Effect of Ketorolac Administration on the Rate of Fracture Nonunion in Operatively Treated Pediatric Long Bone Fractures: A Matched Cohort Analysis

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INTRODUCTION: Nonunion is a rare yet serious complication in pediatric fracture healing, with consequential morbidity and associated economic burden. Association between the administration of ketorolac and increased risk of fracture nonunion in adults has been reported, but data is lacking in the pediatric population This study examines the relationship between postoperative ketorolac administration and nonunion in operatively managed pediatric long bone fractures.

METHODS: A retrospective cohort study was conducted using the TriNetX research network, which encompassed data from the United States, Canada, and Western Europe. 462,260 patients from 52 healthcare organizations satisfied inclusion criteria. Patients under 18 with operatively managed upper or lower limb long bone fractures were included. The exposure of interest was ketorolac administration within 30 days postoperatively in between 2003 and 2023. Nonunion was identified and verified using pertinent medical codes. For both cohorts, absolute risk and hazard ratios were calculated. A P-value of < 0.05 was considered significant.

RESULTS: Results: After propensity score matching 48,778 patients were identified per cohort, with a two year follow-up. In the ketorolac cohort, the incidence of nonunion was 2.19%, compared to 0.93% in the non-ketorolac cohort (hazard ratio (HR): 2.71 (95% CI 2.46, 3.21; P < 0.0001)). Subgroup analyses demonstrated a higher risk of nonunion in lower extremity fractures (HR: 3.45 (95% CI 3.14, 3.75; P <0.0001)) than upper extremity fractures (HR: 2.11 (95% CI 1.84, 2.32; P <0.0001)). The greatest HR for fracture nonunion was observed in the femur, followed sequentially by tibia/fibula, humerus, and finally radius/ulna.

DISCUSSION AND CONCLUSION: This is the largest study to date exploring postoperative ketorolac use and nonunion in operatively managed pediatric long bone fractures. Nonunion is rare in children, occurring in less than 1% of surgically treated patients. Ketorolac administration was associated with a 2-3-fold increase in nonunion risk, with pronounced implications in lower extremity fractures, particularly the femur. Clinicians should weigh the therapeutic advantages of non-opiate analgesia with ketorolac against the risk of nonunion to optimize postoperative pain management and recovery.

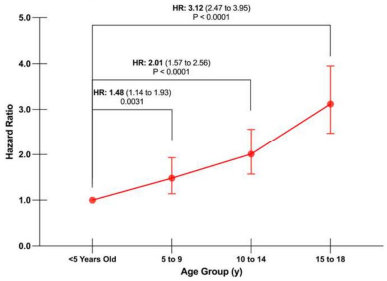

Table 1. Post-Match Characteristics

Characteristic	Ketorolac (48,778) N (Mean or %)	No Ketorolac (48,778) N (Mean or %)	P	Std diff.
Age	9.66 (± 4.62)	9.67 ± 4.61)	0.775	<0.0001
Gender				
Male	30,411 (62.34)	30,448 (62.42)	0.949	0.002
Female	18,367 (37.65)	17,920 (36.73)	0.919	0.019
Race & Ethnicity				
Hispanic	8,392 (17.20)	8,401 (17.22)	0.981	0.001
Asian	1,528 (3.13)	1,521 (3.12)	0.902	0.001
American Indian or Alaskan	351 (0.72)	256 (0.69)	0.261	0.004
Black	5,831 (11.95)	5,851 (12.00)	0.850	0.002
Native Hawaiian	276 (0.57)	269 (0.55)	0.549	0.003
White	30,612 (62.75)	30,603 (62.74)	0.949	0.000
Unknown Race	9,914 (20.32)	10,132 (20.77)	0.070	0.011
BMI Percentile	63.51 (± 33.23)	63.44 (± 31.22)	0.207	<0.0001
Lower Extremity	13,787 (28.26)	13,998 (28.69)	0.886	0.010
Femur	3,922 (28.45)	4,075 (29.11)	0.722	0.015
Tibia/Fibula	9,864 (71.55)	9,923 (70.89)	0.649	0.015
Upper Extremity	34,991 (71.73)	34,780 (71.30)	0.829	0.010
Humerus	19,465 (55.63)	18,875 (54.27)	0.663	0.027
Radius/Ulna	15,525 (44.37)	15,905 (45.73)	0.576	0.027

Table 2. Table of Hazard Ratios

Ketorolac vs No Ketorolac

Measure	N Nonunion (%) Ketorolac	N Nonunion (%) No Ketorolac	Hazard Ratio 95 CI	P-Value
Overall Pre-Match	1,066 (2.19)	2,822 (0.68)	3.49 (3.23, 3.82)	<0.0001
Overall Matched	1,066 (2.19)	453 (0.93)	2.71 (2.46, 3.21)	<0.0001
Lower Extremity	545 (3.96)	206 (1.22)	3.45 (3.14, 3.75)	<0.0001
Femur	191 (1.39)	64 (0.38)	3.76 (3.61, 3.92)	<0.0001
Tibia/Fibula	354 (2.57)	142 (0.84)	2.99 (2.85, 3.17)	<0.0001
Upper Extremity	521 (1.49)	247 (0.71)	2.11 (1.84, 2.32)	<0.0001
Humerus	229 (0.65)	101 (0.29)	2.24 (1.92, 2.54)	<0.0001
Radius/Ulna	292 (0.83)	146 (0.42)	1.89 (1.65, 2.11)	<0.0001

Nonunion by Age - Ketorolac Cohort

Measure	N Nonunion (%)	Hazard Ratio 95 CI	P-Value
<5 Years Old	138 (1.19)	1 (baseline)	-
5 to 9 Years Old	226 (1.47)	1.48 (1.14, 1.93)	0.0042
10 to 14 Years Old	306 (2.68)	2.01 (1.57, 2.56)	<0.0001
15 to 18 Years Old	396 (3.85)	3.12 (2.47, 3.95)	<0.0001