJA 15 years earlier than non-MSD patients, more likely to be on Medicaid, and of minority groups (Table 1). Patients with MSD underwent their TJA more frequently in a teaching hospital (Table 2). Additionally, MSD patients were less likely to have hypertension, coronary artery disease, diabetes mellitus, and hypothyroidism (Table 3). MSD patients had significantly lower Charlson comorbidity index (CCI) scores compared to non-MSD patients ($p < 0.001$).

There were no statistically significant differences in total complications (Odds ratio (OR), 1.15; 95% confidence interval (95% CI), 0.86–1.51; $p = 0.352$), surgical complications (OR, 1.24; 95% CI, 0.94–1.65; $p = 0.132$), or medical complications (OR, 0.79; 95% CI, 0.42–1.49; $p = 0.468$) between the MSD and non-MSD cohorts. MSD patients had higher risks of surgical site infection (0.8% vs. 0.2%; OR, 4.16; 95% CI, 1.03–16.75; $p = 0.044$), and perioperative hemorrhage (2.1% vs. 0.7%; OR, 3.20; 95% CI, 1.32–7.76; $p = 0.010$). Post-operative pneumonia, pulmonary embolism, acute heart failure and in-hospital mortality did not occur in the MSD group (Table 4).

4. Discussion

Although the current literature demonstrates adequate mechanical results and longevity of the hip and knee replacements at short to mid-term follow-up following TJA in MSD patients, there is a paucity of information these patients fare during their in-hospital stay. The purpose of this study was to: (1) compare demographic, hospital characteristics and comorbidities between MSD and non-MSD patients undergoing TJA, and (2) compare the risk of postoperative complications between MSD and non-MSD patients. We found that MSD patients had fewer co-morbidities compared to non-MSD patients, and had no significant difference in overall medical and surgical complication risks following TJA. However, there were significantly increased risks of surgical site

Table 1
Demographic characteristics by musculoskeletal dysplasia (MSD), NIS[a].

Characteristics	Non-MSD[b]	MSD[b]	*p*-value
Total Patients (N)	8,027,181	1,255	<0.001[c]
Age, mean ± SD	65.8 ± 24.4	50.9 ± 35.3	<0.001[c]
Age groups, n (%)			
<40	96,326 (1.2)	287 (22.9)	<0.001[c]
40-49	457,549 (5.7)	203 (16.2)	
50-59	1,701,762 (21.2)	316 (25.2)	
60-69	2,673,051 (33.3)	331 (26.4)	
≥70	3,090,465 (38.5)	118 (9.4)	
Gender, n (%)			
Males	3,162,709 (39.4)	489 (39.0)	0.902
Females	4,864,472 (60.6)	766 (61.0)	
Race, n (%)			
White	6,782,968 (84.5)	998 (79.5)	0.003[c]
African American	577,957 (7.2)	87 (6.9)	
Hispanic	369,250 (4.6)	89 (7.1)	
Asian or Pacific Islander	88,299 (1.1)	45 (3.6)	
Other	208,707 (2.6)	35 (2.8)	
Median household income, n (%)			
1st quartile	1,669,654 (20.8)	267 (21.2)	0.795
2nd quartile	2,119,176 (26.4)	315 (25.1)	
3rd quartile	2,135,230 (26.6)	368 (29.3)	
4th quartile	2,119,176 (26.4)	305 (24.3)	
Payer status, n (%)			
Medicare	4,374,814 (54.5)	427 (34.0)	<0.001[c]
Medicaid	248,843 (3.1)	151 (12.0)	
Private	3,114,546 (38.8)	631 (50.3)	
Self-pay	40,136 (0.5)	15 (1.2)	
Other	248,843 (3.1)	31 (2.5)	
Primary diagnosis, n (%)			
Osteoarthritis	7,714,121 (96.1)	1025 (81.7)	<0.001[c]
Hip Dysplasia	8,027 (0.1)	64 (5.1)	
Aseptic Necrosis	168,571 (2.1)	36 (2.9)	
Other	136,462 (1.7)	129 (10.3)	

Patient demographics showing both musculoskeletal dysplasia (MSD) patients and non-MSD patients. *p*-values shown with $p < 0.05$ representing statistical significance.
[a] NIS, National Inpatient Sample.
[b] MSD, musculoskeletal dysplasia.
[c] Statistically significant.

Table 2
Hospital characteristics by musculoskeletal dysplasia (MSD), NIS[a].

Hospital Characteristics	Non-MSD[b]	MSD[b]	*p*-value
Teaching Status, n (%)			
Teaching Hospital	3,507,878 (43.7)	669 (53.3)	0.002[c]
Non-teaching Hospital	4,519,303 (56.3)	586 (46.7)	
Setting, n (%)			
Rural	1,268,295 (15.8)	164 (13.1)	0.239
Urban	6,758,886 (84.2)	1091 (86.9)	
Bed size, n (%)			
Small	1,364,621 (17.0)	264 (21.0)	0.079
Medium	1,934,551 (24.1)	390 (31.1)	
Large	4,728,010 (58.9)	602 (48.0)	
Region, n (%)			
Northeast	1,332,512 (16.6)	208 (16.6)	0.703
Midwest	2,223,529 (27.7)	338 (26.9)	
South	2,705,160 (33.7)	423 (33.7)	
West	1,621,491 (20.2)	286 (22.8)	
Admission Variables (days)			
Length of Stay, mean ± SD	3.2 ± 0.2	3.3 ± 0.2	0.218

Hospital characteristics in which patients underwent total joint arthroplasty surgery showing both musculoskeletal dysplasia (MSD) patients and non-MSD patients. *p*-values shown with $p < 0.05$ representing statistical significance.
[a] NIS, National Inpatient Sample.
[b] MSD, musculoskeletal dysplasia.
[c] Statistically significant.

infection and perioperative hemorrhage or hematoma in this group, possibly due to the complexity of the surgery and abnormal anatomy encountered.

Early damage to the articular cartilage in MSD patients occurs and is caused by abnormal hyaline cartilage and/or changes in biomechanical joint loading axis due to anatomical deformities. The hip and knee joints, being main weight-bearing joints of the body, are affected earlier than other joints, leading to osteoarthritis ultimately requiring joint arthroplasty [20]. MSD patients in our study were younger and had less comorbidity than non-MSD patients undergoing TJA. This is similar to previous studies showing younger mean age of these patients at the time of surgery

Table 3
Associations between musculoskeletal dysplasia (MSD) and select comorbidities, NIS[a].

Comorbidity, n (%)	Non-MSD[b]	MSD[b]	*p*-value
Hypertension	5,177,532 (64.5)	505 (40.2)	< 0.001[c]
Coronary Artery Disease	1,035,506 (12.9)	69 (5.5)	< 0.001[c]
Congestive Heart Failure	240,815 (3.0)	25 (2.0)	0.351
Diabetes Mellitus	1,525,164 (19.0)	118 (9.4)	< 0.001[c]
Peripheral Vascular Disease	160,544 (2.0)	15 (1.2)	0.328
Cerebrovascular Disease	88,299 (1.1)	5 (0.4)	0.289
COPD (Chronic Lung Disease)	1,188,023 (14.8)	164 (13.1)	0.443
Obesity	1,468,974 (18.3)	282 (22.5)	0.088
Hypothyroidism	1,179,996 (14.7)	98 (7.8)	0.002[c]
Liver disease	56,190 (0.7)	0 (0)	–
Chronic Renal Disease	297,006 (3.7)	41 (3.3)	0.691
Depression	754,555 (9.4)	142 (11.3)	0.294
Deficiency anemia	80,272 (1.0)	18 (1.4)	0.576
Charlson Comorbidity Index, n (%)			
0	4,920,662 (61.3)	914 (72.8)	< 0.001[c]
1	2,143,257 (26.7)	228 (18.2)	
> = 2	963,262 (12.0)	113 (9.0)	

Comorbidity association between both musculoskeletal dysplasia (MSD) patients and non-MSD patients. *p*-values shown with $p < 0.05$ representing statistical significance.
[a] NIS, National Inpatient Sample.
[b] MSD, musculoskeletal dysplasia.
[c] Statistically significant.

Table 4
Associations between musculoskeletal dysplasia (MSD) and perioperative complications, NIS[a]

Complication	Non-MSD[b]	MSD[b]	*p*-value	Adjusted OR (95% CI)
Any Complication, n (%)	1,966,659 (24.5)	339 (27.0)	0.352	1.15 (0.86–1.51)
Surgical, n (%)	1,717,817 (21.4)	314 (25.0)	0.132	1.24 (0.94–1.65)
Surgical site infection	16,054 (0.2)	10 (0.8)	0.044[d]	4.16 (1.03–16.75)[d]
Wound dehiscence	321 (0.004)	0 (0)	–	–
Perioperative hemorrhage or hematoma	56,190 (0.7)	26 (2.1)	0.010[d]	3.20 (1.32–7.76)[d]
Acute postoperative anemia	1,669,654 (20.8)	309 (24.6)	0.138	1.24 (0.93–1.66)
Periprosthetic Joint Infection	3,211 (0.04)	0 (0)	–	–
Mechanical failure	18,463 (0.23)	0 (0)	–	–
Periprosthetic Fracture	0 (0)	0 (0)	–	–
Lower extremity peripheral nerve injury	1,605 (0.02)	0 (0)	–	–
Dislocation	6,422 (0.08)	0 (0)	–	–
Revision TJA	0 (0)	0 (0)	–	–
Irrigation and Debridement	0 (0)	0 (0)	–	–
Medical, n (%)	401,359 (5.0)	50 (4.0)	0.468	0.79 (0.42–1.49)
Acute renal failure	128,435 (1.6)	15 (1.2)	0.669	0.78 (0.25–2.44)
Acute myocardial infarction	24,082 (0.3)	5 (0.4)	0.755	1.37 (0.19–9.72)
Pneumonia	0 (0.0)	0 (0)	–	–
Pulmonary embolism	24,082 (0.3)	0 (0)	–	–
Deep venous thrombosis (DVT)	27,292 (0.34)	0 (0)	–	–
AMS[c]	28,898 (0.36)	5 (0.4)	0.918	1.11 (0.16–7.83)
Urinary tract infection	208,707 (2.6)	25 (2.0)	0.554	0.77 (0.32–1.86)
Blood transfusion	0 (0)	0 (0)	–	–
Acute heart failure	8,027 (0.1)	0 (0)	–	–
Death, n (%)				
In-hospital mortality	8,027 (0.1)	0 (0)	–	–

Associations between both musculoskeletal dysplasia (MSD) patients and non-MSD patients and perioperative complications. *p*-values shown with $p < 0.05$ representing statistical significance. (–) used when *p*-value calculations were not possible due to one or both cohorts not having any occurrences of those complications.
[a] NIS, National Inpatient Sample.
[b] MSD, musculoskeletal dysplasia.
[c] AMS, altered mental status.
[d] Statistically significant.

[10,11,13,17]. Significantly more patients in the MSD group had Medicaid insurance, which would be expected given their musculoskeletal comorbidities that limit their socioeconomic independence.

MSD patients were more likely to be treated at a teaching hospital compared to a private hospital. Considering the technical challenges and theoretically increased complications associated with TJA in MSD patients, it is possible that private surgeons are less likely to operate on this complex patient population. Additionally, Mason et al. reported that there is equal reimbursement for both complex and less complex patients, which has contributed to private practice providers referring these complex patients to the academic sector [21].

MSD results in significantly distorted bony anatomy and muscular contractures which makes TJA challenging in this population [8]. Ain et al., Peltonen et al. and Kim et al., in their small case series, reported increased soft tissue release, capsular release and/or additional bone resection for balancing of the joint in these patients [8,16,17]. Although this leads to increased dissection and surgical exploration requirements, the literature has not shown a higher rate of surgical site infection or post-operative hemorrhage [8,10,12,13]. In contrast, our current study demonstrated

significantly higher rates of surgical site infection ($p = 0.044$) and perioperative hemorrhage ($p = 0.010$). This discrepancy in literature may be due to small sample sizes in previous studies, compared to our larger sample size of a national database.

Although the present study represents the largest cohort assessing MSD patients following TJA, there are several limitations including the inherent limitation of utilizing a national database. Since all the data in NIS was entered by hospital personnel at various hospitals, there is a chance of administrative error and imperfect classification of diseases. The NIS covers only data during each inpatient encounter, and so any complications occurring after the discharge are not accounted for, for example post-operative dislocation. Lastly, due to the low number of MSD patients within each of the 4 MSD subgroups included in the MSD definition used in this study, it was not possible to evaluate the differences in outcomes between each of the four individual MSD subgroups comprising the MSD cohort.

5. Conclusion

The current study found that MSD patients undergoing TJA were younger with less co-morbidity when compared to non-MSD patients, and had no significant difference in overall perioperative medical and surgical complication rates. However, there were significantly increased risks of surgical site infection and perioperative hemorrhage or hematoma in these patients, which is likely due to the abnormal anatomy resulting in increased surgical complexity. In light of the existing literature demonstrating adequate results after TJA in patients with MSD, TJA is a safe procedure in MSD patients with osteoarthritis requiring joint replacement.

Disclosure of Interest

The authors declare that they have no competing interest.

Funding and Ethical Approval

There is no funding source. This study involves a national de-identified database for participant information and is, therefore, exempt from institutional review board approval. It does not contain any studies with human participants or animals performed by any of the authors.

Authors' contribution'

Each author contributed significantly to study design, data collection, data analysis, and editing the manuscript. Dr Patel and Mr Cichos contributed to the initial writing of the paper. Dr McGwin contributed statistical analysis and interpretation. Dr Ghanem contributed oversight, supervision, and final editing of manuscript.

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