

Original Research Article

Clinical outcomes of post-surgery osteoporosis treatment in elderly intertrochanteric fracture patients: a prospective study

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ABSTRACT

Background: This study aims to evaluate the clinical and functional outcomes of administering zoledronic acid in elderly patients undergoing surgical management of hip fractures. The goal is to assess the impact on mortality, postoperative complications, and functional recovery as measured by the modified Harris hip score.

Methods: A prospective study was conducted over 18 months at a tertiary care center in New Delhi, India, involving 42 patients aged 60 and above with intertrochanteric femur fractures. Patients received surgical fixation and standard postoperative care. Zoledronic acid (5 mg) was administered intravenously three months post-surgery. Data on demographics, injury-to-surgery interval, fracture type, DEXA score, and functional outcomes were collected at follow-ups of 6 weeks, 3 months, 6 months, and 12 months.

Results: The mean age of participants was 72.67 years. Zoledronic acid administration was associated with a 9.5% mortality rate. Functional outcomes, measured by the modified Harris hip score, significantly improved from a mean of 42.14 at 6 weeks to 77.68 at 12 months ($p < 0.001$). Younger patients (< 70 years) had significantly better scores at 3 months compared to older patients (> 80 years). However, no significant differences were observed at 6 and 12 months. The mean modified Harris hip scores did not differ significantly between patients with osteopenia and osteoporosis at any time point. Additionally, the type of surgical fixation (intramedullary versus extramedullary) showed no significant impact on functional outcomes.

Conclusions: Zoledronic acid administration in elderly hip fracture patients may reduce mortality and enhance functional recovery. The study supports its use in postoperative care to improve outcomes, although larger, randomized controlled studies are needed to confirm these findings. The results suggest that zoledronic acid can be an effective adjunct therapy in managing osteoporosis-related hip fractures in the geriatric population.

Keywords: Fragility fractures, Osteoporosis, Geriatric fractures, Intertrochanteric femur, Bisphosphonates, Zoledronate

INTRODUCTION

Hip fractures in the elderly are a major concern, leading to significant disability, loss of independence, and high mortality rates. In India, the incidence of hip fractures per 100,000 individuals is 105 for men and 159 for women, with a 1-year mortality rate reaching 42%.¹ These fractures cause considerable morbidity, impair daily activities, and impose substantial public health and economic burdens.

Surgical intervention and early weight-bearing are standard care for intertrochanteric hip fractures, which account for over half of hip fractures in individuals aged 60 and older.² It has been observed that despite surgical fixation of these fractures, the 1-year mortality rate remains significantly elevated, accompanied by heightened risks of cardiovascular, thromboembolic, and respiratory complications.

The etiology of hip fractures in the elderly predominantly involves falls, with osteoporosis being a key factor.³ Osteoporosis, marked by decreased bone mineral density and compromised bone microarchitecture, greatly increases fracture risk from minor trauma.⁴ Despite this, only a few affected individuals receive appropriate pharmacological treatment.⁵ Bisphosphonates, particularly zoledronic acid, are effective in reducing bone turnover, enhancing bone density, and lowering fracture risk. Zoledronic acid, a potent osteoclast inhibitor, has shown superior efficacy in preclinical studies.⁶ Emerging evidence also suggests that bisphosphonates reduce mortality risk.⁷ Additionally, their immunomodulatory properties may improve post-fracture outcomes by mitigating perioperative complications, cardiovascular events, and infections through modulation of inflammatory responses.^{8,9}

Given the significant impact of hip fractures on patient well-being and healthcare resources, optimizing treatment strategies is essential.¹⁰ While surgical management is crucial, postoperative care, including thromboprophylaxis, early mobilization, and nutritional supplementation, enhances recovery.^{12,13}

This study aims to investigate the potential role of zoledronic acid in improving outcomes after surgical fixation of hip fractures. Zoledronic acid may offer multiple benefits such as accelerated healing, reduced complications, and improved survival rates. This study seeks to fill existing knowledge gaps with the goal of enhancing quality of life and improving functional outcomes following geriatric hip trauma.

METHODS

This prospective study aimed to evaluate clinical and functional outcomes following the administration of zoledronate in geriatric patients undergoing surgical management of hip fractures. Clearance was obtained from the institutional ethics committee and the study was conducted over a span of 18 months in Central Institute of Orthopaedics, VMMC and Safdarjung Hospital, New Delhi, India, the study enrolled 42 patients aged 60 and above with intertrochanteric femur fractures resulting from self-fall. Exclusion criteria included patients with known co-morbidities, trauma other than self-fall, immune-compromised status, metabolic diseases, pathological fractures, and hypersensitivity to zoledronic acid. Patients underwent surgical fixation of hip fractures and received standard postoperative care, including thromboprophylaxis with injection enoxaparin 40 mg subcutaneously until discharge, followed by tablet aspirin 75 mg daily, and calcium and vitamin D supplementation. Zoledronic acid (5 mg in 100 ml normal saline) was administered intravenously at 3 months post-surgery as per standard guidelines as very early administration of zoledronic acid has been reported to impair callus formation. Data collection included variables such as age, gender, injury-to-surgery interval, fracture type, DEXA

score, type of surgery, and time to zoledronic acid administration. Follow-ups at 6 weeks, 3 months, 6 months, and 12 months evaluated functional outcomes using the modified Harris hip score. Data were compiled and analyzed using appropriate statistical methods. Although initially planned as a comparative study, it was converted to a single-group descriptive study due to ethical constraints, and the findings were compared with existing literature to assess the role of zoledronic acid.

RESULTS

The study enrolled 42 geriatric patients with intertrochanteric femur fractures, with a mean age of 72.67 years (SD±7.24), ranging from 64 to 95 years. The distribution of age groups was as follows: 61-70 years (45.2%), 71-80 years (40.5%), and >80 years (14.3%). The cohort consisted of 19 males (45.2%) and 23 females (54.8%) (Figure 1).

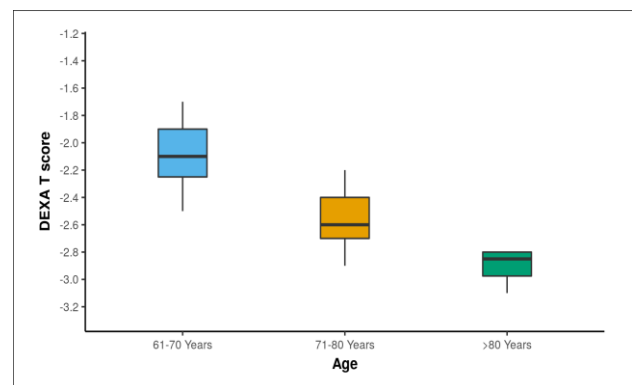


Figure 1: Association of DEXA T score with age.

Regarding fracture characteristics, 52.4% of fractures were on the left side, and 47.6% were on the right side. AO classification revealed type 1 fractures in 14.3% of patients, type 2 in 59.5%, and type 3 in 26.2%. Surgical intervention predominantly involved proximal femur nailing (88.1%), with dynamic hip screw used in 11.9% of cases. This data was skewed in favour of proximal femur nail (PFN) as majority of the fractures (85.7%) were unstable IT fractures requiring intramedullary fixation. The mean injury-to-surgery interval was 11.57 days (SD±3.31), with a median of 11.00 days. All the enrolled participants were operated within 3 weeks of injury after achieving required surgical fitness and more than 60% of the patients were operated in the second week of surgery. The surgery-to-zoledronate administration interval averaged 82.64 days (SD±6.95).

Bone density assessment showed a mean DEXA T score of -2.39 (SD±0.36), among the participants, 33.3% had osteoporosis (T score < -2.5), while 66.7% had osteopenia (T score between -2.5 and -1). The association between age and DEXA T scores was analyzed. Mean DEXA T scores were -2.09 (SD=0.24) for ages 61-70, -2.56 (SD=0.21) for ages 71-80, and -2.83 (SD=0.24) for ages >80. There was a significant difference between the 3 groups in terms of

DEXA T score ($\chi^2=25.912$, $p\leq 0.001$), with the median DEXA T score being highest in the age: 61-70 years group. Younger patients (<70 years) had significantly higher DEXA T scores compared to older patients (>80 years), indicating greater osteoporosis with increasing age.

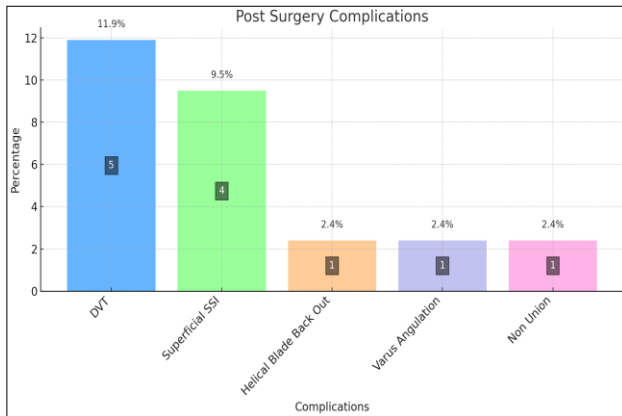


Figure 2: Post surgery complications.

23.8% of our patients suffered from post-surgery complication. 5 patients developed deep venous thrombosis successfully managed by starting the patient on low molecular weight heparin along with 4 patients developed superficial surgical site infections which were successfully managed with culture sensitive antibiotics. 1 patient had a varus angulation following PFN done for unstable IT fracture. 1 patient had a helical blade back out noticed at 6 week follow up of the patient. 1 patient had non-union following PFN done for reverse oblique IT fracture (Figure 3).

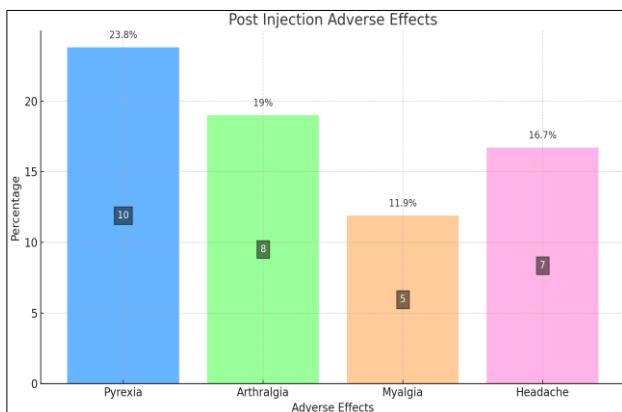


Figure 3: Zoledronic acid infusion related adverse effects.

45.2% of the patients developed infusion related adverse effects. 23.8% patients (N=10) were febrile after administration of zoledronic acid which subsided within 24 to 48 hours of injection. 19% (N=8) patients developed arthralgia, 11.9% patients (N=5) and 16.7% patients (N=7) developed headache all of which subsided within 2 days after being administered with analgesics.

Our study had a mortality rate of 9.5% (N=4) with 2 patients succumbing to cardiac arrest, 1 patient developed an episode of severe pneumonia resulting in respiratory failure and 1 patient suffered from mortality due to a haemorrhagic cerebrovascular accident. The mean age of the participants suffering from mortality was 84.75 years as opposed to 72.67 years being the mean age of participants in our study. All patients suffering from mortality were unstable IT fractures who had undergone proximal femoral nailing. The mean Harris hip score at 3 months was 49.25 as opposed to mean of 53.93 in the study population (Table 1).

Table 1: Mortality at 1 year follow up.

Mortality	Frequency	Percentage
Yes	4	9.5
No	38	90.5

The mean modified Harris hip score increased from a minimum of 42.14 at the 6 weeks timepoint to a maximum of 77.68 at the 12-month timepoint. This change was statistically significant (repeated measures ANOVA: $F=142.9$, $p\leq 0.001$) (Figure 4).

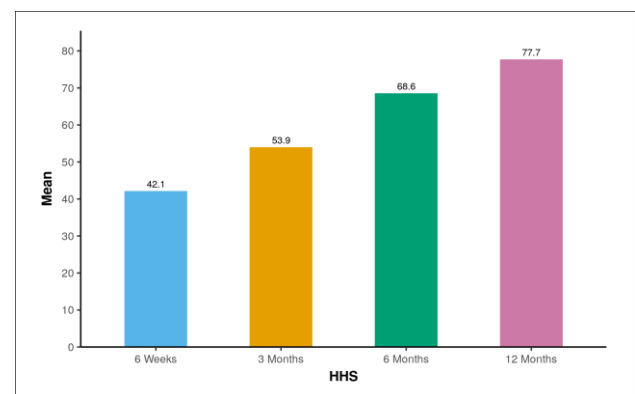


Figure 4: Assessment of change in modified Harris hip score over time.

There was no significant difference between the groups in terms of modified Harris hip score (6 weeks) ($p=0.267$).

Younger age (less than 70 years) was associated with significantly better modified Harris hip score at 3 months ($\chi^2=6.540$, $p=0.038$). However, even though mean modified Harris hip score in younger patients was more than older patients, no significant statistical difference could be found between age and modified Harris hip score at 6 months and 12 months follow ups.

On comparison of overall change in modified Harris hip score over time in the three fracture classification groups. There was a significant difference in the trend of modified Harris hip score over time between the three groups with reverse oblique intertrochanteric fractures reporting significantly lower modified Harris hip score at 3, 6, and 12 month follow up intervals ($p=0.021$) as compared to Boyd

and Griffin type 1 and 2 fractures which showed no significant difference at any follow up.

The overall change in modified Harris hip score over time was compared between patients operated using extramedullary (DHS) and intramedullary fixation (PFN) and no significant difference in the trend of modified Harris hip score over time between the two groups ($p=0.346$).

The change in modified Harris hip score over time was compared in the osteoporosis (T score <-2.5) and osteopenia (T score -1 to -2.5) groups with no significant difference in the trend of modified Harris hip score over time between the two groups ($p=0.305$) (Figure 5).

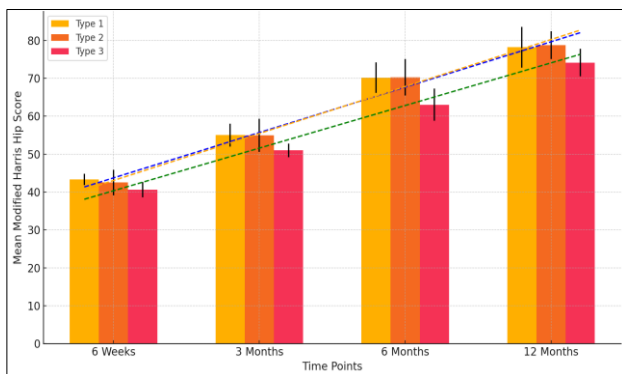


Figure 5: Comparison of Boyd and Griffin fracture classification with change in modified Harris hip score over time.

DISCUSSION

Our study aimed to assess clinical outcomes of post-surgery osteoporosis treatment in elderly patients undergoing surgical fixation of intertrochanteric (IT) fractures. On following up the patients for 1 year, we observed a mortality rate of 9.5% ($N=4$) in our cohort, with causes of death including cardiac arrest, severe pneumonia leading to respiratory failure, and hemorrhagic cerebrovascular accident. Comparatively, Gupta et al in a study conducted at a tertiary hospital in North India, reported a one-year all-cause mortality rate of 28.7% following hip fracture surgery without zoledronic acid, highlighting the significantly lower mortality rate in our study.¹⁴ Additionally, other studies evaluating the impact of zoledronic acid post-hip fracture surgery also showed reduced mortality rates. For instance, in the HORIZON recurrent fracture trial by Lyles et al, a statistically significant reduction in mortality was observed in patients administered zoledronic acid (11.5%) compared to the placebo group (13.3%) with a hazard ratio of 0.72 ($p=0.01$).¹⁵ Similarly, a prospective study by Cengiz et al in Turkey reported a mortality rate of 14.3% in the zoledronic acid group, compared to 34.5% in the control group.¹⁶ Beaupre et al in Canada also noted that bisphosphonate exposure was independently associated

with reduced mortality (7% versus 16%) with an adjusted hazard ratio of 0.92 ($p=0.001$).¹⁷

In our study, the mean age of participants who succumbed was 84.75 years, compared to 72.67 years in the overall study population. All patients who died had unstable IT fractures treated with proximal femoral nailing, and their mean Harris hip score at 3 months was 49.25, lower than the 53.93 observed in the overall population. Due to the small sample size, the statistical significance of these differences could not be determined. Thus, while the results suggest that zoledronic acid may be associated with reduced mortality following hip fracture surgery, the small sample size limits the generalizability of these findings.

We also evaluated functional outcomes of patients operated using the modified Harris hip score. The mean modified Harris hip score improved significantly over time, from 42.14 at 6 weeks to 77.68 at 12 months (repeated measures ANOVA: $F=142.9$, $p\leq 0.001$). Younger patients (<70 years) had significantly better modified Harris hip scores at 3 months, though this difference was not statistically significant at later follow-ups. Fracture classification also influenced functional outcomes, with Boyd and Griffin type 1 and 2 fractures showing greater improvement compared to type 3 fractures. However, no significant difference was found in the modified Harris hip scores at 12 months among the different fracture types.

When comparing surgical fixation methods, no significant difference was observed in the trend of modified Harris hip scores over time between patients treated with intramedullary (PFN) and extramedullary (DHS) fixation ($p=0.346$). Furthermore, no significant difference in functional outcomes was found between patients with osteoporosis (DEXA T score <-2.5) and osteopenia (DEXA T score -1.5 to -2.5), indicating that zoledronic acid may mitigate the negative impact of lower bone density on recovery.

Comparison with existing literature further supports the potential benefits of zoledronic acid. In the study by Cengiz et al, the mean Harris hip scores at 12 months were 81.93 in the treatment group and 72.9 in the control group, a statistically significant difference ($p\leq 0.001$).¹⁶ Gulia et al also reported better functional outcomes in patients treated with zoledronic acid compared to controls ($p<0.005$).¹⁸ These findings align with our observations, suggesting that zoledronic acid may positively influence functional recovery post-surgery.

Our study also analysed surgery-related and zoledronic acid infusion-related complications. Post-surgery, 23.8% of our patients experienced complications, including DVT, superficial surgical site infections, varus angulation, helical blade back-out, and non-union. Literature comparison reveals similar findings; for instance, Gulia et al reported non-union, delayed union, implant failure, and varus angulation following zoledronic acid

administration.¹⁸ Taoka et al observed a 40% incidence of DVT following hip fracture surgery in Japan, indicating that such complications are not uncommon and vary based on hospital protocols and patient-related factors.¹⁹

Zoledronic acid infusion-related adverse effects were reported in 45.2% of our patients, with pyrexia (23.8%), arthralgia (19%), headache (16.7%), and myalgia (11.9%) being the most common. These findings are consistent with other studies. Kotian et al reported pyrexia in 77.5% of patients, while Lyles et al found a lower incidence of infusion-related complications in their randomized control trial.^{15,20} Despite these adverse effects, they were generally mild and self-limiting, resolving within 24-48 hours.

In conclusion, our study indicates that zoledronic acid administration following surgical fixation of osteoporotic peri-trochanteric fractures may reduce mortality and improve functional outcomes. However, further research with larger sample sizes and longer follow-up durations is necessary to confirm these findings and establish the role of zoledronic acid in the management of hip fractures in the geriatric population.

Limitations

The study's limitations include a small sample size, lack of a control group, and potential selection bias, given the patient profile was limited to a tertiary care center and excluded those with comorbidities. Additionally, the observational study design could not adequately control for confounding factors influencing mortality. To further ascertain the role of zoledronic acid in reducing morbidity and mortality post-hip fracture surgery, a larger randomized controlled trial or matched prospective cohort study would be recommended, along with comparative studies of other anti-osteoporotic agents.

CONCLUSION

The findings of our study suggest that zoledronic acid administration may significantly reduce morbidity and mortality following surgical fixation of intertrochanteric fractures in the elderly. The use of zoledronic acid was associated with decreased one-year all-cause mortality compared to existing Indian literature and resulted in improved modified Harris hip scores at 3, 6, and 12-month follow-ups. Notably, AO type 31A3/Boyd and Griffin type 3 intertrochanteric fractures correlated with lower modified Harris hip scores, while no significant difference in functional outcomes, as assessed by the modified Harris hip score, was observed between patients undergoing intramedullary versus extramedullary fixation. Furthermore, a decreased DEXA T-score did not correlate with poorer functional outcomes, possibly due to the role of zoledronic acid, as most enrolled patients were osteopenic. Additionally, older patients demonstrated a higher susceptibility to mortality compared to younger patients.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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