

# Crohn's Disease Increases In-Hospital Lengths of Stay, Medical Complications, and Costs of Care following Primary Total Knee Arthroplasty

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## Abstract

The literature has shown an increase in prevalence of Crohn's disease (CD) within the United States alongside a concomitant rise in primary total knee arthroplasty (TKA) procedures. As such, with these parallel increases, orthopaedic surgeons will invariably encounter CD patients requiring TKA. Limited studies exist evaluating the impact of this disease on patients undergoing the procedure; therefore, this study endeavors to determine whether CD patients undergoing primary TKA have higher rates of (1) in-hospital lengths of stay (LOS), (2) medical complications, and (3) episode of care (EOC) costs. To accomplish this, a nationwide database was queried from January 1, 2005 to March 31, 2014 to identify patients undergoing TKA. The study group, patients with CD, was randomly matched to the controls, patients without CD, in a 1:5 ratio after accounting for age, sex, and medical comorbidities associated with CD. Patients consuming corticosteroids were excluded, as they are at risk of higher rates of adverse events following TKA. This query ultimately yielded a total of 96,213 patients, with 16,037 in the study cohort and 80,176 in the control one. The study compared in-hospital (LOS), 90-day medical complications, and day of surgery and total global 90-day EOC costs between CD and non-CD patients undergoing primary TKA. The results found CD patients undergoing primary TKA had significantly longer in-hospital LOS (4- vs. 3 days,  $p < 0.0001$ ) compared with non-CD patients. CD patients were also found to have significantly higher incidence and odds of 90-day medical complications (25.31 vs. 10.75; odds ratio: 2.05,  $p < 0.0001$ ) compared with their counterparts. Furthermore, CD patients were found to have significantly higher 90-day EOC costs (\$15,401.63 vs. 14,241.15,  $p < 0.0001$ ) compared with controls. This study demonstrated that, after adjusting for age, sex, and medical comorbidities, patients with CD have prolonged in-hospital LOS, increased medical complications, and higher EOC costs following primary TKA. Therefore, it establishes the importance for orthopaedists to adequately counsel CD patients of the potential complications and outcomes following their procedure.

## Keywords

- ▶ total knee arthroplasty
- ▶ Crohn's disease
- ▶ in-hospital lengths of stay
- ▶ 90-day medical complications
- ▶ costs of care

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Crohn's disease (CD) is a chronic relapsing inflammatory bowel disease (IBD) that continues to affect a larger share of the population in North America.<sup>1,2</sup> CD is associated with extraintestinal manifestations (EIM), many of which affect the musculoskeletal system and can present frequently with large joint arthritis, particularly of the knee.<sup>3–6</sup> Arthritis affects up to 44% of patients with IBD, and patients with CD are affected more frequently.<sup>7</sup> The exact pathogenesis is not well understood, but it is believed molecular mimicry plays a role.<sup>8</sup> Dysregulation of the intestinal epithelium leads to increased permeability and translocation of luminal bacteria through the intestinal barrier.<sup>9</sup> The bacteria are believed to have shared epitopes with the articular joints, and the body is unable to differentiate between the two. This triggers an adaptive immune response causing inflammation. Genetic factors also seem to play a role in the autoimmune response as 70% of parent–child pairs and 84% of sibling pairs share the same EIM.<sup>10</sup> Regarding their arthritis, patients with CD may need orthopaedic surgery, and there is paucity in the literature discussing the impact of orthopaedic procedures on patients with CD.<sup>11–13</sup> Therefore, national databases are in a unique position to help begin filling this gap.

To the best of our knowledge, only two studies have used large nationwide databases to study the impact of CD on total knee arthroplasty (TKA) outcomes.<sup>12,13</sup> The study by Ehrenpreis and Zhou found that length of stay (LOS), costs, and mortality rates for knee arthroplasties in CD patients are comparable to the general population.<sup>13</sup> However, this study did not match the case and control groups by medical comorbidities associated with CD and, therefore, did not minimize the effects of confounding. The other study by Gregory et al did control for comorbidities in IBD patients and also found that they were not at an increased risk of serious infections following joint replacement surgery.<sup>12</sup> However, the aforementioned study did not control for additional confounding variables such as depression or hyperlipidemia, which have been shown to be conditions individually associated with CD that result in increased adverse outcomes after TKA.<sup>14–16</sup> More importantly, neither study excluded patients consuming corticosteroids, which the literature has shown, is associated with adverse events.<sup>17–19</sup>

Since the knee joints are commonly affected in CD, and since orthopaedic surgery outcomes in patients with CD are not closely researched in the literature, TKA is an ideal procedure to study regarding its outcomes in this population. TKA is frequently performed, and the number of procedures continues to rise, projected to reach almost a million by 2030.<sup>20</sup> Thus, as the growing population living with CD also continues to age, the number of these patients requiring TKA is likely to increase.<sup>20</sup> Orthopaedic surgeons will then face unique complications with CD patients due to the inherent systemic impacts of the disease. As such, studying the impact of CD on outcomes of TKA procedures is of paramount importance so that healthcare professionals can better implement preoperative risk counseling to their patients.

With the lack of well-powered studies, the purpose of this article is to analyze an administrative claims database to

determine whether patients who have CD undergoing primary TKA have increased (1) in-hospital LOS, (2) 90-day medical complications, and (3) costs of care compared with TKA patients without CD.

## Methods

### Database

To investigate adverse outcomes of CD patients undergoing primary TKA procedures, a retrospective case–control query from January 1st, 2005 to March 31st, 2014 of the 100% Medicare Standard Analytical Files from the PearlDiver (PearlDiver Technologies, Fort Wayne, IN) was performed. The for-fee subscription-based platform contains the deidentified records of over 100 million patients that can be queried using International Classification of Disease, Ninth Revision (ICD-9) and Current Procedural Terminology (CPT) codes. Information available from the supercomputer includes complications, discharge disposition, diagnoses, and costs, in addition to other variables, making it ideal for large retrospective orthopaedic-related research. The study was reviewed by the Institutional Review Board (IRB) and considered appropriate for exempt status of IRB oversight due to the de-identified nature of the data.

### Data Collection

The database was initially queried for all patients undergoing primary TKA using CPT and ICD-9 codes 27447 and 81.54, respectively. CD patients were identified using ICD-9 diagnosis codes 555.0, 555.1, 555.2, and 555.9. The study group included all patients undergoing primary TKA with a concomitant diagnosis of CD. The control group included all patients undergoing TKA without an associated diagnosis of CD. Patients consuming corticosteroids were excluded from the study, as the literature has shown higher rates of adverse events with corticosteroid use.<sup>12,17–19</sup> To minimize the effects of confounding by age, sex, and the following medical comorbidities associated with CD—age, sex, anemia, diabetes mellitus, depression, hypertension, hyperlipidemia, and malnutrition—study group patients were randomly matched to controls in a 1:5 ratio. These conditions were used as they are associated with CD.<sup>14–16,21–26</sup> Successful matching between both groups was indicated by a *p*-value of  $\sim 1$  across potential confounding variables (► **Table 1**). A total of 96,213 TKA patients were identified in the database from January 1st, 2005 to March 31st, 2014 after excluding patients consuming corticosteroids. The query found 16,037 patients with CD and 80,176 without CD.

### Endpoints

The study set out to compare in-hospital LOS, 90-day medical complications, and day of surgery and total global 90-day episode of care (EOC) costs between patients undergoing primary TKA who have CD and those who do not. Medical complications analyzed included ileus, pneumonia, respiratory failure, urinary tract infection, cerebrovascular

**Table 1** Demographic profile for Crohn's disease patients and matched-controls undergoing primary total knee arthroplasty

Demographics	Crohn's disease		Controls		p-Value <sup>a</sup>
	n	%	n	%	
Age (y)					0.99
< 64	2,952	18.41	14,756	18.40	
65–69	5,260	32.80	25,299	31.55	
70–74	3,568	22.25	17,838	22.25	
75–79	2,605	16.24	13,023	16.24	
80–84	1,303	8.12	6,515	8.13	
85<	349	2.18	1,745	2.18	
Sex					0.99
Female	11,195	69.81	55,968	69.81	
Male	4,842	30.19	24,208	30.19	
Comorbidities					
Anemia	425	2.65	2,119	2.64	0.98
Diabetes mellitus	6,863	42.79	34,312	42.80	0.99
Depression	6,855	42.74	34,269	42.74	0.99
Hypertension	14,594	91.00	72,967	91.01	0.99
Hyperlipidemia	12,048	75.13	60,239	75.13	0.99
Malnutrition	156	0.97	774	0.97	0.96

<sup>a</sup>Assessed by Pearson's chi-squared analyses.

accidents, pulmonary emboli, venous thromboemboli, deep vein thromboses, and surgical site infections. Medical complications were defined using ICD-9 codes. Reimbursements were used as a substitute for costs of care.

### Statistical Analyses

Descriptive and statistical analyses were performed by using the open-source programming language R (R, Foundation for Computational Statistics; Vienna, Austria). Pearson's chi-squared analyses were used to compare patient demographics. Mann-Whitney U tests were used to compare LOS and costs between the cohorts. Multivariate logistic regression analysis was used to calculate odds ratios (OR), 95% confidence intervals (95% CI), and *p*-values on the effects of CD on medical complications, while adjusting for age, sex, region, and Elixhauser-comorbidity index (ECI). ECI was used over the traditional Charlson-comorbidity index since studies have shown the former outperforms the latter.<sup>27–30</sup> Due to the number of comparisons being performed, a Bonferroni-correction was performed to reduce the probability of a type I error. Thus, a *p*-value less than 0.002 was considered statistically significant.

## Results

### In-Hospital Lengths of Stay

The study found patients with CD undergoing primary TKA had significantly longer in-hospital LOS (4- vs. 3 days, *p* < 0.0001) compared with patients without CD undergoing the same procedure.

### Medical Complications and Costs of Care

CD patients were also found to have significantly higher incidence and odds of 90-day medical complications (25.31 vs. 10.75; OR: 2.05, 95% CI: 1.95–2.16, *p* < 0.0001) compared with their counterparts. Specifically, the study found CD patients had statistically significant higher frequency and odds of developing ileus (1.13 vs. 0.20%; OR: 4.56, 95% CI: 3.67–5.67, *p* < 0.0001), pneumonia (2.68 vs. 0.83%; OR: 2.42, 95% CI: 2.13–2.75, *p* < 0.0001), respiratory failure (2.48 vs. 0.78%; OR: 2.36, 95% CI: 2.07–2.69, *p* < 0.0001), urinary tract infection (9.78 vs. 4.08%; OR: 2.08, 95% CI: 1.95–2.22, *p* < 0.0001), cerebrovascular accidents (2.04 vs. 0.79%; OR: 1.96, 95% CI: 1.71–2.25, *p* < 0.0001), pulmonary emboli (0.74 vs. 0.37%; OR: 1.62, 95% CI: 1.30–2.01, *p* < 0.0001), venous thromboemboli (2.38 vs. 1.33%; OR: 1.53, 95% CI: 1.36–1.73, *p* < 0.0001), deep vein thromboses (2.04 vs. 1.17%; OR: 1.49, 95% CI: 1.30–1.69, *p* < 0.0001), and surgical site infections (1.42 vs. 0.87%; OR: 1.33, 95% CI: 1.14–1.55, *p* = 0.0002) (► **Table 2**). On the other hand, the study found CD patients did not have a statistically significant higher frequency and odds of developing a myocardial infarction (0.63 vs. 0.32%; OR: 1.44, 95% CI: 1.13–1.85, *p* = 0.0021). Furthermore, CD patients incurred significantly higher 90-day EOC costs (\$15,401.63 vs. 14,241.15, *p* < 0.0001) compared with their counterparts.

## Discussion

CD is a chronic and increasingly prevalent disease associated with substantial burden that affects both the patient and

**Table 2** Comparison of 90-day medical complications among CD patients and matched controls following primary total knee arthroplasty

Medical complications	CD (%)	Controls (%)	OR	95% CI	p-Value <sup>a</sup>
Ileus	1.13	0.20	4.56	3.67–5.67	<0.0001
Pneumonia	2.68	0.83	2.42	2.13–2.75	<0.0001
Respiratory failure	2.48	0.78	2.36	2.07–2.69	<0.0001
Urinary tract infection	9.78	4.08	2.08	1.95–2.22	<0.0001
Cerebrovascular accident	2.04	0.79	1.96	1.71–2.25	<0.0001
Pulmonary emboli	0.74	0.37	1.62	1.30–2.01	<0.0001
Venous thromboemboli	2.38	1.33	1.53	1.36–1.73	<0.0001
Deep vein thromboses	2.04	1.17	1.49	1.30–1.69	<0.0001
Myocardial infarction	0.63	0.32	1.44	1.13–1.85	0.0021
Surgical site infection	1.42	0.87	1.33	1.14–1.55	0.0002
Total medical complications	25.31	10.75	2.05	1.95–2.16	<0.0001

Abbreviations: CD, Crohn's disease; OR, odds ratio; 95%CI, 95% confidence interval.

<sup>a</sup>Adjusted for age, sex, region, and Elixhauser-comorbidity index.

healthcare system. Outside from its intestinal manifestations, CD frequently impacts patients' musculoskeletal systems, specifically knee joints.<sup>5</sup> At the same time, there is also a concomitant rise in demand for primary TKAs.<sup>20</sup> With these parallel increases, it is inevitable that orthopaedic surgeons will encounter CD patients requiring TKA. As such, the purpose of this study is to determine the impact CD has on patients undergoing primary TKA; this was achieved by analyzing a nationwide administrative claims database while controlling for multiple comorbidities associated with the disease as well as having clearly delineated inclusion and exclusion criteria. The present study found that compared with non-CD patients, CD patients undergoing primary TKA had longer in-hospital LOS, increased incidence and odds of medical complications, and higher costs of care.

While the large sample size ensures adequate power, there are still inherent limitations to this study, mostly due to its retrospective nature and use of a large administrative database. The study relies on diagnostic and procedural coding, but there are inevitably going to be inaccuracies with regard to the ICD-9 and CPT diagnostic codes.<sup>31,32</sup> Nonetheless, this study attempted to account, as much as possible, for the potential misclassifications with statistical analyses; what's more, rates of errors are reported to be 1.3% within the Medicare population,<sup>33</sup> but this is unlikely to have had a substantial effect on our findings. Moreover, there is the unavoidable chance of introducing error from variables that cannot be recorded yet still influence postoperative outcomes, such as dosing and/or timing of preoperative antibiotics and surgical sterility techniques.<sup>34,35</sup> The authors also utilized a single insurance database, and as such, the sample used may not be a true cross-sectional representation<sup>36</sup> of the impact of CD following primary TKA. Additionally, there is the possibility that patients in the control cohort may have CD without having being formally diagnosed. For that reason, the effect of CD on TKA may have been underestimated. While the current investigation matched CD patients to a

comparison cohort with various comorbid conditions, such as depression, this may potentially have confounded the results, as these patients with these comorbid conditions are less likely to do well. As such, these comorbid conditions may prolong in-hospital LOS and increase the rates of adverse events and healthcare expenditures that were noted in this study. Furthermore, the diagnosis of CD, the stage of disease which a person is in, and the EIM are dependent on a combination of criteria,<sup>1,3</sup> all of which could potentially impact post-TKA procedure outcomes. Yet, this study is limited with the ability of assessing the specific criteria used, the severity of the disease, and what, if any, EIM were diagnosed. This sheds light on the lack of more meticulous and standardized diagnostic criteria for better ascertaining the sequelae of CD. Thus, despite the limitations presented, this article introduces novel information about a topic that has not previously been studied extensively; as such, the findings reported here can be the foundation for future work that includes more granular data control and collection.

Not many studies discuss the impact of IBD, specifically CD, on non-IBD-related surgeries.<sup>11–13</sup> In a retrospective study of their institution's own database, Kapadia et al compared clinical outcomes of 92 total hip arthroplasty (THA) procedures in patients with ( $n = 23$ ) and without IBD ( $n = 69$ ) from 2001 and 2010 with a mean follow-up period of 49 months, and found higher frequencies of complications in patients with IBD undergoing THA compared with those without IBD.<sup>11</sup> Similarly, Ehrenpreis and Zhou performed a retrospective study and analyzed the Nationwide Inpatient Sample database from 1999 to 2012 of IBD patients undergoing primary TKA ( $n = 21,202$ ) or THA ( $n = 33,783$ ) and found no difference in costs, LOS, and mortality rates between CD and non-CD patients undergoing TKA.<sup>13</sup> In another retrospective study, Gregory et al utilized the MarketScan database from 2006 to 2014 of patients between the ages of 18 and 64 and analyzed the rates of infection within 90 days following the index

procedure.<sup>12</sup> Gregory et al demonstrated that IBD patients were not associated with increased risk of serious infection after controlling for baseline comorbidities.<sup>12</sup> However, they did not report controlling for confounding variables in their CD cohort, only in their IBD cohort; and with the variables they did control for, they did not include depression or hyperlipidemia, which previous papers have demonstrated to be conditions individually associated with CD that result in increased adverse outcomes after TKA.<sup>14–16</sup> Even more, both studies did not exclude patients taking corticosteroids, which has been shown to result in higher rates of adverse events following TKA, which could potentially explain the discrepancies seen in the prior studies and this investigation.<sup>17–19</sup>

Primary TKA patients with CD, after controlling for confounding variables, were found to be at an increased risk of developing the following 90-day medical complications compared with those without CD: ileus, pneumonia, respiratory failure, urinary tract infection, cerebrovascular accidents, pulmonary emboli, venous thromboemboli, deep vein thromboses, and surgical site infections. They were found not to have an increased risk of developing myocardial infarctions; however, the *p*-value was 0.0021, and the cutoff used in our study was 0.002. As stated earlier, Kapadia et al's findings were similar to this study in that they found higher frequencies of complications in IBD patients undergoing THA (*n* = 17) compared with those without (*n* = 51) IBD.<sup>11</sup> Even with the small sample size, absence of control of confounders, and different complications measured, the authors offer insight into the potential association of IBD and total joint arthroplasty complications, which is in line with the present findings. This article also aims to take a step further and emphasize the significance of understanding the impact of a specific IBD, CD, on the outcomes of TKA procedures, especially as CD patients continue to encompass an increasingly larger percentage of TKA patients.

CD accounts for a substantial amount of US healthcare dollars.<sup>37,38</sup> This study found that CD patients incurred significantly higher 90-day EOC costs compared with their non-CD counterparts after controlling for medical comorbidities associated with CD. This is consistent with findings previously reported in the literature with regard to higher inpatient costs for CD patients.<sup>13</sup> These increases in EOC costs can be attributed to the adverse events observed in CD patients undergoing TKA procedures. For example, Kapadia et al found that patients with periprosthetic joint infections after TKA paid almost \$100,000 more in annual costs than their noninfected patient counterparts.<sup>39</sup> Ruppert et al found that the total costs related to venous thromboemboli over 3 months were about \$5,000.<sup>40</sup> Malcolm et al<sup>41</sup> reported that patients with pulmonary complications, such as pneumonia, after TKA paid \$7,078 more than patients without perioperative pulmonary complications.

## Conclusion

Expanding the knowledge of the association between CD and outcomes following TKA procedures can aid clinicians in implementing interventions and in counseling patients prior to treatment. After adjusting for age, sex, and medical comor-

bilities, this study demonstrated that patients with CD have prolonged in-hospital LOS, increased 90-day medical complications, and higher 90-day EOC costs following primary TKA. Larger prospective randomized controlled studies are necessary to further determine the impact of CD, its severity, and its EIM following primary TKA. Nevertheless, this study presently establishes the importance for orthopaedic surgeons to incorporate CD status into the TKA decision-making process; it allows healthcare professionals to adequately educate patients of the potential complications and outcomes that may occur following their procedure.

## Conflict of Interest

None declared.

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