Beta Blockers Associated with Increased Nonunion following Fracture

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INTRODUCTION:
Animal studies have consistently demonstrated increased bone mineral density (BMD), torsional strength, and callus formation with either local or systemic administration of beta blockers (BBs). However, population studies have shown mixed effects on BMD and fracture risk with BB use. The cumulative effect of BBs on skeletal physiology and bone metabolism remains unclear. The goal of this study was to evaluate whether exposure to BB is associated with nonunion after fracture.
METHODS:
Fee-for-service Medicare beneficiaries who had a humerus, forearm, tibia/fibula, or femur fracture were identified by International Classification of Diseases (ICD)-10 and current procedural terminology (CPT) codes from a pool of beneficiates including years 2016-2019. Patients eligible for Medicare via ESRD, SSDI, or on Medicare HMO were excluded. Charleston Comorbidity Index (CCI) was used as a marker of patients' global health based on diagnoses in the year prior to index fracture. Nonunion was identified by ICD-10 or CPT codes during subsequent inpatient, hospital outpatient, and Part B claims over a one-year surveillance from index fracture diagnosis. Patients were classified by BB exposure based on Part D (Pharmacy) claims at any time between 90 days prior to the fracture and one year following the fracture. Chi square and Student's T-tests were performed on categorical and continuous variables, respectively. Logistic regression was performed to evaluate the association between BB use and nonunion, controlling for age, sex, race, and comorbidity.
RESULTS:
Total number of fractures identified was 1,228,931 with 32% of patients having used a beta blocker during the study period. CCI was equal to or greater than two in 58% of patients (70.3% in BB, $p<0.001$). Incidence of nonunion was 2.8% overall. Nonunion patients were more likely male (24.7% vs. 21.8%, $p<.001$) and younger (77 vs. 79 years, $p <.001$), but with similar comorbidity. Beta blockers were associated with a 15% increase in nonunion for all fracture types, after controlling for age, sex, and comorbidity (OR 1.15 [CI 1.12-1.19], $p<.001$).
DISCUSSION AND CONCLUSION:
Results of this study suggest a contradictory influence of BB on skeletal physiology to those of previously published animal models. Much remains to be learned about the effect of beta blockers on bone healing. Clinical data from this study indicates BB use during fracture care is associated with a significant increase in the incidence of nonunion.