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AAHKS Award Paper

The Lawrence D. Dorr Surgical Techniques & Technologies Award: Aseptic Reoperations Within One Year of Primary Total Hip Arthroplasty Markedly Increase the Risk of Later Periprosthetic Joint Infection



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ABSTRACT

Background: Despite the success of primary total hip arthroplasties (THAs), some patients will require an aseptic reoperation within 1 year of the index THA. The goal of this study is to evaluate the risk of subsequent periprosthetic joint infection (PJI) in patients undergoing an aseptic reoperation within 1 year of a primary THA.

Methods: A retrospective review utilizing our institutional joint registry identified 211 primary THAs requiring aseptic reoperation within 1 year following index arthroplasty. A control group of 15,357 primary THAs not requiring reoperation within 1 year was identified. Patients were divided into groups based on time from primary THA to reoperation: (1) within 90 days ($n = 112$ THAs; 40% for dislocation, 34% for periprosthetic fracture) or (2) 91–365 days ($n = 99$ THAs; 37% for dislocation, 29% for periprosthetic fracture). Mean follow-up was 7 years.

Results: Patients undergoing an aseptic reoperation within 90 days had a PJI rate of 4.8% at 2 years, while the 91–365 day group had a PJI rate of 3.2% at 2 years. The control group had a PJI rate of 0.2% at 2 years. Employing a multivariate analysis, reoperation within 90 days of index arthroplasty had an elevated risk of PJI (hazard ratio 8, $P < .001$) as did a reoperation between 91 and 365 days (hazard ratio 13, $P < .001$).

Conclusion: Aseptic reoperations within 1 year following primary THA resulted in an 8- to 13-fold increased risk of subsequent PJI. The risk was similar whether the aseptic reoperation was early (within 90 days) or later (91–365 days).

Level of Evidence: Level III (Prognostic).

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Primary total hip arthroplasty (THA) has been appropriately deemed “the operation of the century” [1,2]. Despite its success, periprosthetic joint infections (PJIs) continue to plague approximately 1%-2% of patients at a cost of approximately \$90,000 per THA PJI [3–7]. More importantly, PJI has been associated with a

350% increased risk of mortality, afflicting 65% of patients by 10 years after PJI [8,9]. It is therefore useful to better define patients who may be at risk for a PJI following primary THA in order to mitigate the risk.

Several studies have identified risk factors for THA PJI and subsequent treatment success [6,10–17]. Unfortunately, despite interest in patient optimization, rates have not substantially improved, and the prevalence will likely only increase as more THAs are performed [4,18]. Some data have indicated that prolonged wound drainage is associated with increased risk of PJI [13,19,20]. Similarly, papers have indicated that early nonelective reoperations for dislocations or periprosthetic fractures have PJI rates between 10% and 33% [21,22]. Consequently, avoiding an early reoperation for aseptic reasons may decrease later PJI rates. However, the data are limited to small series.

Investigation was performed at the Mayo Clinic, Rochester, MN

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The primary purpose of the current study is to determine if there is an elevated risk of PJI for those patients who required an early (within 1 year of primary THA) aseptic reoperation. Secondary outcomes included the rates of aseptic re-revisions, and mortality for those requiring an early aseptic reoperation.

Patients and Methods

After Institutional Review Board approval was obtained, we performed a retrospective review of our institution's total joint registry on all adult patients undergoing a primary THA from 2000 to 2015. All septic reoperations and revisions occurring within the first year for a superficial or deep infection were intentionally excluded. Likewise, patients were excluded if they had a reoperation for persistent wound drainage because that is a known high-risk group [19,20] and distinguishing those cases from early infection can be difficult. Patients were included if they had a previous well-healing wound and sustained an acute event causing wound dehiscence necessitating reoperation. Finally, closed procedures (ie, reduction of a dislocated hip) were excluded.

Patients were then divided into 3 groups: (1) aseptic reoperation within the first 90 days following index primary THA (112 cases), (2) aseptic reoperation between 91 and 365 days following index primary THA (99 THAs), and (3) no reoperations within the first year (15,357 THAs). Thus, in summary, there were 211 patients (211 THAs) with an aseptic reoperation within 1 year. The mean age at index primary THA for the entire group was 65 years (range 18–106). Within 2 years of the aseptic reoperation (groups 1 and 2) or within 2 years of the index primary THA (group 3), 319 patients died, 64 patients were revised, and 175 were lost to follow-up. The mean follow-up for the remaining patients was 7 years for group 1, 6 years for group 2, and 7 years for group 3 (Table 1).

Clinical and radiographic follow-up was routinely performed at 3 months, 1 year, 2 years, 5 years, and every 5 years thereafter. If patients were unable to return for clinical or radiographic follow-up, a questionnaire was mailed for review and patients were requested to send their most current hip radiographs.

The 3 most common indications for an aseptic reoperation following primary THA within the first 90 days were dislocation (45; 40%), periprosthetic fracture (38; 34%), and closed hematoma or seroma (9; 8%) (Table 2). The 3 most common indications for reoperation between 91 and 365 days were dislocation (37; 37%), periprosthetic fracture (29; 29%), and aseptic loosening (14; 14%).

Table 1
Demographics of Study Cohort.

Variable	Days From Primary THA to First Reoperation		
	≤90 d (n = 112)	91–365 d (n = 99)	No Reoperation in the First Year (n = 15,357)
Age at THA, mean (SD)	65.8 (14.8)	64.3 (13.7)	65.1 (14.1)
Age at reoperation, mean (SD)	65.8 (14.8)	65.0 (13.7)	66.1 (14.1)
Gender, n (%)			
Female	65 (58.0)	65 (65.7)	8036 (52.3)
Male	47 (42.0)	34 (34.3)	7321 (47.7)
BMI (kg/m ²), mean (SD)	30.8 (8.2)	29.3 (5.3)	29.5 (6.3)
Charlson Index, mean (SD)	1.7 (2.4)	1.2 (2.0)	1.0 (1.7)
Primary osteoarthritis (%)	64.3	66.7	78.1
Death within 2 y	8	5	306
Lost to follow-up before 2 y	12	10	153
Follow-up, mean (y)	6.8	5.5	7.3

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

Table 2

Indications for Early Aseptic Reoperation Following Primary Total Hip Arthroplasty.

Reason for Reoperation, n (%)	Days From THA to First Reoperation	
	≤90 d (n = 112)	91–365 d (n = 99)
Dislocation	45 (40.2)	37 (37.4)
Periprosthetic fracture	38 (33.9)	29 (29.3)
Hematoma/seroma/effusion	9 (8.0)	1 (1.0)
Aseptic loosening	2 (1.8)	14 (14.1)
Insert dissociation or fracture	3 (2.7)	3 (3.0)
Wound dehiscence	7 (6.3)	
Sciatic nerve injury		1 (1.0)
Other	8 (7.1)	14 (14.2)

THA, total hip arthroplasty.

Statistical Analysis

The data are reported using summary statistics, including means and standard deviations for continuous variables, and counts and percentages for categorical variables. The group of patients with reoperations within 1 year of primary THA was followed starting at their reoperation date until developing a PJI, having an aseptic revision, death, or last follow-up date. Patients without a reoperation within the first year after index surgery were followed starting at 1 year after primary THA until PJI, aseptic revision, death, or last follow-up date. Because PJI was the endpoint of interest, the cumulative incidence of PJI was calculated with competing risks of both other aseptic revisions and death. In addition, risk of PJI, aseptic revision, and mortality were calculated using Kaplan-Meier estimates and reported with 95% confidence intervals (CIs). Hazard ratios (HRs) were estimated using Cox proportional hazard models, treating PJI as the event of interest and censoring at aseptic revision, death, or last follow-up. Other potential risk factors for PJI included age, gender, body mass index (BMI), a diagnosis other than osteoarthritis (OA), and Charlson Comorbidity Index (CCI). Risk factors were assessed individually and in a multivariate model. All statistical tests were 2-sided and *P*-values less than .05 were considered statistically significant.

Results

Reoperation at 90 Days or Less

Patients undergoing an aseptic reoperation within the first 90 days had a PJI rate of 4.8% at 2 years and a PJI rate of 6% at 5 years (Fig. 1). In addition, the risk of an aseptic re-revision in this cohort within 5 years following an index aseptic reoperation within the first 90 days was increased at 12.4% (Table 3).

Reoperation Between 91 and 365 Days

Patients undergoing an aseptic reoperation between 91 and 365 days had a PJI rate of 3.2% at 2 years and a PJI rate of 6.6% at 5 years. In addition, the risk of an aseptic re-revision in this cohort at 5 years following an index aseptic reoperation between 91 and 365 days was 13.3% (Fig. 2).

No Reoperation Within the First Year

Patients not requiring an aseptic reoperation within the first year had a PJI rate at 2 and 5 years of 0.2% and 0.4%, respectively. The frequency of an aseptic revision in this cohort at 5 years was 1.7%.

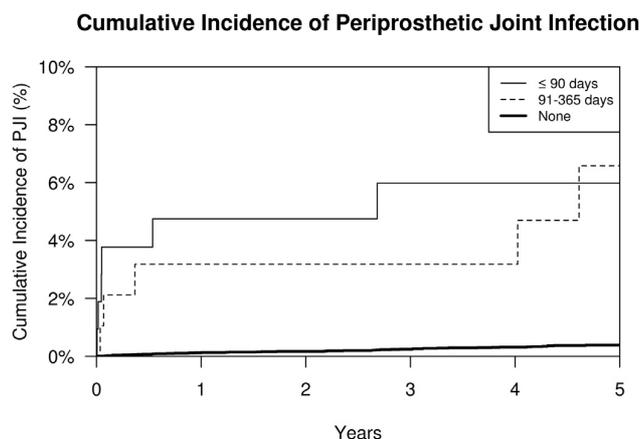


Fig. 1. Cumulative incidence of periprosthetic joint infection over time for patients requiring an early aseptic reoperation, as well as those who did not require reoperation. PJI, periprosthetic joint infection.

Univariate Analysis: Risk of Periprosthetic Joint Infection

Compared to patients without a reoperation within the first year, patients who underwent an aseptic reoperation within 90 days had an elevated risk of PJI (HR 13.54, CI 5.90–31.08, $P < .001$), as did patients who had a reoperation between 91 and 365 days (HR 17.33, CI 7.53–39.88, $P < .001$) (Table 4). In the entire cohort, gender was not found to be a significant risk factor for PJI ($P = .16$) nor was BMI ($P = .20$), while younger age (HR 1.02 per year, CI 1.01–1.03, $P = .01$) was found to be a risk factor for PJI. A diagnosis other than primary OA was associated with an elevated PJI risk (HR 4.13, CI 2.72–6.26, $P < .001$) as did CCI (HR 1.3 per point, CI 1.1–1.4, $P < .001$).

Multivariate Analysis: Risk of Periprosthetic Joint Infection

After accounting for age, gender, BMI, CCI, and diagnosis other than OA, reoperation within 90 days of index arthroplasty had an elevated risk of PJI (HR 7.94, CI 3.14–20.09, $P < .001$) as did a reoperation between 91 and 365 days (HR 13.23, CI 5.69–30.76, $P < .001$).

Multivariate Analysis: Risk of Mortality

For patients requiring a reoperation within the first 90 days, the overall mortality rate at 2, 5, and 10 years following index arthroplasty was 12%, 28%, and 51%, respectively. For patients requiring a reoperation between 91 and 365 days following index THA, the overall mortality rate at 2, 5, and 10 years was 8%, 23%, and 42%, respectively. The mortality at 2, 5, and 10 years following index arthroplasty for those not requiring an early aseptic reoperation was 6%, 16%, and 35%, respectively (Fig. 3).

Table 3

Cumulative Incidence of PJI, Aseptic Revision, and Mortality Rates.

Time to Reoperation	Cumulative Incidences of PJI (95% CI)		Cumulative Incidences of Aseptic Revision (95% CI)		Mortality Rates (95% CI)		
	2 y	5 y	2 y	5 y	2 y	5 y	10 y
Reoperation ≤ 90 d	4.8% (2.0–11.1)	6.0% (2.7–13.1)	8.7% (4.7–16.2)	12.4% (7.3–21.2)	12.2% (5.5–18.5)	28.0% (17.6–37.1)	51.4% (36.7–62.6)
Reoperation 91–365 d	3.2% (1.0–9.7)	6.6% (2.7–15.8)	11.9% (6.8–20.7)	13.3% (7.8–22.6)	8.3% (2.2–14.0)	22.5% (11.3–32.2)	42.2% (24.0–56.0)
No reoperation within 1 y	0.2% (0.1–0.2)	0.4% (0.3–0.5)	0.7% (0.6–0.8)	1.7% (1.5–2.0)	5.6% (5.2–5.9)	15.5% (14.9–16.1)	35.0% (33.9–36.1)

PJI, periprosthetic joint infection; CI, confidence interval.

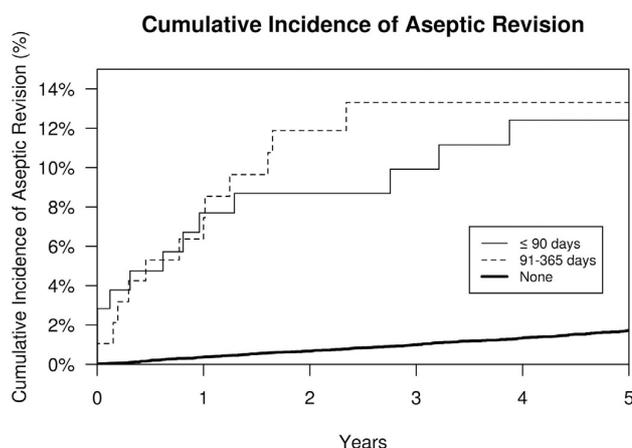


Fig. 2. Cumulative incidence of aseptic re-revision over time for patients requiring an early aseptic reoperation (as well as those who did not require reoperation).

In our multivariate analysis of risk factors for mortality after THA, many variables were significant (Table 5). After adjusting for risk factors with a multivariable analysis, patients requiring an aseptic reoperation between 91 and 365 days had a significantly higher risk for mortality (HR 1.52, CI 1.01–2.29, $P = .05$), while patients undergoing an aseptic reoperation within 90 days of index arthroplasty trended toward an elevated risk of mortality (HR 1.31, CI 0.99–1.76, $P = .07$).

Discussion

The current series demonstrates that patients requiring an early aseptic reoperation within 1 year of primary THA have an 8- to 13-fold increased risk of subsequent PJI. Although this is implicitly thought to be true, the potential reason for this elevated PJI risk is important to discuss. Exposing a healing wound to another insult where oxygen tension is compromised increases the risk of wound contamination [23–25]. Other smaller series have demonstrated similar high rates of complications following early reoperation [21,22]. Our study demonstrates that trauma and recovery related to the primary THA is a time-dependent risk for PJI within the first year. Furthermore, thought must be given to the patient microbiome changes that may occur following the administration of intravenous antibiotics at the time of index THA as well as the physiologic insult of multiple anesthetics.

The 2018 American Joint Replacement Registry annual report identified periprosthetic fracture and dislocation as the most common indications for aseptic revision within 90 days of index arthroplasty [26]. In the current study, dislocations and periprosthetic fractures accounted for over 70% of the early reoperations performed within the first year. Even without the development of a subsequent PJI, those requiring an early aseptic

Table 4
Unadjusted and Multivariate Analysis of Risk Factors Associated With PJI Following Early Aseptic Reoperation.

Parameter	Unadjusted HR PJI	95% CI		P-Value	Adjusted HR PJI	95% CI		P-Value
		Low	High			Low	High	
Age (per 1 y increase)	0.98	0.97	0.99	.015	0.98	0.97	1.00	.027
Male gender	1.35	0.89	2.04	.16	1.27	0.82	1.96	.28
BMI (reference <25 kg/m ²)								
25-29.9	0.99	0.55	1.77	.96	1.02	0.56	1.86	.94
30-39.9	1.02	0.57	1.84	.94	1.08	0.59	1.98	.79
40+	2.01	0.93	4.36	.077	2.03	0.92	4.45	.078
Nonprimary osteoarthritis	4.13	2.72	6.26	<.001	3.36	2.13	5.18	<.001
CCI (per 1 point increase)	1.25	1.15	1.36	<.001	1.18	1.07	1.29	<.001
Reoperation ≤90 d	13.54	5.90	31.08	<.001	7.94	3.14	20.09	<.001
Reoperation 91-365 d	17.33	7.53	39.88	<.001	13.23	5.69	30.76	<.001

BMI, body mass index; CCI, Charlson Comorbidity Index; HR, hazard ratio; CI, confidence interval; PJI, periprosthetic joint infection.

reoperation also had a markedly higher rate of later aseptic revisions. As these are nonelective reoperations with a high risk of complication, preventing the complication leading to reoperation is the best form of treatment.

Dislocation was the most common complication necessitating early aseptic reoperation within the first year following index THA. Optimizing hip stability through operative approach, component positioning and accurate recreation of length and offset are essentials [27,28]. **With the improved wear characteristics** of highly crosslinked polyethylene, larger femoral head sizes have become more common and may help decrease the rate of dislocations in some patients [29,30]. However, it is critical to recognize those patients who may preoperatively be at risk for dislocations through an assessment of their hip-spine relationship [31–33]. Dual mobility has shown promise compared to large femoral heads in the revision setting and a recent study demonstrated successful mid-term follow-up for “high risk” primary THAs [31,34].

Periprosthetic fractures were the second most common indication for early aseptic reoperation within the first year following primary THA in the current study. The 2018 American Joint Replacement Registry annual report demonstrated that **94% of the periprosthetic fractures occurred around a cementless** femoral stem [26]. Surgeons should therefore assess for intraoperative fracture on every case and have a low threshold to use prophylactic wiring in high-risk patients [35,36]. Furthermore, registry studies have shown improved survivorship free from revision in older patients with cemented fixation [37,38]. Therefore, considering cemented femoral implants for patients who are at elevated risk for

fracture (especially females) may decrease the risk of early periprosthetic femur fractures [39–41]. Finally, younger age was found to be a statistically significant risk factor for subsequent PJI following early aseptic reoperation in our multivariate model. The reason for this finding is likely related to the fact that younger patients live longer and may have host factors predisposing them to a THA at a young age.

The exclusion of patients requiring a septic reoperation within the first year following primary THA is notable to our study design. Several studies have previously identified risk factors pertaining to PJI risk following primary THA [6,11,13,15–17]. However, our goal is to evaluate **potentially avoidable early aseptic reoperations** as a potential risk factor for later PJI. By eliminating PJIs occurring within the first year in our cohort, we were able to evaluate the effect on patients undergoing an early aseptic reoperation and compare them to peers who did not have an early reoperation. This assumes that those undergoing an aseptic reoperation during the first year were not destined to develop a PJI within the first year.

Our study has limitations. By its retrospective design we can only establish associations without causation. Furthermore, our multivariate analysis did not include all patient and surgery risk factors (ie, surgeon, approach). The main limitation within our study to this regard is the heterogeneous population requiring aseptic reoperation. The severity of the subsequent reoperations or revisions may harbor an increased risk and was not accounted for beyond designation of an open procedure. For instance, an open reduction of a dislocated hip can be relatively quick and straightforward, whereas a periprosthetic fracture may be much more time-consuming (and thus bearing a higher risk of PJI) [6]. With only 211 early aseptic reoperations within the first year following primary THA over the 16-year study period, we are unable to further stratify the time-dependent nature of a patient’s subsequent risk of PJI. Furthermore, incremental perioperative measures

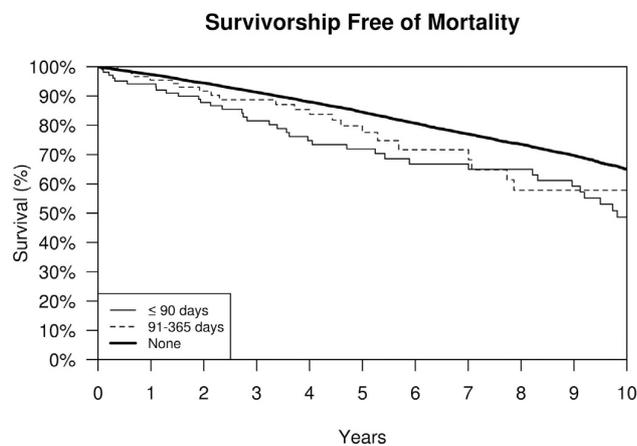


Fig. 3. Kaplan-Meier survivorship curve demonstrating survivorship free of mortality for each study group.

Table 5
Multivariate Risk of Mortality.

Parameter	Adjusted HR PJI	95% CI		P-Value
		Low	High	
Age (per 1 y increase)	1.08	1.08	1.09	<.001
Male gender	1.25	1.18	1.34	<.001
BMI (reference <25 kg/m ²)				
25-29.9	0.75	0.70	0.82	<.001
30-39.9	0.83	0.76	0.91	<.001
40+	1.24	1.07	1.44	.005
Nonprimary osteoarthritis	2.20	2.05	2.35	<.001
CCI (per 1 point increase)	1.23	1.21	1.24	<.001
Reoperation ≤90 d	1.31	0.98	1.76	.069
Reoperation 91-365 d	1.52	1.01	2.29	.047

BMI, body mass index; CCI, Charlson Comorbidity Index; HR, hazard ratio; CI, confidence interval; PJI, periprosthetic joint infection.

intended to minimize the risk of later PJI (ie, dilute betadine wash, extended antibiotics) were not standardized or evaluated [42–45].

In summary, periprosthetic fractures and dislocations accounted for over 70% of early aseptic reoperations following primary THA. The risk of later PJI following an aseptic reoperation within the first year was found to be 8- to 13-fold higher compared to patients not requiring an aseptic reoperation within the first year. In addition, higher rates of any revision and mortality were noted in those who had an early aseptic reoperation. Therefore, an attempt to identify and pre-emptively treat those patients at high risk for periprosthetic fractures and dislocations is essential to decrease early aseptic reoperations and later PJIs.

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