### **OBSTETRIC ANESTHESIA (LR LEFFERT, SECTION EDITOR)**



# **Enhanced Recovery After Cesarean: Current and Emerging Trends**

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#### **Abstract**

Purpose of Review What are the latest enhanced recovery elements for cesarean delivery?

Recent Findings Enhanced recovery after cesarean delivery (ERAC) provides an evidenced-based system to improve maternal outcomes, functional recovery, maternal-infant bonding, and patient experience. Postsurgical recovery has evolved from a one-dimensional pain score to a holistic multidimensional approach emphasizing faster functional recovery. ERAC involves multidisciplinary efforts of the anesthesiologist, obstetrician, nursing, hospital, and patient. Components of ERAC include preoperative patient education, limited fasting, carbohydrate load, limiting opioids intra- and postoperatively, using scheduled non-opioid analgesics and supplementing with advanced therapies for women at higher risk for pain. ERAC protocols reduce opioid consumption, reduce length of stay, and improve maternal and neonatal outcomes.

**Summary** Implementing ERAC standardized care will likely be the most important change you can make in your practice to improve outcomes, improve quality care, help address racial disparities, and minimize opioid exposure and potential for addiction.

Keywords Cesarean delivery · Enhanced recovery · Racial disparity · Opioid use disorder · Maternal outcomes · Length of stay

# Introduction

Enhanced recovery after cesarean (ERAC) provides an evidenced-based system to improve maternal outcomes, functional recovery, maternal-infant bonding, and patient experience. ERAC involves the multidisciplinary team efforts of the anesthesiologist, obstetrician, nursing, hospital, and patient. Cesarean delivery (CD) is the most common surgery in the USA, with a 32% cesarean rate that involves 1.2 million women yearly [1] similar to the rate in many developed countries. The global burden of obstetrical surgical recovery includes approximately 140,000,000 births annually [2] with an estimated 23% global cesarean rate [3]. Hospital length of stay (LOS) for CD has large variations at the provider and facility level [4]. Chronic postsurgical pain for CD affects up to 11% of women 1 year later with nearly 10% having severe pain [3, 5, 6]. ERAC aims to standardize the perioperative care of the

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Department of Anesthesiology, Cedars-Sinai Medical Center, 8700 Beverly Blvd #8211, Los Angeles, CA 90048, USA peripartum patient and helps improve maternal and neonatal outcomes [7, 8, 9••]. Current and emerging ERAC and pain relief strategies will be discussed in this article.

Chronic pain, which often starts as acute pain, has become a major public health problem affecting 20.4% adults in 2019 [10]. Women have more chronic pain (21.7% vs. 19%, P <0.05) and more high-impact chronic pain (8.5% vs. 6.3%, P <.05) than men, even affecting 9-15% of 18-44 year olds [10]. Previous studies have shown an association between higher pain scores after delivery with a higher incidence of postpartum depression and development of chronic pain [3, 6, 11..., 12•]. Higher pain postdelivery has been associated with lower rates of breastfeeding as well as a higher incidence of postpartum depression and chronic pain [13]. Every 10% increase in severe pain postoperatively was associated with a 30% increase in chronic pain 1 year later [14]. Higher analgesic consumption in the first 48 h also has been linked to development of chronic pain [15]. Healthcare disparities in pain and the treatment of pain exist as well [16].

Postsurgical recovery has evolved from focusing on a onedimensional goal of a visual analog scale (VAS) pain score ≤3/10 to a more holistic multidimensional approach. The fundamental goal of experiencing less pain not only reduces an individual's suffering but also improves functional recovery with faster return to the activities of daily living, including



maternal-infant bonding, returning home, and higher satisfaction. ERAC uses an interdisciplinary approach requiring the enrollment of the patient (and her support system), anesthesiology, obstetrics, pediatrics, nursing, lactation specialists, and the hospital. Pregnant women and their partners must be educated prior to coming into the hospital to align expectations of what to do (e.g., clear liquids/carbohydrate load 2 h prior to surgery) and for postoperative physical activity. The intraoperative anesthetic and postoperative pain medications are the easiest ERAC components to change for the anesthesiologist. The postoperative course requires more nursing involvement on the first 1–2 days to help mobilize the mother.

Implementing ERAC standardized care will likely be the most important change you can do in your practice to improve maternal outcomes, improve quality care, help address racial disparities, and minimize opioid exposure and addiction.

### **Preoperative Elements**

Key ERAC preoperative elements include patient education, limiting fasting intervals, and carbohydrate loading.

#### **Patient Education**

Preoperative education prior to the day of surgery is important to engage the patient, manage expectations, reduce anxiety, and help improve patient compliance with ERAC protocols. Many handouts and tools exist, including examples available in the Society for Obstetric Anesthesia and Perinatology (SOAP) ERAC toolkit (www.soap.org). A 2015 UK study found a simple patient information leaflet led to wider patient acceptance of early discharge and a higher rate of earlier discharges even before implementation of other ERAC components [17••]. Patient engagement and shared-decision making may start preoperatively and improve satisfaction and reduce opioid prescriptions [18].

### Limiting NPO Interval and Carbohydrate Loading

The American Society of Anesthesiologists (ASA) guidelines recommend surgical fasting (NPO) for fatty solids 8 h prior, a light meal 6 h prior, and clear liquids 2 h prior to surgery to reduce aspiration risk [19]. Prolonged NPO intervals are usually unnecessary and can lead to hypovolemia and patient dissatisfaction [19]. Data derived from enhanced recovery for colorectal surgery showed that complex carbohydrate (i.e., maltodextrin) loading the evening before and 2-3 h prior to anesthesia with a non-particulate drink can minimize the metabolic stress response, improve postoperative insulin resistance, and lower protein breakdown [20]. This may be omitted for diabetic mothers due to potential for delayed gastric emptying and hyperglycemia. The SOAP ERAC protocol

suggests 16 ounces (~500 mL) of clear apple juice 2 h prior to scheduled cesareans as an easy, acceptable choice [21].

### **Intraoperative Elements**

Multimodal analgesia has become a key component for most surgeries/anesthetics and all enhanced recovery protocols involving medications and techniques beyond routine surgical anesthesia. Analgesic medications may be administered immediately preop, intraop, and continued postoperative. Nonopioid analgesics and techniques are utilized to minimize opioid consumption. However, ERAC goes beyond analgesics (see Table 1).

The intraoperative components of ERAC include start of scheduled acetaminophen (may start preoperatively), NSAIDs, limiting the amount of neuraxial opioid (i.e., morphine), prevention of hypothermia and nausea, and supporting mother-infant bonding, among others [9...]. The routine use of prophylactic vasopressor infusions (e.g., phenylephrine 0.5–1 mcg/kg/min) helps to reduce hypotension induced nausea following spinal anesthesia. Two different classes of prophylactic antiemetics should be used (e.g., 5HT3 antagonist ondansetron, glucocorticoid dexamethasone, and/or D2 receptor antagonist metoclopramide). The suggested doses of neuraxial morphine for cesarean are 1-3 mg epidural or 50-150 mcg intrathecal (IT) to limit opioid side effects. Scheduled acetaminophen 1000 mg (TID or QID) starting preop or intraop and NSAIDs (e.g., ketorolac 30 mg IV after peritoneal closure, followed by either ketorolac (15-30 mg) Q6h, ibuprofen 600 mg Q6h, or naproxen 500 mg Q12h (see Table 2). Prewarming patients before surgery helps to reduce intraoperative hypothermia; intraoperative warming measures are required, including keeping the OR >72 °F/23 °C [9••]. The maximum acetaminophen dose is 4000 mg/24 h, as per FDA approval [22].

### Multimodal Analgesia

Multimodal analgesia may involve regional blocks or wound infusion of local anesthetics and multiple non-opioid analgesics to modify or decrease neuronal transmission of pain, alter physiologic responses to painful stimuli, and reduce opioid consumption, decreasing the potential for postoperative opioid tolerance and development of persistent opioid use.

### Gabapentinoids

Gabapentinoids (i.e., gabapentin and pregabalin) bind to and block the  $\alpha_2\delta$  subunit containing voltage-depending calcium channel and may be effective in reducing postoperative pain. One meta-analysis of non-cesarean patients found gabapentin doses of 900 mg and 1200 mg or pregabalin 150 mg and 300 mg decreased postop opioid use and pain scores [23]. Gabapentin before and for 2 days post-CD decreased pain



**Table 1** Key components of enhanced recovery after cesarean

Preoperative	Intraoperative	Postoperative
Patient education     Limited fasting interval     Carbohydrate loading	<ul> <li>Prevent and treat spinal iduced hypotension</li> <li>Maintain normothermia</li> <li>Intra- and postop nausea and vomiting prophylaxis</li> <li>Optimal uterotonic administration</li> <li>Multimodal analgesia</li> <li>Promote breastfeeding and maternal-infant bonding</li> </ul>	Early oral intake     Early mobilization     Promote resting periods     Early urinary catheter removal     Venous thromboembolism prophylaxis     Continue multimodal analgesia     Breastfeeding support     Promote return of bowel function

Key components of an enhanced recovery after cesarean protocol, modified from Society for Obstetric Anesthesia and Perinatology Consensus, Anesthesia Analgesia 2020, with permission

slightly (4.0 vs 4.7 VAS, P < .05) on movement at 24 h, however with no difference in opiate use or persistent pain scores [24]. A recent meta-analysis found that gabapentinoids were associated with lower postoperative pain intensity, but the difference was not clinically significant ( $\leq 1$  VAS) and associated with more frequent side effects of dizziness and visual disturbances [25•]. Gabapentinoids, while not currently recommended for routine ERAC, may benefit high-risk parturients such as those with chronic pain, opioid use disorders.

# **Regional Blocks for Cesarean Surgery**

Regional blocks useful for cesarean surgery include truncal blocks (TAP, QL) or wound infusion. Overall, these have not been shown to have significant improvement when used in addition to the triad of neuraxial morphine and scheduled acetaminophen and NSAID [9••]. Regional blocks are useful when neuraxial morphine cannot be given, as a rescue

technique for severe pain, or for patients at high risk for severe pain [26••].

#### Transversus Abdominus Plane Block

TAP blocks have been studied for CD but do not provide a routine benefit in addition to neuraxial opioids, except following general anesthesia or when neuraxial opioids need to be omitted [9••]. Posterior or lateral TAP block for cesarean did not confer additional benefits; results are similar to wound infiltration and inferior when compared with IT morphine [27]. Surgical infiltration of the abdominus plane may provide similar results [27].

### **Quadratus Lumborum Blocks**

Many studies have examined the effectiveness of quadratus lumborum (QL) blocks in decreasing post abdominal surgery

**Table 2** Key medication examples enhanced recovery after cesarean

Preoperative	Intraoperative	Postoperative
Carbohydrate load 2 h preop:	Neuraxial morphine:	Multimodal analgesia:
• Clear apple juice 500 ml	• ≤3 mg epidural or	<ul> <li>Acetaminophen 1 g PO Q6h</li> </ul>
Multimodal analgesia:	• ≤150 mcg IT	NSAID, choice of:
• Acetaminophen 1g PO	Nausea Prophylaxis ≥2 agents:	<ul> <li>Ketorolac 30 mg IV Q6h or</li> </ul>
	• 4 mg ondansetron,	• Ibuprofen 600 mg POQ6h or
	• 10 mg metoclopramide,	• Naproxen 500 mg PO Q12h
	• 4 mg dexamethasone	Opioid as PRN only:
	Prevent hypotension:	<ul> <li>Oxycodone 5 mg PO PRN</li> </ul>
	<ul> <li>Phenylephrine infusion 0.5 mcg/kg/min initial, titrate</li> </ul>	
	Multimodal analgesia:	
	Ketorolac 30-mg IV after peritoneal closure	

Key medication examples for enhanced recovery after cesarean of low-risk patients, by phase of care. May give first dose of acetaminophen intraoperative or in PACU if did not receive prior to surgery

PO Per os, IT intrathecal, IV intravenous, PRN as needed, Q every



pain. The anterior QL (QL1) block acts like a TAP block while a posterior QL (QL2) block may spread local anesthetic more medially towards the paravertrebral spaces and inhibit visceral pain in addition to somatic pain [28]. QL block decreased intraoperative and postoperative opioid consumption in patients compared with TAP blocks for abdominal hysterectomies under general anesthesia [29]. In the absence of IT morphine, cesarean patients randomized to QL2 blocks had less postoperative morphine use than the TAP block group [30], and lower morphine usage and VAS pain scores [28]. However, adding QL blocks to patients receiving neuraxial morphine did not significantly change pain scores or reduce opioid consumption. QL2 block did not improve pain scores above IT morphine and scheduled non-opioid analgesics for CD [31•].

### **Local Anesthetic Wound Infusions**

Continuous wound infusions have been used to help control postoperative pain in cesarean delivery and were superior to epidural morphine 2 mg every 12 h with scheduled acetaminophen and diclofenac only as a rescue [32]. In cesarean patients receiving 150 mcg morphine IT with scheduled acetaminophen and systemic ketorolac/ibuprofen, the addition of a continuous wound infusion of ropivacaine 0.2% with ketorolac 30 mg/48 h had no statistically significant difference in pain scores up to 48 h, patient satisfaction, opioid use, or postpartum depression [33]. The difference in the benefit of continuous wound infusion between these two studies is most likely due to the absence of scheduled systemic NSAID in the first study. Most studies have not found a benefit of peripheral local anesthetic nerve blocks in addition to the triad of neuraxial morphine and scheduled non-opioid analgesics of both acetaminophen and NSAID [9., 34].

### Liposomal Bupivacaine

Liposomal formulations provide slow release and thus prolonged effect of a local anesthetic. However, results with liposomal bupivacaine in cesarean delivery have been mixed. A retrospective study found incisional liposomal bupivacaine reduced MMEQ [35]. A prospective study of liposomal bupivacaine in the CD incision did not find significantly reduced pain scores or MMEQ in the first 48 h [34]. A recent study funded by the manufacturer showed liposomal bupivacaine 266 mg plus bupivacaine 50 mg in TAP block reduced 72-h opioid consumption of -16.5 mg, P = 0.012, and had more opioid-spared patients (54% vs 25%, P = 0.001) compared with bupivacaine 50 mg alone [36]. However, 6% of TAP blocks were incorrectly placed on review, and when all treated patients were included in analysis, there was no significant difference in opioid consumption between groups. The additional of intrathecal morphine to liposomal bupivacaine TAP block significantly reduced MMEQ in the first 24 h after CD, but there were no differences in opioid use in the 24–72-h time period, suggesting a lack of prolonged benefit [37]. A recent meta-analysis found perineural liposomal bupivacaine did not provide a clinically important benefit using area under the curve pain scores 24–72 h after injection or in any of the secondary outcomes of pain at rest, time to first analgesic request, or opioid consumption up to 72 h [38]. Regarding the efficacy of liposomal bupivacaine, another recent article and editorial noted a high risk of study bias in 84% of articles showing significant benefits of liposomal bupivacaine and primary study outcomes, compared with only 14% of articles with a low risk of study bias [39, 40•].

### **NMDA Antagonists**

NMDA receptor antagonists are potential analgesics that prevent central sensitization and development of chronic pain [41]. Note that the prevention of neuropathic pain and treatment of acute pain may involve different mechanisms. Opioids may produce hyperalgesia in a dose and time exposure–dependent fashion via NMDA receptor stimulation [14].

#### Ketamine

Ketamine, an NMDA receptor antagonist, has analgesia effect and has been used for prevention of acute and chronic pain, hyperalgesia, and central sensitization and may prevent acute opioid tolerance [12•, 42]. S-Ketamine (dose of 0.5 mg/kg IM followed by 2 mcg/kg/min IV infusion for 12 h) significantly decreased morphine consumption after CD starting at 8 h and by 31% over 24 h, increased time to first morphine use, and trended to reduced hyperalgesia at T10 [43].

### Magnesium

Perioperative magnesium, which also has NMDA antagonist effects, reduced pain scores at 24 h in a meta-analysis of non-obstetric patients and may reduce analgesic consumption in obstetric patients [44]. Magnesium 50-mg/kg decreased pain scores and medication use after general anesthesia for cesare-an [45, 46]. However, a 2006 study with magnesium 50 mg/kg load with 2 g/h, 25 mg/kg load with 1 g/h, or placebo started 1 h prior to cesarean under neuraxial anesthesia did not find a difference in pain severity [47]. A 2017 systematic review found magnesium decreased analgesic requirements and lowered VAS scores after CD [48].

### Dextromethorphan

Dextromethorphan, a non-competitive NMDA antagonist, may decrease both sites of injury pain (primary site) and



outside the injury (secondary site) hyperalgesia that can develop from surgery or trauma [41]. Low dose (30 mg) dextromethorphan provided significant anti-hyperalgesic effects in humans for primary and secondary hyperalgesia and decreases peripheral and central neuronal sensitization in a freeze-injury pain model [49]. A meta-analysis of 21 studies of primarily general, gynecology, and orthopedic surgeries showed perioperative dextromethorphan significantly decreased opioid consumption by 10-mg morphine equivalents and pain scores by almost 1 (10-point pain scale) through 24 h [50]. However, dextromethorphan has not been studied specifically for cesarean; usage in high-risk women may be considered.

### **Alpha-2 Adrenergic Agonists**

The alpha2-adrenergic agonists clonidine and dexmedetomidine have analgesic properties, but the limited evidence for cesareans did not warrant their inclusion in ERAC protocols. However, they may be useful in high-risk patients for pain or tolerance to opioids. Clonidine 1.2 mcg/ml/bupivacaine 0.1% infused epidural postcesarean for 24 h provided good analgesia with no need for supplemental opioids for 70% of parturients with opioid use disorder on buprenorphine [44, 51]. Dexmedetomidine 4 mg IT significantly decreased VAS scores during and immediately after  $(2.1 \pm 1 \text{ vs } 3.6 \pm 1, P < 0.001)$  cesarean surgery [52]. Dexmedetomidine as IV infusion of 0.2–1.4 mcg/kg/h after a load of 1 mcg/kg may also be helpful [26••].

# **Postoperative Elements**

Key postoperative elements of ERAC include early oral intake, early urinary catheter removal (6–12 h) and early mobilization out of bed and attempted ambulation within the first 24 h.

## **Early Oral Intake**

Early oral intake hastens return of bowel function, improves maternal satisfaction, and quickens time to ambulation and discharge without increasing complications such as nausea, vomiting, or infection. Parturients undergoing general anesthesia for cesarean delivery had faster return of bowel function and improved patient satisfaction with early oral feeding in a RCT [53]. Another RCT with general and neuraxial anesthesia patients found faster time to ambulation and earlier discharge in the early feeding cohort following cesarean [54]. Lastly, a Cochrane review found that gum chewing in PACU expedited return of bowel function and decreased length of stay, albeit with low grade evidence [55]. These studies also found no difference in postoperative complications, nausea, and bloating in the early feeding groups.



### **Postop Opioid Use**

ERAC implementations lowered opioid usage with no significant change in postop complication rates, pain scores, or readmission rates. Reduction of opioid consumption can be especially important during the current opioid crisis. ERAC implementation led to a 40% lower morphine equivalent usage (60 mg vs 104 mg), fewer patients requiring opioids within 24 h of discharge (41.1% vs 74.6%, P < 0.001), and no difference in pain scores during inpatient hospitalization [56]. ERAC reduced oxycodone consumption an average of 36 mg/patient after cesarean delivery with no difference in pain scores throughout hospital admission [57]. Similarly, ERAC protocols significantly reduced opioid consumption 38% with lower pain scores (7 vs 8 , P = 0.007) and shorter (2.5 ± 0.5 vs 2.9 ± 1.2 days, P < 0.001) length of stay [58•].

### Length of Stay/Cost Savings

ERAC protocols reduce LOS and cost savings without increasing adverse events such as 30-day readmission rates. Hospitals have a large variation in LOS, with a median discharge of 47% of CD patients within 2 days, with the earlier discharge group being slightly younger, history of prior CD, non-teaching hospital, and having fewer comorbidities [4]. While insurers are required to cover 4-day hospitalization for cesarean, early discharge is allowed if the patient and attending provider agree [59]. An RCT in New York City showed a significantly shorter LOS for women in the ERAC cohort, with the added benefits of increased breastfeeding rates, higher patient satisfaction [60]. In the UK, introduction of ERAC components over a 2-year period time significantly increased POD 1 discharge from 1.6 to 25% and reduced costs [17••].

### **Racial Disparities**

Racial and ethnic healthcare disparities exist in the USA not only for severe maternal morbidity and cesarean delivery rate [61] but also for the recognition and treatment of pain [16]. Severe pain ≥7 VAS was more common in black and Hispanic women, and they were undertreated, receiving significantly fewer oxycodone tablets postpartum days 1 and 2 [62]. Black women have a longer LOS and higher CD rate [63]. Enhanced recovery implementation eliminated racial disparities in LOS with no differences in readmissions or mortality and improved outcomes of pneumonia and ileus following colorectal surgery [64•]. Implicit bias in healthcare professionals may contribute to differences in healthcare outcomes [65•]. Use of ERAS for



cesarean delivery should reduce racial disparities by using standardized universal protocols [66].

#### COVID-19

The Coronavirus (COVID-19) pandemic impacted ERAC as well. NSAIDs are safe to use in COVID-19 patients [67]. COVID-19 may cause hypercoagulability, and VTE prophylaxis may need to be continued for 2–6 weeks [68]. The pandemic has accelerated patients' desire to leave the hospital earlier; our post-ERAC, and post-COVID-19 2-night LOS increased from 12 to 41%, with no harm to mother or baby [69]. Patient expectations and desire to be discharged earlier have significantly decreased LOS during the pandemic.

### **High-Risk Patients**

**Substance Use Disorder** The parturient with a history of substance use disorder may be more difficult to manage pain, especially after surgery. The standard ERAC template serves as an excellent starting point for overall care. In addition to the standard triad of neuraxial morphine, acetaminophen, and NSAID, further pharmacologic approaches may be helpful. Possibilities include postdelivery infusion of epidural local anesthetics/narcotics, alpha-2 adrenergic agonists, NMDA agonists, TAP/QL blocks, or use of gabapentinoids.

Perhaps one of the most important aspects of ERAC is reducing total opioid exposure and the potential for maternal opioid addiction. The risk of opioid naïve parturients becoming chronic opioid use disorder following cesarean was 1/300 [70], representing public health issues affecting an estimated 4000 new mothers per year. Implementation of ERAC reduced morphine mg equivalents (MMEQ) by 40%, from 46 to 28 mg, P < 0.001, in addition to a decrease in peak pain scores by 1 VAS (from 8 to 7), P < 0.01 [58•]. Lower inhospital opioids requirements led to a 35% reduction in opioid discharge prescribing [71]. States have enacted laws to limit opioid prescriptions, decreasing postcesarean discharge opioid prescription by 20 MMEQ [72]. Use of opioids for greater then 5 days increases chances for still using opioids 1 year later [73]. Thus, implementation of ERAC reduces in hospital opioid exposure and discharge opioids and should reduce the incidence of chronic opioid use following cesareans.

**Opioid Use Disorder** Patients with opioid use disorder should be continued on their normal medications (e.g., methadone, buprenorphine) plus extra modalities as discussed above [74]. Suggestions include stepwise multimodal analgesia with options of oral gabapentin 300–600 mg PO Q8h, ketamine 0.5 mg/kg bolus, 2 mcg/kg/min infusion, and/or dexmedetomidine infusion 0.2–1.5 mcg/kg/h after load 1 mcg/kg/10–20 min [26••, 51].

### Conclusion

Enhanced recovery after cesarean provides evidenced-based standardized care for the perioperative period, with benefits for maternal pain relief, mobilization, improved maternal-infant bonding, decreased opioid and rescue medication consumption, and shorter length of stay. With patient engagement started preoperatively, ERAC goals can be achieved, and with greater potential for improvements in chronic opioid use after cesarean, adjustments for higher risk patients, and improvement in racial healthcare disparities. Perhaps the next evolution of ERAC will involve pharmacogenetic testing and certainly "personalized" analgesic management [75].

# **Compliance with Ethical Standards**

Conflict of Interest The authors declare that they have no conflict of interest.

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