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Complications - Infection

Increased Risk of Periprosthetic Joint Infections in Patients With Hypothyroidism Undergoing Total Joint Arthroplasty

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ABSTRACT

Background: Although thyroxine has an important role in modulating the immune system, it has not been associated with periprosthetic joint infection. This study was conceived to examine the association between hypothyroidism and periprosthetic joint infection (PIJ).
Methods: Using an institutional database, the preoperative comorbidities of 32,289 total joint arthroplasties performed between 2000 and 2013 were identified using an International Classification of Diseases, Ninth Revision–based comorbidity index.
Results: In the multivariate analysis, hypothyroidism was found to be an independent risk factor (adjusted odds ratio: 2.46; $P < .0001$). In addition, patients who developed PJI demonstrated higher thyroid-stimulating hormone levels than those without ($P = .04$).
Discussion: Surgeons should be aware of this increased risk of PJI in hypothyroid patients when risk stratifying, and future studies are needed to determine the potential role of thyroxine supplementation.

Despite the success of total joint arthroplasty (TJA), prosthetic joint infection (PJI) remains an infrequent but devastating complication of this procedure. PJI has a significant impact on the patient, with management often requiring multiple operations that may compromise the functional outcomes and health of the patients [1]. Furthermore, PJI places a large economic burden on the health care system [2]. With the rise in the number of TJA procedures being performed, particularly in the elderly, who may have underlying comorbidities, a higher number of PJI cases will be encountered [3]. Thus, it is paramount that every effort is made to minimize the risk of PJI. One successful strategy to minimize complications of TJA in general and PJI in particular is the medical optimization of patients before surgery [4-6]. With the goal of optimizing modifiable risk factors and improving patient selection through risk stratification, many studies have attempted to identify potential PJI risk factors based on comorbidities, number of previous surgeries, demographic variables, and other preoperative characteristics [7-15]. From these studies, many risk factors such as advanced age, malnutrition, coagulopathy, obesity, diabetes mellitus, cirrhosis, human immunodeficiency virus, and prior surgeries or history of infection have been determined to increase the risk of PJI [7,8,12].

Despite the many risk factors associated with PJI, hypothyroidism has not been implicated as an independent risk factor [7,8], despite being an independent marker for mortality [10]. Thyroid hormone is known to play a crucial role in affecting cell metabolism, and the immune system, including the modulation of cell-mediated immunity [16-18]. However, owing to the paucity of studies investigating hypothyroidism, a disorder associated with immune system dysfunction [18] and having a reported prevalence of 18% in the TKA population [7], the influence of thyroid dysfunction and its propensity toward the development of PJI remains unknown.

This study was conceived to examine whether there was an association between hypothyroidism and PJI. We were also interested to see if there were any differences in the organism profile of PJI among patients with and without hypothyroidism. We also examined the influence of the severity of the disease, as measured by the level of thyroid-stimulating hormone (TSH), on PJI.

Materials and Methods

After institutional review board approval, a retrospective study of 26,430 patients undergoing 32,693 TJAs between January 2000

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and January 2013 was performed. All patients who underwent primary or revision total knee or hip arthroplasty were included. Patients undergoing revision TJA for diagnosis of PJI at our institution without prior aseptic TJA were excluded. In instances where the patient had multiple joint reconstructions, each joint was considered as a separate case. After the aforementioned exclusion criteria, 32,289 TJAs were identified in 26,427 patients. Data from an institutional database, including the patient's preexisting comorbidities, including hypothyroidism, were assessed using the Elixhauser comorbidity index [19], an International Classification of Diseases, Ninth Revision–based system, followed by a manual review to confirm a medical history of preoperative hypothyroidism in the medical record. Among the cohort, 4008 TJAs were performed in patients with a history of hypothyroidism and 28,281 TJAs were performed in patients without hypothyroidism (Table 1). Using the institutional electronic database, the following variables were obtained: comorbidities, type of surgery (primary or revision), age, gender, ethnicity, and body mass index. In patients with both a primary and revision surgery occurring at our institution for the same joint, the joint was classified as a revision case.

The diagnosis of PJI was determined based on a cross-match with data from a prospective institutional database constructed from International Classification of Diseases, Ninth Revision codes 996.6, 996.66, 996.67, 998.5, and 998.59. From this query, each joint that underwent arthroplasty was classified as either infected or noninfected. A manual retrospective chart review was performed to confirm that surgery was performed for PJI and to obtain the microbiology profile from intraoperative cultures. In patients with hypothyroidism, TSH levels within 1 month before the index TJA surgery were recorded. TSH and free thyroxine levels were not routinely ordered before or during admission for TJA. A TSH threshold of 5 mIU/L was used to determine whether a patient was clinically euthyroid before surgery. Patient comorbidities were assessed separately using the Elixhauser comorbidity index, a method of quantifying overall health and predicting mortality. Atypical organisms were defined as organisms different than the 5 most common PJI organisms: *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, *Streptococcus species*, *Enterococcus species*, and gram-negative bacilli [20]. Resistant organisms were defined as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*.

Multiple logistic regression analyses were used to identify the predictors of PJI. The Fisher's exact test was used to compare differences in the antibiotic profile (gram positive, antibiotic-resistant organisms, and so forth) between the patients with and without hypothyroidism. Because of the skewed distribution, the Wilcoxon rank-sum test was used to evaluate differences in the TSH levels between those with and without PJI. All statistical analyses were performed with the use of R 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria) using the regression modeling strategies package for the logistic regression. An alpha level of 0.05 was used to determine statistical significance.

Table 1
Patient Demographics.

Demographic Variables	Count ± SD (% or Range)
Gender	
Females	18,252 (57)
Males	14,037 (43)
Age	63.98 ± 12.04 (11-99)
Ethnicity	
White	24,762 (77)
Black	3643 (11.3)
Asian	172 (0.5)
Hispanic	136 (0.4)
Native American/Eskimo	24 (0.07)
Other	3452 (10.7)
BMI	29.49 ± 5.52 (13.1-43.7)
Type of surgery	
TKA	14,577 (45.1)
THA	17,712 (54.9)
Primary	27,648 (85.6)
Revision	4641 (14.4)
Hypothyroidism	
Yes	4008 (12.4)
No	28,281 (87.6)

SD, standard deviation; BMI, body mass index; TKA, total knee arthroplasty; THA, total hip arthroplasty.

Results

Of the 4008 TJAs performed in patients with hypothyroidism, 135 joints developed PJI with an incidence of 3.4% (135 of 4008) compared with 1.4% (384 of 28,281) in patients without hypothyroidism (unadjusted odds ratio [OR]: 2.53) (Table 1). The adjusted OR was 2.46 (95% CI: 1.99-3.05) when controlling for potential confounders, including revisions and joint involvement (Table 2). There was no difference in the body mass index between those with and without hypothyroidism ($P = .71$). Although there was an increased risk of PJI in patients with hypothyroidism, there was no difference in the organism profile between patients with and without hypothyroidism with respect to gram-positive ($P = .60$), gram-negative ($P = .054$), and drug-resistant organisms ($P = .11$; Table 3).

Compared to other preoperative characteristics, hypothyroidism was demonstrated to be the seventh highest risk factor for

Table 2
Multivariate Logistic Regression Analysis of Independent Risk Factors for Periprosthetic Joint Infection.

Risk Factor	Odds Ratio	95% CI	*P* Value
Revision surgery	13.02	9.79-17.32	**<.0001**
AIDS	4.44	2.47-7.99	**<.0001**
Liver disease	2.92	1.66-5.14	**.0002**
Metastatic cancer	2.72	0.95-7.81	.0624
Lymphoma	2.58	0.83-7.99	.1001
Blood loss anemia	2.49	0.82-7.59	.1085
Hypothyroidism	2.46	1.99-3.05	**<.0001**
Weight loss	2.34	0.40-13.75	.3451
Renal failure	2.21	1.47-3.35	**.0002**
Deficiency anemia	1.76	0.86-3.63	.1244
Rheumatic and collagen vascular diseases	1.63	1.16-2.28	**.0050**
Peripheral vascular disease	1.59	0.68-3.68	.2827
Solid tumor without metastasis	1.57	0.73-3.38	.2504
Alcohol abuse	1.49	1.01-2.21	**.0447**
Diabetes without chronic complication	1.42	1.11-1.81	**.0058**
TKA	1.41	1.02-1.95	**.0363**
Congestive heart failure	1.28	0.90-1.82	.1643
Fluid and electrolyte disorders	1.21	0.66-2.22	.5378
Drug abuse	1.15	0.32-4.11	.8283
Depression	1.07	0.81-1.41	.6365
Hispanic ethnicity	1.03	0.36-2.94	.9495
Other neurologic disorders	1.02	0.62-1.65	.9476
Age	1.00	0.99-1.01	.7854
Body mass index	1.00	0.99-1.02	.7069
Valvular disease	1.00	0.69-1.46	.9903
Hypertension	0.96	0.78-1.17	.6596
Black ethnicity	0.93	0.70-1.23	.6081
Native American and Eskimo ethnicity	0.82	0.09-7.44	.8565
Paralysis	0.72	0.09-5.78	.7588
Coagulopathy	0.69	0.33-1.46	.3341
Asian ethnicity	0.38	0.05-2.80	.3402
Other ethnicity	0.00	$0.00\text{-}1.03 \times 10^{24}$	.8433
Pulmonary circulation disorders	0.00	$0.00\text{-}6.02 \times 10^{24}$	.9058
Peptic ulcer disease	0.00	$0.00\text{-}14.83 \times 10^{162}$	.9616

TKA, total knee arthroplasty.
Bold text represents statistically significant values.