Original Article

Increased antibiotic duration improves reoperation free survival after total hip arthroplasty irrigation and debridement

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ABSTRACT

Background: We aimed to determine if reoperation-free survival following irrigation and debridement (I&D) with head and liner exchange of infected primary THA is affected by: 1) postoperative antibiotic duration; 2) patient characteristics; 3) infecting organism; or 4) postoperative versus hematogenous infection.

Methods: Revision THAs from 2006 to 2012 (n = 1184) were observed; 26 underwent I&D with head and liner exchange with mean 4.1-year follow-up. Patients with reoperation for infection (n = 2) versus those without reoperation (n = 24) were analyzed.

Results: Increased postoperative antibiotic therapy duration (p = 0.0333) decreased risk of reoperation for infection.

Conclusion: Chronic antibiotic suppression should be considered following THA I&D with head and liner exchange.

1. Introduction

Numbers of total hip arthroplasty (THA) revisions are projected to increase at a rate more than double that of primary THA.¹ Periprosthetic joint infection (PJI) may result in amputation or mortality and is among the most common indications for THA revision. The cost of PJI to the healthcare system is significant, and estimated to surpass 1.62 billion dollars annually by 2020.² Thus, efforts to increase survivorship following THA revision for PJI are essential.

Irrigation and debridement (I&D) with modular component exchange for the treatment of acute PJI has a success rate of 40–50%.^{3–6} It is generally accepted that more severe infections require longer duration of antibiotic therapy. However, the optimal duration of postoperative antibiotic therapy following I&D with modular component exchange has not yet been established.⁷ Similarly, other predictors of success following THA I&D with head and liner exchange are unclear. Previous investigations of I&D for PJI have included both hips and knees in their cohort, as well as infection following both primary and revision arthroplasties.^{3,8} The conclusions of these studies are confounded by the differing propensities for infection in hip versus knee and primary versus revision arthroplasty.⁹

The aims of our study were to determine if reoperation-free survival

following I&D with head and liner exchange of an acutely infected primary THA is affected by: 1) postoperative antibiotic duration; 2) patient characteristics or surgical factors; 3) infecting organism; or 4) whether the infection was postoperative versus hematogenous.

2. Methods

2.1. Study design

We utilized a retrospective cohort study design. The source population included all patients who underwent revision THA at a single high-volume orthopaedic tertiary referral center from 2006 to 2012 (n = 1184). Inclusion criterion was I&D with head and liner exchange performed for acute PJI (less than 4 weeks of symptoms) following primary THA. PJI was diagnosed using Musculoskeletal Infection Society (MSIS) criteria.¹⁰ Exclusion criteria were treatment for PJI of the same hip prior to I&D with liner exchange, as well as surgery performed less than 2 years prior to the end of the follow-up period. The two cohorts analyzed within the remaining patients (n = 26) were those who required reoperation for infection recurrence (n = 2) versus those who did not (n = 24) (Fig. 1). 12 surgeons fellowship-trained in adult reconstruction performed the cases at a single hospital. The Institutional Review Board at our institution approved this study.

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Fig. 1. Flowchart for identifying all THA I&D with head and liner exchange procedures from 2006 to 2012 and the cohorts analyzed.

After THA I&D with head and liner exchange, all patients were treated with 6 weeks of intravenous antibiotics, followed by a course of oral antibiotics of varying duration. Type and duration of antibiotic therapy were determined by the infectious disease consult service at our institution.

The main study endpoint was reoperation for infection recurrence, as defined by MSIS criteria. Patients revised for any other reason, and those who were not revised, were censored at the end of the follow-up period. The mean durations of clinical follow-up were as follows: 4.1 years (range 0.4–7.7 years) for the entire patient cohort; 1.5 years (range 0.4–6 years) for patients who required reoperation for infection recurrence; and 4.4 years (range 2.0–7.7 years) for patients who did not require reoperation. Though minimum 2-year follow-up was available for all patients, study follow-up of less than 2 years duration was due to reoperation for infection occurring within 2 years of THA I&D with head and liner exchange.

Infecting organism, duration of postoperative antibiotic therapy, reoperation (if any), patient demographics, co-morbidities, and surgical factors were determined by systematic retrospective chart review. All data were recorded on a form standardized for this study.

2.2. Statistical analysis

Fisher's exact test and one-way ANOVA were utilized to compare patient demographics, comorbidities, and surgical factors between the group that required reoperation for recurrent infection and the group that did not. Multivariate survival analysis using Cox regression was built to examine the association between duration of antibiotic therapy and reoperation-free survival. Surgeon random effect was controlled in the Cox model. Standardized differences were calculated to measure the infection recurrence effect size between two groups of infecting organisms. Two groups with an absolute value of standardized difference score greater than 0.1 are considered different. Effect size increases as the standardized difference score approaches 1.0.¹¹ Multivariate Cox regression was used to compare acute postoperative infection (within 4 weeks of primary THA) and acute hematogenous infection (more than 4 weeks after primary THA), controlling for total count of patient comorbidities. Data manipulation and statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc.; Cary, NC).

3. Results

Demographics and distribution of patients within each cohort, and univariate analysis across covariates, are provided in Table 1. Following THA I&D with head and liner exchange, 92.3% of patients remained reoperation-free at mean duration of follow-up of 4.1 years.

Results of the regression model are given in Table 2. Increased duration of postoperative antibiotic therapy (HR 0.997, 95% CI 0.993–0.999, $p = 0.0333$) following THA I&D with head and liner exchange decreased the risk of reoperation for infection. Comorbidities were not associated with risk of reoperation for infection ($p = 0.9159$).

Based on standardized difference scores, the likelihood of reoperation for infection recurrence following THA I&D with head and liner exchange varied with infecting organism (Table 3). The incidence of infection recurrence was highest with non *S. aureus staphylococcal* species, followed by methicillin sensitive *S. aureus* (MSSA). Culture negative and Gram negative organisms had a lower incidence of infection recurrence than other organisms, while non *staphylococcal* Gram positive organisms had the lowest incidence of infection recurrence.

Multivariate analysis did not demonstrate a difference in reoperation-free survival between acute postoperative and acute hematogenous THA infections treated with I&D plus head and liner exchange ($p = 0.7437$).

4. Discussion

Successful treatment of acute PJI following THA is critical to minimizing morbidity, mortality, and cost. The optimal duration of postoperative antibiotic therapy following I&D with modular component exchange is unknown.⁷ Similarly, other predictors of success after THA I&D with head and liner exchange have not been elucidated. Our study aims were to determine if postoperative antibiotic duration, patient/surgical factors, infecting organism, or timing of infection onset affect reoperation-free survival following I&D with head and liner exchange of an acutely infected primary THA. Prior studies with similar aims have been confounded by mixed patient cohorts of hip, knee, primary, and revision arthroplasties, each with different propensities for infection.^{3,7,8}

While our study may provide information helpful in selecting appropriate candidates for THA I&D with head and liner exchange and managing

Table 1

Univariate analysis across covariates among patients who underwent THA I&D with head and liner exchange.

	All Patients (n = 26)	Reoperation for Infection (n = 2)	Reoperation Free (n = 24)	p-value
Age (Mean, SD)	61.7 (10.7)	73 (9.9)	60.8 (10.4)	0.1231
BMI (Mean, SD)	30.4 (7.6)	25.1 (2.9)	31 (7.8)	0.5714
Preoperative CRP (mg/L) (Mean, SD)	186.9 (147.3)	177.6 (155)	185.8 (153.9)	0.9202
Weeks of antibiotic use (Mean, SD)	93.9 (111.7)	64.2 (66.8)	96.4 (115.3)	0.8639
Infecting organism				0.4154
Non <i>S. aureus</i>	20 (76.9)	1 (50)	19 (79.2)	
<i>S. aureus</i>	6 (23.1)	1 (50)	5 (20.8)	
Cells per high-powered field				0.2220
≤ 15	13 (50)	2 (100)	11 (45.8)	
> 15	13 (50)	0 (0)	13 (54.2)	
Tissue pathology				0.1108
Chronic inflammation	17 (65.4)	0 (0)	17 (70.8)	
Not recorded	9 (34.6)	2 (100)	7 (29.2)	
Smoker				0.4800
Yes	13 (50)	0 (0)	13 (54.2)	
No	13 (50)	2 (100)	11 (45.8)	
Alcohol use				1.0000
Yes	14 (53.9)	1 (50)	13 (54.2)	
No	12 (46.2)	1 (50)	11 (45.8)	
Hypertension				1.0000
Yes	13 (50)	1 (50)	12 (50)	
No	13 (50)	1 (50)	12 (50)	
Hypercholesterolemia				0.5292
Yes	8 (30.8)	1 (50)	7 (29.2)	
No	18 (69.2)	1 (50)	17 (70.8)	
Diabetes				1.0000
Yes	5 (19.2)	0 (0)	5 (20.8)	
No	21 (80.8)	2 (100)	19 (79.2)	
Coronary artery disease				0.2215
Yes	3 (11.5)	1 (50)	2 (8.3)	
No	23 (88.5)	1 (50)	22 (91.7)	
History of malignancy				1.0000
Yes	3 (11.5)	0 (0)	3 (12.5)	
No	23 (88.5)	2 (100)	21 (87.5)	
Renal insufficiency				1.0000
Yes	2 (7.7)	0 (0)	2 (8.3)	
No	24 (92.3)	2 (100)	22 (91.7)	
COPD				NA
Yes	0 (0)	0 (0)	0 (0)	
No	26 (100)	2 (100)	24 (00)	

Table 2

Multivariate analysis of risk of reoperation for infection following THA I&D with head and liner exchange.

Predictors	Hazard Ratio	95% CI	p-value
Weeks of antibiotic use	0.997	0.993–0.999	0.0333
Presence of comorbidity	1.017	0.723–1.430	0.9159

them postoperatively, we understand our work has limitations. Given our limited sample size, our study may be vulnerable to type II error. The generalizability of our findings may be hampered by characteristics unique to our study population. In addition, the retrospective study design is inherently restricted by the accuracy of patient records available.

We found 92.3% of patients were reoperation-free after THA I&D with head and liner exchange at mean 4.1 year follow-up. While this

Table 3

Standardized difference scores for reoperation for infection between one infecting organism versus all others. Organisms are listed in order of highest to lowest incidence of reoperation for infection.

Infecting Organism	Standardized Difference Score
Non <i>S. aureus</i> staphylococcal species	0.7979
Methicillin-sensitive <i>S. aureus</i>	0.3962
Culture negative	−0.426
Gram negative	−0.458
Non staphylococcal gram positive	−0.535

*Positive values denote higher incidence of reoperation for infection, while negative values denote lower incidence of reoperation for infection.

success rate is higher than that observed in early studies for I&D with component retention,^{3–6} recent literature reports success rates from 88% to 90%.^{12,13} Newer antibiotic regimens, increased duration of therapy, and inclusion of patients on chronic suppression in the definition of success may all contribute to higher success rates over time.

Our data suggest reoperation-free survival following THA I&D with head and liner exchange improves with longer antibiotic duration. Thus, chronic antibiotic suppression should be considered in all patients following THA I&D with head and liner exchange. However, elderly patients without significant medical co-morbidities are best suited to chronic suppression as antibiotic duration and side effects are minimized in this population.

With our available numbers, we did not find comorbidities were associated with risk of reoperation for infection following THA I&D with head and liner exchange.

We found that identity of the infecting organism affected incidence of reoperation for infection recurrence following THA I&D with head and liner exchange. Infecting organisms in order of highest to lowest incidence of infection recurrence were: non *S. aureus* staphylococcal species, MSSA, culture negative infections, Gram negative organisms, and non staphylococcal Gram positive organisms. Other studies have also established MSSA as a virulent organism in PJI.¹⁴ Gram negative organisms have significant systemic virulence, and culture negative infections make selection of antibiotic therapy difficult. Though counterintuitive, our finding that culture negative and Gram negative infections had favorable outcomes after THA I&D with head and liner exchange is supported by multiple studies.^{3,15–17}

With the numbers available, our data suggest I&D with head and liner exchange is equally successful in eradicating acute postoperative and acute hematogenous infections following primary THA. Fehring et al. also reported that the rate of infection eradication for early postoperative infection¹⁸ was no different than that observed at other time points.¹⁴

Future work includes a multicenter study of acutely infected primary THA treated with I&D with head and liner exchange to increase the sample size of the current study and confirm the generalizability of our findings. Subsequent prospective investigation may further reinforce and expand our findings.

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