Published in final edited form as:
J Arthroplasty. 2012 September ; 27(8): 1507–1512. doi:10.1016/j.arth.2011.12.010.

Patient factors Predict Periprosthetic Fractures Following Revision Total Hip Replacement

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Abstract

We assessed important patient risk factors for postoperative periprosthetic fractures after revision total hip replacement (THR) using prospectively collected Institutional Joint Registry data. We used univariate and multivariable-adjusted Cox regression analyses. There were 330 postoperative periprosthetic fractures after 6,281 revision THRs. In multivariable-adjusted analyses, hazard [95% confidence interval] of periprosthetic fracture was higher for: women, 1.66 [1.32, 2.08], p<0.001; higher Deyo-Charlson comorbidity index of 2, 1.46 (1.03, 2.07) and index of 3+, 2.01 (1.48, 2.73), overall p<0.001; and operative diagnosis, especially previous non-union, 5.76 (2.55, 13.02), overall p<0.001. Hazard was lower in 61–70 year old, 0.64 (0.49, 0.84) and 71–80 year old 0.57 (0.43, 0.76), compared to <60 years (overall p<0.0001). Our study identified important modifiable and unmodifiable risk factors for fractures after revision THR.

Introduction

Due to an aging population and expanding age range and indications for hip replacement, revision total hip replacement (THR) is becoming increasingly common in the U.S. In 2005, 40,800 revision THRs were performed in the U.S., projected to increase by 137% to 96,700/year by the year 2030 [1]. The outcomes of revision THR are not as good as primary THR [2] [3]. Revision THR is technically more challenging procedure than primary THR and is also associated with more complications compared to primary THR [4]. Periprosthetic fracture is one of the most serious feared complications of revision TKR, a complication associated with poor function [5] and higher risk of re-revision [5] and mortality [5] [6].

Several studies have examined the cumulative incidence and risk factors for periprosthetic fractures in large samples of patients with primary THR [7–10]. Few studies have provided estimates of periprosthetic fractures in patients with revision THR [10–13] and most had small sample sizes. To our knowledge, there are no published studies examining risk factors

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for periprosthetic fractures in patients undergoing revision THR, except one study that found female gender and age >70 years to be risk factors [13]. In this study, analyses were only adjusted for age and gender, making the study liable to confounding by other unmeasured important factors, such as body mass index and comorbidity.

Well-designed studies of risk factors of periprosthetic fractures after revision THR are needed, given the impact of periprosthetic fractures on patients and the paucity of data. This much needed information can be used to design interventions to potentially reduce the frequency of periprosthetic fractures, a costly complication.

In this study, our objective was to examine whether patient demographics (age, gender), and clinical characteristics (body mass index (BMI), comorbidity, cardiac disease, operative diagnosis etc.) were associated with the risk of periprosthetic fractures after revision THR.

Methods

Source population

The Mayo Clinic Total Joint Registry is a prospective registry that captures data on every patient undergoing joint replacement at the Mayo Clinic, Rochester, Minnesota. In addition to capturing pre-operative and operative data, the registry also captures post-operative complications focusing especially on revision, fracture, infection and other important clinical outcomes [14]. For this study, we selected the cohort by including every revision THR performed at the AA clinic between 1989 and 2008. This time interval was chosen since all clinical variables of interest (including BMI and American Society of Anesthesiologist (ASA) class) were available in electronic registry datasets for this recent study period.

Study Outcome

The study outcome was the occurrence of a postoperative periprosthetic fracture on postoperative day 1 or later. The occurrence of periprosthetic fracture is captured for every patient after their joint replacement, abstracted from the operative notes or surgeon’s clinical note. We decided a priori to not include same day fractures, since that would include both intra-operative and same day post-operative fractures, which were difficult to differentiate from each other using registry data. Intraoperative fractures were not the focus of this study and likely have different etiology than postoperative fractures.

Predictor variables

We included several demographic and clinical variables as potential risk factors for postoperative periprosthetic fractures following revision THR. Patient demographics included age, categorized as previously (≤60, 61–70, 71–80 and >80 years) [15–17] and gender. Clinical variables included BMI, comorbidity measured with Deyo-Charlson index and peri-/post-operative risk assessed with American Society of Anesthesiologists (ASA) index. BMI (kg/m^2) was categorized as <25, 25–29.9, 30–39.9, or ≥40, as per WHO classification [18] and similar to previous studies [15–16]. We assessed comorbidity with the Deyo-Charlson index [19], which is a validated measure of comorbidity, consisting of a weighted scale of 17 comorbidities (including cardiac, pulmonary, renal, hepatic disease, diabetes, cancer, hemiplegia, HIV etc.), expressed as a summative score [20–21]. American Society of Anesthesiology (ASA) Physical Status score, a validated measure, was categorized as class 1, 2, 3, 4 [22–23]. ASA class was retrieved by a database managed by the Department of Anesthesiology. Operative diagnosis was categorized as loosening/wear/osteolysis, dislocation/bone or prosthesis fracture/instability/non-union or failed prior joint replacement with components removed/infection. The fracture diagnosis included both femoral and acetabular bone fractures as well as implant/prosthesis fractures. Implant fixation was categorized as cemented (if any component was cemented) or uncemented. Previous thromboembolic event (occurrence of deep vein thrombosis or pulmonary embolism; yes/no) or previous major cardiac events (occurrence of arrhythmia, myocardial infarction or congestive heart failure; yes/no), the two common complications of primary THR, were also assessed as covariates, since they may identify patients at higher risk of other perioperative complications. Time period was categorized in 5-year intervals to examine any significant time trends (1989–1993, 1994–98, 1999–2003, 2004–2008).

Statistical Analyses

Summary statistics were calculated for patient demographics and clinical characteristics as mean (standard deviation (SD)) or proportions. We performed univariate Cox regression analyses assessing whether each variable of interest was associated with the outcome, postoperative periprosthetic fracture after revision THR. Both ASA and Deyo-Charlson index were included in the models, since the correlation between them was low (<0.4). The variables assessed included: gender, age (≤60, 61–70, 71–80 and >80 years), body mass index (<25, 25–29.9, 30–39.9, ≥40), Deyo-Charlson index (0, 1, 2, 3 or more), ASA class (1, 2, 3, 4), underlying diagnosis (loosening/wear/osteolysis, previous surgery with components removed, fracture/dislocation, nonunion, infection and other), and prior thromboembolic or cardiac disease. Variables significantly associated in univariate regression with p<0.05 were entered into a backward stepwise multivariable-adjusted Cox regression model, which retained only variables significantly associated with p-value <0.05 (**model 1**). Hazard ratio (HR) and 95% confidence interval (CI) are presented. Sensitivity analyses were performed by including all variables with p-value <0.20 in the univariate analysis in the multivariable-adjusted Cox regression model (**model 2**).

Results

Of the 5,034 patients, who underwent 6,281 revision THRs, the mean age was 65 years, 46% were men and the mean follow-up was 5.6 years (Table 1). 11% were older than 80 years, mean BMI was 29 kg/m^2, 14% had Deyo-Charlson index of 3 or more and 50% were ASA class 3 or higher. The most common underlying diagnosis was loosening, wear or osteolysis in 66% followed by fracture or dislocation in 19%.

Of all periprosthetic fractures, 330 occurred on post-operative day 1 and later (Table 2), which constituted our analytic dataset. Fractures were diagnosed 1 day to 6,118 days postoperative. One-fifth of the periprosthetic fractures occurred between 3–12 months after revision THR and two-thirds occurred later than 12-months.

Risk factors for Postoperative Periprosthetic Fractures

In univariate analysis, we found that female gender, younger age, higher comorbidity indicated by higher Deyo-Charlson index and operative diagnosis were associated with higher risk/hazard of postoperative periprosthetic fracture following revision THR (Table 3). In the multivariable analysis, the same four significant factors from the univariate analyses retained significance (Table 3). We found that women had a 66% higher risk than men. Patients 61–70 and 71–80 year old a 40% lower risk than those younger than 60 years of suffering from a postoperative periprosthetic fracture (Table 3). Patients with Deyo-Charlson index of 2 had 50% higher risk and those with 3 or more, 100% higher risk compared to patients with Deyo-Charlson index of 0. Operative diagnoses of non-union and fracture was associated with 5-times higher risk of periprosthetic fracture. There was a trend towards a slight decrease in fracture rate over time in the multivariable model 1, but it was

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not significant (p=0.06). Sensitivity analyses no meaningful differences in significance or hazards ratios (**model 2**; Table 3).

Discussion

Our study is among the first to assess risk factors for periprosthetic fractures after revision THR in a large prospective cohort. Several important patient characteristics were associated with the risk of postoperative periprosthetic fractures. Female gender, younger age, higher Deyo-Charlson comorbidity index and underlying diagnosis were each independently associated with significantly increased risk of periprosthetic fracture following revision THR. These important findings can better inform both patients and surgeons regarding risk of an important complication allowing for a more informed consent for higher-risk patients. These findings merit further discussion.

Women had significantly higher risk of periprosthetic fractures after revision THR compared to men, a novel finding from our study. These findings confirm similar recent observations from the Scottish registry, that adjusted only for age, gender and primary versus revision surgery [13]. Our study adjusted for several more variables as compared to the previous study [13], confirming that this finding is robust. Several potential explanations exist for this observed difference by gender. A slightly higher risk of falls [24–25] and more recurrent falls [26] have been reported in women, which may put them at higher risk of fracture compared to men. Postmenopausal osteoporosis may be a contributory factor as well. These factors may act synergistically to increase the risk of periprosthetic fractures in women.

Age groups 61–70 and 71–80 were each associated with significantly decreased risk of periprosthetic fractures after revision THR, compared to those 60 years or younger. This finding confirms the report of a similar observation from Scottish registry study [13] and provides this risk estimate for more age categories than those reported in the previous study. A more active lifestyle in younger age and pursuit of active sports [27–28] likely puts younger recipients at higher risk of fracture after revision THR. We examined age *gender interaction in our multivariable-adjusted model and did not find this to be significant (p=0.90).

Increasing Deyo-Charlson index was associated with higher risk of periprosthetic fractures. Specifically, a Deyo-Charlson comorbidity index of 2 or higher was associated with significantly increased risk of periprosthetic fracture after revision THR, compared to score of zero. This is intuitive, but has not been described in the past. We are unable to compare our finding due to lack on any published literature in this area. This finding will need to be confirmed by future studies, which should include large sample size and control for important variables (such as in our study). Our study was not designed to address disease severity and whether comorbidity was optimally managed prior to the surgery in these patients. Further studies should examine whether optimal comorbidity management prior to revision THR can reduce the risk of periprosthetic fractures and improve revision THR outcomes.

An underlying diagnosis of non-union and fracture was associated with significantly higher fracture risk compared to those with loosening, wear or osteolysis. The risk was 5-fold higher in those with non-union and 2-fold higher with fracture, making patients with these diagnoses very high risk categories for postoperative periprosthetic fractures.

Our study is among the first to provide estimates of periprosthetic fractures in a large U.S. cohort of patients with revision THR. An obvious implication of these findings is to inform patients with these risk factors at the time of informed consent that their risk of periprosthetic fracture after revision THR in increased. Thus, younger patients, women and those with higher comorbidity or an underlying diagnosis of non-union should be made aware of their increased risk of periprosthetic fractures after revision TKR, compared to other groups. This would allow for a fully informed preoperative consent.

The frequency of postoperative periprosthetic fracture was 5.3% in 6,281 revision THRs at our medical center in this 20-year study. Our estimates are slightly higher than those previously reported in two large studies, 2.1% in a study of the Swedish National register [10] and 2.8% in a single-center study of 3,265 revision THRs [11], both of which included an earlier period of study than our study. Increasing periprosthetic fracture rate over time has been suspected by some [29–30], although the estimates range widely. This is at least partially attributable to expanding indication of THR to both active younger patients and older osteoporotic patients (risk of falls), both hypothesized to increase periprosthetic fracture risk.

Our study has several limitations. There may be limitations to generalizability of these findings. However, the demographic and clinical characteristics of our cohort are similar to those described in other studies and in other U.S. cohorts. Residual confounding is possible in this cohort study despite our efforts to include important clinical variables in our analyses. It is possible that some of the fractures reported on postoperative day1 or later may actually have been sustained during the surgery leading to misclassification; however, and this is unlikely to be the case in more than a few cases, since periprosthetic fractures are symptomatic and only 4% of all postoperative periprosthetic fractures were sustained between postoperative days 1–30. Study strengths include a large sample size, prospective capture of these events in the registry, and the ability to control for several important covariates and confounders.

In summary, we found that female gender, higher Deyo-Charlson comorbidity index, younger age and an underlying diagnosis of non-union and fracture were each significantly associated with risk of periprosthetic fractures. These findings provide guidance to surgeons and patients with these risk factors regarding their increased risk of periprosthetic fractures. Future studies should examine if targeted interventions for improved comorbidity management may decrease risk of periprosthetic fractures.

Acknowledgments

We thank Youlonda Lochler for assistance in identifying the study cohort and Scott Harmsen for help with statistical analyses. This material is the result of work supported with National Institute of Health (NIH) Clinical Translational Science Award 1 KL2 RR024151-01 (Mayo Clinic Center for Clinical and Translational Research) and the resources and the use of facilities at the Birmingham VA Medical Center, Alabama, USA.

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Table 1

Demographic Features of Study Cohort

	Revision THR (n=6281) Mean (standard deviation) or n (%)
Mean Follow-up, in years	5.6 (4.4)
Female	3,366 (53.6%)
Bilateral	1,247 (19.9%)
Mean age at surgery, in years	65.3 (13.7)
Age Category	
≤60 years	1,985 (31.6%)
61–70 years	1,678 (26.7%)
71–80 years	1,932 (30.8%)
>80 years	686 (10.9%)
Body Mass Index (BMI) in kg/m^2	28.4 (5.8)
BMI Category	
Missing	66 (1%)
Normal, < 25.0 kg/m^2	1,833 (29.5%)
Overweight, 25–29.9 kg/m^2	2,292 (36.9%)
Obese, 30–39.9 kg/m^2	1,845 (29.7%)
Morbidly Obese, ≥ 40.0 kg/m^2	245 (3.9%)
ASA Score	
Missing	33 (0.5%)
1	172 (2.8%)
2	2,961 (47.4%)
3	3,018 (48.3%)
4	97 (1.6%)
Deyo- Charlson Index	1.1 (1.94)
Sum of comorbidities on Deyo-Charlson Index	
0	3,530 (56.2%)
1	1,176 (18.7%)
2	708 (11.3%)
3+	867 (13.8%)
Prior Cardiac Event (MI, CHF, arrhythmia)	
No	5,481 (87.3%)
Yes	800 (12.7%)
Prior Thromboembolic Event	
No	6,043 (96.2%)
Yes	238 (3.8%)
Operative Diagnosis	
Failure: Loose/Wear/Osteolysis	4,173 (66.4%)
Failure: Previous Surgery	713 (11.4%)
Failure: Fracture, Dislocation	1,203 (19.2%)

	Revision THR (n=6281) Mean (standard deviation) or n (%)
Failure: Fracture [b]	− 484 (7.7%)
Failure: Dislocation	− 719 (11.4%)
Failure: Nonunion	31 (0.5%)
Failure: Infection	90 (1.4%)
Failure: Other[a]	71 (1.1%)

[a]Mode of failure not specified

[b]Among the those with fractures as the underlying diagnosis, 169 were prosthesis fractures and 315 bone fractures

Table 2

Frequency of post-operative peri-prosthetic fractures after revision THR

Day 1–30 N (% of Total[a])	Day 31–90 N (% of Total[a])	Day 91–365 N (% of Total[a])	>day 365 N (% of Total[a])	Total (≥Day 1) N (% of Total[a])
15 (4%)	43 (13%)	54 (16%)	218 (66%)	330 (100%)

[a]fractures are represented as proportion of fractures from post-operative day 1 onwards

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Table 3

Univariate and Multivariable-adjusted Hazard of periprosthetic fracture following Revision Total Hip Replacement

Variable	Total (n=6281)	Periprosthetic Fractures (n=330)	Univariate Hazard Ratio (95% CI)	Multivariable [a] model 1 Hazard Ratio (95% CI)	Multivariable[a] model 2 Hazard Ratio (95% CI)
Gender			**p<0.001**	**p<0.001**	**p<0.001**
Male	2,915	114 (4%)	1.00 (ref)	1.00 (ref)	1.00 (REF)
Female	3,366	216 (6%)	1.63 (1.30, 2.04)	1.67 (1.33, 2.10)	1.68 (1.33, 2.11)
Age Category			**p<0.001**	**p<0.001**	**p=0.002**
≤60	1,985	144 (7%)	1.00 (ref)	1.00 (ref)	1.00 (REF)
61–70	1,678	83 (5%)	0.66 (0.50, 0.86)	0.64 (0.49, 0.85)	0.67 (0.51, 0.88)
71–80	1,932	75 (4%)	0.59 (0.44, 0.78)	0.57 (0.43, 0.76)	0.60 (0.45, 0.80)
>80	686	28 (4%)	0.82 (0.54, 1.23)	0.74 (0.49, 1.12)	0.79 (0.52, 1.20)
Body Mass Index, kg/m^2			**p=0.27**		
Normal, < 25.0	1,833	114 (6%)	1.00 (ref)		
Overweight, 25–29.9	2,292	110 (5%)	0.88 (0.67, 1.15)		
Obese, 30–39.9	1,845	92 (5%)	0.98 (0.53, 1.82)		
Morbidly Obese, ≥40.0	245	11 (4%)	0.77 (0.59, 1.00)		
Deyo-Charlson Index			**p=0.003**	**p<0.001**	**p<0.001**
0	3,530	172 (5%)	1.00 (ref)	1.00 (ref)	1.00 (REF)
1	1,176	62 (5%)	1.13 (0.85, 1.51)	1.16 (0.87, 1.55)	1.22 (0.91, 1.64)
2	708	39 (6%)	1.31 (0.92, 1.85)	1.46 (1.03, 2.07)	1.52 (1.06, 2.18)
3+	867	57 (7%)	1.75 (1.30, 2.37)	2.03 (1.50, 2.75)	2.08 (1.52, 2.86)
Operative Diagnosis			**p<0.001**	**p<0.001**	**p<0.001**
Failure: Loose/Wear/Osteolysis	4,173	221 (5%)	1.00 (ref)	1.00 (ref)	1.00 (REF)
Failure: Previous Surgery	713	35 (5%)	1.08 (0.76, 1.54)	1.14 (0.80, 1.63)	1.19 (0.83, 1.70)
Failure: Fracture	484	37 (8%)	1.85 (1.30, 2.62)	1.78 (1.25, 2.53)	1.86 (1.30, 2.64)
Failure: Dislocation	719	27 (4%)	1.01 (0.68, 1.51)	0.94 (0.63, 1.40)	0.92 (0.61, 1.38)
Failure: Nonunion	31	6 (19%)	6.00 (2.66, 13.53)	5.75 (2.54, 12.99)	5.79 (2.55, 13.14)
Failure: Infection	90	1 (1%)	0.44 (0.06, 3.13)	0.38 (0.05, 2.71)	1.19 (0.83, 1.70)
Failure: Other	71	3 (4%)	0.81 (0.26, 2.52)	0.72 (0.23, 2.26)	0.77 (0.25, 2.41)
ASA class			**p=0.06**		**p=0.14**

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Variable	Total (n=6281)	Periprosthetic Fractures (n=330)	Univariate Hazard Ratio (95% CI)	Multivariable [a] model 1 Hazard Ratio (95% CI)	Multivariable[a] model 2 Hazard Ratio (95% CI)
1	172	17 (10%)	1.00 (ref)		1.00 (REF)
2	2,961	172 (6%)	0.71 (0.43, 1.18)		0.75 (0.45, 1.26)
3	3,018	132 (4%)	0.62 (0.38, 1.03)		0.64 (0.38, 1.09)
4	97	7 (7%)	1.39 (0.58, 3.36)		1.20 (0.48, 3.09)
Prior Cardiac event			**p=0.43**		
No	5,481	301 (5%)	1.00 (ref)		
Yes	800	29 (4%)	0.86 (0.58, 1.25)		
Prior Thromboembolic Event			**p=0.16**		**p=0.13**
No	6,043	325 (5%)	1.00 (ref)		1.00 (REF)
Yes	238	5 (2%)	0.53 (0.22, 1.28)		0.50 (0.21, 1.23)