Opioids and NSAIDs Are Both Associated with Nonunion Following Geriatric Fracture

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Purpose: The question of whether nonsteroidal anti-inflammatory drugs (NSAIDs) impair fracture healing has been long debated, but there is also concern regarding the potential negative effect of opioids on bone healing. This has been demonstrated in both animal and observational research. The purpose of this study was to evaluate potential association between NSAIDs and opioids with fracture union using a large database.

Methods: Medicare beneficiaries with a humerus, forearm, tibia/fibula, or femur fracture were identified by ICD-10 and CPT codes from 2016-2019. Patients eligible for Medicare via ESRD (end-stage renal disease), SSDI (Social Security Disability Insurance) or on Medicare HMO (health maintenance organization) were excluded. Charlson Comorbidity Index (CCI) was used as a marker of patients' global health based on diagnoses prior to index fracture. Patients were classified by drug exposure based on Part D (Pharmacy) claims at any time between 90 days prior to the fracture and 1 year following the fracture. Nonunion was identified by ICD-10 or CPT codes during subsequent encounters during 1-year surveillance from index fracture. Chi-squared and Student t-tests were performed on categorical and continuous variables, respectively. Logistic regression used to evaluate the association between medication use and nonunion, controlling for age, sex, race, and CCI.

Results: Total number of fractures meeting inclusion criteria was 253,266. The overall absolute rate of nonunion at 1 year was 3.9%. This rate was 2.5% (95% confidence interval [CI] 2.4-2.6) among those not taking either opioid or NSAID, and 4.2% (95% CI 4.1-4.3) among those taking any NSAID or opioid. Patients exposed to opioids (odds ratio [OR] 1.52) and prescription NSAIDs (OR 1.40) had higher incidence of nonunion diagnosis. There was a dose-dependent association in both NSAID and opioid exposure with increasing relative risk per each prescription fill. Patients exposed to greater than 240 morphine milligram equivalents within the first 3 months post-fracture had the highest association with nonunion (OR 2.09). Pre- and post-fracture NSAID use conferred a greater rise in OR of nonunion when compared to chronic opioid use (1.82 vs 1.62, respectively). Use of opioid and NSAIDs following fracture had a summative effect in terms of association with nonunion (OR 2.13).

Conclusion: Both opioids and NSAIDs were associated with a higher prevalence of nonunion diagnosis after fracture in this large cohort, and they demonstrated a summative effect as well. Further understanding regarding how these medications impact fracture healing is needed.