

OVARIAN CANCER IN FOCUS

Current Developments in the Management of Ovarian Cancer

Section Editor: Robert L. Coleman, MD

Enhanced Recovery After Surgery for Ovarian Cancer



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H&O What are the protocols that constitute enhanced recovery after surgery (ERAS) in ovarian cancer?

SD The precise protocols vary somewhat among institutions, but they include early feeding, opioid-sparing analgesia, and euvolemia. Early feeding is important because healing and outcomes tend to be better in patients who receive good nutrition. In the past, we withheld nutrition from patients for a long period after surgery in an effort to improve recovery, but the truth is that early feeding is better. Regarding opioid-sparing analgesia, we have taken multiple steps to reduce the amount of opioids patients use after surgery. In our own practice, we have reduced opioid use in the first 48 hours after surgery by more than 90%. Although opioids are an indispensable part of postoperative pain management, they can be overused, which is a problem because they cause side effects such as constipation and drowsiness. Patients generally feel better when they use lower doses of opioids and stop taking them sooner.

I believe that euvolemia, or a neutral fluid balance, is perhaps the most critical aspect of enhanced recovery. We used to give patients a lot of fluids to keep them hydrated and reduce the risk for kidney damage. Because we tend to exaggerate good things, however, we started to give more and more fluids—as much as 10 to 20 L of saline solution during surgery. One problem with that approach is that each liter of saline solution contains approximately the same amount of sodium as 50 servings of potato chips, so 10 L of normal saline delivers the sodium load of 500 bags of potato chips.

Excreting all that sodium takes a long time, so edema often develops in a patient's extremities, face, and abdomen. If swelling occurs in the intestines, bowel function is slow to recover. In a trial published in the *New England Journal of Medicine* in 2018, with Myles as the first author, the patients randomly assigned to receive normal fluids did just as well or possibly better than those randomly assigned to receive restricted fluids. I would not interpret these trial results to mean that more hydration is better, however. In this trial, neither arm was overhydrated in my opinion—one arm was

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appropriately hydrated and the other was slightly underhydrated. We should be looking at getting the balance just right; this varies according to the patient, surgical approach, and duration of the operation.

The more elements of ERAS that hospitals implement, the better the patients do. I am working on a manuscript right now about an international cohort of

more than 2000 patients who have undergone gynecologic surgery. We have found that patients do slightly better if 1 or 2 elements are implemented, and far better

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if 10 or 11 elements are implemented. Each additional element shortens the length of hospital stay by 8% to 12%.

In 2016, our group published a 2-part set of international guidelines for ERAS in *Gynecologic Oncology*. These guidelines have been popular—they are one of the top downloads for the journal—so a lot of people have been reading them.

H&O Why is ERAS considered revolutionary in surgical care?

SD A lot of what we do in surgery is based on dogma—protocols that have been handed down from teacher to student. ERAS has brought evidence-based care to perioperative management. Although what happens during surgery is extremely important, we have learned that perioperative care is also a major determinant of outcomes. When perioperative care is optimized, patients fare better, and we are able to reduce the cost of care and open up space in hospitals by discharging patients earlier. Everyone wins—the surgeons, the patients, and the administrators.

H&O When was ERAS introduced in ovarian cancer, and how widespread is its use?

SD ERAS was first introduced in colorectal surgery in the 1990s, and only later was it used in ovarian cancer surgery. We adopted this approach across the board for all our gynecologic surgeries at the Mayo Clinic starting in 2011. Given the complexity of ovarian cancer surgery and its inherent risks, the articles we published were focused on that topic. I have taken steps to publicize this approach through talks at national meetings and grand rounds, and a lot of surgeons have taken to it. So I would say that nearly all gynecologic oncologists are familiar with the concept and may be making attempts to implement it. The problem is that many institutions are not implementing

it to its full potential. If ERAS is to work, everyone on the surgical team needs to be on the same page—not just the surgeon. Specific steps must be taken before surgery, during surgery, and after surgery. Otherwise, we should not refer to the approach as ERAS.

H&O What are the documented benefits of ERAS?

SD First, ERAS has been shown to reduce the length of stay in the hospital. Our study published in *Obstetrics and Gynecology* in 2013 found that ERAS reduced the hospital stay by an average of 4 days, without changing the readmission rate. This study also found that ERAS reduced opioid use during the first 24 hours after surgery by 80%, with no change in pain scores. Our study published in 2016 in *Obstetrics and Gynecology*, with Kalogera as the first author, found that reductions in opioids and fluids reduced the rate of ileus by approximately 50%, with quicker restoration of gastrointestinal function. Complication rates are stable at worst and decreased at best after ERAS is implemented. Regarding cost, in our 2013 study, we were able to save approximately \$750,000 in 6 months. We also have shown improvements in patient satisfaction with ERAS.

MD Anderson was one of the early adopters of ERAS after the Mayo Clinic and is doing an excellent job with it. Dr Larissa Meyer at MD Anderson led an important study, published in *Obstetrics and Gynecology* in 2018, in which patient-reported outcomes were shown to be significantly improved with enhanced recovery. The results were striking. For example, a 72% reduction in opioid use occurred in patients in the ERAS group. In addition, patients managed with ERAS returned to normal function after an average of 3 rather than 13 days.

H&O Which members of the health care team are involved in the administration of ERAS?

SD In addition to the surgeons, we include anesthesiologists, pharmacists, residents and fellows, nurses, operations managers, and administrators. It is very important for the nurses to be on board; they are usually very happy after we explain that the patients are being discharged earlier because they are recovering earlier, not because we are simply trying to get them out of the hospital more quickly. A surgeon who explains the benefits of ERAS and obtains buy-in from all the members of the team will be more successful than an authoritarian surgeon in getting this approach implemented.

H&O What are the next steps in the implementation of ERAS?

SD I am one of the content experts for an Agency for Healthcare Research and Quality (AHRQ) grant under which we are working to implement ERAS in 750 service lines over 5 surgical specialties during the next 5 years. Dr Elizabeth Wick, a colorectal surgeon at the University of California San Francisco, and Dr Clifford Ko, Director of the American College of Surgeons Division of Research and Optimal Patient Care, are leading this government-funded project. Patients in colorectal surgery and in orthopedics have already been enrolled, and gynecology is the next surgical specialty in which patients will be enrolled in the spring of 2019.

The AHRQ Safety Program for Improving Surgical Care and Recovery is a free program in which coaching calls and webinars are used to teach institutions how to implement ERAS; I encourage people to visit <https://qi.facs.org/isctr/> to learn more and sign up.

H&O What are the research opportunities for ERAS?

SD Although we have made a great deal of progress in optimizing our perioperative care pathways, these will continue to evolve as more surgeons gain experience with ERAS and test new hypotheses. In addition to the areas already discussed, such as the use of bowel preparation and regional analgesia, a number of ERAS elements still need additional investigation, including the use of pharmacologic adjuncts, the impact of carbohydrate loading, and the importance of the stress response on recovery. A growing number of pharmacologic adjuncts, such as intravenous lidocaine, dexamethasone, clonidine, ketamine, magnesium, and esmolol, have purported benefits that include reduced opioid tolerance, less pain, and reduced inflammatory responses following surgery. Although the use of gabapentin, acetaminophen, and celecoxib is common, we do not yet understand the optimal pharmacologic cocktail for patients before, during, and after surgery. Various biochemical derangements are muted with some of these interventions, but what is statistically

significant may not always be clinically relevant. So, at the same time that reducing inflammation and stress are likely to be important, the most important endpoints in revised ERAS pathways should remain length of stay, complication rates, and patient-reported outcomes. Carbohydrate loading has been associated with modest benefit, including reduced insulin resistance, and many companies have begun to advocate for specific (and often expensive) formulations, such as “immune-nutrition.” These new products require unbiased investigation to identify the most efficacious and cost-effective formulations.

Disclosure

Dr Dowdy has received a Safety Program for Improving Surgical Care and Recovery grant from the Agency for Healthcare Research and Quality.

Suggested Readings

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