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Surgical Approach to Total Hip Arthroplasty Affects the Organism Profile of Early Periprosthetic Joint Infections

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Background: The optimal approach for total hip arthroplasty (THA) remains hotly debated. While wound complications following the direct anterior approach are higher than with other approaches, the organism profile of periprosthetic joint infections (PJIs) by approach remains unknown. Our goal was to compare the organism profiles of PJIs following direct anterior and non-anterior THA.

Methods: We retrospectively reviewed 12,549 primary THAs (4,515 direct anterior and 8,034 non-anterior) that had been performed between January 2012 and September 2019 at a university-affiliated single-specialty orthopaedic hospital to identify patients with an early postoperative PJI. Criteria used for the diagnosis of a PJI were the National Healthcare Safety Network, which screens for PJI that occurs within 90 days of index arthroplasty, and the Musculoskeletal Infection Society guidelines. Patient demographic information and organism characteristics were recorded for analysis.

Results: We identified 84 patients (38 who underwent the direct anterior approach and 46 who underwent the non-anterior approach) with an early postoperative PJI following primary THA (0.67% total THA PJI rate, 0.84% direct anterior THA PJI rate, and 0.57% non-anterior THA PJI rate). The direct anterior THA cohort had a significantly lower body mass index and American Society of Anesthesiologists score than the non-anterior THA cohort (29.5 versus 35.2 kg/m^2, $p < 0.0001$; 2.29 versus 2.63, $p = 0.016$, respectively). Regarding organism profile, patients in the direct anterior THA cohort had significantly more monomicrobial gram-negative infections than the non-anterior THA cohort (4 versus 0, $p = 0.038$). We did not identify any demographic risk factors other than approach for gram-negative PJI. There were no significant differences in methicillin-resistant *Staphylococcus aureus,* methicillin-sensitive *Staphylococcus aureus,* coagulase-negative Staphylococcus, obligate anaerobes, polymicrobial, or PJIs due to other organisms by approach.

Conclusions: Direct anterior THA approaches have a greater risk of monomicrobial gram-negative PJI, likely due to the unique microbiome of the inguinal region. While targeted infection prophylaxis may reduce these infections, it is not entirely effective on its own. Future studies with larger sample sizes are required to help us develop more targeted perioperative infection prophylaxis.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

The optimal surgical approach for total hip arthroplasty (THA) is one of the most hotly debated topics in total joint arthroplasty (TJA) today[1-3]. The majority of THAs that are performed worldwide are done through either a posterior or lateral approach[4], but direct anterior approaches are gaining in popularity because of their marketability and a possible earlier functional recovery[5-9]. Unfortunately, there are a number of disadvantages with the direct anterior THA, one of which is an increased rate of wound complications and a higher risk of periprosthetic joint infection (PJI), especially in obese patients[10-15]. At our center, regardless of approach, prolonged wound drainage, superficial infections, and deep infections

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account for 55% of all THA complications[16]. Thus, there is substantial interest in identifying measures to prevent, detect, and treat wound complications following all variations of THA.

While relatively uncommon, a PJI is arguably the most devastating TJA complication. Despite developments in perioperative risk factor mitigation and infection prophylaxis, the incidence of PJI following THA still remains around 1%[17]. Importantly, the infecting pathogens impact treatment success following PJI. For example, gram-negative, methicillin-resistant *Staphylococcus aureus* (MRSA), and polymicrobial PJIs are negative predictors of treatment success[18-24]. The importance of understanding the specific organism profiles of each surgical procedure, as well as each surgical approach, is therefore paramount to successfully reducing the incidence and improving the treatment of PJIs.

Interestingly, to our knowledge, very few studies have evaluated the organism profiles of THA PJIs by approach. Ilchmann et al. found more gram-negative infections in anterior compared with lateral approach THAs, but this finding did not reach significance ($p = 0.26$)[10]. Achermann et al. noticed more *Cutibacterium* (formerly *Propionibacterium*) *avidum* infections after starting to perform more anterior-based THAs, but they attributed this finding to higher patient body mass index (BMI)[25]. Therefore, the purpose of our study was twofold. First, we sought to compare the organism profiles of THA PJIs by direct anterior and non-anterior approaches. Second, we wanted to compare the demographic and risk factor profiles of our patients with THA PJIs with direct anterior and non-anterior approaches. We hypothesized that direct anterior THAs would have a different organism profile than non-anterior THAs, and thus may require unique strategies to prevent PJI.

Materials and Methods

Direct anterior and non-anterior primary THA PJIs from a university-affiliated single-specialty orthopaedic hospital were retrospectively reviewed. Data from 12,549 patients who underwent primary THA from January 2012 to September 2019 were reviewed to identify cases of PJI that occurred within 90 days of the index arthroplasty. PJIs that occurred within 90 days were chosen because we believe that early infections are more likely related to approach, while late infections are more likely related to hematogenous spread. Infections were screened for with use of the Centers for Disease Control and Prevention National Healthcare Safety Network (NHSN) criteria[26], and PJIs were confirmed using the Musculoskeletal Infection Society (MSIS) criteria[27]. To ensure that we captured all of the patients with early PJIs from our institution who may have sought treatment at another institution, our 90-day follow-up of all 12,549 patients was cross-referenced with data from both the Medicare Bundled Payments for Care Improvement (BPCI) program and the Statewide Planning and Research Cooperative System (SPARCS) database for New York State.

Standard operating rooms with similar staffing and personnel were used for all of the primary THAs. Institutional policy required that all of the scrubbed personnel wore a surgical helmet and a body exhaust suit. Primary THAs were performed by 20 experienced orthopaedic surgeons. Surgical approach was chosen based on surgeon preference and expertise. All of the direct anterior approaches were performed through the interval described by Matta et al.[28]. The non-anterior THA cohort included patients who underwent posterior, northern, direct lateral, and anterolateral approaches, all in the lateral decubitus position. Any patient with a confirmed PJI following primary THA for a femoral neck fracture, conversion THA, or simultaneous bilateral THA was excluded.

Over the study period, several notable changes occurred at our institution. Importantly, all of the changes occurred with both the direct anterior and non-anterior THA cohorts. Prior to 2013, thromboembolic prophylaxis was surgeon-dependent, although most preferred low-molecular-weight heparin. From January 2013 through April 2014, robust institutional guidelines recommended low-molecular-weight heparin for prophylaxis, and from May 2014 onward, those guidelines recommended aspirin instead of low-molecular-weight heparin. For preoperative antimicrobial prophylaxis, all of the patients undergoing primary THA received expanded gram-negative antimicrobial prophylaxis (EGNAP)[29,30] with a gram-negative agent (1 dose of 2 g of aztreonam if the patient age was ≥75 years, the weight was ≥120 kg, or the creatinine clearance [CrCl] was <20 mL/min, or 3 to 5 mg/kg of gentamicin) and either 2 g of cefazolin for 24 hours, 1 preoperative dose of 15 to 20 mg/kg of vancomycin if MRSA-positive, or 1 preoperative dose of 900 mg of clindamycin if the patient was severely allergic to penicillin or cephalosporin for gram-positive coverage. Additionally, our institution began an intrawound vancomycin powder and dilute povidone-iodine lavage protocol (VIP) for high-risk patients undergoing THA in January 2014, as defined by Iorio et al.[31], and began using VIP for all patients undergoing THA in January 2016, regardless of preoperative risk[32]. Based on a separate analysis that we performed, the VIP did not affect the organism profile of our 90-day primary THA PJIs. Finally, patients who were positive for *S. aureus* underwent preoperative nasal decolonization with chlorhexidine wipes and povidone-iodine ointment to the nares. All preoperative surgical site preparation was performed using chlorhexidine scrub or povidone-iodine wash if the patient was allergic to chlorhexidine.

After confirmation of PJI, the patient age, sex, BMI, presence of diabetes mellitus (DM) or rheumatoid arthritis (RA), American Society of Anesthesiologists (ASA) classification, and organism characteristics were collected via electronic medical database query, followed by manual chart review for confirmation. The infecting organisms were identified and grouped after consultation with our infectious disease colleagues and infection control department. The incidence of the following organisms and organism groups was then compared by approach: methicillin-sensitive *S. aureus* (MSSA), MRSA, coagulase-negative Staphylococcus species, gram-negative species, obligate anaerobes, polymicrobial infections, culture-negative infections, and "other" infections. Since polymicrobial PJIs are known to lead to worse outcomes compared with monomicrobial PJIs[24], following the precedent set by Aggarwal et al.[33], individual organisms in the polymicrobial

TABLE I Patient Demographics of THA PJI by Approach*

Demographics	Anterior (N = 38)	Non-Anterior (N = 46)	P Value
Age† *(yr)*	63.0 ± 12.5	60.8 ± 8.4	0.357
Male sex	68.4%	52.2%	0.181
BMI† *(kg/m²)*	29.5 ± 5.5	35.2 ± 6.5	**<0.001**
DM	7.9%	19.6%	0.210
RA	0.0%	6.5%	0.248
ASA classification†	2.29 ± 0.6	2.63 ± 0.6	**0.016**

*THA = total hip arthroplasty, PJI = periprosthetic joint infection, BMI = body mass index, DM = diabetes mellitus, RA = rheumatoid arthritis, and ASA = American Society of Anesthesiologists. Boldface indicates p values that reached significance. †The values are given as the mean and standard deviation.

category were excluded from grouping in any of the other categories. Additionally, none of the monomicrobial infections belonged to >1 category. Only organisms that were identified before or during the first revision for infection after primary THA, and not during any subsequent revision surgeries, were included in our analysis.

Statistical analyses were performed using GraphPad Prism version 8.3.0 (GraphPad Software). The demographics of patients with direct anterior and non-anterior THAs were compared using Fisher exact tests and t tests for categorial and numerical variables, respectively. The organism types were compared using Fisher exact tests. Significance was set at $p < 0.05$.

The present study was exempt from human-subjects review by our institutional review board as part of our institutional quality improvement program.

Results

In total, we identified 84 patients with an early PJI following primary THA as defined by the NHSN and MSIS criteria[26,27]. Our overall primary THA PJI rate from January 2012 to September 2019 was 0.67% (84 of 12,549). Our direct anterior THA PJI rate was 0.84% (38 of 4,515) and our non-anterior THA PJI rate was 0.57% (46 of 8,034). Demographic data for the 2 PJI cohorts are listed in Table I.

On average, patients who underwent direct anterior THA complicated by PJI had significantly lower BMI and ASA scores than the non-anterior THA PJI cohort (29.5 versus 35.2 kg/m², $p < 0.001$; 2.29 versus 2.63, $p = 0.016$, respectively). While the direct anterior cohort had more men, fewer patients with DM, and fewer patients with RA, these trends did not reach significance ($p = 0.181$, $p = 0.210$, and $p = 0.248$, respectively).

Importantly, analysis of organism profile by THA approach demonstrated that the direct anterior THA cohort had significantly more monomicrobial gram-negative infections than the non-anterior THA cohort (4 versus 0, $p = 0.038$) (Table II). Monomicrobial gram-negative infections included 2 cases of *Enterobacter cloacae,* 1 case of *Klebsiella aerogenes,* and 1 case of *Citrobacter koseri.* Only 1 of the 4 gram-negative THA PJIs occurred after starting the VIP protocol in all of the THAs that were performed from 2016 onward. Further demographic analyses comparing these 4 patients with those without monomicrobial or polymicrobial gram-negative growth revealed no significant differences or trends toward differences with sex, age, BMI, DM, RA, or ASA class. Additionally, none of these 4 patients were immunocompromised, were on chronic corticosteroids, or had any other documented gram-negative infection within the year prior to their THA.

Of the polymicrobial infections in the direct anterior THA cohort, 3 (60%) of the 5 patients had at least 1 gram-negative species, and 2 (40%) of the 5 patients had at least 1 Enterococcus species. Of the non-anterior THA cohort, only 2 (22%) of the 9 patients with polymicrobial infection had a gram-negative species, and 4 (44%) of the 9 patients had an Enterococcus species. The number of polymicrobial infections with gram-negative growth did not significantly differ by approach (60% versus 22%, $p = 0.266$). Individual organisms for each polymicrobial PJI are listed in Table III.

No significant differences were found by approach for monomicrobial MRSA, MSSA, coagulase-negative Staphylococcus, culture-negative, obligate anaerobic, polymicrobial, or "other" infections. The 6 cases of monomicrobial "other" infections in the direct anterior cohort included 4 cases of *Streptococcus agalactiae,* 1 case of *Streptococcus mitis,* and 1 case of *Streptococcus sanguinis.* The 6 cases of monomicrobial "other" infections in the non-anterior cohort included 6 cases of *S. agalactiae.* No vancomycin-intermediate or resistant *S. aureus,* vancomycin-resistant Enterococcus, acid-fast bacteria, or fungal infections were identified in either cohort.

Discussion

At our institution in 2019, Aggarwal et al. demonstrated that patients undergoing direct anterior THA are 2.2 times more likely to develop a PJI compared with patients

TABLE II Infecting Organisms of THA PJI by Approach*

Organism	Anterior (N = 38)	Non-Anterior (N = 46)	P Value
MRSA	4 (10.5%)	5 (10.9%)	>0.999
MSSA	15 (39.5%)	20 (43.5%)	0.825
Coagulase-negative	4 (10.5%)	3 (6.5%)	0.696
Gram-negative	4 (10.5%)	0 (0.0%)	**0.038**
Culture-negative	0 (0.0%)	2 (4.3%)	0.499
Polymicrobial	5 (13.2%)	9 (19.6%)	0.560
Obligate anaerobe	0 (0.0%)	1 (2.2%)	>0.999
Other	6 (15.8%)	6 (13.0%)	0.762

*THA = total hip arthroplasty, PJI = periprosthetic joint infection, MRSA = methicillin-resistant *Staphylococcus aureus,* and MSSA = methicillin-sensitive *S. aureus*. Boldface indicates p values that reached significance.

TABLE III Infecting Organisms of Polymicrobial THA PJI*

Approach	Organism
Anterior (n = 5)	
Case 1	*Streptococcus agalactiae, Peptostreptococcus asaccharolyticus*
Case 2	*Pseudomonas aeruginosa*†, *Enterococcus faecalis,* Corynebacterium species
Case 3	*Pseudomonas aeruginosa*†, *Enterococcus faecalis*
Case 4	MRSA, *Pseudomonas aeruginosa*†
Case 5	MSSA, *Cutibacterium acnes*
Non-anterior (n = 9)	
Case 1	MSSA, MRSE†, *Enterococcus gallinarum*
Case 2	*Finegoldia magna*§, *Enterococcus faecalis, Staphylococcus lugdunensis, Streptococcus agalactiae*
Case 3	MSSA, Corynebacterium species
Case 4	MSSA, *Streptococcus agalactiae*
Case 5	MSSE‡, *Pseudomonas aeruginosa*†
Case 6	*Pseudomonas aeruginosa*†, *Providencia stuartii*†, *Enterococcus faecalis*
Case 7	MSSA, Corynebacterium species
Case 8	MRSE‡, *Enterococcus faecalis*
Case 9	MRSE‡, *Propionibacterium granulosum*

*THA = total hip arthroscopy, PJI = periprosthetic joint infection, MRSA = methicillin-resistant *Staphylococcus aureus,* MSSA = methicillin-sensitive *Staphylococcus aureus,* MRSE = methicillin-resistant *Staphylococcus epidermidis,* and MSSE = methicillin-sensitive *Staphylococcus epidermidis*. †Denotes gram-negative organism. ‡Denotes coagulase-negative Staphylococcus. §Denotes obligate anaerobe.

undergoing non-anterior THA (odds ratio: 2.2, 95% confidence interval = 1.1 to 3.9, p = 0.006; infection rate: 1.22% direct anterior versus 0.63% non-anterior, p = 0.023)[13]. As a follow-up to that paper, the present study demonstrates that direct anterior and non-anterior approach THA PJIs have different organism profiles, which has important implications for infection prevention and treatment. Specifically, there were significantly more monomicrobial gram-negative PJIs with direct anterior THAs compared with non-anterior THAs (4 versus 0, p = 0.038). Furthermore, there was a trend toward more polymicrobial PJIs with gram-negative growth following direct anterior THAs compared with non-anterior THAs, but this finding did not reach significance (60% versus 22%, p = 0.266). Patients who had PJIs after undergoing direct anterior THA had a significantly lower BMI (29.5 versus 35.2 kg/m^2, p < 0.001) and were of a significantly lower ASA class (2.29 versus 2.63, p = 0.016) compared with non-anterior THA PJIs.

Our findings of more gram-negative infections in the direct anterior cohort is novel but not surprising. It is well-described that humans have location-specific microbial colonization based on a number of factors, including skin folds and proximity to the genitourinary and gastrointestinal tracts[34]. Importantly, these differing microbiomes have been shown to cause location-specific surgical site infections. For example, Aboltins et al. reported that gram-negative infections are more common in the hip than in the knee[35], which authors such as Tande and Patel believe reflects the influence of the body's natural flora on inoculating skin incisions[36-39]. The upper-extremity literature suggests that the skin microbiome of the shoulder leads to high rates of *Cutibacterium acnes* after total shoulder arthroplasty and shoulder arthroscopy[40-42]. In spine surgery, lumbosacral operations appear to have the highest rate of gram-negative surgical site infections, a finding attributed to the lumbosacral area's proximity to fecal and urinary flora[43]. Lastly, in the vascular literature, it appears that groin-based incisions for graft placement have higher infection rates and may be more susceptible to graft colonization with gram-negative species[44,45].

While it is believed that most gram-negative PJIs are due to urinary tract infection-related bacteremia and urosepsis[20], numerous authors report that the genitourinary tract, the gastrointestinal tract, and the inguinal fold harbor gram-negative species that can lead to surgical site infections[29,35-39]. Thus, the significantly greater incidence of early monomicrobial gram-negative PJIs in our direct anterior approach cohort supports the notion that surgical site affects the organism profile of PJIs. Additionally, since a lower BMI and lower ASA class do not appear to be associated with gram-negative infections, approach appeared to be the only risk factor for gram-negative THA PJI.

In response to an increase in gram-negative THA PJIs, our institution began using EGNAP for THA in 2012[29]. Bosco et al. found that the introduction of EGNAP significantly decreased the overall THA PJI incidence as well as the incidence of monomicrobial gram-negative THA PJIs[30]. Furthermore, Aggarwal et al. reported that using EGNAP and VIP together led to a large decrease in direct anterior THA PJI and a moderate decrease in non-anterior THA PJI[13]. They hypothesized that the use of EGNAP was particularly effective at decreasing direct anterior THA PJI rates due to its higher risk of gram-negative infections.

In the current study, all of the monomicrobial gram-negative infections in the direct anterior THA cohort occurred after the introduction of EGNAP, although only 1 of the 4 infections occurred after the introduction of VIP in 2016 to all patients undergoing THA. Clearly, there is more to be learned regarding the prophylaxis of gram-negative PJI. These data have our institution considering additional measures to eliminate gram-negative PJI regardless of surgical approach. One possible intervention is the use of >1 dose of gram-negative antimicrobial prophylaxis, similar to the use of cefazolin for up to 24 hours after an incision, based on the Surgical Care Improvement Project guidelines[46,47]. Additionally, there may be some utility to culturing and decolonizing the inguinal fold prior to surgery, similar to the way we preoperatively decolonize the nares of MRSA. Despite the small number of early monomicrobial gram-negative THA PJIs reported in this series, we believe that both EGNAP and VIP play a role in reducing THA

PJI, especially with THA that is performed using a direct anterior approach.

Importantly, while there was no significant difference in polymicrobial infection rates in our study or the study by Ilchmann et al.[10], 22% of our non-anterior THA approach patients with polymicrobial PJIs had at least 1 gram-negative species. In contrast, 60% of our polymicrobial direct anterior THA PJIs had at least 1 gram-negative species. While these numbers still seem to favor more gram-negative species in the direct anterior THA cohort, it does suggest that there remains a nonzero chance that non-anterior approaches are at risk for gram-negative infections and thus may similarly benefit from EGNAP and VIP.

Limitations

There are several limitations to this study. Most importantly, these data are from a single institution and, despite having performed nearly 13,000 THAs during the study period, due to our low infection rate, our PJI sample size was small. As a result, while there were significantly fewer gram-negative infections in our non-anterior THA cohort, larger multicenter trials could be performed to confirm our findings. Additionally, patient data from 20 different surgeons were included; thus, differing surgical techniques and experience could have impacted our findings. Importantly, having multiple surgeons is also beneficial since this may improve the general applicability of our findings; all of the institutional protocols were developed with input from these surgeons, and all of the surgeons were required to follow the same institutional protocols for TJA, allowing for a uniform data set. Since all of the patients in this study were treated in a major metropolitan area with its own bacterial profile, the findings may not be generalizable to other locales. This is especially important given that PJI organism profiles are known to differ geographically[33]. Finally, we do not know the percentage of patients who had postoperative follow-up; thus, it is possible that some early THA PJIs were missed. Despite the limitations of this study, we will continue to identify the organism profiles of different orthopaedic surgical site infections and work to improve our perioperative infection prophylaxis.

Conclusions

THA PJI organism profiles differ based on surgical approach. We found that direct anterior THA approaches were associated with more gram-negative infections compared with non-anterior THA approaches. While EGNAP and VIP may help reduce THA PJI after direct anterior THA, they are not effective on their own, and other infection prophylaxis measures must be considered. Future studies with larger sample sizes that help define the organism profiles of PJI after THA will allow us to further tailor our perioperative infection prophylaxis. ■

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