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Original Research Article

Comparative Study of Incidence of Delayed Healing and Failure of Fracture Union in Subjects with Fractures of Neck of Femur in Patients on Versus Without Steroid Therapy: A Prospective Study

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Abstract:

Aim: To compare the incidence of delayed healing and fracture union failure in patients with femoral neck fractures receiving systemic steroid therapy versus those without steroid exposure in a prospective cohort design.

Materials and Methods: A prospective observational study was conducted over 24 months involving 200 patients (100 with steroid therapy, 100 without) presenting with femoral neck fractures. Patients were followed at 6 weeks, 12 weeks, 24 weeks, and 52 weeks post-operative. Radiographic assessment was performed using anteroposterior and lateral hip radiographs. Statistical analysis included Chi-square test, Mann-Whitney U test, and logistic regression analysis. P-value <0.05 was considered statistically significant.

Results: The incidence of delayed union was significantly higher in steroid-treated patients (34%) compared to non-steroid group (12%, p=0.002). Fracture nonunion rates were 16% in steroid group versus 4% in control group (p=0.008). Mean time to union was 18.2±4.6 weeks in steroid group versus 12.4±3.2 weeks in control group (p<0.001). Harris Hip Score at 12 months was significantly lower in steroid group (68.4±12.3 vs 82.1±8.9, p<0.001). Complications including AVN were more frequent in steroid-treated patients (18% vs 6%, p=0.012).

Conclusion: Systemic steroid therapy is an independent risk factor for delayed fracture healing and nonunion in femoral neck fractures. Patients on chronic steroid therapy require early surgical intervention, close radiographic monitoring, and potentially augmentative strategies to promote bone healing. These findings underscore the importance of identifying steroid-exposed patients at risk and implementing preventive measures.

Keywords: Femoral Neck Fracture, Steroid Therapy, Delayed Union, Nonunion, Prospective Study, Orthopedic Trauma.

Introduction

Femoral neck fractures represent a significant orthopedic injury with substantial morbidity and mortality, particularly in the aging population. The healing of femoral neck fractures depends on multiple biological, mechanical, and clinical factors. The femoral neck's unique vascular anatomy, characterized by an end-artery blood supply originating from the medial and lateral femoral circumflex arteries, renders fractures in this region particularly vulnerable to nonunion and avascular necrosis. The incidence of nonunion after internal fixation of femoral neck fractures ranges from 20-35% in elderly patients and up to 15-25% in younger populations.

Systemic corticosteroid therapy, commonly used in the management of chronic inflammatory conditions including rheumatoid arthritis, systemic lupus erythematosus, polymyalgia rheumatica, and chronic obstructive pulmonary disease, has been implicated as a risk factor for impaired fracture healing. Corticosteroids exert multifaceted effects on bone metabolism and fracture healing through several mechanisms: (1) inhibition of osteoblast differentiation and function, (2) promotion of osteocyte apoptosis, (3) impaired angiogenesis at the fracture site, (4) reduced expression of bone morphogenetic proteins (BMPs) and other growth factors essential for osteogenic differentiation, (5) altered immune response affecting the inflammatory phase of fracture healing, and (6) development of glucocorticoid-induced osteoporosis with reduced bone mineral density[7].

The clinical significance of this research lies in the need to identify high-risk patients and implement preventive and therapeutic strategies to optimize outcomes in this challenging patient population. This prospective study was designed to systematically evaluate the incidence of delayed

healing, nonunion, and associated complications in patients with femoral neck fractures stratified by steroid exposure status, with the hypothesis that systemic steroid therapy significantly increases the risk of delayed union and nonunion.

Materials and Methods

Study Design and Setting: A prospective observational cohort study was conducted at a tertiary orthopedic care center over a 24-month period. The study protocol was approved by the Institutional Ethics Committee, and informed written consent was obtained from all participants.

Study Population and Inclusion Criteria: Two hundred patients with confirmed femoral neck fractures were enrolled and stratified into two groups: Group A (n=100) comprised patients receiving systemic steroid therapy (≥7.5 mg prednisolone or equivalent daily for ≥3 months prior to fracture), and Group B (n=100) comprised age-matched and comorbidity-matched patients without steroid exposure.

Inclusion criteria: (1) Age ≥40 years, (2) Radiographically confirmed femoral neck fracture (Garden classification I-IV), (3) Treated with internal fixation using femoral neck screws or plates within 72 hours of injury, (4) Ability to comply with follow-up protocol, (5) Minimum 12-month follow-up period.

Clinical profile

- Age, sex, BMI, menopausal status, smoking, alcohol, family history of hip fracture, prior fragility fractures, fall history, and comorbidities (RA, CKD, malabsorption).
- Detailed steroid history: dose, duration, cumulative exposure, and indication for therapy.

Densitometry and imaging

- DXA T-scores at femoral neck, total hip, and lumbar spine, classifying normal, osteopenia, or osteoporosis; vertebral fracture assessment if height loss or back pain.
- FRAX 10-year probabilities (major osteoporotic and hip fracture) with and without BMD, explicitly capturing glucocorticoid use.

Laboratory and fracture pattern Baseline labs: calcium, phosphate, ALP, creatinine, 25(OH)D, CBC, TSH, and tests for secondary causes (e.g., hypogonadism) as needed. Fracture characteristics (low-trauma mechanism, intra- vs extracapsular pattern) and time to fracture, comparing severity and BMD between steroid and non-steroid groups. **Exclusion criteria:** (1) Pathological fractures, (2) Previous hip surgery on the ipsilateral side, (3) Active infection or osteomyelitis, (4) Severe cognitive impairment, (5) Patients requiring anticoagulation therapy with warfarin.

Radiographic Assessment Radiographic evaluation was performed using standardized anteroposterior and lateral hip radiographs at baseline and at 6 weeks, 12 weeks, 24 weeks, and 52 weeks post-operatively. Union was assessed using standardized criteria: (1) Bridging callus visible on both anteroposterior and lateral radiographs, (2) Loss of fracture line visibility, (3) Progressive sclerosis at fracture margins, and (4) Load-bearing capability without hardware failure. Delayed union was defined as lack of radiographic evidence of union at 12 weeks post-operatively. Nonunion was defined as absence of radiographic union at 24 weeks with no further healing progression.

Functional Assessment: Functional outcomes were assessed using the Harris Hip Score (HHS) at baseline (preoperatively), 6 weeks, 12 weeks, 24 weeks, and 52 weeks post-operatively. The HHS is a validated, surgeon-administered scoring system with a maximum score of 100, where higher scores indicate better functional outcomes.

Observation Tables

Table 1: Baseline Demographic and Clinical Characteristics

Demographic Variable	Steroid Group (n=100)	Non-Steroid Group (n=100)	p-value
Mean Age (years ± SD)	57.3 ± 11.2	56.8 ± 10.9	0.647
Male: Female ratio	42:58	45:55	0.721
Mean BMI (kg/m²)	24.6 ± 3.8	24.2 ± 3.5	0.425
Diabetes Mellitus, n (%)	34 (34%)	28 (28%)	0.358
Hypertension, n (%)	58 (58%)	52 (52%)	0.401
Osteoporosis, n (%)	46 (46%)	38 (38%)	0.228
Mean Serum Creatinine (mg/dL)	1.2 ± 0.4	1.1 ± 0.3	0.156
Preoperative Hemoglobin (g/dL)	10.8 ± 1.6	11.2 ± 1.4	0.089

Table 2: Characteristics of Steroid Therapy in Study Group

Steroid Characteristics	Number of Patients	Percentage	Mean ± SD
Indication for Steroid Therapy			
\Quad Rheumatoid Arthritis	42	42%	--
\Quad COPD	28	28%	--
\Quad Systemic Lupus Erythematosus	18	18%	--
\Quad Polymyalgia Rheumatica	12	12%	--
Mean Daily Steroid Dose (mg PE*)	--	--	12.8 ± 6.4
Cumulative Steroid Dose (g PE*)	--	--	2,847 ± 1,236
Duration of Steroid Therapy (years)	--	--	5.8 ± 3.2
Concurrent Immunosuppressive Therapy, n (%)	34	34%	--
Mean Bone Mineral Density (T-score)	--	--	-2.4 ± 0.8
*PE = Prednisolone Equivalent			

Table 3: Radiographic and Clinical Outcomes at Follow-Up

Radiographic Outcome	Steroid Group (n=100)	Non-Steroid Group (n=100)	p-value
Union at 12 weeks, n (%)	62 (62%)	86 (86%)	0.001
Delayed Union (>12 weeks), n (%)	34 (34%)	12 (12%)	0.002
Nonunion at 24 weeks, n (%)	16 (16%)	4 (4%)	0.008
Avascular Necrosis, n (%)	18 (18%)	6 (6%)	0.012
Hardware Failure, n (%)	12 (12%)	4 (4%)	0.062
Infection (Deep SSI), n (%)	8 (8%)	6 (6%)	0.769
Mean Time to Union (weeks ± SD)	18.2 ± 4.6	12.4 ± 3.2	<0.001
Successful Union by 24 weeks, n (%)	84 (84%)	96 (96%)	0.012

Table 4: Harris Hip Score and Functional Outcomes

Functional Outcome	Steroid Group	Non-Steroid Group	p-value
HHS at 12 weeks (mean ± SD)	52.3 ± 14.2	64.8 ± 11.6	<0.001
HHS at 24 weeks (mean ± SD)	61.8 ± 13.5	76.2 ± 10.4	<0.001
HHS at 52 weeks (mean ± SD)	68.4 ± 12.3	82.1 ± 8.9	<0.001
Patient Satisfaction (Excellent), n (%)	38 (38%)	72 (72%)	<0.001
Return to Baseline Function, n (%)	32 (32%)	68 (68%)	<0.001
Assistive Device Dependency at 52 weeks	42 (42%)	18 (18%)	<0.001

Results

Baseline Characteristics: Two hundred patients met inclusion criteria and were enrolled in the study. Baseline demographic characteristics were well-balanced between groups (Table 1). Mean age was 57.3±11.2 years in the steroid group and 56.8±10.9 years in the control group (p=0.647). Gender distribution was similar between groups (male: female ratio 42:58 in steroid group vs 45:55 in control group, p=0.721). Comorbidities including diabetes mellitus, hypertension, and osteoporosis were similarly distributed between groups. Mean body mass index (BMI) was 24.6±3.8 kg/m² in steroid group versus 24.2±3.5 kg/m² in control group (p=0.425).

Steroid Therapy Characteristics: Among the 100 steroid-treated patients, the most common indications for steroid therapy were rheumatoid arthritis (42%), COPD (28%), systemic lupus erythematosus (18%), and polymyalgia rheumatica (12%) (Table 2). Mean daily steroid dose was 12.8±6.4 mg prednisolone equivalent, with a cumulative steroid dose of 2,847±1,236 g prednisolone equivalent. Mean duration of steroid therapy prior to fracture was 5.8±3.2 years. Thirty-four patients (34%) were receiving concurrent immunosuppressive therapy. Mean bone mineral density T-score was -2.4±0.8, indicating moderate to severe osteoporosis.

Radiographic Outcomes: Radiographic union at 12 weeks post-operatively was achieved in 62 patients (62%) in the steroid group compared to 86 patients (86%) in the non-steroid group (p=0.001). Delayed union (defined as lack of union at 12 weeks but eventual union by 24 weeks) occurred in 34 patients (34%) in the steroid group versus 12 patients (12%) in the non-steroid group (p=0.002).

Nonunion at 24 weeks was documented in 16 patients (16%) in the steroid group versus 4 patients (4%) in the non-steroid group (p=0.008). Mean time to union was significantly prolonged in steroid-treated patients: 18.2±4.6 weeks versus 12.4±3.2 weeks in controls (p<0.001). By 52 weeks follow-up, successful union was achieved in 84 patients (84%) in the steroid group compared to 96 patients (96%) in the control group (p=0.012).

Complication Rates: Avascular necrosis (AVN) was identified in 18 patients (18%) in the steroid group versus 6 patients (6%) in the non-steroid group (p=0.012). Hardware failure including screw loosening or loss of fixation occurred in 12 patients (12%) in the steroid group versus 4 patients (4%) in the control group (p=0.062). Deep surgical site infection was similar between groups (8% in steroid group vs 6% in non-steroid group, p=0.769). No statistically significant difference was noted in thromboembolic events between groups.

Functional Outcomes: Harris Hip Score at 12 weeks post-operatively was significantly lower in steroid-treated patients (52.3±14.2) compared to controls (64.8±11.6, p<0.001). This difference persisted at 24 weeks (61.8±13.5 vs 76.2±10.4, p<0.001) and at 52 weeks (68.4±12.3 vs 82.1±8.9, p<0.001). Patient satisfaction levels (excellent outcome) were achieved in 38% of steroid-treated patients versus 72% of controls (p<0.001). Return to baseline functional status by 52 weeks was achieved in only 32% of steroid-treated patients compared to 68% of controls (p<0.001). Assistive device dependency at 52 weeks follow-up was significantly higher in the steroid group (42%) compared to controls (18%, p<0.001).

Statistical Analysis: Data were analyzed using SPSS Statistics version 26 (IBM Corporation, Chicago, IL). Categorical variables were compared using Chi-square test, with Fisher's exact test applied when expected cell frequencies were <5. Continuous variables were assessed for normality using Shapiro-Wilk test and compared using independent samples t-test for normally distributed data or Mann-Whitney U test for non-normally distributed data. Logistic regression analysis was performed to identify independent risk factors for delayed union and nonunion, with odds ratios (OR) and 95% confidence intervals (CI) calculated. Time-to-event analysis was performed using Kaplan-Meier survival analysis with log-rank test. P-value <0.05 was considered statistically significant.

Discussion

This prospective study represents a comprehensive examination of fracture healing outcomes in 200 patients with femoral neck fractures stratified by systemic steroid exposure. The findings provide substantial evidence that systemic corticosteroid therapy constitutes a significant independent risk factor for delayed fracture healing and nonunion in this patient population, with implications for clinical management and prognostication. Multiple interconnected mechanisms contribute to steroid-induced impairment of fracture healing.The 34% incidence of delayed union in steroid-treated patients represents a clinically significant complication requiring prolonged immobilization, delayed weight-bearing rehabilitation, and increased risk of secondary complications. Nonunion presents a treatment challenge requiring surgical intervention, potentially including vascularized bone grafting, revision fixation, or arthroplasty. The prognostic implications are substantial, as nonunion frequently results in chronic pain, functional impairment, and reduced quality of life.

The elevated AVN rate in steroid-treated patients (18% vs 6%, p=0.012) deserves particular emphasis given the catastrophic consequences of femoral head collapse. Multiple contributing factors likely operate synergistically: (1) steroid-related bone quality deterioration increases mechanical instability and displacement at the fracture site, (2) impaired angiogenesis from steroid effects reduces collateral blood flow to the femoral head, (3) steroid-induced osteonecrosis may reflect direct toxic effects on osteocytes independent of fracture-related ischemia, and (4) altered lipid metabolism and marrow adiposity associated with steroid use may contribute to osteonecrosis pathogenesis. The development of AVN substantially impairs functional outcomes, as evidenced by persistently low Harris Hip Scores in affected patients. Of the 18 patients with AVN in the steroid group, mean HHS at 52 weeks was 54.2±16.4 compared to 72.8±10.2 in steroid-treated patients without AVN, indicating profound functional impairment.

Patient satisfaction levels (excellent outcomes in 38% of steroid group vs 72% of controls) underscore the significant impact on quality of life. Assistive device dependency at 52 weeks (42% in steroid group vs 18% in controls) reflects ongoing functional limitations and increased risk of falls, particularly concerning given that osteoporosis in this population places patients at further fracture risk. The fact that only 32% of steroid-treated patients returned to baseline functional status compared to 68% of controls demonstrates that steroid exposure significantly impairs long-term rehabilitation potential. This has important implications for patient counseling, rehabilitation planning, and social support services in this population.

Concurrent immunosuppressive therapy (present in 34% of steroid-treated patients) may synergistically impair healing through additional suppression of the inflammatory phase of fracture healing, though statistical interaction was not formally tested in this analysis. More frequent radiographic assessment (every 4-6 weeks rather than standard 8–12-week intervals) enables early detection of delayed union or nonunion, permitting timely intervention before progression to established nonunion. Weight-bearing progression should be guided by radiographic evidence of healing rather than standard protocols. Prolonged protective weight-bearing may be necessary to prevent hardware failure and displacement. Where clinically feasible,

consideration should be given to steroid dose reduction or tapering around the time of fracture injury to reduce immunosuppression during critical early healing phases, provided underlying disease activity permits.All steroid-treated patients with fractures should receive concurrent bone-protective therapy including calcium, vitamin D, and bisphosphonates (particularly if BMD T-score <-2.0), as supported by current guidelines for glucocorticoid-induced osteoporosis prevention.

Several limitations merit acknowledgment. First, the study was conducted at a single tertiary center, potentially limiting generalizability to other healthcare systems with different surgical expertise or rehabilitation protocols. Second, indication-specific effects of steroid therapy were not systematically analyzed; different underlying diseases (rheumatoid arthritis vs COPD vs SLE) may carry inherent inflammatory or metabolic effects independent of steroid exposure. Third, adherence to rehabilitation protocols was not formally quantified, potentially confounding functional outcome differences. Fourth, specific surgical techniques and implant types were not standardized, potentially affecting outcomes independent of steroid effects. Fifth, the study population was predominantly elderly (mean age 67.3 years), limiting applicability to younger patients.

These findings align with prior observational studies implicating steroids as risk factors for impaired fracture healing. However, the magnitude of effect (16% nonunion rate in steroid group vs 4% in controls) is substantially higher than reported in some studies, potentially reflecting the older age of participants and higher burden of comorbidities. The time-to-union difference of 5.8 weeks is also more substantial than reported in some smaller series, possibly reflecting the rigorous radiographic standardization employed in this study.

Future Directions: Future research should investigate: (1) mechanistic studies of steroid effects on callus histology and bone quality in animal fracture models, (2) randomized trials comparing augmentation strategies (BMPs, PRP, teriparatide) in steroid-treated patients with femoral neck fractures, (3) investigation of whether steroid tapering around the time of fracture injury improves outcomes, (4) comparison of different fixation techniques (percutaneous pinning vs open reduction internal fixation) in steroid-treated patients, and (5) long-term follow-up studies examining late complications including osteoarthritis and AVN progression.

Conclusion

The findings underscore the importance of: (1) recognizing steroid exposure as a significant independent risk factor in fracture risk stratification, (2) implementing early surgical intervention in steroid-treated patients, (3) considering biological or pharmaceutical augmentation strategies, (4) implementing enhanced radiographic surveillance protocols, and (5) ensuring bone-protective therapy.

Steroid-treated patients with femoral neck fractures represent a high-risk population requiring individualized management strategies, close radiographic monitoring, and aggressive rehabilitation. Further research should focus on optimizing treatment protocols and testing novel augmentation strategies in this challenging patient cohort. These findings have substantial implications for orthopedic surgeons, internists, and rheumatologists managing patients with chronic corticosteroid therapy who sustain femoral neck fractures.

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