



A Commonsense Patient-Centered Approach to Multimodal Analgesia Within Surgical Enhanced Recovery Protocols

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“Enhanced recovery” in the context of a surgical patient is both a plan and a goal at the same time. The goal is faster convalescence after surgery with positive outcomes and no complications. The plan takes the form of an enhanced recovery protocol (ERP) or clinical pathway specific to a surgical procedure, a concept pioneered by Professor Henrik Kehlet from Denmark decades ago.¹ Over time, this basic concept has evolved and has become arguably too complex. With over twenty elements frequently included in modern ERPs, it is not surprising that consistent implementation and adherence are lacking.² Not all of these elements are critical, and a study of an ERP for bowel resection has demonstrated that three are particularly important: 1) laparoscopic (minimally invasive) approach; 2) early termination of intravenous fluid; and 3) early mobilization (getting out of bed).³

This last element is critically dependent on effective pain management. Because the objective of achieving analgesia does not exist in a vacuum and must be balanced with the goal of early mobility, today’s standard for pain management in the perioperative period is multimodal analgesia or using more than one analgesic agent with different mechanisms of action.⁴ While a single analgesic agent has the potential to provide complete postoperative pain management alone, it often comes at a significant cost. Consider these two extremes: continuous spinal anesthesia and opioid-only analgesia. Continuous spinal anesthesia, which may involve an infusion of local anesthetic into the cerebrospinal fluid, is arguably the most effective regional analgesic technique available.⁵ In the case of lower extremity arthroplasty, a continuous spinal anesthetic will provide complete postoperative pain relief; however, it will also result in complete immobility and prevent the patient from participating in any physical therapy. For the same surgery, opioid-only analgesia may also provide effective pain management, but it may also render the affected patient unconscious, depress respirations, and precipitate nausea, vomiting and constipation, which can also negatively impact postoperative rehabilitation. Additionally, persistent postoperative opioid use has been identified as a common adverse outcome after surgery.⁶ Given these examples, it is clear why multimodal analgesia has become the cornerstone of all ERPs.

Available data suggest that the increasing number of non-opioid analgesic modalities decreases total opioid usage and opioid-related side effects,⁷ and different patterns of non-opioid analgesic utilization have been identified among

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anesthesiologists based on the type of surgery and patient factors.⁸ The scientific mechanisms of postoperative pain have been described elsewhere.⁹ A practical application of a multimodal analgesic strategy should be patient- and procedure-specific and consider the source, transmission, and processing of the expected surgical pain (Figure 1). We present one commonsense approach using total knee arthroplasty (TKA) as an example below written in a way to facilitate discussions with patients and family members.

Source of Pain

TKA is one of the most common surgical procedures in the United States and reliably generates severe pain in most patients.¹⁰ TKA involves removal of the arthritic surfaces of the knee joint and implantation of manufactured prostheses. Localized pain and inflammation are caused by incising and cauterizing skin, subcutaneous layers, and muscle as well as osteotomies (“bone cutting”)

of the tibia, femur, and patella and nerve injury. Pain at the surgical site may be relieved by non-steroidal anti-inflammatory drugs (NSAIDs) or the more selective cyclooxygenase-2 inhibitors (e.g., celecoxib), local anesthetics administered around the knee joint, and cryotherapy (i.e. applying ice to affected areas) with or without compression.¹¹ All surgical patients should be eligible for these interventions unless contraindications exist.

Transmission of Pain

Afferent pain signals are carried from the surgical site to the central neuraxis via peripheral nerves. For certain types of surgery, regional anesthesia techniques (i.e., targeting one area of the body with local anesthetics) can effectively interrupt nerve transmission from the periphery to the spinal cord. These nerve blocks can provide sufficient anesthesia to make general anesthesia unnecessary for some surgeries (e.g., spinal anesthesia for knee

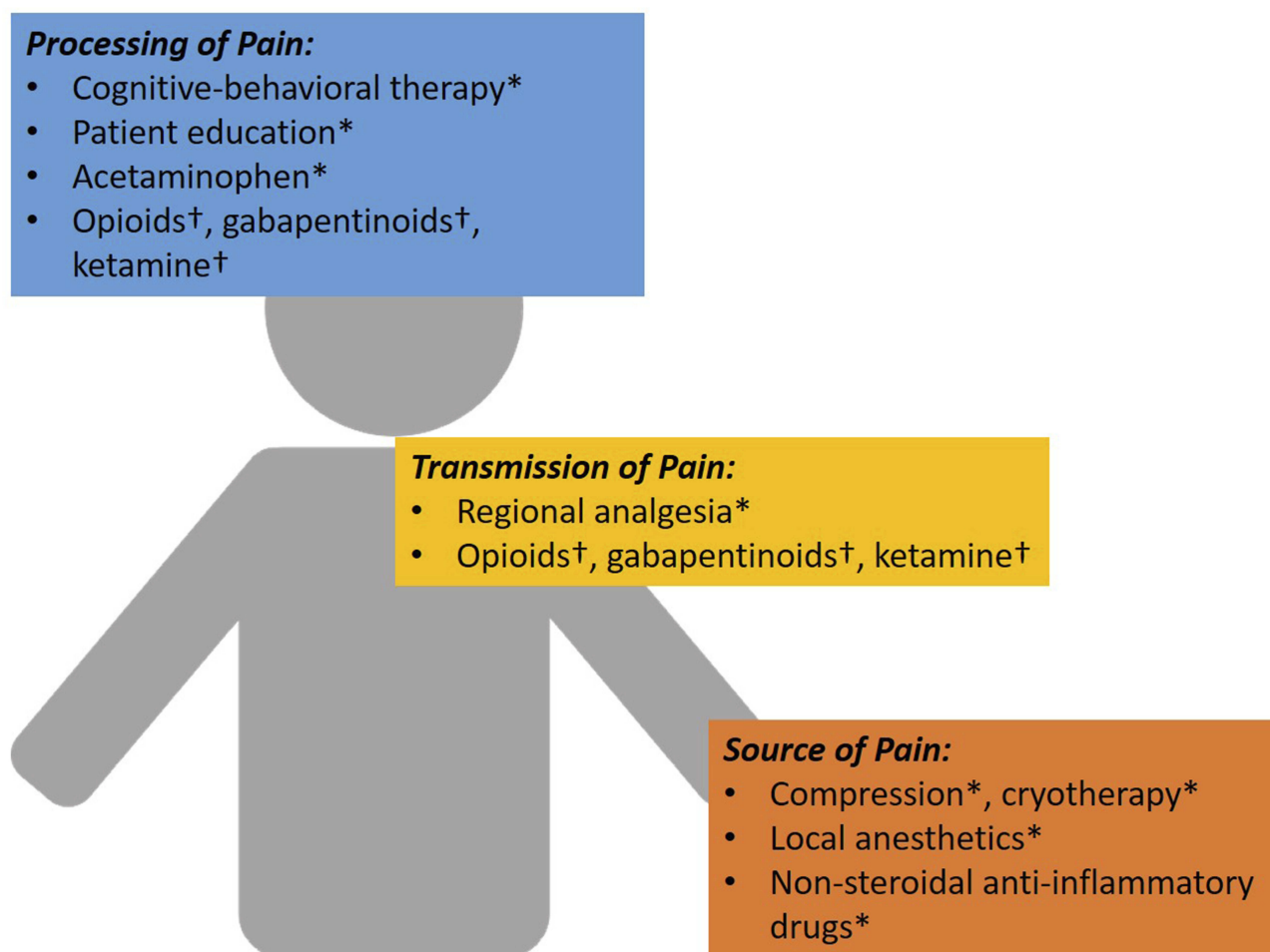


Figure 1 A simple paradigm for applying a multimodal analgesic strategy taking into consideration the source, transmission, and processing of the expected surgical pain; *=Routine and should be available to all patients unless contraindicated; †=Not routine and given only as indicated.

replacement or brachial plexus block for hand surgery). Advances in these techniques using perineural or epidural catheters (i.e., regional analgesia) can extend the duration of target-specific pain relief further into the postoperative period. When this duration matches the expected trajectory of pain resolution after surgery, there may be little need for additional systemic analgesics. For TKA, regional analgesia is well-established as part of the multimodal regimen,^{4,11} but the trajectory of pain resolution may commonly extend beyond the 3-day duration of most regional analgesic techniques.¹²

Another important consideration for patients undergoing major surgery is central sensitization. In simple terms, this entails recruitment of neurons at the level of the spinal cord that normally do not transmit pain and results in expansion of the originally painful area (i.e., hyperalgesia). Opioids indirectly stimulate descending inhibitory pathways in the spinal cord that decrease the transmission of painful signals to the brain.¹³ Gabapentinoids decrease the hyperexcitability of neurons in the spinal cord responsible for central sensitization.¹⁴ Ketamine acts on N-methyl-D-aspartate receptors and, in subanesthetic doses, has been recommended for acute postoperative pain management.¹⁵ Further, ketamine may also exert beneficial effects in decreasing central sensitization.¹⁶ It is our opinion that non-pharmacologic interventions, local anesthetics, and NSAIDs should be administered to all surgical patients who do not have contraindications. However, opioids, gabapentinoids, and ketamine should only be used when indicated. Common factors to consider include patient history, especially comorbid conditions and preoperative analgesic use, preoperative physical function, surgical technique, and the availability of a 24/7 acute pain service that can respond to inadequately treated pain in a timely manner.

Processing of Pain

Pain processing is both physiological and psychological. By definition, postoperative pain will be an individualized experience.¹⁷ Previous studies demonstrate that pain catastrophizing is a risk factor for the development of chronic pain following TKA.¹⁸ For some patients with chronic pain undergoing major surgery, combining cognitive-behavioral therapy with physical therapy may improve postoperative outcomes.¹⁹ Cognitive-behavioral interventions are time- and labor-intensive and are unfortunately not available everywhere.²⁰ Access to and use of basic patient education available online with regard to

postoperative analgesic options and safe opioid management are limited.^{21,22} A relatively simple intervention of setting patients' expectations regarding pain after TKA, providing a more detailed pain scale, and educating patients regarding their postoperative pain medications has been shown to decrease the utilization of opioids after surgery.²³

In terms of pharmacology, paracetamol or acetaminophen acts centrally and should be given to all surgical patients unless contraindicated. Although its exact mechanisms of action are not completely understood, analgesia may result from activation of descending serotonergic (inhibitory) pain pathways, interfering with prostaglandin synthesis, and interacting with the endocannabinoid system.²⁴ Other systemic analgesics with supraspinal activity include opioids, gabapentinoids, and ketamine.^{9,11,13,14,16}

Putting It All Together

The implementation of multimodal analgesia within ERPs is best viewed as a checklist and not a recipe. When following a recipe, each ingredient should be included in a recommended amount and added in a stepwise fashion in order to avoid a culinary disaster. This is not the case with multimodal analgesia. Each analgesic item within an ERP should be considered for the eligible surgical patient; included in the regimen if there are no contraindications and/or there are specific indications; and individualized in terms of dosing and frequency based on the patient's prior medication use history and comorbid conditions.

An example of one institution's multimodal analgesic regimen included in an ERP for TKA patients is illustrated in **Box 1**. While the regimen includes multiple interventions and medications, it may be adapted to meet the needs of the individual patients.⁴ Some patients who are opioid-naïve may not need any scheduled opioid after surgery and will respond to as-needed administration only. For all TKA patients, spinal anesthesia is strongly preferred for intraoperative anesthesia²⁵ and will eliminate the need for systemic analgesics during surgery. Patients who take opioids chronically before surgery should continue this regimen in the perioperative period. Patients on medication-assisted treatment for opioid use disorder require special consideration with regard to perioperative pain management.²⁶ Today, the use of opioids for breakthrough pain relief post-TKA has not been eliminated for most patients in the United States even in the setting of robust multimodal analgesia and patient education.²³ However, the integration of non-pharmacologic interventions and non-opioid

Box 1 Sample Perioperative Multimodal Analgesic Regimen Included in an Enhanced Recovery Protocol for Total Knee Arthroplasty Patients

| Before Surgery |
|---|
| <ul style="list-style-type: none"> • Counsel the patient on inpatient fall prevention and expected pain trajectory. • Assess each patient's medical and substance abuse history, pain medication history, drug allergies, and intolerances to analgesic medications. • Give acetaminophen 1000 mg and celecoxib 400 mg by mouth if no contraindications exist. • Insert an adductor canal catheter under ultrasound guidance in the regional anesthesia induction area ("block room"); add infiltration between the popliteal artery and capsule of the knee (IPACK) block if the surgeon does not routinely perform local infiltration analgesia at the end of surgery. • If applicable, continue the patient's chronic outpatient analgesics on the day of surgery and postoperatively. • For the chronic pain or opioid-tolerant patient, consider giving a single dose of gabapentin 300–600 mg by mouth (lower dose in elderly and renal insufficiency). |
| During Surgery |
| <ul style="list-style-type: none"> • Recommend and perform spinal anesthesia (local anesthetic only) unless refused by the patient or contraindicated (then proceed with general anesthesia). • For the patient who does not receive spinal anesthesia, intravenous opioids may be administered as needed based on reactivity to painful stimuli. • For the opioid-tolerant patient who receives general anesthesia, consider intraoperative low-dose ketamine infusion (0.5 mg/kg bolus followed by 0.25 mg/kg/hr infusion). • Encourage surgeons to perform local infiltration analgesia (ropivacaine 0.2% 150 mL with epinephrine 2.5 mcg/mL and ketorolac 30 mg) before closure; if not an option, perform IPACK block preoperatively. |
| After Surgery |
| <ul style="list-style-type: none"> • Provide routine cryotherapy with or without compression based on institutional practice. • Prescribe scheduled acetaminophen 1000 mg by mouth every 6 hrs unless contraindicated (reduce the dose in patients with impaired liver function). • Prescribe scheduled celecoxib 200 mg by mouth twice a day for up to 5 days then continue as needed (avoid if history of gastric ulcer or renal insufficiency). • Short-acting oxycodone may be prescribed on a scheduled basis 5–10 mg every 6 hrs for the first 1–2 days after surgery; replace with the patient's preoperative opioid regimen when applicable. • For breakthrough pain relief, prescribe short-acting oxycodone tablets (e.g., 5 mg) by mouth and hydromorphone intravenously (e.g., 0.2 mg) every 4 hrs as needed. • Initiate perineural infusion of ropivacaine 0.2% (basal rate 6 mL/hr; patient-controlled bolus 5 mL, lockout 30 min) via adductor canal catheter immediately after surgery. • Provide daily monitoring of the patient's pain experience, achievement of functional goals, and overall recovery through hospital discharge and adjust medications and interventions as needed. • Counsel the patient on outpatient opioid use and safe storage following discharge and recommend provision of a tapering schedule for prescribed outpatient opioids based on the patient's prior 24 hr opioid use; continue non-pharmacologic interventions and non-opioid analgesics on an as-needed basis. • For the patient taking opioids chronically before surgery, communicate the discharge analgesic plan with the outpatient prescribing physician. |

analgesic modalities including regional anesthesia techniques effectively decreases opioid consumption and should be considered routine.^{4,11,23}

In order to be successful, ERPs must be accepted by both healthcare practitioners and patients. Ethical concerns have been raised about the "weaponization" of ERPs with the goal of eliminating all postoperative opioids even in patients on long-term opioids. We appreciate that an important goal of ERPs should be to minimize the need for postoperative opioids whenever possible and practical

through effective multimodal analgesia. However, we assert that the intended goal of ERPs, particularly for severely painful surgical procedures (e.g., total joint replacement), is incorporation of "opioid-sparing" rather than "opioid-eliminating" pain management strategies.²⁷ Opioids as a class of analgesic drugs continue to have a role in postoperative pain management, and the reality is that many patients presenting for surgery today are already on long-term opioids preoperatively. These patients may rightfully fear "oligoanalgesia" due to the

deliberate underutilization of opioids in the perioperative period. The ethical application of ERPs emphasizes that pain is a subjective experience, and all ERPs should continue to promote personalized pain medicine in the hospital postoperatively and post-discharge. A recent article describing a multidisciplinary patient-specific opioid prescribing and tapering protocol after lower extremity arthroplasty suggests a reasonable goal of return to baseline opioid use after recovery from surgery.²⁸

In conclusion, there has been tremendous progress in the field of acute perioperative pain medicine. Effective pain management to facilitate early mobility is a critical element of modern ERPs for surgical patients. The use of multimodal analgesia has decreased the over-reliance on opioids for postoperative pain relief with regional anesthesia techniques targeting the specific site of pain and systemic non-opioid and non-pharmacologic interventions expanding coverage across the complex network of pain mechanisms. While opioids have yet to be eliminated from the postoperative period, and may well never be, the effectiveness of multimodal analgesia is well proven and has become the standard for perioperative pain management.

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