ERAS 2.0 – opportunities and challenges: A review

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Structured Abstract

Importance: Enhanced Recovery After Surgery (ERAS) is a global surgical quality improvement initiative now firmly entrenched within the field of perioperative care. While ERAS is associated with significant clinical outcome improvements and cost savings in numerous surgical specialties, there are still several opportunities and challenges that deserve further discussion.

Observations: Uptake and implementation of ERAS® Society Guidelines, together with ERAS-related research has increased exponentially since inception of the ERAS movement. Opportunities to further improve patient outcomes include addressing frailty, optimizing nutrition, prehabilitation, correction of preoperative anemia, and improving uptake of ERAS worldwide including low- and middle-income countries. Challenges facing enhanced recovery today include implementation, carbohydrate loading, reversal of neuromuscular blockade and bowel preparation. The COVID19 pandemic poses both a challenge and an opportunity for ERAS.

Conclusions: To date, ERAS has achieved significant benefit for patients and health systems, however improvements are still needed particularly in the areas of patient optimization and systematic implementation.

Relevance: Now more than ever, particularly during this time of global crisis, the ERAS method of delivering care is what is required to take surgery and anesthesia to the next level, bringing improvements in outcomes to both patients and health systems.

Introduction

This review is a sequel to a previous article on Enhanced Recovery After Surgery (ERAS) and the work of the ERAS® Society published in 2017.[1] Since then the concept of fast-track surgery initiated by Henrik Kehlet, and further developed as enhanced recovery by the ERAS® Society, has expanded exponentially and come to influence change in protocols for surgery and anesthesia in many disciplines (Table 1). The approach of evidence-based perioperative care, with teams controlling the entire care pathway has inspired medical organizations worldwide to follow and promote ERAS principles,[2-5] and has led to large international collaborations with the ERAS® Society.[6] ERAS has spread worldwide with implementation in more than 25 countries (Figure 1). The interest is demonstrated by the number of ERAS-related publications, now exceeding 4000, since the ERAS® Society was founded in 2010. These publications involve different hospitals, healthcare systems and financial systems and show benefits from adopting this method of delivering care. Patients managed according to ERAS principles can expect faster recovery, fewer complications, and may live longer; health systems can expect reduced cost of care.[1,7]

ERAS is a constantly evolving program based on the best currently available evidence in perioperative care. This narrative review describes how the ERAS® Society has continued to develop since inception, highlights opportunities and challenges in the field of enhanced recovery today, and finally, discusses how ERAS represents an opportunity to manage the problems for surgery arising from the COVID-19 pandemic, alongside the challenges that need to be overcome to implement ERAS into daily practice.[8]

ERAS Today

ERAS® Society guidelines

The first ERAS consensus statement[9] was published in 2005 and heralded a paradigm shift in perioperative care for colorectal surgery, emphasizing multidisciplinary work, patient partnership, evidence-based interventions and audit. This led to a global change in practice over the subsequent 15 years. The ERAS® Society has now published guidelines in 20 specialties (including updates) with several more in development (Table 1). Collectively, the

ERAS® Society guidelines have been cited more than 6000 times and downloaded more than 700,000 times.

The ERAS® Society has also published a framework for the development of guidelines so that uniformity is maintained, and that guidelines don't contradict each other.[10] The guidelines serve professionals and healthcare organizations but need also be acceptable to patients and stakeholders. Impartial grading of evidence level and recommendation strength is also vital. The Delphi process is useful especially in instances where there is low-quality evidence. Validity and applicability of guidelines have to be tested clinically; this is achieved by multicenter audit as performed for several ERAS® Society guidelines.[11-13] The ERAS® Interactive Audit System (EIAS) is a monitoring platform for audit and research. Data fields may be modified as necessary to test specialty-specific guidelines.[14]

Implementation and sustainability

For ERAS programs to be successful, data show that there is little room for improvisation and efforts to implement ERAS properly should not be underestimated.[15] Implementation of ERAS should be systematic, involve a multidisciplinary team and can be facilitated by support of ERAS experts to ease the complexity of the implementation process.[16] A successful ERAS implementation program should cover the evidence-based principles of ERAS with team-oriented training. The essential elements are data collection and monitoring of outcomes using an audit system with comprehensive review during regular multidisciplinary meetings.[15,16] The goal is to document to what extent the items of the ERAS guidelines are being used (compliance). Teams work together to iterate towards increased guideline compliance which translates to improved clinical outcomes. These principles have been confirmed in over 90,000 patients entered into the EIAS database representing 250 units worldwide (Figure 1).

Multidisciplinary team

Fundamental components of an ERAS program include the multidisciplinary approach required to ensure successful implementation of ERAS but also that sustainability of the program is achieved. The core ERAS team typically consists of a surgeon, anesthesiologist, ERAS coordinator, nurse, allied healthcare professionals (AHP) and a manager.[17] The team

should establish clear communication between all disciplines and departments related to the patient journey. ERAS is different from other surgical interventions as it changes perioperative management, increases communication between clinical teams and promotes ongoing commitment from staff and patients to ensure optimal deployment.[18] Lack of collaboration remains a barrier to successful implementation of ERAS[1,19] as is a lack of communication between multidisciplinary team members.[20]

The importance of nurses and AHPs cannot be overemphasized as these team members perform many of the day-to-day tasks required to achieve high ERAS compliance.[21] This is particularly the case postoperatively when early mobilization may be resource intensive[22-24] and early feeding may not be considered a priority.[25] Some evidence suggests that ERAS reduces overall nursing workload.[26] The optimal mobilization and rehabilitation strategies in ERAS still need to be assessed both in general surgery,[27] and in orthopedics for post discharge rehabilitation.[28]

Are all ERAS care elements justified?

A current controversy in the field of enhanced recovery relates to how many individual elements need be included in an ERAS protocol. The inclusion of multiple elements is criticized as too complex and some authors claim that only 5-7 are needed.[29] The answer lies in the process behind the ERAS® Society Guidelines where care elements are included only if evidence suggests improvement in outcomes. Several publications have shown that the more ERAS elements in use the better the outcomes.[11-13,30] Another argument that some make is that certain elements are considered "standard of care", so why include them in a protocol? Elements considered standard, however, may differ between surgeons, hospitals, and countries.[31] The ERAS® Society's scientific approach is to include all the elements shown to improve outcomes instead of trying to define a minimum number of elements. In addition, some elements are likely to change over time. It is then the responsibility of the individual unit to include as many of the ERAS elements as possible, which in turn translates to improved outcomes.[11-13,30]

Health economics

While surgeons and anesthesiologists describe benefits of ERAS in terms of clinical outcome improvements, these benefits must be translated into the language of health system administrators. These individuals are typically the ones who make the decisions to fund surgical quality improvement initiatives. This begs the question "is ERAS considered value-based surgery?"

There has been numerous health economic analyses[32] of ERAS programs across the surgical spectrum performed showing cost savings ranging between US$655 - $16447/patient (Table 2). Communication of cost savings to administrators may be facilitated by discussing the return-on-investment ratio (ROI). A recent ROI analysis of the implementation of multiple ERAS guidelines in Canada demonstrated that the ROI was 7.3, meaning that every dollar invested in ERAS brought $7.3 in return,[7] showing that ERAS definitively provides value.[32]

What is real ERAS?

While ERAS is at the forefront of interest of anesthesia and most surgical specialties, the actual application of these principles, as originally proposed by the ERAS® Society, is far from being universally adopted. Many surgical professionals claim they "do ERAS". Still, national data on colorectal surgery reveals prolonged hospital stays – contradicting its widespread use.[8] "Doing ERAS" does not mean that the guidelines are followed as revealed in a recent global survey.[33]

In addition, not all ERAS training programs necessarily translate to better practice or outcomes. A recent report from a nationwide Spanish implementation program based on protocols, lectures and instructions[13] reduced length of stay (LOS) by 1 day. In healthcare systems of the Netherlands[34] and Canada,[35] implementation was more structured and complemented by audit - these programs reported 2-4 day reductions in LOS with similar baseline LOS as the Spanish study. ERAS training *per se* does not guarantee better results. The final determining factor is how well the unit can change and comply with the ERAS protocol.

A common missing factor is monitoring and audit. Constant analysis of practice is the key to success for any surgical unit. The audit needs to assess not just outcomes and basic processes, as in most quality registries, it must also include all ERAS guideline elements and it needs to be continuous,[36,37] as opposed to sampling.

Opportunities for improved outcomes

Addressing frailty

Management of the metabolic stress response to surgery is a crucial feature of ERAS protocols.[1] This has come into focus with recent insights into the role of malnutrition and frailty as contributors to complications. With an aging population presenting for major surgery there has been recognition that frailty itself is a major risk factor for complications and reduced postoperative life expectancy. Frailty is different from old age and is characterized by a reduced reserve to tolerate complications.[38] Complications such as delirium and postoperative reduction in functional capacity can lead to prolonged rehabilitation and permanent loss of function especially in the elderly.[39] Therefore, it is essential to identify those patients who are frail (using a validated frailty assessment tool) and ensure optimal interventions to reduce the impact of surgery and reduce medications that can increase risk of delirium.[40-42] A multidisciplinary team model focusing on care of the older patient is key for optimal care and reduces hospital readmission.[40,42]

Optimizing nutrition

Nutritional status is a critical factor for recovery after major surgery. Prevalence of nutritional risk is reportedly above 20% in colorectal cancer surgery,[43] and is considerably higher for patients with gastroesophageal and pancreatic cancers. Sarcopenia, sarcopenic obesity and myosteatosis, and presence of preoperative inflammation coupled with the postoperative inflammatory responses to major surgery[44] further increase this risk. Recent data, however, reveal that ERAS abrogates this increased risk to a large extent.[45]

All patients scheduled for major surgery require a nutritional risk assessment, and if needed, up to 10-14 days of nutritional treatment preoperatively.[46] In addition, a recent meta-analysis in patients undergoing surgery for gastrointestinal cancer confirmed that

preoperative immune modulating nutrition, when given for 5-7 days preoperatively reduced postoperative infectious complications and LOS significantly when compared with isocaloric isonitrogenous feeds or a normal diet.[47]

Most colorectal and liver surgery patients can have an adequate oral diet as early as the first postoperative day, since ERAS protocols help gut motility in the postoperative phase and enhance the capacity to return to normal diet.[48] However, this may take longer in patients undergoing gastroesophageal or pancreatic surgery. These patients may need oral nutritional supplements in addition to their diet. Artificial nutrition in the form of tube feeding or parenteral nutrition should be reserved only for patients unable to fulfill needs with oral nutritional supplementation.[46]

Studies on post-discharge nutrition have not shown significant benefits. It is possible that this is because post-discharge supplements evoke feelings of satiety and reduce the intake of food.[49] Nevertheless, post-discharge oral nutritional supplements should be considered in high-risk patients with an inadequate food intake as they have been shown to reduce the rate of deterioration in muscle mass and improve tolerance to adjuvant therapies in cancer patients.[49]

Prehabilitation

Prehabilitation is the concept of preparing patients preoperatively to withstand the challenges of surgical stress especially in those who are comorbid and frail as decline in functional status in these patients may result in loss of independent living status.[50] The preoperative time is viewed as a “teachable moment” as patients may be more receptive to improving their health. There are many areas of prehabilitation, with multimodal the most described, addressing three major areas: exercise, nutrition and psychological support.[50]

There is emerging evidence about the benefit of prehabilitation before major abdominal and cardiothoracic surgery. Reduced overall complications, including pulmonary and cardiac complications, have been observed.[51] However, given the heterogeneity of studies to date, randomized studies are needed to confirm the role of prehabilitation for specific patients

and surgical procedures, including the benefit on immediate and long-term outcomes within ERAS programs.

Correction of preoperative anemia

Preoperative anemia is common and is one of the key risk factors for all causes of morbidity and mortality in patients undergoing major surgery.[52] Blood transfusion does not mitigate risk because it is associated with other risks including transfusion reactions, poorer oncological outcomes and reduced 5-year survival.[53] All patients should therefore be screened preoperatively to detect the cause of anemia and correct the hemoglobin concentration as much as possible prior to major surgery.[54] The opportunity for preoperative correction depends on the urgency of surgery. New safer intravenous iron formulations have shown promise in many studies and provide rapid restoration of total body iron stores even in patients with anemia of chronic disease.[54] The PREVENTT study, however, showed that preoperative intravenous iron was not superior to placebo in reducing the need for blood transfusion.[55] However there was increased postoperative hemoglobin and reduced complications in the treatment group.[55] Future studies should focus on the combination of intravenous iron and erythropoietin as both seem to be effective and safe in the different phases of perioperative care.[54]

Improving uptake of ERAS in low- and middle-income countries (LMIC)

The Lancet Commission on Global Surgery in 2015 reported that 5 billion people do not have access to safe, affordable surgical and anesthesia care when needed.[56] An unmet need of 143,000,000 procedures per year exist in low- and middle-income countries (LMIC) with an immense loss of global productivity.[56] In particular securing surgery for almost 50% of the population in LMIC that are children is very cost-effective. Life-long treatment for a child with HIV costs US$300,000 while a hernia repair costs only US$50.[57]

Implementation of ERAS pathways in LMIC will provide opportunities to improve the quality of perioperative care and reduce healthcare costs. However, it will also require significant changes in how care is delivered.[58] There are many challenges and barriers to implementing ERAS care in LMIC including fundamental healthcare problems like malnutrition, obesity and

HIV that impact the complexity of surgery, complication rates and LOS.[59,60] First steps of ERAS implementation in LMIC should consist of discussions among stakeholders including ministries of health, hospital systems, physicians, nurses and nutrition specialists.[33,58] Specific ERAS guidelines tailored for LMIC are under development. Implementation of ERAS care in LMIC can be an important addition to facilitate the Global Surgery 2030 goals to improve patient outcomes, service efficiency and reduce hospital bed days.[56]

Challenges and controversies

An overarching challenge is to fill the knowledge gaps with high-quality research. The ERAS® Society has published recommendations for publishing on ERAS,[36] as part of its aim to improve clinical research.

Carbohydrate loading

Preoperative carbohydrate drinks tailored to elicit an insulin release have low osmolality and approximately 12% carbohydrate content (based mainly on maltodextrins and some salt). Taken before surgery, they mitigate several negative effects of overnight fasting.[61] Preoperative carbohydrates result in a reduction of postoperative insulin resistance, less hyperglycemia and reduced need for insulin treatment[62] with preservation of both skeletal muscle and, for patients undergoing cardiac surgery, cardiac muscle function. In addition, preoperative carbohydrate drinks reduce preoperative discomfort and anxiety, headache, postoperative nausea and vomiting, pain and the inflammatory response without increasing the risk of pulmonary aspiration. These benefits have translated into mainly shorter length of stay in major abdominal surgery but not in reduced complications, as reported by 2 meta-analyses.[63,64] However, the quality of some of the underlying evidence and the failure to show reduced complications has caused the use of preoperative carbohydrates to remain controversial.

There is marked variation in carbohydrate drinks and their composition have direct impact on their physiological effect and safety. Sports drinks (with carbohydrate concentrations of 6-8 %) are not made to elicit an insulin response and, therefore, are not recommended for preoperative use. Many products containing carbohydrates have been advocated for

preoperative use, but only few have been properly tested. Therefore, users should demand that producers provide data on their specific formula confirming that their product is tested for safety and efficacy before being used.

In patients with diabetes the combination of preexisting hyperglycemia and/or delayed gastric emptying due to autonomic neuropathy may coexist, thus putting them at risk of poor perioperative glucose control and pulmonary aspiration, respectively.[65] There is little evidence in this area, with one small study suggesting it was safe in patients with well-controlled diabetes taking their morning medication.[65] Moreover, as patients with Type I diabetes are insulin deficient, rather than insulin resistant, these drinks are not recommended in this group.

Neuromuscular blockade, its reversal and postoperative recovery

Adequate neuromuscular management consisting of appropriate choice of neuromuscular blocking drug, and monitoring of neuromuscular blockade and reversal is important in anesthesia and contributes to improved outcome.[66]

Deeper levels of neuromuscular blockade facilitate lower insufflation pressures during laparoscopy, thereby improving surgical space by relaxation of the abdominal wall.[67] This has been associated with less postoperative pain and improved recovery.[66,67]

Reversal of neuromuscular blockade is necessary to prevent delayed recovery of muscle function.[66] Approximately 5% of patients experience a major pulmonary complication after non-cardiac surgery.[68] Inadequate reversal of neuromuscular blockade increases the risk of pulmonary complications.[66] Recent studies report that selective relaxant binding agents provide a rapid and complete reversal of common steroidal neuromuscular blocking agents without adverse effects found with other drugs.[66,68] The benefits of these new agents of neuromuscular blockade reversal include fewer pulmonary complications, reduced LOS and reduction in 30-day unplanned readmission after major abdominal surgery.[69,70]

Bowel Preparation

ERAS Guidelines have advised against mechanical bowel preparation (MBP) for colonic surgery and have advocated MBP selectively for rectal surgery. This was based on the prevailing evidence that did not show a benefit of MBP alone when compared with no preparation.[71] However, there has been a resurgence in interest in oral antibiotics (OAB) in combination with MBP or on their own for colorectal surgery. A recent meta-analysis[72] showed that when compared with MBP alone, a combination of OAB with MBP was associated with significantly lower rates of surgical site infection (SSI), anastomotic leak, 30-day mortality, postoperative ileus and overall complications, with no increase in *Clostridium difficile* infection. Although there was no difference in SSI and anastomotic leak rates when a combination of MBP+OAB was compared with OAB alone, the combination resulted in a reduction in 30-day mortality and incidence of postoperative ileus. However, one of the limitations of this meta-analysis was that it was heavily influenced by the results of cohort studies (63,080 participants) as there were only 6437 participants from randomized controlled trials (RCTs). Nevertheless, when RCTs alone were considered, the combination of MBP+OAB resulted in a significantly lower SSI rate than MPB alone.[72]

Two RCTs[73,74] have been published since the meta-analysis,[72] one comparing MBP+OAB with no bowel preparation[73] and the other OAB alone with no bowel preparation[74] in patients undergoing elective colectomy. When these studies[73,74] were added to the previous meta-analysis,[72] the overall results were unaltered,[75] once again because of the weighting of the cohort studies.

This suggests that OAB should be considered in all patients undergoing elective colorectal surgery. Since there is no definitive evidence on the equivalency of combined MBP+OAB with OAB alone, there is a need for a high-quality study with participants randomized to receive no preparation, OAB alone, or a combination of MBP+OAB to provide a definitive answer to this question.[75] In addition, there remains a question related to the microbial homeostasis that may impact outcomes in studies from different countries.[76]

COVID-19: a challenge and an opportunity

The COVID-19 pandemic has caused several major changes in healthcare around the world and its financial impact is just beginning. Surgery and surgical patients have had to stand back and make room for patients in need of acute and intensive care related to COVID-19 infection.[77] Operating rooms have been transformed to ICU facilities and doctors, nurses and AHPs have been rapidly retrained to manage patients with COVID-19. Overall, there has been a remarkable change of practice that few believed possible.

This massive and rapid change in daily practice[78,79] is in stark contrast to what the normal pace of change has been for surgery and anesthesia. It usually takes 15 years or more to establish a change in clinical care. For COVID-19 many units around the world have made extraordinary changes in just 15 days. This would never have been possible without a common will to solve a huge problem and employ everyone's expertise from the surgical floor to hospital management. All these groups working together ensured that the goal was met.

This is where the opportunity for the future of surgery and anesthesia lies.[8] Surgery and anesthesia need to seize the opportunity and use the momentum of change adopted during the COVID-19 pandemic to modernize perioperative care. Modern technology, such as telemedicine, has been employed to avoid unnecessary in-person visits. We believe that this is also the opportunity to get proper ERAS up and running. Now is the time to establish what surgical care has required for a long time – multidisciplinary teams that work outside of traditional silos with the common goal to improve outcomes for patients. ERAS brings modern monitoring and audit to obtain control of the entire perioperative process and will lead to much needed improvement in surgical outcomes.

Conclusion

To date, the ERAS method of delivering care has achieved significant benefit. In the next phase of ERAS, high-quality research produced rapidly and at low cost is needed to take surgery and anesthesia to the next level. During this time of global crisis, perioperative care

412 providers must unite and make the changes that will bring further enhancements for
413 patients and health systems.
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Legend Figure 1. The Figure shows spread of the ERAS® Society Implementation Program and use of the ERAS® Interactive Audit System (EIAS) in different countries worldwide as of November 2020.

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