Enhanced recovery after cesarean delivery: a challenge for anesthesiologists

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Abstract
Enhanced recovery after cesarean (ERAC) delivery is an evidence-based, multi-disciplinary approach throughout pre-, intra-, post-operative period. The ultimate goal of ERAC is to enhance recovery and improve the maternal and neonatal outcomes. This review highlights the role of anesthesiologist in ERAC protocols. This review provided a general introduction of ERAC including the purposes and the essential elements of ERAC protocols. The tool used for evaluating the quality of ERAC (ObsQoR-11) was discussed. The role of anesthesiologist in ERAC should cover the areas including management of peri-operative hypotension, prevention and treatment of intra- and post-operative nausea and vomiting, prevention of hypothermia and multi-modal peri-operative pain management, and active pre-operative management of unplanned conversion of labor analgesia to cesarean delivery anesthesia. Although some concerns still remain, ERAC implementation should not be delayed. Regular assessment and process improvement should be imbedded into the protocol. Further high-quality studies are warranted to demonstrate the effectiveness and efficacy of the ERAC protocol.

Keywords: Cesarean delivery; Cesarean section; Enhanced recovery after surgery

Introduction
Enhanced recovery after surgery (ERAS) was firstly introduced by Kehlet in 1997 to reduce the length of hospital stay in open sigmoid resections.[1] In China, the first ERAS Congress was established in 2015 and since then a series of Chinese Experts Consensus has been published regarding this topic.[2] Today, ERAS has infiltrated a broad range of surgical specialties and these years various guidelines have been published and updated by experts from all over the world. Although ERAS protocols have been successfully implemented across many subjects and institutions, the uptake of ERAS in obstetrics is lagged behind. Not until 2018, ERAS society released guidelines for cesarean delivery (CD)[3] and to date relevant data are limited in the literature.

Purposes of Enhanced Recovery After Cesarean Delivery

CD is the most common major abdominal surgery in the world and women, however, face dual challenges after CD of being post-partum and post-operative.[4] The enhanced recovery after cesarean (ERAC) delivery protocols may effectively address these advantages for women after CD.

Accelerating recovery and decreasing the length of hospital stay

The global CD rate reached an unprecedented high of 21% in 2015[5] and did not seem to decrease these years.[6] In the United States, the CD rate increased to 32% in 2017[7] with over 1.27 million procedures performed annually. In China, even higher rate of 36.7% was observed in 2018. Although great efforts have been made to decrease the CD rate, the improved peri-operative care of obstetric patients is also crucial.[8] As the majority of obstetric patients are young and healthy, they are potential for rapid recovery and motivated to return to normal state of functioning to care for the baby. On the contrary, enhanced recovery may benefit healthcare system by reducing waste of scarce medical resources and reduce the overall cost of healthcare.[9] Evidence has shown that ERAC protocols can help reducing the length of hospital stay (LOS) by 7.8% or...
4.86 h overall ($P < 0.001$) and decrease the total post-operative cost by 8.4% or $642.85 per patient overall ($P < 0.001$).\[10\]

**Improving maternal outcomes and satisfaction**

Unlike other surgical specialties, CD may have some unique characteristics. One is unexpectable, so it is difficult to make a plan. Unplanned CD is associated with negative emotion and affected mother-infant bonding, and makes mother feel sadness, disappointment, and even depressed.\[11\] Even when CD is planned, women also face the unique dual challenges: recovering from major abdominal surgery and taking care of the baby. Efforts to enhance post-operative recovery may help to improve bonding and breastfeeding, as well as reduce the incidence of post-partum depression.\[11-13\]

**Reducing maternal morbidity and mortality**

CD is associated with the increasing risk of maternal and neonatal morbidity and mortality.\[14\] Nearly one-half of the maternal deaths occur in the post-partum period and are related to intra-operative complications.\[6\] Hypertensive disorders, cardiovascular diseases, hemorrhage, and infection are the leading causes of maternal death.\[15\] However, more than 60% of pregnancy-related deaths might be preventable.\[16\] So the ERAS society recommended the “optimized” pathway specifically for woman who has the priori modifiable risks to optimize the management of these maternal comorbidities (ERAS CD Expanded Program),\[17\] including hypertension, diabetes, anemia, smoking, etc.\[3\] These complex women may need a team-based peri-operative care to reduce the operative risks and enhance their outcomes.\[17\]

**Limiting opioid use and prescribing post-operatively**

Opioids are frequently used and prescribed after CD, but they should be used at lowest effective dose for shortest duration to minimize the potential risks to the mother as well as the breastfed baby.\[18,19\] American College of Obstetricians and Gynecologists committee recently released recommendations for post-partum pain management. A stepwise, multi-modal and non-opioid analgesia approach was recommended as the first-line therapy after CD.\[20\] Similarly, ERAS society also recommended an opioid-sparing, multi-modal post-operative protocol with the combination of pre-operative education and share-decision making intervention to limit opioid use in obstetrics.\[17,21\] For anesthesiologists, we should make efforts to optimize the pain management ensuring patients get effective pain control while limiting opioid use to avoid the potential risks of excessive opioid exposure including opioid withdrawal syndrome and the opioid crisis.\[22\]

**Developing an optimized ERAC protocol**

With the increasingly robust literature regarding ERAS in general, many organizations began to address ERAS for CD. Similar to other ERAS protocols, ERAC is also an interdisciplinary approach including anesthesiology, obstetricians, nurses, neonatologists, pediatrics, pharmacists, hospital administration, and the supporting systems. The principles of ERAC cover the whole phase of CD, but there is wide variability in elements of published ERAC protocols [Table 1]. Society guidelines for CD have two specific pathways.\[17\] The “focused” (normal) pathway for both scheduled and unscheduled CD, starting at 30 to 60 min before incision to hospital discharge, summarizes the evidence-based pre-, intra-, post-operative care elements and recommendations\[17\] [Table 1]. While the “optimized” (complex) pathway, as mentioned before, discussed broad antenatal topics of patient education and counseling for those complex and comorbid women, and the immediate neonatal care at delivery.\[3,17,21\] More recently, Society of Obstetric and Perinatology (SOAP) released ERAC Consensus Statement developed for scheduled CD, but some of the elements can also be applied to unscheduled CD [Table 1]. The committee identifies a few essential elements which are indispensable in ERAC (emphasized by asterisks *) and provides a series of patient education materials to help with the successful implementation of the protocol.\[23\] These excellent resources provide details to develop the ERAC pathway in your institution which describes many dimensions of enhanced recovery goals.

**Evaluation of the Quality of Recovery After CD (ObsQoR-11)**

Quality of recovery (QoR) score QoR-40\[24\] and QoR-13\[25\] have been extensively used and validated as tools to measure the recovery outcomes after non-obstetric surgeries. However, both of them are not maternal-focused and do not cover some aspects related to CD. For example, most CDs are performed under neuraxial anesthesia. The recovery aspects of neuraxial anesthesia are a bit different from that of general anesthesia. Besides some physiological variables, we should take the physical, emotive, cognitive, and functional outcomes into account. For maternal population, the ability to care for the baby is the key element of recovery after CD. Recently, Ciechanowicz et al.\[26\] developed the first obstetric-specific, 11-item QoR score which derived from QoR-40. ObsQoR-11 can evaluate the quality of recovery by measuring several key elements, including physical comfort (nausea and vomiting, dizziness, shivering), pain relief, physical independence (mobilizing, personal hygiene), and emotional state (in control, comfortable), with some items related to neuraxial anesthesia and the ability to care for the baby (breastfeeding, holding the baby). The ObsQoR-11 is a reliable, valid, and responsive tool for assessment in obstetrics. However, the QoR-11 is not generalizable and developed only for the scheduled population. Further work is warranted to investigate its validation in unscheduled population.

**Role of Anesthesiologist in ERAC**

When we develop our ERAC protocols, we need to think about the interventions according to the elements in ObsQoR-11 tool. For anesthesiologists, we may focus on these specific components which can be tackled by us and ultimately improve the quality of ERAC.
Management of peri-operative hypotension

In the 2016 American Society of Anesthesiologists Practice Guidelines for Obstetric Anesthesia, neuraxial techniques including epidural, spinal, and combined spinal-epidural are recommended for most CD. However, these techniques are associated with some maternal and neonatal/fetal side effects. Maternal hypotension, primarily caused by vasodilation, is commonly seen during CD. The severity of hypotension depends on the speed of onset of neuraxial anesthesia and the dose of neuraxial medication. Maternal hypotension leads to a series of symptoms including intra-operative nausea and vomiting (IONV), dyspnea and dizziness frequently after severe hypotension. Severe hypotension may decrease the uteroplacental flow and increase the incidence of fetal acidosis which may be detrimental to the fetus. Fluid therapy and vasopressors are considered the gold standard for treatment and prevention of maternal hypotension. Both colloid preloading and crystalloid coloading can be used to prevent maternal hypotension to some extent. But unfortunately, it is still unclear what is the most optimal fluid therapy and whether crystalloid or colloid or both to be effective enough to prevent hypotension. Both too little and too excessive fluid during CD can have adverse effects. There are mounting evidence supporting that fluid therapy guided by flow base hemodynamic monitors (eg, CO monitors, echo for assessing volume status, SV estimation) can improve peri-operative outcomes. But the implementation in obstetric population is sparse. Vasopressors, however, can effectively prevent and treat hypotension and are recommended to be used routinely and preferably prophylactically. Pure α-agonist drug (phenylephrine) is the first-line vasopressor as it can directly counteract vasodilation. Although those with a mild β-agonist drug (norepinephrine, metaraminol) may be more beneficial for hemodynamics, more evidence-based data are need to support its value in obstetrics. The effective norepinephrine bolus dose to prevent hypotension in 90% of women undergoing elective CD (ED90) is 6 µg. Recently, Ngan Kee found the estimated dose equivalent to phenylephrine 100 µg was norepinephrine 8 µg when given as a bolus to treat the first episode of hypotension. Moreover, changing position of parturient after spinal anesthesia by tilting the operating table or using a wedge may improve the maternal hemodynamics, but more evidence is needed to confirm these findings. By combining use of vasopressor, fluid therapy, and tilt-position, the ultimate target aim is to maintain the systolic arterial pressure above 90% of baseline.

Table 1: Peri-operative elements recommended by ERAS Society and SOAP.

| ERAS society recommendations | SOAP consensus statement |
|-----------------------------|--------------------------|
| Preoperative elements       |                          |
| Anesthetic medications      | Limit fasting interval    |
| Fasting                     | Non-particulate liquid carbohydrate loading |
| Carbohydrate supplementations| Patient education         |
| Anti-microbial prophylaxis   | Lactation/breastfeeding preparation and support |
| Skin wash/vaginal preparation| Hemoglobin optimization   |
| Prevention of intra-operative hypothermia |                          |
| Intra-operative elements    |                          |
| Pre- and intra-operative management | Intravenous fluid optimization |
| Abdominal/vaginal anti-microbial cleaning | Prevent and treat spinal anesthesia induced hypotension |
| CD surgical techniques      | Maintain normothermia     |
| Peri-operative fluid management | Optimal uterotonic administration |
| Neonatal immediate care/ delayed cord clamping | Initiate multi-modal analgesia |
| Post-operative elements     |                          |
| ERAS sham feeding/chewing gum | Early oral intake         |
| Nausea and vomiting management | Glycemic control         |
| Analgesia                   | Early mobilization        |
| Peri-operative nutritional care/early feeding | Promotion of resting periods |
| Glucose control             | Promotion of return of bowel function |
| Thromboembolism prevention  | Early urinary catheter removal |
| Early mobilization          | Venous thromboembolism prophylaxis |
| Urinary drainage management | Multi-modal analgesia     |
|                           | Facilitate early discharge |
|                           | Anemia remediation        |
|                           | Breastfeeding             |

*Essential elements. ERAS: Enhanced Recovery After Surgery; SOAP: Society of Obstetric and Perinatology.*
Prevention and treatment of intra- and post-operative nausea and vomiting

Nausea and vomiting are frequent during CD than other non-obstetric surgery. There are many underlying causes. Spinal anesthesia induced acute sympathetic blockade may hyperactivate the gastro-intestinal tract. Acute hypotension causes cerebral ischemia and activates the vomiting center. Peri-operative use of opioids and some surgical procedures (uterine exteriorization, intra-abdominal saline irrigation) are also contributing factors. IONV/post-operative nausea and vomiting (PONV) is a major stressor for women and their family. IONV may offer significant challenge to the operating surgeon and also a potential risk of aspiration. Several interventions are commonly used for IONV/PONV.

**Preventive measures:**

- Preventive vasopressor infusion combined with fluid loading may decrease the incidence of hypotension-associated IONV and maintain uterotential perfusion. Combination of at least two IV anti-emetics with different mechanism of action, for example, 5-HT3 antagonists, glucocorticoid, and D2 receptors antagonists, is suggested. A meta-analysis showed that 4 to 5 mg dose regimen of systemic dexamethasone can effectively prevent PONV not IONV due to delayed onset of action. While metoclopramide (10 mg) alone decreased IONV not PONV because of the low efficacy. Generally, combinations of treatments are better than single agents for IONV as well as early PONV.

**Prevention of hypothermia**

Peri-operative hypothermia (core temperature <36°C) can occur rapidly after spinal anesthesia during CD and the thermoregulation will be altered for several hours. In general population, peri-operative hypothermia is associated with poor outcomes including infection, myocardial ischemia, coagulopathy, shivering, reduced drug metabolism, prolonged LOS, and poor patient satisfaction. However, the outcomes in obstetric patients have rarely been investigated as core temperature is difficult to be monitored during CD. But neonatal hypothermia may lead to respiratory distress syndrome, hypoglycemia, and neonatal mortality (especially in preterm and very low birth weight). ERAS society recommended that “Appropriate patient temperature is needed to apply warming devices and avoid hypothermia (recommendation grade: strong).” Active warming (IV fluid combined with force-air warming) can effectively reduce peri-operative hypothermia and shivering, improve maternal thermal comfort, facilitate bonding, and faster PACU times. A modest increase of OR temperature (>72°F/22°C) may reduce the rate of maternal and neonatal hypothermia.

**Multi-modal peri-operative pain management**

Peri-operative pain control is the key component of ERAS protocol, as high pain will make it difficult for mother to care for the baby, delay early mobilization, and even induce anxiety and depression. Multi-modal peri-operative pain management including various techniques and medications should be used to reduce pain, enhance recovery and reduce opioid use. Long-acting neuraxial opioid (morphine) is the gold standard for pain control during and after CD but accompanied by some adverse effects including pruritus, nausea, and respiratory depression. Evidence showed that approximately 50% women experienced mild respiratory depression after neuraxial morphine. Recently, the SOAP committee developed a consensus statement to promote patient risk stratification and patient-centered respiratory monitoring after neuraxial morphine administration. Opioids can also be given intravenously or intramuscularly. But much attention should be paid to maternal and neonatal adverse effects, especially to breastfeeding infant. The US Food and Drug Administration advised that codeine should be avoided in breastfeeding women due to the morphine poisoning to the infants. Scheduled NSAIDS (unless there are contraindications) and acetaminophen decreasing opioids and side effects by 30% to 50%, should be considered as the mainstay of analgesia after CD. Local anesthetic techniques including wound infiltration, nerve block (eg, quadratus lumborum or transversus abdominis plane [TAP] block) with ultrasound guidance may provide good analgesic effect. A recent study showed that TAP block provided clinically similar outcomes (including numerical pain rating scores, the need for rescue medication, side effects, and patient satisfaction) as intra-thecal morphine (100 µg) after CD. The quadratus lumborum block after CD was also effective for post-operative pain control as a part of a multi-modal approach. But note that these techniques are performed when neuraxial morphine cannot be given, or as a rescue technique for breakthrough post-operative pain.

Active pre-operative management of unplanned conversion of labor analgesia to cesarean delivery anesthesia

For planned or scheduled CD, anesthesiologists may be more involved in the intra- and post-operative period. But for unplanned CD, especially when the epidural catheter is in situ, the pre-operative management may be the most challenging practice for anesthesiologists to confront with. Unplanned CD in labor is urgent and can be traumatic. If the conversion or the “top-up” epidural dosing fails, delayed operation will be detrimental to the fetus and raise the risks of anesthesia-related complications. Repeated spinal anesthesia after failure conversion can lead to high level blockade and hypotension. Unplanned conversion to general anesthesia is associated with high risks of maternal aspiration, failed airway management, maternal hemorrhage, and delayed neonatal respiration. So, the reliable, safe, and timely conversion is crucial. Early and active pre-operative management of conversion should be started once the patient consents to CD. A small bolus before transport and a repeated bolus in OR can be used to test the catheter and accelerate the induction. Accurate and quick assessment of the surgical level should be made to avoid the unintended high level blockade and facilitate the anesthesiologists to make a decision whether to continue induction or choose an alternate technique. Appropriate epidural solution can also accelerate the induction. In a meta-analysis evaluating different solutions for extending epidural analgesia for emergency CD, the author recom-
mended the combined solution of 2% lidocaine with epinephrine, fentanyl, and bicarbonate can fasten the onset.\textsuperscript{[57]} Another point of noting is that active management of labor analgesia in which the anesthesiologists participate in optimizing the quality and density of analgesia, the progress of labor, the diagnosis, and the treatment of breakthrough pain will help safe and successful conversion of labor analgesia to anesthesia.\textsuperscript{[58]}

Conclusions

In general, ERAC is an approach to promote maternal and neonatal healthcare through the utilization of standardized protocols and guidelines. Although this patient population is ideal for implementation of ERAC, to date, the supportive data are sparse and no completed randomized controlled trials of ERAC exist in the literatures. Among them, unplanned CD takes a high proportion in the total number of CD, large scale clinical trials are also warranted to test the feasibility of ERAC protocol in unplanned CD. One concern is that we might delay large-scale ERAS implementation until high quality data are available. But we believe that ERAC protocol is promising and should not be delayed because robust evidence has demonstrated the effectiveness and efficacy of each component of ERAC. Certainly, close audit and feedback should be used regularly to improve the quality of ERAC.\textsuperscript{[59]} The other concern is how to precisely define “recovery” after CD, as the concept “recovery” means different things to different people. We should focus on a complete recovery including post-discharge care and follow-up as it may take months for women to reach their pre-operative functional level based on their expectations and social circumstances. Interestingly, in China, there has a traditional practice after childbirth so-called “post-partum confinement” or “sitting the month” focusing mainly on social support rituals, for example, prolonged rest, special diet, and personal hygiene.\textsuperscript{[60]} Within-culture differences between Western and Asian, patient’s expectation of recovery may be quite different. Finally, ERAC is just the beginning toward developing optimized pathway across pregnancy. In the future, enhanced recovery may be considered for all the women giving birth to help them quickly return to the physical and mental functioning status while reducing medical expenses and wastes of medical resources.

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Conflicts of interests

None.

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