



Editorial

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NSAIDs, are they dangerous for pancreatic surgery?

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Appropriately controlling acute postoperative pain is associated with improved recovery and postoperative outcomes. Postoperative pain should be controlled in the most effective and safest manner with the fewest side effects possible. Multimodal analgesia is a combination of various analgesics with different mechanisms of action that have additive or synergistic effects when taken together [1]. This allows for a lower total analgesic dose and fewer side effects, reducing the opioid requirement. Several drugs are currently used for multimodal treatment strategies, including nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, gabapentinoids, N-methyl-D-aspartate receptor antagonists, glucocorticoids, lidocaine, alpha 2 agonists, and local anesthetics for regional blocks.

NSAIDs are effective non-opioid analgesics that are widely used in the perioperative setting. The primary mechanism of action is the inhibition of the cyclooxygenase (COX) enzyme, which blocks the inflammatory response by preventing the formation of prostaglandins. NSAIDs are categorized on the basis of their selectivity for COX-1 and COX-2. Non-selective NSAIDs block both enzymes, and the side effects of these drugs are mainly due to COX-1 inhibition, which is associated with a disturbance in vascular homeostasis [2].

The side effects of NSAIDs on renal function [3-6], cardiac events [7-9], perioperative bleeding [10-12], wound healing [13,14], and gastrointestinal events [15] have been assessed, with some concerning findings. However, the results are controversial and the evidence is not conclusive.

NSAIDs have been shown to have a strong analgesic effect similar to opioids [16-19], with similar acute postoperative pain control. This makes them suitable for reducing opioid consumption and thus improve bowel function [17,20]. However, safety concerns regarding postoperative anastomotic complications have recently been raised. Since NSAIDs can impair collagen deposition and angiogenesis, the strength of anastomosis is thus decreased [21,22]. Kotagal et al. [16], in their study of 398,752 patients undergoing gastrointestinal surgery, found that the administration of ketorolac was associated with an increased risk of readmission and reintervention due to anastomosis complications (odds ratio [OR]: 1.20, 95% CI [1.06, 1.36]). According to another large-scale retrospective cohort study, NSAIDs were found to increase the risk of anastomotic leaks (OR: 1.70, 95% CI [1.11, 2.68], P = 0.01) in patients undergoing bariatric or colorectal surgery [23].

Yoon et al. [24] retrospectively investigated the association between postoperative NSAID use and clinically relevant postoperative anastomotic leakage (postoperative pancreatic fistula [POPF] or hepatojejunostomy anastomotic leakage [HL]), in > 4,000 patients. The authors found a higher incidence of HL within the first 5 postoperative days in the group that received NSAIDs postoperatively (OR: 3.11, 95% CI [1.86, 5.21]). However, the overall incidence of HL was too low (1.9%) to allow for the role of NSAIDs to be analyzed as a risk factor for postoperative HL using binary logistic regression analysis. In addition, NSAID use was not a risk factor for POPF in that study [24].

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Therefore, the question regarding whether NSAIDs should be used during pancreatic surgery remains unclear. There are numerous risk factors for postoperative anastomotic complications, including advanced age, large anastomotic tension, infection, neo-adjuvant chemotherapy, co-existing inflammation for postoperative anastomotic complications, the use of vasopressors, and the skill of the surgeons. In addition, the cumulative dose of NSAIDs may be a more important risk factor than the use of NSAIDs [25]. To define the association between postoperative NSAID use and anastomotic complications and to find the optimal dose of NSAIDs, well-controlled and large-scale prospective studies are needed.

NSAIDs are central to the opioid-sparing multimodal analgesia technique. However, results have been inconclusive regarding the effect of early postoperative NSAID use and anastomotic leakage [25,26]. While NSAIDs can be safely used at an optimal dose and timing, a protocol for acute postoperative pain control should be established for postoperative NSAID use that involves a multidisciplinary discussion including both anesthesiologists and surgeons.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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