

Brown, KM, Saunders, MM, Kirsch, T, Donahue, HJ, Reid, JS. Effect of COX-2-Specific Inhibition on Fracture-Healing in the Rat Femur. *J Bone Joint Surg.* 2004;86A(1):116-123.

The purpose of this study was to determine if the postoperative delivery of a COX-2-specific inhibitor altered the healing of rat femur fractures to the same degree as conventional NSAIDs in humans. This was achieved by observing the biomechanical, morphological, histological, and radiographic properties at four, eight, and twelve weeks after a nondisplaced femoral fracture was created in adult rats. There are too few studies that examine these effects and such knowledge can be crucial in developing a protocol for postsurgical pharmacological treatment for long bone fractures.

Fifty-seven rats were used for this study by dividing them into 3 groups of 19. Some animals from each group were sacrificed at 4, 8, and 12 weeks postoperatively. One group was the control, receiving no drug, a second group received indomethacin (1mg/kg/d), and the final experimental group received celecoxib (3mg/kg/d) with all treatment starting on the first postoperative day. The femoral fracture was made according to the methodology described by Bonnarens and Einhorn. Radiographic analysis was determined with anteroposterior and lateral xrays of all femurs to reveal any callus formation and maturity as well as bridging bone formation on the four cortices at each time point. Blinded, independent investigators graded the radiographs. Histological analysis was determined through a modification of the classification system of Goldberg et al. This system is centered on the relative percentages of fibrous tissue, cartilage, woven bone, and mature bone in the callus. Blinded, independent investigators graded the fractures for histological analysis. Mechanical analysis was achieved through 3-point bending to determine femoral and fracture callus strength. Load, and displacement were recorded, and bending stiffness, failure load, displacement, bending moment, and fracture location in both femurs. Statistical analysis was determined with a power analysis for sample size, an alpha level at 0.05 and 80% power. Results reveal that at 4 and 8 weeks bone healing was more prevalent in the experimental groups. There was no significant difference between the celecoxib group and the control at any time as far as mechanical strength and radiographic healing are concerned. There were no significant findings between groups at 12 weeks.

The strength of recommendation using the *SORT* for this research is a *B* as it is a therapeutic animal study and therefore has limited-quality patient-oriented evidence. Using the *AAOS Levels of Evidence for Primary Research Question* this research is given a level 2 as the animal subjects make this a lesser quality randomized control trial.

Clinically this study is relevant to Athletic Training as it is important to know what medications our patients may be taking post-operatively and the effect these treatments can have on fracture healing of long bones, particularly the femur. If the bone healing is hindered due to pharmacological effects this can have implications for the progression of rehabilitation. Patients should be aware that their rehabilitation may not progress according to protocol timelines due to potential healing impairment if they are taking conventional NSAIDs postoperatively. Conversely, they should also be educated that if they are taking a COX-2 specific inhibitor, their femoral fracture healing should not be negatively affected by the medication postoperatively.