The Effect of Opioids, Alcohol, and Nonsteroidal Anti-inflammatory Drugs on Fracture Union

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KEYWORDS

• Fracture • Nonunion • Opioids • Alcohol • NSAIDs

KEY POINTS

- Retrospective clinical studies show a negative correlation between opioids and fracture healing, but there is no study that can determine direct causality.
- Animal models suggest that alcohol has an inhibitory effect on osteoblast proliferation and leads to a detrimental effect on fracture healing.
- Animal models have suggested that NSAIDs are a risk factor for nonunion; however, retrospective studies on human fracture data have failed to definitively link NSAIDs and nonunion.
- There are limited data to allow for clinical guidelines regarding opioids, alcohol, and NSAIDs on fracture union; rather, the prescribing physician should be cognizant of the potential effects.

INTRODUCTION

Fracture union is a complex process that is intimately related to the biologic and mechanical environments at the fracture site. Improper fracture fixation ranging from undersized intramedullary nails to overstiffened plate constructs can create an unfavorable mechanical environment for fracture union (Fig. 1 and Fig. 2). In the biologic environment, a multitude of cells and molecules are found at fracture sites within hours, and work to provide a framework for fracture repair. There are multiple inflammatory cells found at fracture sites within hours of the injury, and play an influential role in hematoma formation and the early stages of fracture healing within the first 5 days.[1] A multitude of factors influencing fracture union have been suggested including nutritional status; endocrine disorders; smoking; fracture location; fracture energy; fracture pattern; and medications, including steroids, chemotherapy agents, and nonsteroidal anti-inflammatory drugs (NSAIDs).[1] External factors influencing fracture union have come under increasing scrutiny in efforts to reduce the rates of nonunion or delayed union. Particularly, patient nutritional status and smoking status have proven to be influential in fracture healing as a result of altering the molecular environment at the fracture site.[1] Several medications have also come under consideration for their theoretic ability to alter the early inflammatory pathway and the later molecular environment involved in the formation of new bone. For

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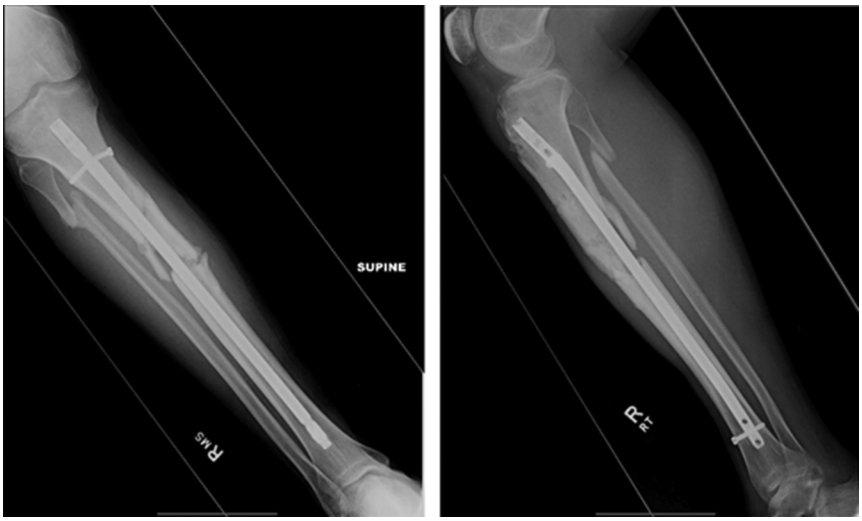

Fig. 1. Atrophic nonunion resulting from an undersized tibial nail.

example, there is a theoretic risk of chronic corticosteroid use leading to impaired fracture union because of the inhibition of osteogenic differentiation of mesenchymal stem cells, but this has not been proven in clinical studies.[1]

Although there is no standard definition of nonunion, it is generally accepted that nonunion is defined as a lack of complete bone healing within a specified time frame, typically between 6 and 9 months.[1] Nonunion is a known complication of the operative and nonoperative management of fractures. The rate of fracture nonunion has been estimated to be between 5% and 10%.[2] The effects of fracture nonunion are detrimental to the patient and the health care system. Some estimates of tibial shaft nonunions suggest that the median health care cost of nonunion versus union was more than two times greater, despite nonunions representing only 12% of tibial fractures overall.[3] With the increasing focus on patient outcomes and the awareness of external factors that influence fracture union, surgeon- and patient-controlled variables are being increasingly studied. Although smoking is generally accepted as detrimental to fracture healing, a less discussed patient factor is alcohol. Some studies demonstrate an association between alcohol use and impaired

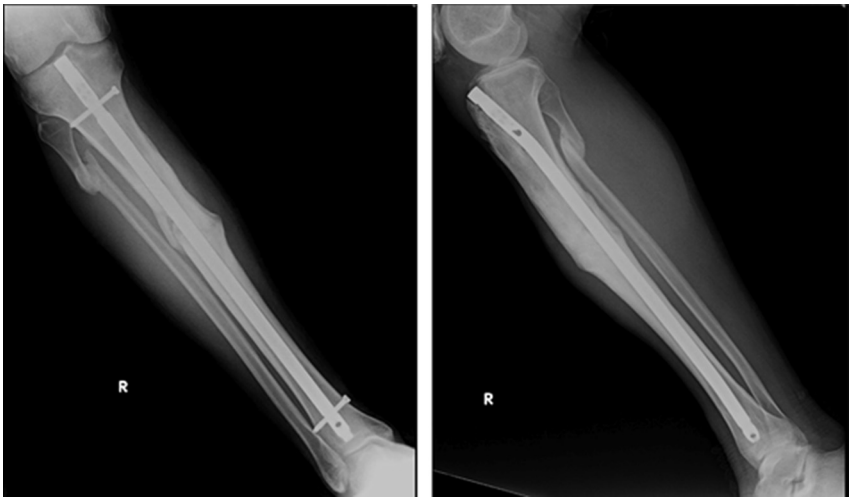

Fig. 2. Fracture union following nonunion surgery with intramedullary nail exchange.