

# Fracture healing and NSAIDs

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## Clinical question

Do nonsteroidal anti-inflammatory drugs (NSAIDs) increase risk of fracture nonunion or impede healing?

## Bottom line

Limited RCT data suggest NSAIDs do not impair fracture healing. Cohort studies associating NSAIDs with fracture nonunion are likely showing that patients with nonhealing (painful) fractures use more analgesics. As NSAIDs provide pain relief equivalent or superior to other analgesics, often with fewer side effects, patients should not be denied their short-term use for fractures.

## Evidence

- Adults—2 RCTs (N=140) of predominantly middle-aged women with Colles fractures randomized to flurbiprofen (14 days)<sup>1</sup> or piroxicam (20 mg/d for 8 weeks)<sup>2</sup> versus placebo:
  - No difference in recovery time, physiotherapy needs, malunion or nonunion,<sup>1</sup> functional recovery, or healing.<sup>2</sup>
  - Superior pain relief with NSAIDs (both trial arms allowed acetaminophen if required).
  - Limitations: about 20% lost to follow-up; small numbers.
- Children—1 RCT (N=336)<sup>3</sup> of children with arm fractures randomized to ibuprofen or acetaminophen and codeine:
  - No difference in fracture nonunion at 1 year.
  - Ibuprofen provided equivalent pain relief with less functional impairment and fewer adverse effects.
- Quasi-RCT of adults with acetabular fractures requiring heterotopic ossification prophylaxis<sup>4</sup> is misleading. Patients with less-serious injuries and different surgical approach (not randomized to NSAIDs or radiation for prophylaxis) were analyzed in the “non-NSAID” arm.

## Context

- Retrospective cohort and case-control studies associating NSAIDs with nonunion<sup>5-8</sup> are confounded by differing injuries,<sup>7</sup> smoking rates,<sup>7,8</sup> and treatments.<sup>8</sup> They demonstrate *association*, not *causation*.<sup>6</sup> Opioid use is also associated with nonunion. Patients with nonhealing (painful) fractures are probably just more likely to use analgesics.
- Rate of nonunion of long-bone fractures is 1% to 6%.<sup>5-7</sup>
- NSAIDs provide good postsurgical pain relief in adults,<sup>9</sup>

and are superior to acetaminophen or codeine and equivalent to acetaminophen plus codeine (with fewer adverse events) for pediatric musculoskeletal injury.<sup>10</sup>

- Some animal studies demonstrate that supranormal doses of NSAIDs impair bone healing.<sup>11,12</sup>

## Implementation

Appropriate pharmacologic and nonpharmacologic (splints or fracture reduction) treatment for patients with painful fractures should be a priority in all emergency departments. Some patients (especially children) with fractures have analgesia unnecessarily delayed<sup>13</sup> or do not receive analgesia in the emergency departments.<sup>14</sup> Preventing fractures is obviously ideal, but when they do occur, patients should not be denied NSAIDs for short-term pain relief. 🌿

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