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Does Timing of Previous Intra-Articular Steroid Injection Affect the Post-Operative Rate of Infection in Total Knee Arthroplasty?

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ABSTRACT

Intra-articular steroid injections are widely used for symptomatic relief of knee osteoarthritis. This study used a national database to determine if there is an association between preoperative intra-articular knee injection at various time intervals prior to ipsilateral TKA and infection. The incidence of infection within 3 months (2.6%, OR 2.0 [1.6–2.5], $P < 0.0001$) and 6 months (3.41%, OR 1.5 [1.2–1.8], $P < 0.0001$) after TKA within 3 months of knee injection was significantly higher than our control cohort. There was no significant difference in patients who underwent TKA more than 3 months after injection. Ipsilateral knee injection within three months prior to TKA is associated with a significant increase in infection.

Osteoarthritis is second to only ischemic heart disease as a cause of work disability in men over 50 years of age in the United States [1]. Intra-articular corticosteroid injections have been shown to provide short-term relief from pain due to moderate and end stage osteoarthritis of the knee [2–4]. An advantage of intra-articular injections over systemic anti-inflammatories is to provide high concentrations of corticosteroid in the synovial fluid and synovial cells to reduce local inflammation while concurrently minimizing the systemic effects of the drug [5]. The pain relief provided by injections can delay the need for total knee arthroplasty (TKA) in patients who are too young, unwilling or medically unfit for the procedure [6]. Studies have estimated that approximately 22%–39% of patients who fail conservative measures and undergo total knee arthroplasty have had an intra-articular steroid injection prior to the procedure [7–10]. While these injections are common, risks of the procedure include tendon rupture [11,12], articular cartilage degeneration [13], and septic arthritis including periprosthetic joint infection (PJI) [10,14].

Conflicting evidence exits regarding the association of preoperative intra-articular steroid injection and increased risk of postoperative PJI following TKA [7–10]. Three studies have reported that injections given more than 8–12 months prior to TKA were not associated with increased risks of PJI [7–9], while one study suggested that steroid injections given within eleven months prior to TKA are associated with a significant increase in the rate of deep infection [10]. These few existing studies are likely underpowered, and examine variable time periods between injection and TKA.

The goal of the present study was to use a national database to determine if an association exists between preoperative intra-articular knee injections at different time points and post-operative PJI after TKA. Our hypothesis was that recent ipsilateral knee injection would be associated with an increased rate of PJI following TKA.

Materials and Methods

All data were derived from the PearlDiver Patient Records Database (www.pearldiverinc.com; PearlDiver Inc, Fort Wayne, Indiana). This insurance-based database of patient records contains procedural volumes, patient demographics, and average charge information for patients with International Classification of Diseases, 9th Revision (ICD-9) diagnoses and procedures or Current Procedural Terminology (CPT) codes. Data for the present study were derived from the Medicare database within the PearlDiver records, which have a total of over 100 million individual patient records from 2005 to 2011. Access to the database was granted by PearlDiver Technologies for the purpose of academic research. The database was stored on a password-protected server maintained by PearlDiver.

The database was queried for TKA using CPT 27447. Large joint injection was queried using CPT 20610. To assure that the injection was performed in the knee and not on other large joints such as the shoulder or hip, only patients with large joint injections performed for the following knee-related ICD-9 codes were included: 715.26, 715.16, 715.36, 715.96, 719.66, 717.96, 717.89, 717.8, and 719.46. CPT codes were used in favor of ICD-9 procedure codes because CPT modifiers were necessary to determine laterality of the injection and TKA. The resulting TKA and knee injection cohorts were then divided into "left" and

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"right" cohorts using the CPT modifiers for left (LT) and right (RT). Patients that were coded as having bilateral injections with subsequent unilateral surgery were included, as were patients with unilateral or bilateral injections with subsequent bilateral surgery by the same methods. Injections or TKA without laterality specified by CPT modifier were excluded.

Patients who subsequently underwent TKA after ipsilateral knee injection were identified using Boolean coding to determine patients who underwent left TKA after left knee injection and those who underwent right TKA after right knee injection. These patients were then divided into three separate cohorts: TKA within 3 months after ipsilateral knee injection, TKA between 3 and 6 months after ipsilateral knee injection, and TKA between 6 and 12 months after ipsilateral knee injection.

A matched control cohort of TKA without any prior documented knee injection was then created. The final control cohort comprised of the maximum number of available patients in the database that underwent TKA without any prior ipsilateral knee injection that could be included and matched to the average distribution of the three study groups to achieve a statistically similar distribution of five key variables: age, gender, obesity, smoking status and diabetes. The sequential matching algorithm first matched based on age, then gender, then obesity, diabetes and finally smoking.

The demographics of the matched control cohort and three study cohorts were recorded from the database and subsequently compared. Postoperative PJI was characterized by either a diagnosis or procedure for wound or deep infection within 3 or 6 months after TKA using the CPTs 20005, 27030 and ICD-9s 996.66, 996.67, 996.69, 998.51, and 998.59.

Statistical comparisons of cohort demographics and postoperative infections were completed with Pearson χ^2 analysis. For all statistical comparisons, $P < 0.05$ was considered significant. SPSS version 21 for Macintosh (IBM, Armonk, New York) was used for all statistical calculations.

Results

The study included 35,890 unique patients who underwent primary TKA. The matched control cohort included 13,650 patients who did not receive an injection prior to TKA, while the matched study groups included 5313 patients who underwent TKA within 3 months after knee injection, 8919 patients who underwent TKA between 3 and 6 months following knee injection, and 8008 patients who underwent TKA between 6 and 12 months following knee injection. Demographics, including sex, age, obesity status, diabetes, and smoking status of each cohort are presented in Table 1. There were no statistically significant differences between any of the study groups.

The incidence of infection within 3 months (2.6%, OR 2.0 [1.6–2.5], $P < 0.0001$) and 6 months (3.41%, OR 1.5 [1.2–1.8], $P < 0.0001$) after TKA within 3 months of knee injection was significantly higher than our control cohort. There was no significant difference in infection rates in patients who underwent TKA between 3–6 months or 6–12 months after ipsilateral knee injection compared to our control cohort. The incidences of postoperative infection within 3 and 6 months after TKA for each cohort are presented in Table 2 and Fig. 1 with statistical comparisons presented in Table 3.

Discussion

The rate of deep infection within 1 year following TKA is estimated to be 1% [15,16]. While low, this devastating complication subjects the patient to increased morbidity and mortality and often revision surgery. Given the low incidence of PJI following primary TKA, studies investigating the relationship between pre-operative ipsilateral intra-articular knee injections and postoperative PJI have been underpowered [7–9]. In the present study, a national database was used to obtain an adequate sample size to demonstrate a significant increase in postoperative PJI in patients who underwent ipsilateral knee injections within three months prior to TKA. There was no association between PJI and TKA in patients who had the injection more than three months prior to TKA.

Previous studies examining infection following arthroplasty and its association with pre-operative steroid injections have been insufficiently powered with high variability in the interval between injection and subsequent arthroplasty [7–9]. Given the potentially devastating consequences of PJI, determining this relationship is of high clinical importance. Three studies have reported that prior steroid injection was not associated with an increased risk of post-operative infection following TKA [7–9]. Joshy et al compared 32 patients with PJI following TKA and a control group of 32 non infected TKA patients in a retrospective matched cohort study and determined that there was no significant difference between the two groups [8]. Horne et al recently performed a similar retrospective case control study which compared 40 patients who developed post-operative wound infection or required revision surgery for infection, and 352 patients who underwent TKA without post-operative infection [7]. 32% of patients received steroid injections prior to surgery in the control group compared with 39% in the infected group. Average time of last injection prior to TKA in the study was 16 months, with a range of 1 month to 45 years. They determined that prior steroid injection was not associated with an increased risk of post-operative PJI ($P = 0.44$). Desai et al has performed the largest study investigating the effect of steroid injection on infection rates following TKA [9]. The group compared 90 knees that received injections with 180 knees that did not, and reported no cases of deep infection in either group. They did report 2 cases of superficial infection following injections given at 18 months prior to TKA and five cases in the control group. No correlation was determined between timing of injection and risk of infection, and they concluded that there was no association between prior injection and post-operative infection.

One prior study reported that steroid injections prior to TKA may be associated with an increased incidence of PJI [10]. Papavasiliou et al

Table 1
Cohort Characteristics.

	0–3 Months		3–6 Months		6–12 Months		Matched Controls		Statistical Analysis		
Total number	5313		8919		8008		13,650		*P*: 0–3 Month vs control	*P*: 3–6 Month vs control	*P*: 6–12 Month vs control
Demographics	n	(%)	n	(%)	n	(%)	n	(%)			
Female	3637	(68.5%)	6105	(68.5%)	5474	(68.4%)	9334	(68.4%)	0.936	0.926	0.982
Male	1676	(31.5%)	2814	(31.5%)	2534	(31.6%)	4316	(31.6%)			
Age < 65 years	517	(9.7%)	737	(8.3%)	655	(8.2%)	1243	(9.1%)	0.192	0.030	0.021
Age 65–69 years	1312	(24.7%)	2154	(24.1%)	1854	(23.2%)	3267	(23.9%)	0.280	0.721	0.197
Age 70–74 years	1326	(25.0%)	2289	(25.7%)	2196	(27.4%)	3545	(26.0%)	0.157	0.618	0.060
Age 75–79 years	1150	(21.6%)	1962	(22.0%)	1816	(22.7%)	2993	(21.9%)	0.688	0.912	0.205
Age 80–84 years	721	(13.6%)	1245	(14.0%)	1106	(13.8%)	1862	(13.6%)	0.917	0.511	0.741
Age ≥ 85 years	288	(5.4%)	532	(6.0%)	381	(4.8%)	739	(5.4%)	0.986	0.084	0.038
Comorbidities	n	(%)	n	(%)	n	(%)	n	(%)			
Obesity (BMI >30)	1258	(23.7%)	2003	(22.5%)	1807	(22.6%)	3118	(22.8%)	0.227	0.510	0.650
Smoking	678	(12.8%)	1062	(11.9%)	880	(11.0%)	1608	(11.8%)	0.066	0.789	0.082
Diabetes mellitus	2483	(46.7%)	4357	(48.9%)	4027	(50.3%)	6566	(48.1%)	0.093	0.277	0.002