The Epidemiology of Fracture Nonunion in 18 Human Bones: Analysis of a Payer Database that Includes ~90.1 Million Patients

Robert D. Zura, MD[1]; Ze Xiong, MS[2]; Thomas Einhorn, MD[3]; J. Tracy Watson, MD[4]; Robert F. Ostrum, MD[5]; Michael Prayson, MD[6]; Gregory J. Della Rocca, MD, PhD, FACS[7]; Samir Mehta, MD[8]; Zhe Wang, MS[9]; R. Grant Steen, PhD[10]

[1]Louisiana State University Health Science Center, New Orleans, Louisiana, USA;
[2]North Carolina State University, Raleigh, North Carolina, USA;
[3]Boston University Medical Center, Boston, Massachusetts, USA;
[4]St. Louis University Dept. of Ortho Surgery, Saint Louis, Missouri, USA;
[5]UNC Department of Orthopaedics, Chapel Hill, North Carolina, USA;
[6]Wright State Orthopaedic Surgery, Dayton, Ohio, USA;
[7]University of Missouri School of Medicine, Columbia, Missouri, USA;
[8]Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA;
[9]North Carolina State University, Raleigh, North Carolina, USA;
[10]Bioventus LLC, Durham, North Carolina, USA

Purpose: The rate of nonunion is generally accepted as 5% to 10% of all fractures. Nonunion risk is related to the severity of injury and/or surgical tactics used for fixation, but nonunion is not fully explained by these factors alone. Certain patient factors are modifiable, which could potentially have a strong impact on patient care, perioperative decision making, and patient counseling. We test a hypothesis that fracture characteristics and patient-related risk factors assessable by the clinician at presentation can predict the risk of fracture nonunion.

Methods: This was an inception cohort study in a large payer database of patients in the United States. Patient-level health claims for medical and drug expenses were compiled for approximately 90.1 million patients. Study inclusion was limited to patients with a coded bone fracture in calendar year 2011. The final database collated 257 patient variables for each fracture. Variables included patient demographic descriptors, treatment procedures as per CPT codes, comorbidities as per ICD-9 codes, and drug prescriptions as per National Drug Code Directory (Red Book) codes. Continuous enrollment in the database was required for 12 months after fracture, to allow sufficient time to capture a nonunion diagnosis. Logistic regression was used to calculate odds ratios (ORs) for variables associated with nonunion.

Results: Among 313,256 fractures in 18 bones, the nonunion rate was 4.7%. Elevated nonunion risk was associated with a more complex fracture (eg, open fracture, multiple fractures), high body mass index, smoking, and alcoholism. Females had more fractures, but males were more prone to nonunion. Multivariate ORs for nonunion are generally small (<2.0), which may explain why nonunion has been so hard to predict. Fracture complexity is a key determinant, but nonunion rate also varies with fracture location: scaphoid, tibia + fibula, and femur are most likely to suffer nonunion. Nonunion ORs were significantly increased for risk factors including: number of fractures, use of NSAIDs (nonsteroidal anti-inflammatory drugs) + opiates, operative treatment, open fracture, anticoagulant

use, rheumatoid + osteoarthritis, opioid use, diabetes, anticonvulsant use, osteoarthritis, high-energy injury, osteoporosis, male gender, smoking, benzodiazepine use, insulin use, vitamin D deficiency, antibiotic use, obesity, and diuretic use (all, multivariate P <0.001). Surprisingly, nonunion risk associated with opioid use accrued largely to patients who were using opioids prior to fracture, rather than to patients who took opioids to treat pain secondary to fracture.

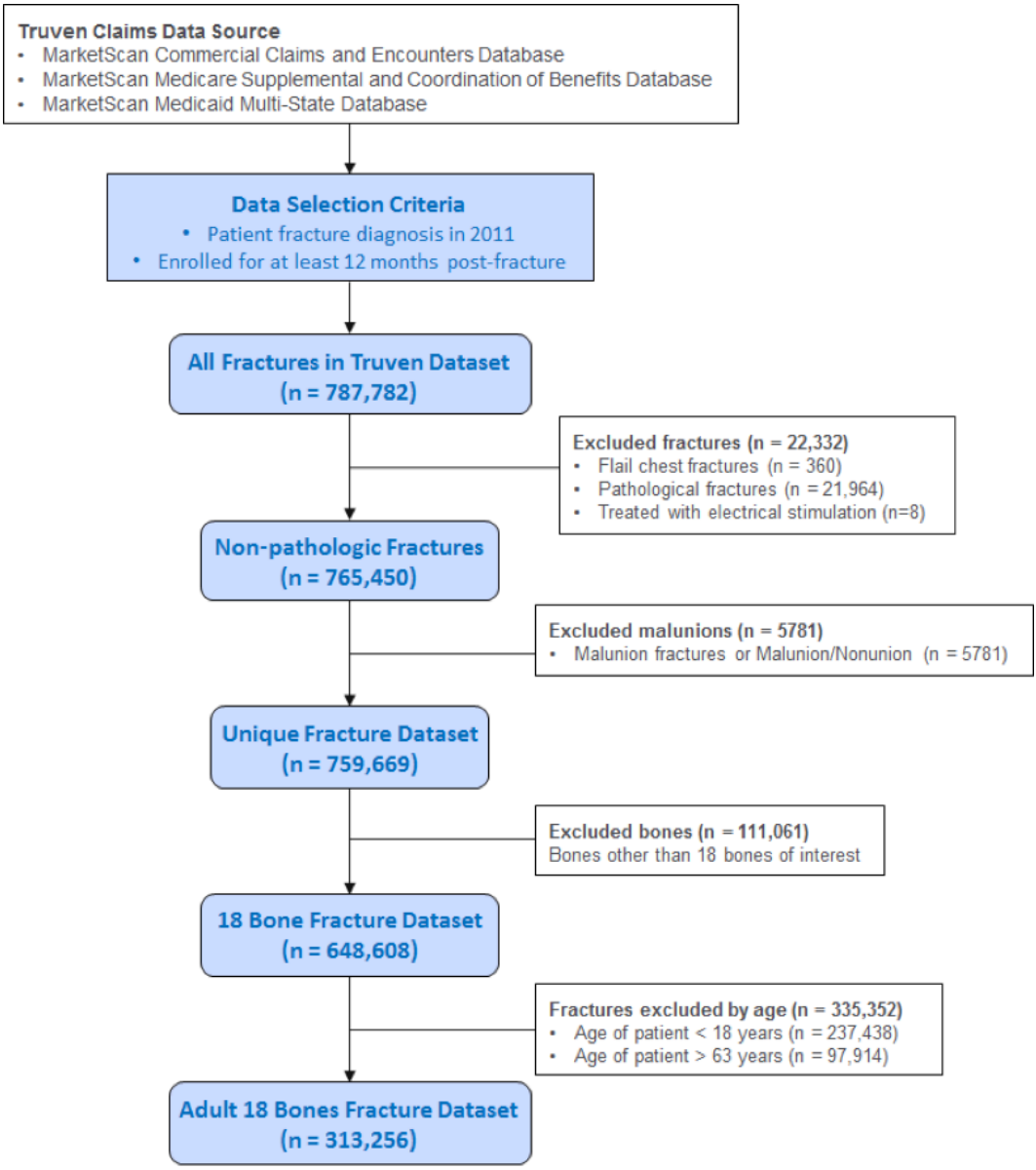

Figure 1. CONSORT diagram showing how the analytic sample was assembled.

See pages 49 - 106 for financial disclosure information.

Conclusions: Nonunion is a function of fracture complexity, fracture location, medication use, and disease comorbidity. The interplay of risk factors is complex, but it may become possible to predict nonunion. Certain medications that have a significant impact on fracture nonunion can be modified in the perioperative period to minimize risk of nonunion. Chronic opioid exposure is a strong risk factor for nonunion.