Risks of Nonunion and Revision Surgery with Early Bisphosphonate Use in Surgically Treated Proximal Femoral Fractures

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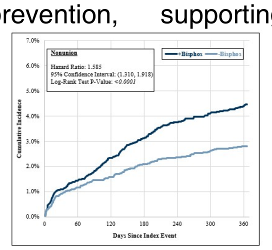
INTRODUCTION: Bisphosphonate therapy is essential to prevent secondary fractures in the geriatric population, but the optimal timing for initiation to avoid disrupting fracture healing remains unclear. This study evaluates the impact of immediate versus delayed bisphosphonate therapy on nonunion and revision surgery rates following proximal femoral fracture repair.

METHODS: Data were obtained from the TriNetX US Collaborative Network for patients aged 50 and older undergoing surgical repair of proximal femur fractures between January 2002 and October 2023. Two cohorts were compared: bisphosphonate use within six weeks post-fracture fixation (+Bisphos) and no bisphosphonate use within six weeks post-fracture (-Bisphos). Subanalysis examined bisphosphonate initiation at 6 weeks to 3 months or 3 to 6 months versus no treatment at 3 and 6 months. Additional analysis assessed vertebral and other osteoporotic fracture risks when therapy was delayed to 6 versus 6 to 12 months. Propensity score matching balanced cohorts, and hazard/risk ratios were calculated.

RESULTS: Of 109,838 patients, 7,215 were in each cohort after matching. Early bisphosphonate use increased nonunion (HR: 1.585, $p < 0.05$) and revision surgery risks (HR: 1.242, $p < 0.05$). Delaying therapy to 6 weeks to 3 months maintained elevated revision rates compared to no therapy within 3 months (RR: 1.833, $p < 0.05$). Initiation at 3 to 6 months showed no difference in revision surgery rates compared to no therapy within the first 6 months (RR: 1.156, $p = 0.47$). Vertebral (RR: 0.866, $p = 0.35$) and other osteoporotic fracture risks (RR: 0.966, $p = 0.71$) were unaffected by delaying therapy up to 6 months.

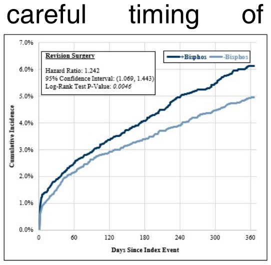
DISCUSSION AND CONCLUSION: Early bisphosphonate use significantly increases nonunion and revision surgery risks. Deferring therapy for up to six months reduces these risks without compromising vertebral or osteoporotic fracture prevention, supporting careful timing of bisphosphonate initiation to optimize fracture healing.



Number At Risk*	0	60	120	180	240	300	360
+Bisphos	7,215	7,111	7,045	6,990	6,943	6,917	6,898
-Bisphos	7,215	7,131	7,100	7,064	7,045	7,025	7,013

Patients are censored if their record falls within the analysis time window

Figure 1: Cumulative incidence of nonunion with hazard ratio



Number At Risk*	0	60	120	180	240	300	360
+Bisphos	7,215	7,035	6,973	6,921	6,856	6,820	6,772
-Bisphos	7,215	7,060	7,004	6,971	6,933	6,892	6,858

Patients are censored if their record falls within the analysis time window

Figure 2: Cumulative incidence of revision surgery with hazard ratio

Effect of Delayed Bisphosphonate Therapy on New Vertebral and Osteoporotic Fractures After Propensity Score Matching

Bisphosphonates prescribed 6 months post index vs. bisphosphonates prescribed 6 to 12 months post index							
Measure	6 months (N)	6-12 months (N)	6 months Proportion	6-12 months Proportion	Risk Ratio	95% CI	*P*
Vertebral Fracture	84	97	8.8%	10.1%	0.866	(0.656, 1.144)	*0.35*
Osteoporotic Fracture	229	237	23.9%	24.7%	0.966	(0.825, 1.132)	*0.71*

Table 4: Effect of Delayed Bisphosphonate Therapy on New Vertebral and Osteoporotic Fractures After Propensity Score Matching

Effect of Delayed Bisphosphonate Therapy on Revision Surgery and Nonunion After Propensity Score Matching

Bisphosphonates prescribed 6 weeks to 3 months post index vs. no bisphosphonates prescribed 3 months post index							
Measure	+Bisphos 6 weeks to 3 months (N)	-Bisphos 3 months (N)	+Bisphos 6 weeks to 3 months Proportion	-Bisphos 3 months Proportion	Risk Ratio	95% CI	*P*
Revision Surgery	66	36	7.2%	3.9%	1.833	(1.234, 2.723)	*<0.05*
Nonunion	33	22	3.6%	2.4%	1.500	(0.881, 2.552)	*0.13*

Bisphosphonates prescribed 3 to 6 months post index vs. no bisphosphonates prescribed 6 months post index							
Measure	+Bisphos 3 to 6 months (N)	-Bisphos 6 months (N)	+Bisphos 3 to 6 months Proportion	-Bisphos 6 months Proportion	Risk Ratio	95% CI	*P*
Revision Surgery	52	45	5.6%	4.9%	1.156	(0.784, 1.704)	*0.47*
Nonunion	32	15	3.5%	1.6%	2.133	(1.163, 3.913)	*<0.05*

Table 3: Effect of Delayed Bisphosphonate Therapy on Revision Surgery and Nonunion After Propensity Score Matching