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ORIGINAL ARTICLE

Risk factors for early infection following hemiarthroplasty in elderly patients with a femoral neck fracture

Dirk Zajonz[1,2] · Alexander Brand[1] · Christian Lycke[1] · Orkun Özkurtul[1] · Jan Theopold[1] · Ulrich J. A. Spiegl[1] · Andreas Roth[1] · Christoph Josten[1] · Johannes K. M. Fakler[1]

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Abstract

Purpose Periprosthetic joint infections (PJI) after hemiarthroplasty for geriatric femoral neck fractures are a devastating complication that results in serious morbidity and increased mortality. Identifying risk factors associated with early infection after HA for hip fractures may offer an opportunity to address and prevent this complication in many patients. The aim of this study was to evaluate preoperative risk factors for early PJI after HA in hip fracture patients.

Methods From January 2010 to December 2015, 312 femoral neck fractures (AO/OTA 31-B) in 305 patients were included in this single-center, retrospective study. PJI was defined according to the Centers for Disease Control (CDC) definition of deep incisional surgical site infection. Early infection referred to a postoperative period of 4 weeks. Binary univariable and multivariable regression analysis with backward elimination was applied to identify predictors of PJI.

Results Median age of all patients was 83.0 (IQR 76–89) years. We identified 16 (5.1%) early PJI which all required surgical revision. Median length of in-hospital stay (LOS) was 20.0 (IQR 10–36) days after PJI compared to 10.0 (8–15) days without deep wound infection. In-hospital mortality was 30.8 vs. 6.6%, respectively. Preoperative CRP levels (OR 1.009; 95% CI 1.002–1.018; $p=0.044$), higher BMI (OR 1.092; 95% CI 1.002–1.189; $p=0.044$) and prolonged surgery time (OR 1.013; 95% CI 1.000–1.025; $p=0.041$) were independent risk factors for PJI. Excluding infection following major revision due to mechanical complications identified preoperative CRP levels (OR 1.012; 95% CI 1.003–1.021; $p=0.007$) and chronic glucocorticoid therapy (OR 6.314; 95% CI 1.223–32.587; $p=0.028$) as risk factors, a clear trend was seen for higher BMI (OR 1.114; 95% CI 1.000–1.242; $p=0.051$). A cut-off value at CRP levels ≥ 14 mg/l demonstrated a sensitivity of 69% and a specificity of 70% with a fair accuracy (AUC 0.707).

Conclusion Preoperative serum CRP levels, higher BMI and prolonged surgery time are independent predictors of early PJI. Excluding PJI secondary to major revision surgery revealed chronic glucocorticoid use as a risk factor apart from preoperative CRP levels.

Keywords Femoral neck fracture · Hip fracture · CRP · Periprosthetic joint infection · Surgical site infection · Hemiarthroplasty · Obesity · Glucocorticoids

Purpose

Hip fractures in the elderly population are highly frequent and yet expected to rise exponentially over the next years [1, 2]. Intracapsular femoral neck fractures in geriatric patients are most commonly treated with hemiarthroplasty (HA) [3]. HA provides short operating times and quick mobilization [4] which are essential for geriatric patients presenting in an emergent and potentially life-threatening situation. Rapid restoration of the preoperative ambulatory capacity of these frail patients can be achieved with HA which may also have a beneficial effect on mortality rates within the

Dirk Zajonz and Alexander Brand equally contributed to this article.

✉ Johannes K. M. Fakler
Johannes.fakler@medizin.uni-leipzig.de

[1] Department of Orthopaedics, Trauma Surgery and Plastic Surgery, University Hospital of Leipzig, Liebigstr. 20, 04103 Leipzig, Germany

[2] ZESBO–Zentrum zur Erforschung der Stütz- und Bewegungsorgane, Semmelweisstraße 14, 04103 Leipzig, Germany

first year after surgery [5]. However, periprosthetic joint infections (PJI) after hemiarthroplasty for hip fractures are a devastating complication that results in serious deterioration of patients´ daily function and quality of life [6] and an increased 1-year mortality [7]. PJI are observed in 2–7% in this group of patients [7–10] which represents a considerably higher infection rate compared to approximately 1% after elective total hip arthroplasty (THA) [11].

Identifying risk factors associated with early infection after HA for hip fractures may offer an opportunity to address and prevent this potential complication by preoperative arrangements in many patients. But only limited data are available specifically focusing on the risk profile of HA [12] which is different from that of scheduled total hip arthroplasty (THA) [13].

Thus, the aim of this study was to evaluate risk factors for early PJI after bipolar HA in elderly hip fracture patients.

Methods

From January 2010 to December 2015, 312 femoral neck fractures (AO/OTA 31-B) in 305 patients were included in this single-center, retrospective study. Inclusion criteria were an age of 55 years or older, initial treatment with HA, a minimum follow-up of 4 weeks and a complete data set. Patients that received HA secondary to a failed internal fixation of a femoral neck fracture and those with a pathological fracture due to malignancy were excluded (Fig. 1). All included patients or their legal representative gave written informed consent. The study was approved by the local Ethics Committee at the University of Leipzig (Ref.no. 171-16/ek-25042016).

Apart from patient age, the body mass index (BMI) and medication was recorded (Table 1). Comorbidities were graded according to the American Society of Anaesthesiologists (ASA) score [14]. PJI was defined according to the Centers for Disease Control (CDC) definition of deep incisional surgical site infection [15]. An infection was categorized as early, if it occurred within 4 weeks after surgery [16]. In addition, PJI related to the initial implantation of HA were defined as primary PJI. If PJI was not present at the time of major revision surgery due to mechanical implant complications, but thereafter they were defined as secondary PJI. Blood samples for routine laboratory parameters, in particular CRP and total leukocyte count, were drawn immediately after admission to the emergency room.

All surgeries were performed in general anesthesia and all patients received a single-shot of 1.5 g cefuroxime (or clindamycin in case of hypersensitivity to penicillin or cefuroxime) prior to surgery. A bipolar endoprosthesis (DePuy, Warsaw, USA) was implanted using the Hardinge approach. After preparation of the medullary canal a plug was inserted and pulsatile jet-lavage was applied before cementing and implanting the stem. No pulsatile jet-lavage was used in uncemented HA. Patients were mobilized with full weight-bearing postoperatively.

The Shapiro–Wilk test was used to test continuous variables for normal distribution. Not normal distributed values are given as median and interquartile range (IQR 25–75 percentile). The following statistical tests were applied: binary univariable and multivariable regression analysis with backward selection, receiver-operating-characteristic curve (ROC curve) and area under the curve (AUC). All statistical computations were performed using SPSS version 24.0 (Chicago, IL, USA). *p* values less than 5% were considered as significant.

Results

Female patients represented 78% ($n=237$) and male patients 22% ($n=68$) of the study population. Median age of all patients was 83.0 (IQR 76–89) years. In the observed period

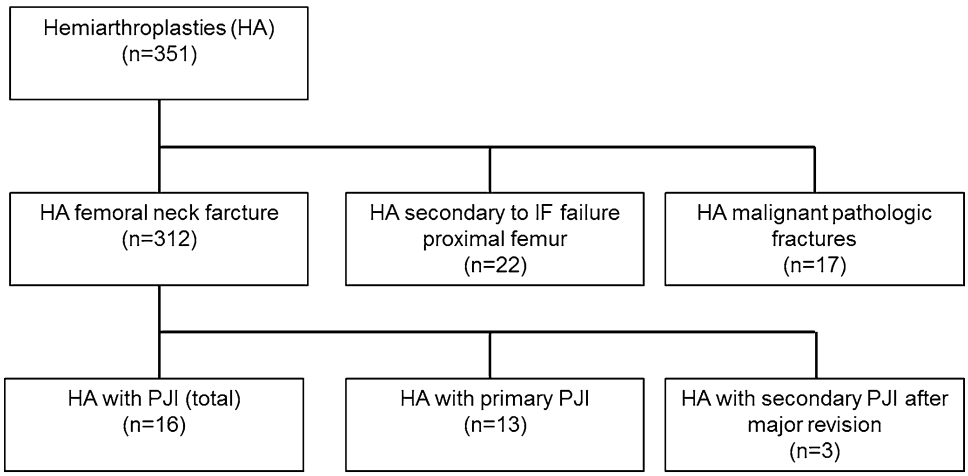

Fig. 1 Flowchart of performed hemiarthroplasties (HA)

Table 1 Baseline characteristics of 312 femoral neck fractures treated with hemiarthroplasty

	Total study cohort ($n=312$)
Age, median (IQR)	83.0 (76.3–89.0)
Females	78%
ASA classification	
I	2 (0.6)
II	69 (22.1)
III	235 (75.3)
IV	6 (1.9)
BMI, median (IQR)	24.1 (22.0–27.0)
Leucocyte count, median (IQR)	10.0 (8.0–13.4)
CRP (mg/l), median (IQR)	5.6 (1.6–19.9)
CRP ≥ 5 mg/l	162 (51.9)
Diabetes mellitus	99 (31.7)
Active skin disease (at site of surgical incision)	7 (2.2)
Anti-platelet drugs	103 (33.0)
Anticoagulants	43 (13.8)
Glucocorticoids	18 (5.8)
Immunosuppressant drugs (other than glucocorticoids)	8 (2.6)

Values are given as absolute numbers and percentage (parenthesis), if not otherwise specified

seven patients were treated with HA on both sides due to a subsequent medial femoral neck fracture at the contralateral side. Baseline characteristics of all 312 included HA are exhibited in Table 1.

We identified a total of 16 (5.1%) early PJI which all required surgical revision. 13 (4.2%) PJI occurred after primary HA and 3 (0.9%) PJI were attributed to secondary revision surgery related to implant complications (one periprosthetic fracture, two dislocations), because no infection was found at the time of revision surgery (Fig. 1). Median length of in-hospital stay (LOS) was 20.0 (IQR 10–36) days after PJI compared to 10.0 (8–15) days without deep wound infection. In-hospital mortality was 13% ($n=5$) vs. 6.7% ($n=20$), respectively. Univariable regression analysis revealed BMI, preoperative CRP levels, diabetes mellitus, active skin disease at the site of the surgical approach, glucocorticoid use and duration of surgery as significant risk and prognostic factors for early PJI. No significant association was found for age, sex, ASA score, leucocyte count, anti-platelet drugs, anticoagulants, immunosuppressants other than glucocorticoids, time of operation and experience of the surgeon (Table 2).

Multivariable regression analysis with backward elimination including the variables age, sex, BMI, ASA, diabetes, chronic glucocorticoid use, active skin disease at the site of surgery, preoperative CRP levels and operation time was used to identify independent risk factors for early PJI. Preoperative CRP levels, higher BMI and prolonged surgery time were independent predictors for PJI. (Table 3). The same variables were included in the second model referring to 13 primary PJI and excluding three cases of secondary infection due to major aseptic revision surgery. Preoperative CRP levels and chronic glucocorticoid use were found to be independent risk factors. A clear trend was demonstrated for the BMI (Table 4). In order to determine a cut-off value for preoperative serum CRP levels indicating risk of primary PJI a ROC curve was calculated. It showed a sensitivity of 69% and a specificity of 70% at levels ≥ 14 mg/l with a fair accuracy (AUC 0.707). A cut-off value of ≥ 14 mg/l was present in 99 (32%) patients.

Discussion

Our study revealed that preoperative elevated CRP levels, higher BMI and prolonged surgery are independently associated with an increased risk of early PJI after HA for femoral neck fracture in elderly patients. To exclude a potential influence of major revision surgery secondary to mechanical implant complications on PJI, we analyzed the primary PJI in a separate multivariable regression model. This model revealed elevated preoperative CRP levels and chronic glucocorticoid therapy as independent predictors. A clear trend was seen for BMI. A cut-off value for CRP indicating a higher risk for primary PJI was calculated at 14 mg/l with a sensitivity of 69%, a specificity of 70% and a fair accuracy (AUC 0.707).

PJI after hemiarthroplasty for hip fractures is a devastating complication that results in a 1-year mortality of 33–43% [6, 7, 10]. Only limited data is available on CRP as a predictor of PJI. C-reactive protein (CRP) is a routinely measured biochemical marker for inflammation synthesized in the

Table 2 Univariable analysis of risk and prognostic factors for early total periprosthetic infection ($n=16$) in 312 hemiarthroplasties

	PJI-free group ($n=296$)	PJI group ($n=16$)	OR (95% CI)	p
Age, median (IQR)	83.5 (76.3–89.0)	81.0 (75.5–85.0)	0.956 (0.903–1.012)	0.121
Females	232 (78.4%)	11 (68.6%)	0.607 (0.203–1.810)	0.370
ASA classification			1.607 (0.491–5.257)	0.433
I	2 (0.7)	0 (0)		
II	67 (22.6)	2 (12.5)		
III	221 (74.7)	14 (87.5)		
IV	6 (2.0)	0 (0)		
BMI [median (IQR)]	24.0 (22.0–27.0)	26.7 (22.0–29.1)	1.105 (1.016–1.201)	0.019*
Leucocyte count, median (IQR)	9.8 (8.0–13.3)	11.7 (7.7–14.8)	1.008 (0.987–1.030)	0.456
CRP (mg/l), median (IQR)	5.2 (1.6–19.0)	14.7 (3.1–26.9)	1.008 (1.000–1.016)	0.045*
Diabetes mellitus	90 (30.4%)	9 (56.3%)	2.943 (1.063–8.147)	0.038*
Active skin disease (at site of surgical incision)	5 (1.7%)	2 (12.5%)	8.314 (1.481–46.677)	0.016*
Anti-platelet drugs	98 (33.1%)	5 (31.3%)	0.918 (0.310–2.716)	0.878
Anticoagulants	40 (13.5%)	3 (18.8%)	1.496 (0.415–5.391)	0.538
Glucocorticoids	15 (5.1%)	3 (18.8%)	4.323 (1.111–16.820)	0.035*
Immunosuppressive drugs (other than glucocorticoids)	7 (2.4)	1 (6.3%)	2.752 (0.318–23.833)	0.358
Cementless HA	32 (10.7%)	1 (6.3%)	0.550 (0.070–4.303)	0.569
Surgery time (min), median (IQR)	70.0 (56.0–84.0)	77.0 (66.0–124.3)	1.014 (1.002–1.027)	0.024*
Operation at night shift (8 p.m–8 a.m.)	64 (21.6%)	2 (12.5%)	0.523 (0.116–2.366)	0.400
Senior surgeon	261 (88.2%)	15 (93.8%)	1.889 (0.233–15.287)	0.551

Values are given as absolute numbers and percentage (parenthesis), if not otherwise specified

*$p<0.05$

Table 3 Multivariable analysis of risk and prognostic factors for early total periprosthetic infection ($n=16$) in 312 hemiarthroplasties

	β	OR (95% CI)	p
BMI [median (IQR)]	0.088	1.092 (1.002–1.189)	0.044
CRP (mg/l), median (IQR)	0.009	1.009 (1.000–1.018)	0.044
Surgery time	0.013	1.013 (1.000–1.025)	0.041

Table 4 Multivariable analysis of risk and prognostic factors for early primary periprosthetic infection ($n=13$) in 309 hemiarthroplasties

	β	OR (95% CI)	p
BMI [median (IQR)]	0.108	1.114 (1.000–1.242)	0.051
CRP (mg/l), median (IQR)	0.012	1.012 (1.003–1.021)	0.007
Glucocorticoids	1.843	6.314 (1.223–32.587)	0.028

liver and adipose tissue within 6 h in response to bacterial infection, inflammatory disease or tissue trauma [17]. Buchheit et al. [7] found a higher proportion of patients with PJI after HA for femoral neck fracture in a group of 30 patients with CRP levels > 50 mg/l compared to 74 patients with levels < 50 mg/l (13.3 vs. 1.4%). Of note, patients with CRP levels > 50 mg/l received additional diagnostic work-up and, if necessary, treatment which almost doubled time to surgery from 3.8 to 7.4 days. Nonetheless, a 1-year mortality of 33% was reported [7]. Pfitzner et al. [18] determined a threshold of 5 mg/l to predict PJI in patients scheduled for primary hip or knee arthroplasty. Consequently, the authors recommended additional preoperative diagnostic work-up in patients with CRP levels > 5 mg/l to exclude bacterial infection. That recommendation cannot automatically be transferred to patients with a femoral neck fracture, since approximately 50% of patients with a femoral neck fracture present with CRP levels > 5 mg/l as demonstrated previously [19] and confirmed in this study population. However, raising the cut-off level to 14 mg/l as in our study would decrease the cohort at risk only to roughly one-third. Moreover, the cause of elevated CRP levels often remains unclear, since mild to moderate CRP elevations may also originate from tissue trauma, obesity, diabetes or aseptic inflammatory disease [20–22]. Irrespective of increased preoperative CRP levels, a substantial delay of surgery due to extensive preoperative diagnostics should be avoided in these patients, because it is associated with higher morbidity [23] and mortality [5].

Obesity is a recognized risk factor for PJI after scheduled primary THA [24, 25]. In patients treated with HA after femoral neck fracture Cordero-Ampuero [12] reported an association of obesity and PJI occurring more than 3 months after surgery. Visualization of the surgical situs in obese patients can be technically demanding and may

require larger surgical incisions. Moreover, close proximity of the surgical incisions to densely germinal colonized intertriginous areas add to an increased risk of wound infection [26–28]. This may also be of interest in obese hip fracture patients in which overhanging, enlarged intertriginous areas of the groin extend closely to the site of surgical incisions required for an approach to the hip joint. On the contrary, BMI was not confirmed as a risk factor by de Jong et al. [10]. An explanation could be a different standard antibiotic prophylaxis (SAP) regimen. Jong et al. [10] administered 1–3 g of cefazolin adapted to body weight compared to our SAP with 1.5 g cefuroxime. Both SAPs are compliant with current guidelines [29]. However, Lübbeke et al. [30] exhibited recently that a standard dose of 1.5 g cefuroxime might not be adequate in patients with a BMI ≥ 35 or body weight ≥ 100 kg and recommended doubling of cefuroxime dosage in those patients.

The role of chronic glucocorticoid therapy and immunosuppression on PJI after hip arthroplasty is discussed controversially. Cordero-Ampuero et al. [12] exhibited an increased risk of PJI after HA in patients receiving glucocorticoid treatment. In young patients with rheumatoid and juvenile rheumatoid arthritis a higher rate of PJI was also demonstrated for those on steroid therapy [31]. In contrast, de Jong et al. [10] and Lau et al. [32] could not identify glucocorticoid therapy as a risk factor. These results resemble our findings that identified chronic glucocorticoid use as an independent risk factor for PJI only after primary surgery. After including PJI that occurred after revision due to implant complications an association was only seen in univariable regression analysis. Conflicting results are also reported in transplant patients scheduled for THA. Solid organ transplant patients on glucocorticoid and immunosuppressant therapy demonstrated a higher risk of PJI after total hip arthroplasty (THA) [33]. But the rate in PJI in transplant patients seems to depend on the type of transplanted organ [33] as well as the perioperative antibiotic regimen [34]. In a small series of lung transplant patients no PJI occurred. The authors recommended prolonged postoperative antibiotics at least until wound healing [34].

The influence of a surgery time on PJI after HA for femoral neck fractures is discussed controversially [9, 10, 13, 32]. Ridgeway et al. [9] and Lau et al. [32] found no association with surgical site infection. On the contrary, Dale et al. [13] reported higher PJI rates after short operation times. This was confirmed by de Long et al. [10], but they also exhibited an independent association with prolonged surgery time after stratifying operation times into short (≤ 45 min), reference (45–90 min) and long (≥ 90 min).

Diabetes showed a significant association with PJI in univariable, but not in multivariable analysis with backward elimination. Previous studies failed to demonstrate an influence of diabetes on surgical site infection [12, 32]. This might be explained by findings of Chrastil et al. [35] demonstrating an increased risk of PJI for preoperative hyperglycemia, but for increased HbA1c levels. No associations with PJI were demonstrated for anti-platelet or anticoagulant therapy in our study which is in line with other studies [10, 32].

Limitations of this study include the retrospective design which potentially implicated a study bias. Although numerous confounding variables were considered in the multivariable regression model, unknown or unmeasured confounders were likely disregarded which is inherent to all retrospective studies. Moreover, the time of the fracture incidence was not documented and the time interval from fracture to drawing of blood samples may have influenced preoperative CRP levels. Finally, the study was limited to single trauma center. Other hospitals may have a variable infrastructure and treatment protocols with a potential impact on outcomes and PJI rates.

Conclusion

Preoperative serum CRP levels are independent predictors of early PJI in elderly patients treated with HA following a femoral neck fracture, but accuracy at the calculated cut-off value of 14 mg/l is only moderate. Higher BMI and a longer operating time were also independently associated with early PJI. Excluding PJI secondary to major revision surgery revealed chronic glucocorticoid use as an additional risk factor. Awareness of these risk factors and consideration in perioperative treatment protocols offer an opportunity to decrease this devastating complication in a fragile patient cohort.

Compliance with ethical standards

Conflict of interest The authors declare that no competing interests exist.

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