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Multimodal Analgesia Guidelines for Surgical Practice

Most surgical patients experience some degree of pain after surgery. Despite the near-universal use of short courses of opioids perioperatively, as many as 80% of patients report moderate to extreme postoperative pain.[1-2] Surgical pain is multifactorial and, depending on the procedure, may involve nociceptive pain associated with incision and surgical injury, visceral pain associated with disruption of visceral structures, neuropathic pain secondary to nerve damage or transection and the inflammatory response to tissue damage. Compounding pain caused by the surgery itself, many patients present with conditions that are acutely painful or have a history of chronic pain. Thus, perioperative pain is often complex and multifactorial. Despite the ubiquity of pain in surgical practice, pain is poorly understood by many medical professionals and is seldom taught in medical schools, 96% of which have no dedicated pain medicine module.[3] A better understanding of pain and the interventions that can be therapeutically applied to alleviate is among the most important aspects of better opioid stewardship and safer, effective analgesia.

Pain is best addressed by simultaneously intervening at multiple points in the physiological pathways involved in the transmission of pain signals. By selecting pharmacological agents that act on different channels, enzymes, and receptors, surgeons can leverage the additive and synergistic mechanisms of analgesia provided by complementary medications to treat pain more comprehensively. At the same time, surgeons and anesthesiologists also have a powerful array of regional anesthetic and analgesic interventions at their disposal which, if used widely and consistently, have the potential to provide anatomically selective anesthesia and analgesia, further reducing the need for analgesics. Evidence supporting the concomitant use of regional and nonopioid pharmacologic analgesia for acute perioperative pain is strong, and the possibility that such multimodal approaches may reduce the incidence of chronic postsurgical pain (CPSP) may additionally motivate surgical care teams to use multiple modes of pain control for all their patients.[4,5-10]

An obvious, common-sense approach to reducing our national reliance on opioids is to ensure that every surgical patient is offered nonopioid analgesics. Despite evidence in support of alternatives to opioids, physicians and hospitals frequently fail to offer surgical patients more than one mode of pain control. While virtually every surgical patient in the U.S. receives opioid analgesia, the likelihood of receiving a single nonopioid analgesic after surgery ranges from 43% to 99% depending on the institution, while the likelihood of receiving two nonopioid agents ranges from 8% to 92%.[11] The consistent delivery of multimodal analgesia remains an area of opportunity for reducing perioperative opioid use.

Opioid monotherapy often fails to achieve adequate analgesia and exposes patients to both increased immediate risk of Opioid-Related Adverse Drug Events (ORADEs) and long-term risk of dependence and addiction. For some surgical patients, scheduled Acetaminophen APAP and a Non-Steroidal Anti-Inflammatory (NSAID) provide adequate analgesia. For others, the addition of one or more nonopioid therapies may reduce or eliminate perioperative opioid requirements while simultaneously improving pain control and the speed of recovery.[12-14] Appropriate use of the nonopioid therapies described below may significantly improve perioperative pain management. Surgeons and anesthesiologists who modify their clinical practices to employ more multimodal pharmacologic and nonpharmacologic approaches may deliver better, safer patient care while simultaneously protecting their communities from the harm associated with unused opioid medications.

When selecting multimodal analgesic medications and interventions, surgeons and anesthesiologists must contend with the lack of high-quality, procedure-specific evidence for many of the suggestions outlined in the pathways below.[15] Further research is urgently needed to determine the quality of evidence and strength of recommendations for many elements in these pathways. That said, the absence of conclusive findings must be weighed against the incontrovertible evidence of the immediate and long-term harms caused by an overreliance on opioid analgesia,

and clinicians are encouraged to consider the relatively safe risk profiles of the many nonopioid options available. Surgeons and anesthesiologists must partner with researchers, pharmacists, and nurses to define and implement safe and effective analgesic protocols that incorporate available and evolving evidence in a way that is compatible with their unique practice settings.

Practice Recommendations

1. Surgeons and anesthesiologists are encouraged to use multimodal analgesia and adopt the following principles when managing perioperative pain:

a. Use nonopioid approaches as first-line therapies.
b. Use several pharmacological agents and/or regional anesthetic/analgesic interventions for pain control rather than relying on opioid monotherapy.
c. Use opioids primarily as rescue medications.
d. Emphasize realistic, functional pain management goals with patients.
e. Use empathic language when discussing pain.

2. Before every surgery, surgeons and anesthesiologists are encouraged to discuss the neuraxial and regional anesthetic techniques that may apply to each case and the risks and benefits of each.

a. Surgical teams are encouraged to work together to select the modes of neuraxial anesthesia, peripheral nerve or plane blocks, single-shot blocks, and/or catheter placement for Continuous Wound Infiltration (CWI) that are safe, effective and best suited to each patient to reduce postoperative pain and opioid consumption.
b. Surgeons may wish to consider wound infiltration with amide anesthetics and/or, in appropriate patients, installation of intraperitoneal local anesthetic (IPLA).
c. Collaboration between surgeons and anesthesiologists may require the restructuring of operative workflows to efficiently facilitate the wider use of regional anesthetic interventions.
d. Ideally, a plan for altering the approach to regional anesthesia/analgesia will be in place before surgery in the event that a laparoscopic procedure must be converted to an open procedure.
e. It is advised that patients be informed of the risks and benefits of regional anesthesia/analgesia and that patient consent be obtained before surgery for the use of any appropriate regional anesthesia/analgesia in the case that such an approach becomes indicated if not initially planned.
    i. It is recommended that standard preoperative consent forms be amended to facilitate the use of any appropriate regional anesthetic and analgesic interventions.
f. Surgical and anesthesiology teams can work with hospitals to ensure that they are credentialed and have the equipment necessary to perform these opioid-sparing procedures.

3. Anesthesiologists are encouraged to consider the use of opioid-sparing or opioid-free anesthesia protocols when clinically appropriate.

4. Surgical clinicians are encouraged to consider the use of preoperative and intraoperative medications that may contribute to reduced postoperative pain and analgesic requirements and are encouraged to use

nonopioid analgesics in the postoperative period.

a. Strongly consider concomitantly prescribing scheduled APAP and an NSAID for the treatment of perioperative pain.

i. It is suggested that APAP be used pre-, intra-, and postoperatively for any surgical patient in whom it is not contraindicated. ii. It is recommended that NSAIDs be strongly considered for pre- and postoperative pain management unless contraindicated. Although NSAIDs have in the past been avoided out of surgical, renal, and bleeding concerns, more recent research supports the perioperative benefits of these medications for the majority of surgical procedures.

b. Low-dose, sub-dissociative ketamine is an effective analgesic that can be opioid-sparing during and following many different surgeries. It may be particularly beneficial for patients with chronic pain or opioid dependence.

c. IV lidocaine is an effective analgesic; it is recommended that its routine intra- and postoperative administration be supported by appropriate education and hospital policies.

d. Alpha-agonists (dexmedetomidine, clonidine), N-methyl-D-aspartate receptor (NMDA) antagonists in addition to ketamine (magnesium) and esmolol are agents that may have analgesic benefits for some patients.

e. Consider using an amine-reuptake inhibitor (e.g., duloxetine, venlafaxine) or a gabapentinoid when CPSP is anticipated or when managing patients with pre-existing chronic pain conditions. Consider coordinating with primary care or pain clinicians who can manage the ongoing use of these agents.

f. Consider the use of topical medications for pain control, including topical lidocaine and diclofenac.

g. Consider advocating for or conducting further research into pharmacological agents that have limited evidence or pre-clinical evidence supporting their potential use as analgesics.

5. Surgical clinicians are encouraged to familiarize themselves with the identification and targeted treatment of different types of perioperative pain and comorbid pain conditions.

a. Consider NSAIDs, APAP, and glucocorticoids for somatic pain or pain with an inflammatory component.

b. For pain with a tension or spastic component, consider muscle relaxants or antispasmodics.

c. For pain with a neuropathic component, consider gabapentinoids and/or topical and Intravenous (IV) lidocaine.

d. For chronic neuropathic, musculoskeletal, or abdominal pain, consider an amine-reuptake inhibitor (e.g., duloxetine, venlafaxine).

6. Opioids are best reserved for pain that is severe or limits function despite the use of nonopioid treatments.

a. When opioid analgesia is used, the concurrent receipt of opioids and nonopioid analgesics can reduce the patient's total opioid requirements and improve pain management.[16]

b. Monoproducts of opioids, including oxycodone, hydromorphone, and morphine sulfate, are preferred over combination products that contain APAP. This allows APAP to be taken preferentially and used as a first-line agent with a lower risk of supratherapeutic dosing or accidental poisoning.[17]

c. It is advised that postoperative opioids be tapered or discontinued as soon as possible.

d. It is recommended that surgical patients who received no opioid analgesia in the last 24 hours of hospitalization not be discharged with a prescription for an opioid.

7. Surgical teams are encouraged to integrate multimodal treatment strategies and pathways into their computerized physician order entry systems to facilitate the seamless adoption and safe delivery of novel medications.

8. Nonpharmacologic options can be used concomitantly with medications and regional anesthesia for the treatment of all types of pain.

9. Surgical teams are encouraged to consider the use of opioid-sparing multimodal perioperative pain management as suggested in the pain management options outlined below for:

a. Colorectal
b. Cholecystectomy
c. Appendectomy
d. Ventral abdominal wall repair
e. Inguinal herniorrhaphy
f. Mastectomy
g. Breast Biopsy, Lumpectomy +/- sentinel lymph node biopsy (SLNB)
h. Thoracotomy

NOTE: The principles of enhanced recovery pathways and the analgesic interventions suggested in these sample pain management pathways can be applied to surgical procedures beyond those addressed here.

Opioid-Sparing Multimodal Perioperative Pain Pathways

For Common Surgical Procedures

The following recommendations are derived from existing enhanced recovery pathways (ERPs), a comprehensive literature review and expert opinion. The clinical judgment of surgeons and anesthesiologists must always supersede suggested clinical care pathways.

The following pathways offer comprehensive lists of interventions that may be useful for improving perioperative pain management and limiting patient opioid exposure. Surgical teams are encouraged to select from these options the pharmacological and regional anesthetic interventions that are best suited to each patient and procedure. It is in no way intended that most or all of the interventions listed below be used for any one patient or procedure. For **every** patient, the risks and benefits of **every** intervention and combination of interventions must be carefully weighed in consultation with the patient and the entire surgical team. Patients undergoing minimally invasive procedures will generally require fewer, low-risk multimodal analgesic options; patients undergoing major surgeries may benefit from more extensive, possibly higher-risk, multimodal analgesic interventions. For the vast majority of patients, it is recommended that multimodal analgesic interventions be carefully selected from the sample pain pathways below to address pain at multiple anatomic and physiological junctures.

The interventions included in the procedure-specific lists of possible multimodal pharmacological agents and regional anesthetic and analgesic techniques below are divided into the preoperative, intraoperative, immediate postoperative, and discharge periods. They are further loosely organized into the following categories:

1. Interventions that are recommended for the majority of patients appear under the heading "Recommend" for the relevant perioperative period.

2. Interventions that may be useful additions to an opioid-sparing multimodal analgesic regimen in patients without contraindications appear under the heading "Consider."

3. Beneath the "Recommend" and "Consider" categories are additional "Consider" pain management interventions that may be relevant to patients undergoing major and/or open procedures that are anticipated to produce moderate-to-severe postoperative pain. Consider also for patients who may benefit from more comprehensive pain management regimens, including those receiving chronic opioid therapy for pain, those receiving naltrexone, buprenorphine, or methadone for addiction treatment, those with a history of refractory or difficult-to-control postoperative pain and patients who request opioid-free surgery.

The pathways below are limited to considerations of pain and analgesia. Many of the recommendations for nonopioid anesthesia and analgesia presented below are derived from existing ERPs. Surgeries conducted using comprehensive enhanced recovery protocols have been demonstrated to result in reduced postoperative pain and analgesic requirements, and surgeons and anesthesiologists may consider developing and implementing full ERPs at their institutions where feasible and clinically appropriate.

It is recommended that multimodal analgesic regimens be tailored to safely meet the needs of individual patients. It is also recommended that medication selection and dosages be adjusted based on patient-specific factors, including organ function, comorbidities, home medication regimens, and previous medication intolerances. Several of these drugs and blocks when administered together or in combination with anesthetic drugs or opioids can contribute to perioperative bradycardia, dysrhythmias, hypotension, local anesthetic toxicity, renal disease, respiratory depression, somnolence, and other adverse effects. The risk of these adverse effects can be decreased by eliminating certain drug-drug combinations, giving a single dose and/or reduced dosages of certain drugs, and timing the administration of certain drugs so that they

do not reach peak levels simultaneously. Anesthesiologists and surgeons must understand the administration instructions, benefits, and risks of each block, drug, and block/drug combination, and are encouraged to consult a pharmacist for guidance regarding the use of the agents in these pathways as needed.

At Preoperative Consultation:

1. Educate all patients and caregivers on reasonable postoperative expectations. It is important to emphasize that some pain following surgery is normal and that the elimination of pain can conceal valuable clinical information. Patients and caregivers may be further counseled that mild pain can be a helpful tool for moderating patient activity.
2. Families and caregivers are encouraged to take measures to ensure that the patient has adequate rest and respite from work and family obligations following surgery in order to facilitate optimal postoperative healing.
3. It is advised that patients and caregivers be educated that improvements in function are as important as improvements in pain intensity. It is important to stress that some limitations in function are to be expected following surgery and will resolve as healing progresses.
4. Involve patients and family or caregivers in the development of a pain management plan, emphasizing both the immediate and long-term risks of opioid use and the benefits of multimodal analgesia, including nonpharmacologic modalities.
5. Screen patients for elevated risk of developing Opioid Use Disorder (OUD). Consider providing a behavioral health referral and additional psychosocial support for high-risk patients.
6. Identify and provide appropriate care for patients receiving chronic opioid therapy (COT) or Medications for Opioid Use Disorder (MOUD) and those with untreated OUD.
7. Screen patients for an elevated risk of developing CPSP. Consider the early involvement of pain medicine service and/or additional psychosocial support systems.
8. Advise patients that prehabilitation with smoking cessation, daily physical activity, increased protein intake in the week before surgery, and a protein drink before surgery may speed recovery and indirectly reduce the duration and intensity of postoperative pain.
9. Discuss over-the-counter (OTC) pain medications with your patient ahead of time and encourage them to have this medication on hand before surgery.
10. Direct patients to where they can find out what their financial obligation will be for the upcoming procedure so that they can plan ahead and not be surprised by a large bill.

Opioid-sparing Multimodal Analgesic Pathway for *Colorectal Surgeries*

Preoperative Recommendations	Consider for Preoperative Use

• APAP 1000 mg PO once	• Cyclooxygenase (COX)-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)
	• Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[18]
	• Gabapentin 300-600 mg PO once OR pregabalin 75-150 mg PO once (adjust the dose for age, renal function)[19-20]
	  ○ Caution with concomitant sedative prescribing, including opioids.
	  ○ Efficacy and safety evidence is mixed.

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to the procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique: • Laparoscopic repair is associated with less postoperative pain[21-26] Operative anesthesia: • Minimize or avoid induction opioids and minimize intraoperative maintenance opioids • Infiltration of local amide anesthetic at the surgical sites[27] Pharmacologic agents: • APAP 1000 mg IV if more than 6 hours since the last dose and the patient cannot take PO, with a goal of administering a dose every 6 hours • Ketorolac 15 mg IV at closure, unless contraindicated or an NSAID was administered preoperatively	Operative anesthesia: • Opioid-free total intravenous anesthesia (TIVA) (e.g., propofol, dexmedetomidine, lidocaine, and ketamine)[28] Regional anesthesia, consider[29-31] • Transversus abdominis plane (TAP) block (single shot or continuous infusion) • Quadratus lumborum (QL2 or TQL) block[32] • Erector spinae block[33] • Rectus sheath block[34] • Consider the use of bupivacaine for incisional and/or regional analgesia.[34-36] ○ Liposomal formulations lack evidence in terms of cost vs benefit. • Consider instillation of intraperitoneal local anesthetic (IPLA)[37-38] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max dose 150 mg) +/- 1-3 mg/kg/hr IV infusion[39-42] • It is recommended that infusion be stopped if and when incisional and/or regional

	bupivacaine product is administered ● Esmolol loading dose of 0.5 mg/kg IV bolus over one minute followed by 0.01-0.05 mg/kg/min IV infusion[43-44] ● Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion OR 4 gm IV given over 30-60 minutes at the close of case[45-48]

Consider for Intraoperative Use

For major open colorectal surgeries or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:

- Ketamine 0.1-0.3 mg/kg IV bolus once pre-incision +/- ketamine 0.1-0.3 mg/kg/hr IV infusion[49-52]
- Dexmedetomidine 0.8-1 mcg/kg IV bolus + 0.2-0.8 mcg/kg/hr IV infusion[52-58]
- Catheter placement for continuous wound infusions with amide anesthetic

Regional analgesia:

- Neuraxial analgesia: spinal, thoracic epidural anesthesia (TEA) or combined spinal and epidural anesthesia (CSEA)[59]
  - For patients with thoracic epidural, consider administering a bolus prior to incision and/or running an infusion intraoperatively

Postoperative Recommendations	Consider for Postoperative Use
APAP 1 g PO every 6-8 hours until pain is resolved. Use IV APAP only for patients in whom oral and PR administration are contraindicated ***PLUS*** ● Nonpharmacological interventions	● Ketorolac 15 mg IV every 6 hours for 24-48 hours followed by ○ NSAID (ibuprofen 600 mg PO every 6 hours ○ ***OR*** naproxen 500 mg PO every 12 hours) ○ ***OR*** COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ○ ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved ● Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO 1 to 2 times daily (adjust for age, renal function)[60] ● Lidocaine 1-2 mg/kg/hr IV infusion[39-42] - Avoid if bupivacaine product used or continuous wound infusion continued ● Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches)

For major open colorectal procedures or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:

- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[49-52]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[53-55,58]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if bupivacaine or other forms of wound infusion or epidural amide anesthetic are continued)

Regional analgesia:

- Continuous wound infusion with amide anesthetic
- Continued epidural adjunctive analgesia

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia, that patients receiving opioid therapy be maintained on multimodal analgesic agents as clinically appropriate and that opioid monotherapy be avoided.

Initiate opioid treatment with:

- Oxycodone IR 5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-15 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:

- Tramadol 50-100 mg PO every 4 hours
- Hydromorphone IR 2 mg PO every 4 hours as needed

For pain not controlled by oral opioids, if the patient has strict NPO, or for severe breakthrough pain, consider:

- Hydromorphone 0.5 mg IV every 2 hours as needed

Discharge Recommendations	Consider for Prescription on Discharge

• APAP 1 g PO every 6 to 8 hours until pain is resolved
• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches)
• For opioid-naïve patients, prescribe between 0 and 15 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent) for open, or between 0 and 10 tablets for laparoscopic colectomy.
	• NSAID (ibuprofen 600 mg PO every 6 hours
	  ○ ***OR*** naproxen 500 mg PO every 12 hours)
	  ○ ***OR*** COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours
	  ○ ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
	• For patients who benefitted from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoids upon discharge.
	-It is suggested that the discharge dosing regimen match the inpatient dosing regimen.
	-It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.

Multimodal Analgesic Pathway for *Cholecystectomy*

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Gabapentin 300-600 mg PO once ***OR*** pregabalin 75-150 mg PO once (adjust dose for age, renal function)[60-63] • Tizanidine 4 mg PO once[64-65]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to the procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique:[66] • Laparoscopic surgery is associated with less postoperative pain • Low-pressure (10-12 mm Hg) peritoneum if surgically feasible • Saline lavage and suction after removal of the gallbladder if there is spillage of bile • Aspiration of pneumoperitoneum gas Operative anesthesia: • Minimize or avoid induction opioids, and minimize intraoperative maintenance opioids • Infiltration of local amide anesthetic at the surgical sites[67] Pharmacologic agents: • Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[67, 82-83] • Ketorolac 15 mg IV, unless contraindicated or an NSAID was administered preoperatively	Operative anesthesia: • Opioid-free/sparing total intravenous anesthesia (TIVA) (e.g., propofol, dexmedetomidine, lidocaine, and ketamine)[56] • Instillation of IPLA[69-74] Regional anesthesia, consider: • Rectus sheath block[75] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion[39-41,56,76-78] • Esmolol loading dose of 0.5 mg/kg IV bolus over one minute followed by 0.01-0.05 mg/kg/min IV infusion[79-81] • Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion ***OR*** 4 gm IV given over 30-60 minutes at the close of case[45-48]

Consider for Intraoperative Use

For open cholecystectomy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Ketamine 0.1-0.3 mg/kg IV bolus once pre-incision +/- 0.1-0.3 mg/kg/hr IV infusion[49-52,84]
- Dexmedetomidine 0.8-1 mcg/kg/hr IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[60,85-86]

Regional anesthesia:
- Neuraxial analgesia: spinal, TEA or CSE[76,87-89]

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- TAP block[90]
- Quadratus lumborum block[90]
- Subcostal TAP blocks[91]
- Bilateral T6 erector spinae plane (ESP) single-shot blocks[33,92]
- Catheter placement for continuous wound infusions with local anesthetic

Postoperative Recommendations	Consider for Postoperative Use
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Nonpharmacological interventions	• Lidocaine 5% patch once daily, applied adjacent to incision (up to three patches

For open cholecystectomy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, use the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:

- Gabapentin scheduled 300-600 mg PO 1 to 3 times daily OR pregabalin 50-150 mg PO 1 to 2 times daily[63]
- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hrs[49-52,84]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if other forms of wound infusion or epidural amide anesthetic are continued)[39-42]

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

Initiate opioid treatment with:

- Oxycodone IR 5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-15 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:

- Tramadol 50-100 mg PO every 4 hours
- Hydromorphone IR 2 mg PO every 4 hours as needed

For pain not controlled by oral opioids, if patient strict NPO or for severe breakthrough pain, consider:

- Hydromorphone 0.5 mg IV every 2 hours as needed

Discharge Recommendations	Consider for Discharge
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS***	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches)

• NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
• COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
• For opioid-naïve patients, prescribe between 0 and 10 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent) for laparoscopic cholecystectomy and between 0 and 15 tablets for open cholecystectomy.
	• For patients who benefitted from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoid upon discharge.
	  ○ It is recommended that the discharge dosing regimen match the inpatient regimen.
	  ○ It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.

Opioid-sparing Multimodal Analgesic Pathway for Appendectomy

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[82] • Gabapentin 300-600 mg PO once ***OR*** Pregabalin 75-150 mg PO once (adjust dose for age, renal function)[19-20,62]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique: • Laparoscopic repair is associated with less postoperative pain[94-95] Operative anesthesia: • Minimize or avoid induction opioids and minimize intraoperative maintenance opioids. • Infiltration of local amide anesthetic at surgical sites[38,96]	Operative technique: • Single-port technique Operative anesthesia: • Opioid-free/sparing TIVA (e.g., propofol, dexmedetomidine, lidocaine, and ketamine)[28] • Instillation of IPLA[97-98] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion[39-41] • Esmolol loading dose of 0.5 mg/kg IV bolus over 1 minute followed by 0.01-0.05 mg/kg/min IV infusion[43-44,99-100] • Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion ***OR*** 4 gm IV given over 30-60 minutes at the close of case[45-48]

	Regional anesthesia, consider: ● TAP block[30,101] ● Quadratus lumborum block[32]

Consider for Intraoperative Use

For open appendectomy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Ketamine 0.1-0.3 mg/kg IV bolus once pre-incision +/- 0.1-0.3 mg/kg/hr IV infusion[49-52]
- Dexmedetomidine 0.8-1 mcg/kg/hr IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[58,54,102]

Regional Anesthesia:
- Consider epidural/spinal/CSEA as sole mode of anesthesia or as adjunctive analgesia[103-104]
  - Consider preoperative TEA placement
  - For patients with a thoracic epidural, consider providing a bolus prior to incision and/or running infusion intraoperatively
- Consider placing a catheter for continuous wound infusion with amide anesthetic

Postoperative Recommendations	Consider for Postoperative Use

● APAP 1 g PO every 6 to 8 hours ***PLUS***
● Ketorolac 15 mg IV every 6 hours for 24-48 hours followed by
  ○ NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
  ○ COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
● Lidocaine 5% patch topically once daily, applied adjacent to incision (up to 3 patches)[105]
● Nonpharmacological interventions
	● Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO once or twice daily (adjust dose for age, renal function)

For open appendectomy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[49-52]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[54]
- Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO once or twice daily
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if other forms of wound infusion or epidural amide anesthetic are continued)[39-42]

Regional anesthesia:

- Continuous wound infusion with amide anesthetic[60]

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

Initiate opioid treatment with:

- Oxycodone IR 5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-15 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:

- Tramadol 50-100 mg PO every 4 hours
- Hydromorphone IR 2 mg PO every 4 hours as needed

For pain not controlled by oral opioids, if patient strict NPO or for severe breakthrough pain, consider:

- Hydromorphone 0.5 mg IV every 2 hours as needed

Discharge Recommendations	Consider for Discharge

• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS***
• NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
• COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
• Lidocaine 5% patch once daily, applied adjacent to incision (up to three patches)
• For opioid-naïve patients, prescribe between zero and 10 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent) for open or laparoscopic appendectomy.[106]
	• For patients who benefitted from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoids upon discharge.
	  ○ It is recommended that the discharge dosing regimen match the inpatient regimen.
	  ○ It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.

Opioid-Sparing Multimodal Analgesic Pathway for *Ventral Abdominal Wall Repair*

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once) • Dexamethasone 0.1-0.2 mg/kg IV given slowly	• Gabapentin 300-600 mg PO once ***OR*** pregabalin 75-150 mg PO once (adjust dose for age, renal function)[19-20,107]

preoperatively or at induction[18]	

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique: • A laparoscopic approach is associated with less postoperative pain[108] • When feasible, use mesh for all ventral hernia repairs • Use of sutureless, self-gripping mesh may result in lower analgesic requirements than the use of transfascially sutured mesh[109-111] Operative anesthesia: • Minimize or avoid induction opioids, and minimize the use of intraoperative maintenance opioids • For large defects, consider preoperative placement of thoracic epidural, bolus, and/or running basal dose during procedure[112-113] • Local anesthetic infiltration into the peritoneal, musculofascial, and subdermal tissue planes at incision sites[114] Regional analgesia, consider: • TAP block[90,107,115-117] • Quadratus lumborum block[32] • Oblique subcostal TAP block[91] • Rectus sheath block[34] Pharmacologic agents: • Ketorolac 15 mg IV at closure, unless contraindicated or an NSAID was administered preoperatively[118]	Operative technique: • Opioid-free/sparing TIVA (e.g., propofol, dexmedetomidine, lidocaine, and ketamine)[28] • For minor procedures, consider anesthesia with local or regional anesthesia only[37] • Instillation of IPLA[37] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion[39-42] • Esmolol loading dose of 0.5 mg/kg IV bolus over 1 minute followed by 0.01-0.05 mg/kg/min IV infusion[43-44] • Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion ***OR*** 4 gm IV given over 30-60 minutes at the close of case[45-48]

Consider for Intraoperative Use
For large defects or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate: Pharmacologic Agents: • Ketamine 0.1-0.3 mg/kg IV bolus once pre-incision +/- ketamine 0.1-0.3 mg/kg/hr IV infusion[49-52] • Dexmedetomidine 0.8-1 mcg/kg IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[58,54-55] Regional Anesthesia: • Catheter placement for continuous wound infusion with amide anesthetic[119-120] • Neuraxial anesthesia: spinal, TEA, or CSEA[118,121]

Postoperative Recommendations	Consider for Postoperative Use
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Nonpharmacological interventions	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • Cyclobenzaprine 5-10 mg PO 3 times daily as needed ***OR*** metaxalone 800 mg PO 3 to 4 times daily as needed for pain caused by muscle spasms • Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO once or twice daily (dose adjusted for renal function, age)[60]

For major defects or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Regional Anesthesia:

- Continuous wound infusion with amide anesthetic
- Continued epidural adjunctive analgesia[122]

Pharmacologic Agents:

- Ketamine 0.1-0.3 mg/kg IV bolus +/- ketamine 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[49-52]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[54]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if other forms of wound infusion or epidural amide anesthetic are continued)[39-42]

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

Initiate opioid treatment with:

- Oxycodone IR 5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-15 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:

- Tramadol 50-100 mg PO every 4 hours
- Hydromorphone IR 2 mg PO every 4 hours as needed

For pain not controlled by oral opioids, if patient strict NPO or for severe breakthrough pain, consider:

- Hydromorphone 0.5 mg IV every 2 hours as needed

Discharge Recommendations	Consider for Discharge
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • For patients who benefited from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoids upon discharge.

every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • For opioid-naïve patients, prescribe between 0 and 10 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent).	○ It is suggested that the discharge dosing regimen match the inpatient dosing regimen. ○ It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.

Opioid-sparing Multimodal Analgesic Pathway for *Inguinal Herniorrhaphy*

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[82] • Gabapentin 300-600 mg PO once ***OR*** pregabalin 75-150 mg PO once (adjust dose for age, renal function)[19-20] • Tizanidine 4 mg PO twice daily[64+65]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique: • Laparoscopic repair is associated with less postoperative pain.[109] • There are no recommendations for one particular open mesh technique, prosthesis type, or mesh fixation technique over another due to limited available pain data.[123] Operative anesthesia: • Minimize or avoid induction opioids, and minimize intraoperative maintenance opioids. Pharmacologic agents: • Ketorolac 15 mg IV at closure, unless contraindicated or an NSAID was administered preoperatively[124]	Operative anesthetic technique: • Opioid-free/sparing total intravenous anesthesia (TIVA) with propofol, dexmedetomidine, lidocaine, and ketamine[28,125] • Local anesthetic infiltration at surgical sites[126-127] • Consider the use of bupivacaine products for incisional and/or regional analgesia.[35-36] -Liposomal formulations are lacking evidence in terms of cost vs benefit. Regional anesthesia, consider: • IL/IH block Inguinal nerve block[128] • TAP block[129] • "Double TAP": (IL/IH and TAP block)[130-131] • Paravertebral blocks[126,132-133] • Erector spinae plane block[88] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion[39-40,134] • Esmolol loading dose 0.5 mg/kg IV bolus over 1 min followed by 0.01-0.05 mg/kg/min IV infusion[43-44]

	• Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion OR 4 gm IV given over 30-60 minutes at the close of case[45-47]

Consider for Intraoperative Use

For open inguinal hernia repair or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:

- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion[47-52]
- Dexmedetomidine 0.8-1 mcg/kg IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[54-55,58,125]

Regional Anesthesia:

- Catheter placement for continuous wound infusions with amide anesthetic[64-66]

Postoperative Recommendations	Consider for Postoperative Use
• APAP 1 g PO every six to eight hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Nonpharmacological interventions	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • Tizanidine 4 mg PO twice daily[64-66]

For open herniorrhaphy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:

- Gabapentin 300-600 mg PO one to three times daily OR pregabalin 75-150 mg PO once or twice daily[60]
- Ketamine 0.1-0.3 mg/kg IV bolus +/- ketamine 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[49-52]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[54]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if other forms of wound infusion or epidural amide anesthetic are continued)[39-40,134]

Regional Analgesia:

- Continuous wound infusion with amide anesthetic

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

Initiate opioid treatment with:

- Oxycodone IR 5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-15 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:

- Tramadol 50-100 mg PO every 4 hours
- Hydromorphone IR 2 mg PO every 4 hours as needed

For pain not controlled by oral opioids, if patient strict NPO or for severe breakthrough pain, consider:

- Hydromorphone 0.5 mg IV every 2 hours as needed

Discharge Recommendations	Consider for Discharge

• APAP 1 g PO every six to eight hours until pain has resolved ***PLUS***
• NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
• COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved[1-3]
• For opioid-naïve patients, prescribe zero to 10 tablets of oxycodone 5 mg (or equivalent opioid monoproduct)
	• Lidocaine 5% patch once daily, applied adjacent to incision (up to three patches)
	• Tizanidine 4 mg PO twice daily for seven days[64-65]
	• For patients who benefited from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoid upon discharge.
	  ○ It is suggested that the discharge dosing regimen match the inpatient regimen.
	  ○ It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.

Opioid-Sparing Multimodal Analgesic Pathway for *Mastectomy With or Without Implant-Based or Flap Reconstruction*

Preoperative Recommendations	Consider for Preoperative Use
APAP 1000 mg PO COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[138] Gabapentin 300-600 mg PO once ***OR*** Pregabalin 75-150 mg PO once (adjust dose for age, renal function)[19-20,139] Venlafaxine 37.5 mg PO daily for 2 weeks, beginning the day prior to procedure for the prevention of chronic post-mastectomy pain (CPMP)[140] (caution with the concomitant use of methylene blue) EMLA cream 5 g on the sternal area 5 minutes before surgery, and 15 g on the supraclavicular area and axilla at the end of the operation and daily for 4 days for the prevention of CPMP[141]
It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.	
Intraoperative Recommendations	**Consider for Intraoperative Use**

Operative technique: Preserve axillary nerves whenever possible Operative anesthesia: Minimize or avoid induction opioids and minimize intraoperative maintenance opioids Regional anesthesia, consider: Paravertebral nerve block[142] Pectoral nerve block (Pecs)[143-144] Pecs I and II block after induction prior to incision Serratus plane blocks ESP block Consider adding dexamethasone or dexmedetomidine to PVB to enhance the quality and duration of peripheral nerve blocks Pharmacologic agents: Ketorolac 15 mg IV, unless contraindicated or an NSAID was administered preoperatively[145-147]	Operative anesthesia: Opioid-free/sparing TIVA (e.g., propofol, dexmedetomidine, lidocaine, and ketamine)[28, 148-149] Administer local anesthetic at incision sites before making the incision, and infiltrate into skin, subcutaneous tissue, and the chest wall (+/- axilla, drain site) prior to closure[150-151] For large incisions, surgeons must be mindful of limits on total quantity of local anesthetic injected and may opt to defer infiltration until after removal of the breast Bupivacaine products infiltrated prior to incision and prior to closure[35-36] Pharmacologic agents: Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion (stop if and when bupivacaine products are administered)[40,42,152-156] Esmolol loading dose of 0.5 mg/kg IV bolus over 1 minute followed by 0.01-0.05 mg/kg/min IV infusion[43-44] Magnesium sulfate 30-50 mg/kg followed by 6-20 mg/kg/hr IV infusion OR 4 gm IV given over 30-60 minutes at the close of case[45-48]
Consider for Intraoperative Use	
For patients undergoing flap-based reconstruction or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate: Pharmacologic Agents: Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion[49-52] Dexmedetomidine 0.8-1 mcg/kg IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[54] Regional Anesthesia: Catheter placement for continuous wound infusion of amide anesthetic Epidural placement for adjunctive analgesia	
Postoperative Recommendations	**Consider for Postoperative Use**
APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** Nonpharmacological interventions	NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) OR COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours may reduce incidence of CMPS (avoid if bupivacaine products used or wound infusion of amide anesthetic continued)[42,152-156] Lidocaine 5% patch once daily, applied adjacent to incision

	(up to 3 patches) Gabapentin 300 mg PO daily, titrated to 300 mg PO 3 times daily[157] Cyclobenzaprine 5-10 mg PO 3 times daily as needed ***OR*** methocarbamol 750 mg PO 4 times daily as needed for pain caused by muscle spasms

For patients undergoing flap-based reconstruction or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:
Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[49-52]
Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours
Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if bupivacaine products or other forms of wound infusion or epidural amide anesthetic are continued)[40,42,152-156]
Regional Anesthesia:
Continuous wound infusion with amide anesthetic
Continued epidural or paravertebral adjunctive analgesia

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

Initiate opioid treatment with:
Oxycodone IR 5-10 mg PO every 4 to 6 hours as needed ***OR***
Morphine IR 5-15 mg PO every 4 to 6 hours as needed
For pain not controlled with above opioid options, consider:
Tramadol 50-100 mg PO every 4 hours
Hydromorphone IR 2 mg PO every 4 hours as needed
For pain not controlled by oral opioids, if patient strict NPO or for severe breakthrough pain, consider:
Hydromorphone 0.5 mg IV every 2 hours as needed

Discharge Recommendations	Consider for Discharge
APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) For opioid-naïve patients, prescribe between 0 and 20 tablets of oxycodone 5 mg (or equivalent opioid monoproduct) for simple mastectomy +/- SLND or	Venlafaxine 37.5 mg PO daily for up to 10 days may reduce risk of chronic post-mastectomy pain[362] Topical diclofenac 1% gel, apply 2 g around surgical site 4 times daily

between 0 and 30 tablets for MRM or ALND	
It is recommended that assessment for post-mastectomy pain syndrome (PMPS) be a component of long-term follow-up of breast surgery patients and that management of PMPS be initiated upon diagnosis. It is suggested that surgeons consider early referral of patients with persisting pain to a pain specialist. Therapies may include: Lidocaine 5% transdermal patch, apply up to 3 patches around incision site daily Topical diclofenac 1% gel, apply 2 g around surgical site 4 times daily Gabapentin 300 mg PO once daily, titrated to 300 mg PO 3 times daily[157] Surgical excision of neuroma (for non-resectable neuromas, consider an infiltration of area with bupivacaine products)[35-37] Liposomal formulations lack evidence in terms of cost vs benefit. Treatment of PMPS with regional nerve blocks Intercostal nerve blockade[158] Stellate ganglion blockade Paravertebral blockade Thoracic plane blocks Superficial or deep serratus plane block[159-160] Physical therapy Acupuncture or other nonpharmacologic interventions	

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