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Clinical Research

What Factors Are Associated With Implant Revision in the Treatment of Pathologic Subtrochanteric Femur Fractures?

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Abstract

Background Limiting reoperation or revision after operative stabilization or endoprosthetic reconstruction of a pathologic subtrochanteric femur fracture reduces morbidity, but how best to achieve this remains controversial. Endoprosthetic reconstruction offers durable mechanical stability but may not be most appropriate in patients who are frail or who are not expected to survive more than a few months. For that reason, cumulative incidence survival (looking at the endpoint of reoperation or revision with death as a competing risk) and factors associated with revision after surgical stabilization or reconstruction—both of which remain poorly characterized to date—would help surgeons make better decisions on behalf of these patients.

Questions/purposes We analyzed patients who were operatively treated for pathologic subtrochanteric femur fracture, and we asked: (1) What is the cumulative incidence of reoperation and revision at 3 months, 1 year, and 2 years after surgery for pathologic subtrochanteric femur fracture in patients undergoing each treatment type with death as a competing risk? (2) What are the factors associated with implant revision after operative treatment of pathologic subtrochanteric femur fracture? (3) What is the overall survival of patients in this population after surgery? (4) How do clinical and surgical factors along with the frequency of complications compare in this population by operative treatment?

Methods Between January 2000 and December 2020, 422 patients underwent surgery for completed proximal femur pathologic fractures. After excluding patients with non-subtrochanteric femur fractures (71% [301]), fractures caused by primary tumors of bone (< 1% [2]), and insufficient data (1% [6]), we included 113 patients who underwent operative treatment of completed pathologic subtrochanteric femur fractures. Our study period spanned 20 years because although implant trends may have shifted, the overall operative objective for pathologic subtrochanteric femur fractures—restoring function and alleviating pain, regardless of the extent of bony union—have remained relatively unchanged during this period. Median follow-up time was 6 months (range 1 month to 20.6 years). Intramedullary nailing (IMN) was performed in 68% (77) of patients, proximal femur replacement (PFR)

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Ethical approval for this study was obtained from the Massachusetts General Hospital Institutional Review Board (protocol # 2024P000054).
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was performed in 19% (22), and open reduction and internal fixation (ORIF) was performed in 12% (14) of patients. IMN was performed in patients with a poor prognosis but in whom fracture stabilization was felt to be advantageous. In instances of complex fractures in which adequate reduction could not be achieved, ORIF was generally performed. PFR was generally performed in patients with a better prognosis in which long-term implant survival and patient function were prioritized. We found a higher proportion of women in the IMN group (73% versus 32% in PFR and 50% in ORIF; p = 0.001). Rapid growth tumors (Katagiri classification) were found in 25% of patients with IMN, 27% with PFR, and 43% with ORIF. The primary outcome was the cumulative incidence of reoperation or revision surgery after initial stabilization. Competing risk analysis with death as a competing event was performed to estimate the cumulative incidence for reoperation and revision. Factors associated with revision surgery were identified using the Cox proportional hazards model, which rendered HRs. All analyses were adjusted to control for potential confounders.

Results The cumulative incidence for reoperation at 2 years was 5% (95% confidence interval [CI] 4% to 6%) for IMN, 15% (95% CI 9% to 22%) for PFR, and 32% (95% CI 15% to 50%) for ORIF (p = 0.03). The cumulative incidence for revision at 2 years was 4% (95% CI 3% to 4%) for IMN, 4% (95% CI 2% to 6%) for PFR, and 33% (95% CI 15% to 51%) for ORIF (p = 0.01). Factors associated with revision surgery were radioresistant tumor histology (HR 8.5 [95% CI 1.2 to 58.9]; p = 0.03) and ORIF (HR 6.3 [95% CI 1.5 to 27.0]; p = 0.01). The 3-month, 1-year, and 2-year overall survival was 80% (95% CI 71% to 87%), 35% (95% CI 26% to 45%), and 28% (95% CI 19% to 36%), respectively. Thirty-day postoperative complications did not differ by fixation type, but 90-day readmission was highest after ORIF (3 of 14 versus 4 of 22 in PFR and 4% [3 of 77] in IMN; p = 0.03) Periprosthetic joint infection (PJI) was more common after salvage PFR (2 of 6) than primary PFR (1 of 22) (p = 0.04).

Conclusion Primary PFR may be preferred for pathologic subtrochanteric femur fractures arising from radioresistant tumor types, as the cumulative incidence of revision was no different than for IMN while restoring function, alleviating pain, and offering local tumor control, and it less commonly develops PJI than salvage PFR. In complex fractures not amenable to IMN, surgeons should consider performing a PFR over ORIF because of the lower risk of revision and the added benefit of replacing the pathologic fracture altogether and offering immediate mechanical stability with a cemented endoprosthesis. Future studies might evaluate the extent of bone loss from local tumor burden, and this could be quantified and analyzed in future studies as a covariate as it may clarify when PFR is advantageous in this population.

Level of Evidence Level III, therapeutic study.

Introduction

One-third of pathologic femur fractures undergoing operative intervention involve the subtrochanteric region [6, 10, 26]. Pathologic subtrochanteric femur fractures are subject to forces that may contribute to malunion, nonunion, and implant breakage [4, 15, 25]. As such, appropriate surgical treatment must be selected to ensure fracture stabilization for the duration of the patient's life. However, there is no clear consensus for the surgical management of these fractures [15]. Treatment modalities include intramedullary nailing (IMN), open reduction and internal fixation (ORIF), and endoprostheses. A recent meta-analysis of 544 patients from 19 studies found that IMN was performed 75% of the time with a revision rate of 7.2%, whereas endoprosthetic reconstruction was performed 21% of the time with a revision rate of 8.9% in standard prostheses and 2.5% in tumor endoprostheses [15]. Further, prior studies report variable rates of implant revision, between 0% and 26% after IMN [8, 10, 13, 23, 27, 35, 36], and lower rates after endoprosthetic reconstruction [13, 35]. Endoprostheses also carry unique risks and benefits when compared with IMN, such as higher rates of intraoperative and mechanical complications (such as dislocation [8, 35]) and infection because of the larger dissection required [3, 14, 16]. At the same time, endoprostheses allow for en bloc resection of the tumor, which removes the pathologic bone that was the cause of mechanical insufficiency and replaces it with a cemented implant that offers immediate mechanical stability and does not rely on the need for a fracture to heal. The proportion of revisions following ORIF has also been reported as high as 23% [37].

While operative treatment of these fractures is widely endorsed, conflicting data exist regarding the best strategy for management [15], as endoprosthetic reconstruction offers durable mechanical stability but may not be most appropriate in patients who are frail or patients whose anticipated survival is measured in weeks or months [10]. Prior studies have evaluated which implant approach is best after failure for pathologic femur fractures [10], specifically reporting the rate and modes of failure after salvage. Notably, while controversy exists in managing pathologic subtrochanteric fractures, cumulative incidence for implant revision using death as a competing risk has not been defined, which is particularly meaningful in patients with metastatic disease. Furthermore, factors associated with implant revision after operative stabilization are not known, particularly with respect to tumor histology and radiobiology, which may equip surgeons with parameters to consider preoperatively when selecting the appropriate treatment modality. We sought to address this gap in knowledge by describing such factors to better inform

implant selection and treatment decision-making for this population.

We asked: (1) What is the cumulative incidence of reoperation and revision at 3 months, 1 year, and 2 years after surgery for pathologic subtrochanteric femur fracture in patients undergoing each treatment type with death as a competing risk? (2) What are the factors associated with implant revision after operative treatment of pathologic subtrochanteric femur fracture? (3) What is the overall survival of patients in this population after surgery? (4) How do clinical and surgical factors along with the frequency of complications compare in this population by operative treatment?

Materials and Methods

Study Design and Setting

In this retrospective, comparative study, we screened the electronic medical records of patients with osseous metastatic disease, lymphoma, or multiple myeloma at our institution, a large, urban academic tertiary referral center, between January 2000 and December 2020. Despite advances in fracture fixation over the past 20 years, the treatment principles for pathologic fractures have remained relatively constant. Compared with fractures caused by trauma in the absence of a tumor, the operative objective for pathologic subtrochanteric femur fractures is to restore function and alleviate pain regardless of the degree of bony union. Therefore, the algorithm for implant selection has remained relatively constant over this span of time; surgeons may choose endoprosthetic reconstruction with PFR in patients with better prognosis, while immediate stabilization with IMN or ORIF may be preferred for those with limited life expectancy. For this reason, we chose a study span of 20 years to include patients treated using this implant decision-making algorithm.

Patients

Adult patients (≥ 18 years of age) treated operatively for completed, neoplastic, pathologic femur fracture in the subtrochanteric region (within 5 cm distal to the lesser trochanter) were included. Included patients were adjudicated radiographically for subtrochanteric femur fracture, and neoplasm was verified from core needle biopsy or surgical pathology results. Exclusion criteria were being < 18 years of age, subtrochanteric femur fracture because of trauma, femur fractures not involving the subtrochanteric region, non-myelomatous primary tumors of bone, insufficient records, and loss to follow-up within 1 year of initial surgery. We did not exclude patients who died within 1 year of surgery because one of the study objectives was to determine the overall survival of this population.

Between January 2000 and December 2020, 422 patients underwent surgery for completed pathologic fractures of the proximal femur. We excluded 301 patients who had fractures outside the subtrochanteric region. Of the remaining 121 patients, two were further excluded because their fractures were caused by primary bone tumors, and six were excluded because of insufficient data (Fig. 1). A comprehensive review of records, surgical management, oncologic treatment, and clinical course was performed in the final cohort of 113 patients.

Description of Treatment and Follow-up

All index procedures were performed at a tertiary academic institution. All patients underwent surgical management for a pathologic subtrochanteric femur fracture using one of three modalities: open and/or closed IMN, ORIF, or proximal femur replacement (PFR). In general, IMN was used in patients with short anticipated survival whom the surgeon felt would benefit from immediate fracture stabilization. In instances of complex fractures where adequate reduction could not be achieved with IMN, ORIF was generally used. PFR was generally chosen in patients with better prognosis where long-term implant survival and patient function were prioritized.

IMN generally involved a long, antegrade, reamed cephalomedullary nail that was locked distally. We used the cannulated Trochanteric Fixation Nail system (DePuy Synthes Inc). ORIF consisted of any combination of plates and screws, fixed-angle devices such as blade plates, or dynamic constructs, such as sliding hip screws. PFR consisted of modular, cemented endoprostheses. We used the Global Modular Replacement System (Stryker Inc). Most patients received perioperative chemotherapy (74% [83 of 113]) and/or radiotherapy (65% [73 of 113]) (Table 1).

Patients were followed at 2 and 6 weeks postoperatively, and regularly (3, 6, 12 months, and at least annually) thereafter for evaluation until date of death or most recent contact. Death was confirmed using public death records. In patients with metastatic disease to the skeleton, a follow-up time of < 2 years was clinically anticipated, as median survival may be shorter than 6 months [1, 30]. At the end of our study period, 17% (19 of 113) of patients remained alive, with a median (range) follow-up time of 8 months (1 month to 8.6 years), and three surviving patients achieved at least 2 years of follow-up. The median (range) follow-up time for the entire cohort was 6 months (1 month to 20.6 years).

Study Population and Descriptive Data

The median (range) age at the time of surgery was 64 years (34 to 87), and 62% (70 of 113) of patients were women

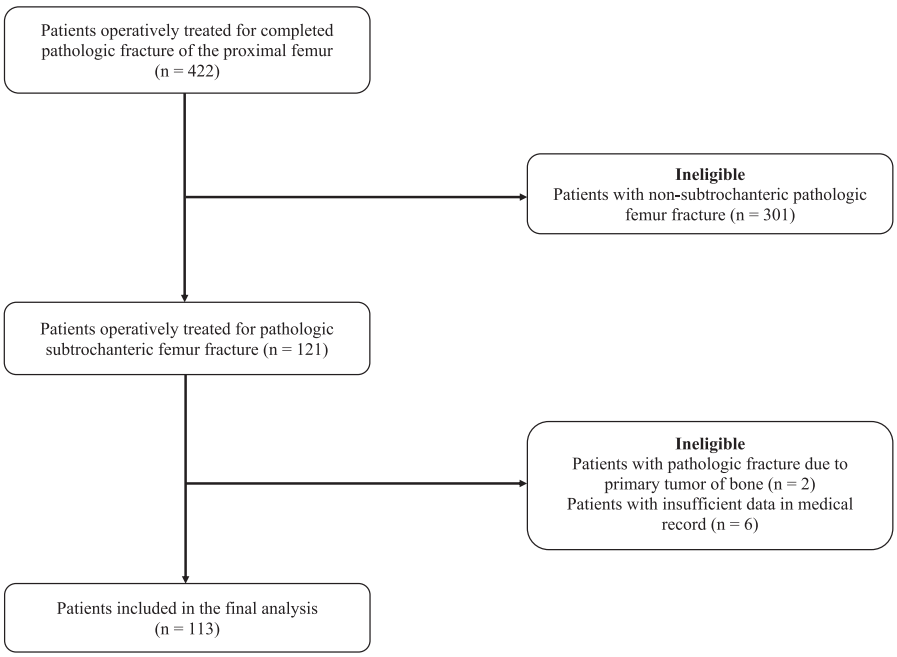

Fig. 1 Study flow diagram.

(Table 1). The treatment groups differed in terms of the proportion of women (IMN 73% [56 of 77], PFR [7 of 22], and ORIF [7 of 14]; p = 0.001) and the proportion of patients who received preoperative chemotherapy (IMN 69% [53 of 77], PFR [9 of 22], and ORIF [7 of 14]; p = 0.04). Despite these differences, our analyses attempted to control for potential confounding by adjusting for age, gender, and age-adjusted Charlson Comorbidity Index (CCI) in all analyses, then additionally performing an exploratory univariable regression to identify any additional potentially confounding variables to include in a multivariable Cox proportional hazards model. The most common primary histologic types of cancer were metastatic breast (36% [41 of 113]), lung (14% [16 of 113]), and prostate (12% [13 of 113]) carcinoma, followed by multiple myeloma (9% [10 of 113]) (Supplemental Table 1; http://links.lww.com/CORR/B350®). IMN was performed most commonly in 68% (77 of 113) of patients, followed by PFR (19% [22]), and ORIF (12% [14]). The median (range) preoperative hemoglobin was lowest in patients treated with IMN (10.1 g/dL [6.7 to 14.8] versus 10.8 g/dL [7.1 to 13.2] in PFR and 12.0 g/dL [6.4 to 14.9] in ORIF; p = 0.03).

Variables, Data Sources, and Bias

Data were obtained from longitudinally maintained orthopaedic oncology registries from a large, tertiary academic medical center. Data on demographic variables including age, gender, primary tumor histologic type and location, histologic growth as described by Katagiri et al. [18], BMI, age-adjusted CCI, smoking status, tumor radiobiology, radiotherapy, chemotherapy, fixation type, preoperative hemoglobin, operative time, estimated blood loss (EBL), and hospital length of stay (LOS) were collected.

We took steps to try to mitigate the impact of the most likely kinds of bias in a study of this design. Selection bias was present because implant type and surgical treatment were not randomized, and decision-making was made on an individualized basis for each patient. With this in mind, we controlled for confounding in our analyses. To try to minimize the risk of errors in data abstraction, two members of the study team (ATV, KGB) independently abstracted data from the medical records, and any disagreements were adjudicated by a third author (MRG).

Primary and Secondary Study Outcomes

Our primary outcome was the cumulative incidence of reoperation and revision after surgical fixation of pathologic subtrochanteric femur fracture with death as a competing risk. Secondary outcomes included factors associated with revision surgery, overall survival, and differences in clinical and surgical factors (including operative time, EBL, and LOS), complications, and 90-day readmissions. For the purposes of this analysis, we considered radioresistant tumors to include renal cell carcinoma, thyroid carcinoma, and sarcomatous tumors [29]. Certain histologic subtypes of thyroid cancer display

Table 1. Demographic characteristics of patients with pathologic subtrochanteric femur fracture

Characteristic	IMN (n = 77)	PFR (n = 22)	ORIF (n = 14)	p value
Age in years	65 (55-72)	63 (53-75)	69 (62-75)	0.66
Women	73 (56)	32 (7)	50 (7)	0.001
Primary tumor				0.11
Breast carcinoma	44 (34)	23 (5)	14 (2)	
Lung carcinoma	12 (9)	14 (3)	29 (4)	
Prostate carcinoma	9 (7)	18 (4)	14 (2)	
Multiple myeloma	9 (7)	0 (0)	21 (3)	
Renal cell carcinoma	3 (2)	14 (3)	7 (1)	
Other[a]	23 (18)	32 (7)	14 (2)	
Histologic growth[b]				0.08
Slow	57 (44)	32 (7)	43 (6)	
Moderate	18 (14)	41 (9)	14 (2)	
Rapid	25 (19)	27 (6)	43 (6)	
Tumor radiobiology				0.08
Radiosensitive	90 (69)	73 (16)	71 (10)	
Radioresistant	3 (2)	18 (4)	14 (2)	
Prostate carcinoma, blastic	8 (6)	9 (2)	14 (2)	
BMI in kg/m^2	25 (23-31)	27 (20-28)	30 (21-33)	0.49
Age-adjusted CCI	9 (8-11)	9 (8-10)	9 (9-10)	0.43
Smoking status				0.35
Never	62 (48)	55 (12)	50 (7)	
Former	32 (25)	32 (7)	50 (7)	
Current	5 (4)	14 (3)	0 (0)	
Radiotherapy	65 (50)	59 (13)	71 (10)	0.75
Preoperative	44 (34)	27 (6)	29 (4)	0.25
Postoperative	42 (32)	41 (9)	50 (7)	0.83
Chemotherapy	77 (59)	68 (15)	64 (9)	0.52
Preoperative	69 (53)	41 (9)	50 (7)	0.04
Postoperative	45 (34)	50 (11)	43 (6)	0.89
Follow-up in months	5 (3-19)	4 (2-11)	7 (4-25)	0.48

Data presented as median (IQR) or % (n).
[a]The full list of primary tumors is available (Supplemental Table 1; http://links.lww.com/CORR/B350).
[b]Histologic growth as described by the Katagiri scoring system [18].

varying degrees of radioresistance, which is why we categorized them as such for our study [22, 28, 32]. Radiosensitive tumors were all others except for osteoblastic prostate carcinoma, which we evaluated separately, as it is sclerotic and behaves like bisphosphonate-associated fractures in the proximal femur with difficult-to-reduce transverse fracture patterns [19]. A reoperation was any procedure that used an approach through the same incision. A revision was any reoperation wherein some or all the components of the previous implant were removed or exchanged. We defined complications as deep venous thromboses (DVT), pulmonary emboli (PE), pneumonia, urinary tract infection (UTI), neurovascular injury, and miscellaneous complications, including acute kidney injury and bacteremia. Complications were not pooled during analysis.

Ethical Approval

Ethical approval for this study was obtained by the Massachusetts General Hospital Institutional Review Board (protocol # 2024P000054).

Statistical Analysis

Data were analyzed with bivariate analysis and provided as descriptive statistics. We reported continuous variables as

median (IQR) and compared them using the nonparametric Kruskal-Wallis test. Dichotomous variables were provided as frequencies (percentages) and compared using chi-square tests, with the Fisher exact test for those with < 5 observations. All tests were two-sided, and an α of 0.05 was considered significant. Kaplan-Meier analysis was performed to assess overall survival in the whole cohort. The Cox proportional hazards model was used to estimate overall survival for each treatment group using age, gender, and age-adjusted CCI as covariates in the model to control for potential confounding. Competing risks analyses were performed to render cumulative incidences for reoperation and revision at 2 years using death and/or loss to follow-up as competing events, adjusting for age, gender, and age-adjusted CCI to control for potential confounding. Differences between groups were assessed using Fine-Gray test for subdistribution hazards. An exploratory univariable logistic regression was performed to generate unadjusted HRs for potentially confounding parameters including age, gender, BMI, age-adjusted CCI, smoking status, tumor radiobiology, radiotherapy, chemotherapy, operative treatment, preoperative hemoglobin, operative time, EBL, and LOS. A subsequent multivariable Cox proportional hazards model was used to render adjusted HRs for parameters significantly associated in univariable logistic regression ($p < 0.10$) along with potentially confounding parameters including age, gender, and age-adjusted CCI. Stata SE 17.0 (StataCorp LLC) was used for all analyses.

Results

Cumulative Incidence of Reoperation and Revision

The cumulative incidence for reoperation at 2 years was 5% (95% confidence interval [CI] 4% to 6%) for IMN, 15% (95% CI 9% to 22%) for PFR, and 32% (95% CI 15% to 50%) for ORIF ($p = 0.03$) (Fig. 2A). The cumulative incidence for revision at 2 years was 4% (95% CI 3% to 4%) for IMN, 4% (95% CI 2% to 6%) for PFR, and 33% (95% CI 15% to 51%) for ORIF ($p = 0.01$) (Fig. 2B).

Reoperation was performed after IMN in 6% (5 of 77) of patients, PFR in 3 of 22 patients, and ORIF in 5 of 14 patients (Table 2). The most common reasons for reoperation were implant revision (10 of 12) and postoperative hematoma treated with irrigation and debridement (2 of 12; both after PFR). The most common reasons for revision were nonunion (5 of 10) and infection (2 of 10) (Table 3). Periprosthetic joint infection (PJI) was more common after salvage PFR (2 of 6) than primary PFR (1 of 22) ($p = 0.04$).

Factors Associated With Implant Revision

After controlling for potentially confounding variables such as age, gender, and age-adjusted CCI, we found radioresistant tumor histology (HR 8.5 [95% CI 1.2 to 58.9]; $p = 0.03$) and ORIF (6.3 [95% CI 1.5 to 27.0]; $p = 0.01$) to be associated with implant revision (Table 4).

Overall Survival

The 3-month, 1-year, and 2-year overall survival was 80% (95% CI 71% to 87%), 35% (95% CI 26% to 45%), and 28% (95% CI 19% to 36%), respectively (Fig. 3A). A log-rank test for equality of survivor functions showed no difference in overall survival by implant type at 90 days, 1 year, and 2 years after initial surgery (Fig 3B). Cox proportional hazards, adjusted for age, gender, and age-adjusted CCI, additionally revealed no differences in 2-year overall survival between implant types (PFR HR 0.6 [95% CI 0.3 to 1.3]; $p = 0.24$; ORIF HR 0.6 [95% CI 0.3 to 1.4]; $p = 0.26$; reference = IMN).

Clinical and Surgical Factors and Complications

Patients undergoing PFR experienced a greater median (range) operative time (150 minutes [94 to 314] versus 98 minutes [45 to 410] in IMN and 143 minutes [117 to 208] in ORIF; $p = 0.005$) (Table 2). Patients treated with PFR also displayed higher median (range) EBL (625 mL [200 to 3600] versus 300 mL [20 to 1800] in IMN and 475 mL [200 to 900] in ORIF; $p = 0.01$) and LOS (8 days [1 to 33] versus 5 days [2 to 28] in IMN and 7.5 days [3 to 15] in ORIF; $p = 0.04$).

Overall, the frequencies of complications were as follows: DVT 5% (6 of 113), PE 1% (1 of 113), UTIs 4% (5 of 113), developed pneumonia 4% (4 of 113), neurovascular injury 1% (1 of 113), and miscellaneous complications 3% (3 of 113), including acute kidney injury (n = 2) and bacteremia (n = 1) (Table 2). One patient undergoing PFR developed a transient sciatic nerve palsy from hematoma compression that resolved after hematoma evacuation. Thirty-day postoperative complications did not differ by fixation type. Readmission within 90 days occurred in 10 patients: 3 after ORIF, 4 after PFR, and 3 after IMN ($p = 0.03$). Ten deaths occurred within the first 30 days of surgery but did not differ by treatment (Table 2).

Discussion

Pathologic fractures in the subtrochanteric region severely worsen patients' quality of life, causing pain, loss of function, and reduced life expectancy, and they often initiate a period of dependent care. Although surgery is commonly indicated in this context, debate continues about how to choose the right approach for each patient. Most studies

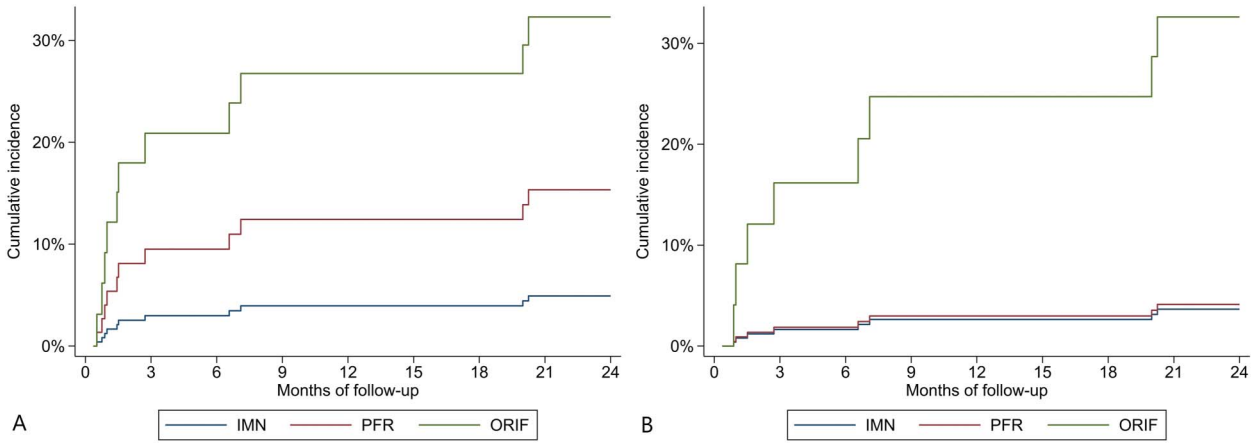

Fig. 2 Cumulative incidence of (**A**) reoperation and (**B**) revision by operative treatment type. A competing risk analysis with death as a competing risk was performed using age, gender, and age-adjusted CCI as covariates to control for potential confounding. A color image accompanies the online version of this article.

focus on three main treatment strategies: IMN, ORIF, and endoprostheses such as PFR [35]. Each modality is associated with unique complications and different rates of reoperation and revision, underscoring the importance of careful consideration during treatment selection [15]. Our study aimed to address this gap by investigating the cumulative incidence for reoperation and implant revision and factors associated with revision surgery across these fixation modalities in a large group of patients treated for pathologic subtrochanteric femur fractures. We found that PFR had a higher 2-year cumulative incidence of reoperation compared with IMN, primarily because of the more common use of irrigation and debridement procedures for postoperative hematoma. However, the cumulative incidence of implant revision was no different between the two methods. Furthermore, patients who underwent ORIF or had radioresistant tumor histology were at higher risk for revision surgery after adjusting for potential confounding factors.

Table 2. Clinical and surgical factors and 30-day complications by type of operative management

	IMN (n = 77)	PFR (n = 22)	ORIF (n = 14)	p value
Clinical and surgical factors				
Operative time in minutes	98 (72-142)	150 (116-238)	143 (126-181)	0.005
EBL in mL	300 (175-600)	625 (300-800)	475 (350-770)	0.01
Length of stay in days	5 (3-8)	8 (4-13)	7.5 (5-9)	0.04
Medical complications				
90-day readmission	4 (3)	18 (4)	21 (3)	0.03
DVT	4 (3)	14 (3)	0 (0)	0.13
PE	1 (1)	0 (0)	0 (0)	0.79
Pneumonia	4 (3)	5 (1)	0 (0)	0.74
UTI	5 (4)	0 (0)	7 (1)	0.50
Other[a]	3 (2)	5 (1)	0 (0)	0.67
Surgical complications				
Infection	3 (2)	5 (1)	0 (0)	0.71
Neurovascular injury[b]	0 (0)	5 (1)	0 (0)	0.12
Reoperation	6 (5)	14 (3)	36 (5)	0.007
Revision	5 (4)	5 (1)	36 (5)	< 0.001
Death within 30 days	10 (8)	9 (2)	0 (0)	0.45

Data presented as median (IQR) or % (n).
[a]Other medical complications included acute kidney injury (n = 2) and bacteremia (n = 1).
[b]Sciatic nerve palsy because of compression by hematoma that resolved after hematoma evacuation.

Table 3. Characteristics and interventions for revisions and reoperations

Age in years	Gender	Primary tumor[a]	Operative treatment	Revision or reoperation	Reason for surgery	Surgical intervention	Time to reoperation in months
69	Woman	Breast	IMN	Revision	Nonunion	ORIF and iliac crest autograft	7
52	Woman	Breast	IMN	Revision	Nonunion	PFR	21
57	Man	Myeloma	IMN	Revision	Nonunion	Irrigation and debridement and nail exchange	36
46	Man	Myeloma	ORIF	Revision	Nonunion	Hardware removal and long-stemmed THA	20
73	Man	Prostate, blastic	ORIF	Revision	Nonunion	PFR	3
75	Woman	Thyroid	ORIF	Revision	Implant failure	Revision to PFR (Qx1) followed by DAIR plus for PJI (Qx2)	1
75	Man	Lung	ORIF	Revision	Implant failure	PFR	2
50	Woman	Melanoma	ORIF	Revision	Disease progression	Revision to PFR (Qx1) followed by DAIR plus for PJI (Qx2)	32
71	Man	Colorectal	IMN	Reoperation	Infection	Irrigation and debridement	1
76	Woman	Breast	IMN	Revision	Infection	Irrigation and debridement and nail exchange (Qx1) followed by PFR (Qx2)	7
70	Man	Renal cell	PFR	Revision	PJI	DAIR plus	1
68	Woman	Breast	PFR	Reoperation	Hematoma	Irrigation and debridement	1
52	Woman	Breast	PFR	Reoperation	Hematoma	Irrigation and debridement	2

Qx1 = first reoperation; Qx2 = second reoperation.
[a]Primary tumors were carcinomatous unless otherwise specified.

Limitations

Our study had several limitations that should be acknowledged. First, selection bias may have influenced the results, as treatment strategy was based on the preoperative profile of patients and the anticipated response to systemic treatment. IMN was typically chosen for patients with more (or more severe) medical comorbidities who were thought not to be sufficiently fit for a larger intervention (endoprosthetic reconstruction or ORIF) or those with diffuse metastatic disease and poor prognosis in terms of expected overall survival. In contrast, PFR was preferred for patients with a better prognosis in whom surgeons prioritized implant durability and patient function over surgical risk. To address this source of bias, we adjusted all regression analyses for age, gender, and age-adjusted CCI. Age-adjusted CCI is a widely used measure of comorbidity and has been shown to accurately predict survival in cancer patients [39]. Although the American Society of Anesthesiologists (ASA) classification is also validated, it was not documented in about 35% of the cases included in our study. We consider age-adjusted CCI superior because of its numerical range from 0 to 37 compared with the limited 6 ASA classes, only 4 of which are clinically meaningful in a study such as ours. Second, this was a retrospective, observational study, which was limited to identifying associations but cannot comment on cause-effect relationships. However, the surgical indications applied in our study are likely consistent with those from other cancer-specialized centers. Third, the limited sample size for our study may have reduced statistical power, potentially resulting in us missing between-group differences. For instance, the proportion of patients with DVT was 14% for those undergoing PFR, and it was 4% in patients treated with IMN; this difference, however, was not statistically significant ($p = 0.13$). Surgeons should exercise caution when interpreting these differences and the underlying statistics, as they may be limited by our study sample. Finally,

Table 4. Factors associated with revision after operative treatment of pathologic subtrochanteric femur fracture

Factor	HR (95% CI)	p value
Age	1.0 (0.9-1.1)	0.98
Women (ref. = men)[a]	0.4 (0.1-1.7)	0.20
Age-adjusted CCI	1.1 (0.7-2.0)	0.66
Radiobiology (ref. = radiosensitive)[a]		
Radioresistant	8.5 (1.2-58.9)	0.03
Prostate carcinoma, blastic	1.1 (0.1-12.3)	0.97
Operative treatment (ref. = IMN)[a]		
PFR	0.6 (0.1-5.9)	0.66
ORIF	6.3 (1.5-27.0)	0.01

[a]For categorical variables, we compared each alternative to a reference category (ref.). For example, the risk of revision with PFR or ORIF was compared to IMN as the reference. Age is represented as a per-year increase because it was included as a continuous variable for this analysis.

the wide CIs seen in some areas of our multivariable analysis, particularly in the Cox regression to identify factors associated with revision surgery, suggest that sparse-data bias may have been present [20]. Practicing surgeons in this field should be aware of such bias to appropriately contextualize findings when applying them to clinical practice.

Cumulative Incidence of Reoperation and Revision

Despite higher cumulative incidence of reoperation in PFR and ORIF, there was no difference in cumulative incidence of revision between PFR and IMN. It is important to compare these outcomes separately, as reoperations for hematoma removal involve significantly less morbidity than implant revisions for nonunion or PJI. Nonunion was the most common cause for revision or reoperation in 5 of 13 patients, which followed IMN in 3 patients and ORIF in 2 patients. In patients initially treated with IMN and ORIF, conversion to PFR is a common salvage option, particularly when there is mechanical insufficiency because of poor bone stock or substantial bone loss [10, 17, 21]. However, of the six patients who underwent IMN and ORIF and revision to PFR as salvage, two of these subsequently developed PJI and were treated with an additional procedure consisting of debridement, antibiotics, and implant retention (DAIR plus) (Table 3). DAIR plus has been shown to be effective as two-stage revision in the setting of PJI of oncologic megaprostheses in patients who cannot withstand two-stage revision surgery [11], although any reoperation, if avoidable, is preferable in the sick patient. These findings highlight a higher infection rate for salvage procedures with PFR than primary PFRs (33% versus 5%; p = 0.04), which is consistent with reported findings for salvage PFR [5]. Thus, primary PFR performs better than salvage PFR in this population, and the cumulative incidence of implant revision was no different between IMN and PFR, which should be considered in patients with sufficient estimated survival and low estimated morbidity who may be at higher risk of developing an indication for implant revision, such as nonunion, mechanical failure, or progressive bone loss caused by radioresistant tumor.

Factors Associated With Implant Revision

After adjusting for potential confounding factors, we found ORIF and radioresistant tumor types to be associated with

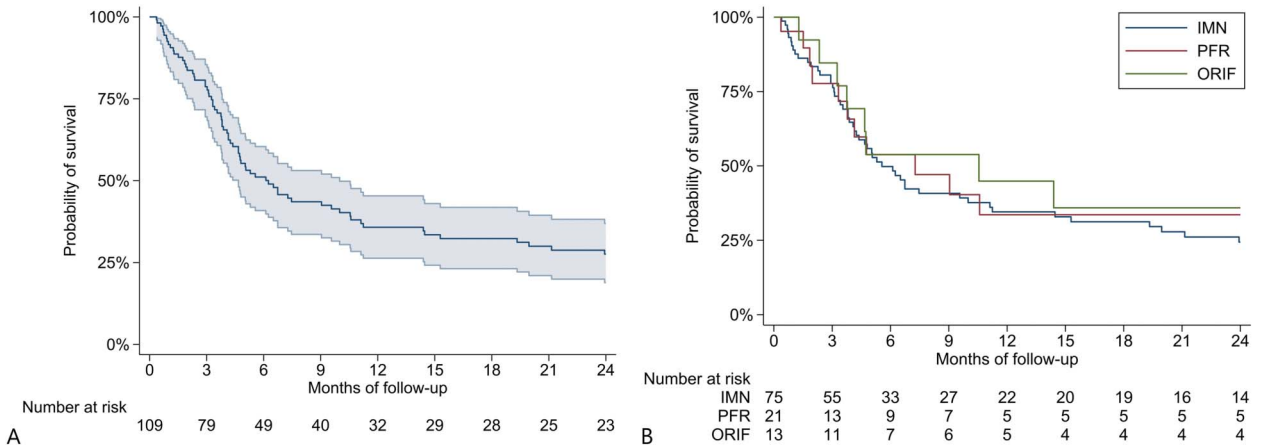

Fig. 3 Kaplan-Meier survival analysis of overall survival for (**A**) the entire cohort and (**B**) by implant type. (**A**) The shaded area represents the estimated 95% CI of survival probability. The median overall survival was 6 months (95% CI 4 to 10). (**B**) Cox proportional hazards, adjusted for age, gender, and age-adjusted CCI, revealed no differences in 2-year overall survival between implant types (PFR HR 0.6 [95% CI 0.3 to 1.3]; p = 0.24; ORIF HR 0.6 [95% CI 0.3 to 1.4]; p = 0.26; reference = IMN). A color image accompanies the online version of this article.

implant revision. Notably, treatment with PFR was not associated with revision when compared with IMN. This aligns with reports indicating high revision rates (up to 23%) after ORIF, especially for subtrochanteric fractures in pathologic bone [37]. Further, prior studies report rates of revision varying between 0% to 26% after IMN [8, 13, 23, 27, 34–36] and lower rates after endoprostheses [13, 35]. Although preoperative or postoperative chemotherapy and radiotherapy were not associated with revision, as previously suggested by Willeumier et al. [36], tumor radiobiology was associated. Our findings showed that radioresistant tumors had a higher revision risk compared with radiosensitive tumors, but osteoblastic prostate carcinoma had no increased risk of revision. We evaluated tumor radiobiology because radiosensitive tumors, after systemic chemotherapy and local radiotherapy, may respond favorably and behave like nonpathologic bone with some propensity to remodel. In contrast, radioresistant osseous lesions continue to behave pathologically and may progress to nonunion if not resected, subsequently resulting in revision [29]. Further, we analyzed osteoblastic prostate carcinoma separately because its sclerotic bone behaves like bisphosphonate-associated, transverse fractures [19], which might increase the theoretical risk of implant revision. However, we did not find a higher risk of revision compared with radiosensitive tumors in this group. Tumor radiobiology should be considered when selecting a treatment strategy for pathologic subtrochanteric femur fracture, as radioresistant tumors are at increased risk for implant revision, as are patients undergoing ORIF. Therefore, in patients with radioresistant tumor types, orthopaedic surgeons should consider performing primary endoprosthetic reconstruction over IMN.

Overall Survival

Overall survival decreased precipitously during the first postoperative year in our study from 80% at 3 months to 35% at 1 year, and then this leveled somewhat near the 2-year mark at 28% without differences between treatment strategy. These survivorships are higher than published rates at all time points for patients undergoing stabilization for pathologic femur fractures, with ranges of 49% to 52%, 33%, and 14% to 19% at 6 months, 1 year, and 2 years postoperatively, respectively [31, 35, 36]. Furthermore, those published reports included completed and impending pathologic fractures at follow-up of 6 to 14 months, but we evaluated only patients with completed fractures at a median follow-up of 6 months. Prior research found poorer overall survival at longer follow-up times in patients with completed pathologic fractures [12]. This finding suggests the impact of improvements in oncologic care over time, which is particularly relevant to the orthopaedic oncologist when considering use of PFR to manage pathologic subtrochanteric femur fractures. As progress in oncologic treatment continues to improve, more surviving patients may functionally benefit from endoprosthetic reconstruction over other fixation types when managing this entity.

Clinical and Surgical Factors and Complications

The higher operative time and EBL in patients undergoing PFR in our study was consistent with more extensive dissection necessary for exposure, particularly compared with IMN [38]. Additionally, patients who were stabilized with IMN experienced lower 90-day readmission rates, with no difference in 30-day mortality between groups (Table 2). In patients potentially nearing the end of their lives, minimizing morbidity and mortality that may precipitate from the physiologic insult of surgery, prolonged hospital or rehabilitation stays, or hospital readmissions should be of paramount concern [10]. Decision-support tools, such as PATHFx, exist to help estimate likelihood of survival after pathologic fracture fixation [2, 9], and instruments such as the Pathologic Fracture Mortality Index may predict 30-day postoperative morbidity and mortality to augment this determination [24, 33]. Furthermore, minimizing physiologic insult is crucial for patients who would benefit from expeditious resumption of systemic treatment or radiotherapy during active oncologic treatment to reduce risk of disease recurrence or progression [7]. In this context, we found IMN to afford the lowest EBL in patients with the lowest average preoperative hemoglobin, likely due to the less invasive necessary surgical exposure, along with the lowest rate of 90-day readmission. With the aid of decision-support instruments in patients for whom estimated postoperative survival is higher and estimated surgical morbidity is low, endoprostheses have been shown to have lower incidence of mechanical failure and higher implant survival rates compared with IMN [13], which is consistent with the findings of our study.

Conclusion

In patients with pathologic subtrochanteric femur fractures arising from radioresistant tumor types, primary PFR may be preferred over IMN by restoring function, alleviating pain, and offering local tumor control as the pathologic bone will be unlikely to respond to systemic treatment or radiotherapy. In complex fractures not amenable to IMN, surgeons should consider performing a PFR over ORIF because PFR was observed to be associated with reduced morbidity, lower risk of revision, and the added benefit of offering immediate mechanical stability with a cemented

endoprosthesis without relying on a fracture to heal in pathologic bone. Similarly, patients with large defects or more severe bone loss, in whom construct stability to ensure bone healing cannot readily be achieved, may benefit from endoprosthetic reconstruction. Future studies should compare long-term implant survival of PFR and IMN, as well as prospectively assess functional outcomes in patients with metastatic disease with favorable response to systemic treatment. Furthermore, the extent of bone loss because of local tumor burden should be quantified and analyzed in future studies, as this may additionally indicate PFR in this population.

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