Surgical technical evidence review for gynecologic surgery conducted for the Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery

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BACKGROUND: The Agency for Healthcare Research and Quality, in partnership with the American College of Surgeons and the Armstrong Institute at Johns Hopkins, developed the Safety Program for Improving Surgical Care and Recovery, which integrates principles of implementation science into adoption of enhanced recovery pathways and promotes evidence-based perioperative care.

OBJECTIVE: The objective of this study is to review the enhanced recovery pathways literature in gynecologic surgery and provide the framework for an Improving Surgical Care and Recovery pathway for gynecologic surgery.

STUDY DESIGN: We searched PubMed and Cochrane Central Register of Controlled Trials databases from 1990 through October 2017. Studies were included in hierarchical and chronological order: meta-analyses, systematic reviews, randomized controlled trials, and interventional and observational studies. Enhanced recovery pathways components relevant to gynecologic surgery were identified through review of existing pathways. A PubMed search for each component was performed in gynecologic surgery and expanded to include colorectal surgery as needed to have sufficient evidence to support or deter a process. This review focuses on surgical components; anesthesiology components are reported separately in a companion article in the anesthesiology literature.

RESULTS: Fifteen surgical components were identified: patient education, bowel preparation, elimination of nasogastric tubes, minimization of surgical drains, early postoperative mobilization, early postoperative feeding, early intravenous fluid discontinuation, early removal of urinary catheters, use of laxatives, chewing gum, peripheral mu antagonists, surgical site infection reduction bundle, glucose management, and preoperative and postoperative venous thromboembolism prophylaxis. In addition, 14 components previously identified in the colorectal Improving Surgical Care and Recovery pathway review were included in the final pathway.

CONCLUSION: Evidence and existing guidelines support 29 protocol elements for the Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery in gynecologic surgery.

Key words: Agency for Healthcare Research and Quality, enhanced recovery after surgery, enhanced recovery pathway, gynecologic surgery, Improving Surgical Care and Recovery, patient safety, review

Introduction

A multistakeholder partnership among the Agency for Healthcare Research and Quality (AHRQ) (funder), the American College of Surgeons (ACS), and the Johns Hopkins Medicine Armstrong Institute for Patient Safety and Quality has developed the Safety Program for Improving Surgical Care and Recovery (ISCR), a national effort to assist hospitals in implementing pathways for surgical patients that incorporates evidence-based practices to >750 hospitals across multiple surgical procedures over the next 5 years. This program will cover 5 surgical areas including colorectal surgery (CRS), orthopedics, gynecology, bariatrics, and emergency general surgery. This expansive project aims to assist hospitals in improving perioperative care through implementation of evidence-based enhanced recovery pathways (ERP).

ERP have reduced complications, shortened length of stay, improved patient satisfaction, and reduced costs for a variety of operations across specialties, including gynecology. The effectiveness of these programs is directly related to a

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AJOG at a Glance

Why was this study conducted?

To review the literature on enhanced recovery pathways in gynecologic surgery and identify the evidence-based components that will comprise the pathway for gynecologic surgery within the Safety Program for Improving Surgical Care and Recovery.

Key findings

Evidence and existing guidelines support 29 protocol elements for the Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery in gynecologic surgery.

What does this add to what is known?

This study provides a detailed evidence-based enhanced recovery pathway specifically focused on gynecologic surgery that will serve as the reference pathway during the Agency for Healthcare Research and Quality national effort to assist hospitals in implementing evidence-based pathways for surgical patients to >750 hospitals across multiple surgical procedures including gynecologic surgery over the next 5 years.

hospitals' ability to promote high compliance with each pathway process. Adherence to these pathways appears to have a dose-response effect on clinical outcomes.[1] Successful and sustainable implementation goes beyond protocol development, requiring integration across patient units, timely feedback of performance data sharing, senior executive support, as well as ongoing educational sessions.[2] As such, the Safety Program for ISCR will provide extensive resources beyond the ERP including access to outcome registries, performance benchmarking, educational materials, leadership training, and contemporary implementation science tools.

The objective of this article is to systematically review the literature supporting the individual components that most commonly comprise the ERP in gynecologic surgery and develop a comprehensive AHRQ Safety Program for ISCR pathway tailored to gynecologic surgery for widespread dissemination and implementation.

Materials and Methods

This study was conducted in parallel with the AHRQ Safety Program for ISCR review in CRS and adhered to the methodology originally developed for the CRS review with minor modifications to accommodate special circumstances in gynecologic surgery.[3] Two subject-matter experts reviewed existing ERP in gynecologic surgery and developed a list of the individual interventions that were most commonly adopted. Considering that evidence for implementation of individual components in gynecologic surgery is often derived from the CRS literature, this list was compared to the list of components discussed in the CRS and anesthesia review to avoid redundancy. The current study includes only components that are unique to gynecologic surgery, components that contain a good body of evidence derived directly from gynecologic surgery, or components that are different enough between the 2 specialties that a special review of the gynecologic surgery literature is warranted. The list of the components included in the ISCR pathway in gynecologic surgery is presented in Table 1. A summary of the protocol components, associated outcomes, and whether these are supported by literature and society guidelines is presented in Table 2, while a summary of the actual society guidelines for the protocol elements is presented in Table 3. To insure proper guidance for future implementation, the final pathway for gynecologic surgery incorporates all the ERP elements presented in the current review, in addition to elements relevant to gynecologic surgery presented in the CRS and anesthesia review (ie, skin preparation and carbohydrate loading) (Table 4).

A separate PubMed literature search was performed for each pathway component for articles published before October 2017. The search strategy is presented in the Supplemental Table and was in agreement with the principles of the search in the CRS review conducted for the AHRQ program. The literature was limited to gynecologic surgery and was only broadened to include literature from CRS if there was no literature available in gynecologic surgery and the component had not been reviewed in detail in the CRS or anesthesia review. If there were substantial differences in the interpretation of the literature between the 2 specialties, the reasons guiding the variable interpretation were critically reviewed. In accordance with the CRS review and given the extensive body of literature existing for each component individually, a hierarchical method of inclusion was followed and was based on study design: the most current well-designed systematic reviews (SR) or meta-analyses (MA) were included along with any randomized controlled trials (RCT) or high-quality interventional or observational studies published after the SR or MA. Studies should have reported on the following variables to be included: sample size, surgical procedure category, comparator (varied by component), and main outcome (varied by component). Exclusion criteria included: (1) no data on the variables of interest as detailed above; (2) study size <10 patients; (3) non-English language; and (4) non-SR. Results are presented in narrative form. The rating of quality of the evidence was based on the GRADE system as previously published by Guyatt et al.[4]

Results

Preoperative

Patient education. Rationale: Preoperative education may improve patient outcomes through expectation setting and adherence to postoperative protocols.

Evidence: We identified 2 RCT that met inclusion criteria. One RCT compared written vs verbal preoperative information in patients undergoing hysterectomy and bilateral salpingo-oophorectomy for endometrial cancer.[5] Patients who received written

information had significantly lower length of stay (3.47 vs 4.36, $P = .03$), lower mean visual analog scale value for postoperative pain (5.7 vs 6.8, $P < .01$), and used less pain medication daily (2.26 vs 2.89, $P = .0120$). The second RCT compared patients undergoing abdominal hysterectomy who received either usual care protocol or an efficacy-enhancing teaching protocol preoperatively.[6] Participants in the intervention group ambulated longer than participants in the usual care group (330 vs 156 seconds, $P = .043$). However, there were no significant differences between the groups in preoperative self-efficacy scale score, State Anxiety Inventory score, pain scores on the visual analog scale, vital capacity, preventable complications (atelectasis, pneumonia, paralytic ileus, and deep vein thrombosis), length of stay, and health status questionnaire scores at 6 months postoperatively.

Summary: While the synthesis of the evidence suggests a potential relationship between preoperative patient education and improved postoperative pain and ambulation, quality evidence informing the optimal method and efficacy of education is lacking. However, there is no evidence of any risk to counseling. We recommend that patients should routinely receive preoperative education.

Level of evidence: low

TABLE 1
List of elements to be evaluated for gynecologic surgery protocol for Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery

Preoperative
Patient education
Immediately preoperative
Bowel preparation
Intraoperative
Minimize drains
a. No routine nasogastric intubation
b. No routine peritoneal drains
Postoperative
Early mobilization
Early alimentation
Early urinary bladder catheter removal
Prevention of ileus
a. Laxatives
b. Chewing gum
c. Alvimopan
Early intravenous fluid discontinuation
Additional evidence-based perioperative interventions
Surgical site infection bundle
Glucose management
Preoperative venous thromboembolism prophylaxis
Postoperative venous thromboembolism prophylaxis

Kalogera. Enhanced recovery and gynecologic surgery. Am J Obstet Gynecol 2018.

Immediate preoperative

Bowel preparation. Rationale: Use of preoperative bowel preparation (mechanical bowel preparation [MBP] alone, oral antibiotics [OA] alone, or combination of both) has been hypothesized to decrease the risk of surgical site infections (SSI) and possibly anastomotic leak in CRS. However, its use has been associated with physiologic derangements such as dehydration, electrolyte abnormalities, need for prolonged fasting, as well as patient dissatisfaction, potentially hindering postoperative recovery.

Evidence: We found 1 SR,[7] 2 MA,[8,9] and 2 RCT published after the SR[10,11] investigating the utility of MBP in the setting of benign laparoscopic gynecologic surgery or vaginal prolapse surgery without bowel resection. All studies concluded that use of bowel preparation did not improve intraoperative visualization, bowel handling, and overall ease of performance of the procedure during gynecologic laparoscopic surgery even when handling large uteri or operating on patients with a higher body mass index.

There are no studies examining the safety and efficacy of bowel preparation (MBP alone, OA alone, or combination of both) following laparotomy for gynecologic surgery with or without bowel resection. We were able to identify only 1 RCT that studied the use of preoperative enemas during gynecologic laparotomy surgery.[12] Perioperative complications, surgical field visualization, efficacy of bowel packing, and surgeon and patient satisfaction were compared following no preoperative enema vs sodium chloride enema vs soap-suds enema. Of note, patients who were expected to have extensive surgery or entry in the bowel lumen were excluded. There were no differences in time of return of bowel function, time to oral intake and mobilization, or wound and perioperative complications. However, enema use was associated with greater patient dissatisfaction. In addition, there were no differences in surgeons' satisfaction overall as well as with regards to the efficacy of operative view and bowel packing.

Data were extrapolated from the CRS literature to inform best practices for bowel preparation in patients undergoing laparotomy for gynecologic diseases who are at risk for having a bowel resection. Based on 5 MA it was concluded that, "Despite the possibility

TABLE 2
Summary of improving surgical care and recovery gynecologic surgery protocol components, associated outcomes, and support from literature and/or guidelines

Intervention	Outcome(s)	Studies	Population	Evidence	Guidelines
Preoperative					
Patient education	↓/— LOS, ↓/— pain	2 RCT	GS	c	e
Immediate preoperative					
Bowel preparation					
a. MBP	— SSI	MIS GS: 1 SR, 2 MA, 2 RCT CRS: 4 MA	MIS GS/CRS	d	e
b. Oral antibiotics only	↓ SSI	CRS: 3 OS	CRS	b	f
c. Oral antibiotics with MBP	↓ SSI	CRS: 1 MA	CRS	b	f
Intraoperative					
Minimize drains					
a. No routine nasogastric intubation	— AL, — time to bowel function return, —PONV, ↑ patient discomfort	2 RCT	GS	a	e
b. No routine peritoneal drains[g]	— AL, — SSI, — reoperation, — mortality	2 MA, 2 RCT, 2 OS	GS	a	e
Postoperative					
Early mobilization	↓ Time to bowel function return	1 RCT	GS	b	e
Early alimentation	↓ Time to flatus, ↓ LOS, ↓ infectious complications	2 SR, 1 MA	GS	a	e
Early urinary bladder catheter removal	↓ UTI	GS: 1 MA, 1 RCT AS: 1 MA	GS/AS	a	e
Prevention of ileus					
a. Laxatives	↓ Time to bowel function return, ↓/— LOS	3 RCT, 3 CT	GS	a	e
b. Chewing gum	↓ Time to bowel function return, ↓ ileus, ↓/— LOS	5 RCT	GS	a	e
c. Alvimopan	↓/— Time to bowel function return (based on type of surgery)	1 MA, 1 RCT	GS/AS	c	f
Early intravenous fluid discontinuation	↓ LOS, ↓ complications	1 MA, 1 OS	GS/AS	a	e

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that combined bowel preparations cause physiologic derangements in the preoperative period, combined PO antibiotic and MBP is recommended in the ISCR protocol because of the evidence that this practice decreases SSI."[3] Due to the lack of relevant RCT in gynecologic surgery, it is worth reviewing in greater depth how ERP incorporating the use of bowel preparations have performed in comparison to ERP that do not. Lippitt et al[13] demonstrated that introduction of a

TABLE 2
Summary of improving surgical care and recovery gynecologic surgery protocol components, associated outcomes, and support from literature and/or guidelines *(continued)*

Intervention	Outcome(s)	Studies	Population	Evidence	Guidelines
Additional evidence-based perioperative interventions					
SSI bundle	↓ SSI	3 CT	GS	[a]	[f]
Glucose management	↓ SSI	Non-GS: 1 MA GS: 2 RCT	Cardiac, AS GS	[b]	[e]
Preoperative VTE prophylaxis	↓ VTE	2 SR, 1 OS, 1 CC	GS/MIS	[a]	[e]
Postoperative VTE prophylaxis	↓ VTE	3 SR, 1 MA, 2 CT	GS	[a]	[e]

AL, anastomotic leak; *AS*, abdominal surgery; *CC*, case-control study; *CRS*, colorectal surgery; *CT*, clinical trial; *GS*, gynecologic surgery; *LOS*, length of stay; *MA*, meta-analysis; *MBP*, mechanical bowel preparation; *MIS*, minimally invasive; *OS*, observational study; *PONV*, postoperative nausea and vomiting; *RCT*, randomized controlled trial; *SR*, systematic review; *SSI*, surgical site infection; *UTI*, urinary tract infection; *VTE*, venous thromboembolism.

[a] Component where all evidence supported given practice; [b] Component where evidence was indirect, but supported given practice; [c] Component where evidence was mixed (some showing benefit, some showing no effect) regarding given practice; [d] Component where evidence showed no effect of given practice; [e] Component where all guidelines supported given practice; [f] Component that is not included in existing guidelines; [g] Until more conclusive evidence is available, routine peritoneal drainage should be considered only in patients with high likelihood of postoperative pelvic collections or undergoing low anterior resection with anastomosis within 6 cm from anal verge and no concurrent temporary diversion.

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5-point SSI prevention bundle significantly reduced the infection rate from 33−7% in a cohort of ovarian cancer patients undergoing cytoreductive surgery with colon resection. However, well-established ERP in gynecologic surgery have eliminated the use of bowel preparation without negatively affecting SSI or anastomotic leak rates.[14,15] Furthermore, SSI reduction bundles that did not incorporate bowel preparation have been similarly successful in decreasing the incidence of SSI to as low as 2.4% among ovarian cancer patients undergoing cytoreductive surgery with bowel resection.[16,17] Since well-designed ERP protocols have been successful in achieving very low SSI rates, the number needed to treat to prevent 1 case of SSI by incorporating bowel preparations is quite high. Many patients would thus be exposed to the risk of physiologic derangements and general dissatisfaction with questionable benefit. This highlights the potential for differing recommendations between specialties.

Of the 5 MA from the CRS literature, 4 MA focused exclusively on comparing outcomes between MBP vs no MBP.[18−21] All 4 MA concluded that use of MBP did not result in a decrease in overall mortality, SSI, anastomotic leak rate, or reoperation compared to no MBP. The fifth MA compared combination of OA plus MBP to MBP alone.[22] In this study, combination of OA plus MBP compared to MBP alone significantly reduced the rate of total SSI (7.2 vs 16%, $P < .001$) and incisional SSI (4.6% vs 12.1%, $P < .001$) but did not reduce organ space SSI (4% vs 4.8%, $P = .56$). Although there has not yet been a RCT comparing directly OA alone vs OA plus MBP, evidence from observational studies suggests that OA alone may result in a comparable decrease in the rate of SSI compared to OA plus MBP for colorectal resections (ileocolic resection, partial colectomy, total colectomy, rectal resection).[23−25] Notably, in a recent ACS-National Surgical Quality Improvement Program analysis of 40,446 patients undergoing elective CRS, OA alone significantly reduced SSI, anastomotic leak, and major morbidity compared to no bowel preparation, while combined use of OA with MBP offered no additional benefit in improving these outcomes compared to OA alone.[24] These studies are limited by their retrospective nature as well as by the possibility that MBP was not captured because of lack of documentation, while OA use may be better documented as it is a prescribed medication.

Summary: There is strong evidence to suggest that oral MBP before minimally invasive gynecologic surgery does not offer any benefit and should be abandoned. Evidence from the CRS literature suggests that the use of oral MBP alone does not appear to decrease SSI and its use is thus discouraged. If bowel preparation is desired, we recommend considering use of OA along with MBP or OA alone with a focus on patients at high risk of needing a colorectal resection as part of the gynecologic procedure. However, physicians should weigh the risks associated with their use against the theoretical benefit of decreasing SSI. Data from nonrandomized studies suggest that bowel preparation may be omitted within a well-developed ERP that incorporates a SSI reduction bundle even when bowel resection is anticipated.

Level of evidence: moderate

Intraoperative

Minimize drains.

a. *No routine nasogastric intubation*

Rationale: The routine use of nasogastric tubes (NGT) may result in significant patient discomfort and dissatisfaction, increased rates of pulmonary complications, delays in return of bowel function, and prolongation of hospital stay with no patient benefit.[26]

Evidence: A limited number of reports specifically focused on the use of routine NGT in gynecologic surgery are available. In a RCT of postoperative NGT

decompression vs no NGT in 109 gynecologic oncology patients undergoing extensive intraabdominal surgery, use of NGT increased patient discomfort, did not decrease the rate of abdominal distention or nausea and vomiting, and delayed time to first flatus and clear liquid diet.[27] There was no change in the rate of anastomotic leak or other postoperative complications including aspiration. No patient among the non-NGT group required reinsertion of an NGT postoperatively. In another randomized trial of 122 patients undergoing surgery for gynecologic malignancies comparing early oral feeding to NGT decompression followed by feeding at first passage of flatus, the NGT group experienced later return of bowel function, delayed resumption of general diet, and longer hospital stay.[28] NGT reinsertion was required in only 10% of the non-NGT patients for subocclusive symptoms, half of which had underlying anatomic etiologies to explain their symptoms (lymphocyst, urinoma, and intestinal adhesions). Up to 88% of patients with NGT reported discomfort associated with the tube. Frequency of nausea, vomiting, and postoperative complications were the same between groups. These findings are in agreement with the evidence review conducted for the CRS pathway.[3]

Summary: There is strong evidence to suggest that routine NGT offers no clinical benefit, causes significant patient discomfort, and should thus be avoided.

Level of evidence: high

b. *No routine peritoneal drains*

Rationale: Prophylactic use of peritoneal drains may prevent, control, or assist in earlier diagnosis of postoperative fluid collections that can serve as a nidus of infection and lead to increased infectious complications including anastomotic bowel dehiscence.

Evidence: A 2017 Cochrane Database review on the use of retroperitoneal drainage vs no drainage following lymphadenectomy in patients with gynecologic malignancies included 4 RCT with 571 patients. The authors concluded that drainage was not associated with reduced rates of lymphocyst formation. On the contrary, use of surgical drains increased rates of symptomatic lymphocyst formation when the pelvic peritoneum was left open[29]; a MA reported similar conclusions.[30] In a RCT examining the use of retroperitoneal drainage after complete paraaortic lymphadenectomy, the authors observed that the drainage group had a higher rate of complications, symptomatic lymphocysts and ascites, and longer hospital stay.[31]

With regards to the use of prophylactic pelvic drainage following bowel surgery, most of the literature is derived from CRS. The evidence review recently conducted for the CRS pathway concluded that prophylactic peritoneal drainage should be avoided with the possible exception of patients undergoing low rectal anastomoses (within 6 cm of the anal verge).[3,32–35] However, some characteristics of patients with gynecologic malignancies may render them at higher risk for complications compared to colorectal patients, such as resection of multiple organ sites, extensive peritoneal resection, ascites, peritoneal carcinomatosis, and poor nutritional status. We identified only 1 observational study in the gynecologic oncology literature that addressed the use of prophylactic pelvic drainage following large bowel resection in patients with ovarian cancer.[36] The majority of these patients underwent rectosigmoid resection (55.8%) or rectosigmoid resection coupled with additional large bowel resection (37.2%). Although use of drains was associated with an earlier diagnosis of anastomotic leak, there was no difference between groups in overall outcomes including need for reoperation, length of stay, time to chemotherapy, or 30-day and 90-day mortality.

We found only 1 RCT on the use of prophylactic drainage in minimally invasive gynecologic surgery.[36] The use of surgical drains did not result in decreased perioperative morbidity including febrile morbidity in women undergoing laparoscopy-assisted vaginal hysterectomy.

Summary: Evidence suggests that the prophylactic use of peritoneal or retroperitoneal drains does not confer benefit following lymphadenectomy in gynecologic surgery. Routine peritoneal drains should be avoided unless there is a rectal anastomosis within 6 cm of the anal verge without concurrent diversion or the patient is at high risk for postoperative pelvic collections.

Level of evidence: moderate

Postoperative

Early mobilization. Rationale: Early mobilization may protect against muscle atrophy and deconditioning following surgery and reduce pulmonary and thromboembolic-associated complications.

Evidence: Data examining the impact of early mobilization as a single intervention in postoperative recovery are limited. We identified 1 RCT that examined the effect of a bundle of interventions including chewing gum, early oral hydration, and early mobilization on resumption of bowel function following gynecologic surgery.[37] In this study, there were 8 intervention groups (no intervention, single intervention, 3 interventions, and any combination of 2 out of 3 interventions group). Although the investigators focused on the comparison of the 3-intervention group compared to the rest of the groups, the early mobilization group, at least by numeric comparison, was associated with earlier return of bowel function compared to the no-intervention group. The evidence review conducted to support the CRS pathway[3] concluded that although data are limited and no specific postoperative mobilization protocol is recommended, prolonged bed rest is harmful.

Summary: Existing literature suggests that early mobilization may be beneficial for postoperative recovery. Prolonged bed rest should be avoided.

Level of evidence: moderate

Early alimentation. Rationale: Early oral feeding may hasten postoperative recovery by improving nutritional status and accelerating return of bowel function.

Evidence: Early postoperative feeding is defined as resumption of oral fluid and/or solid food intake within 24 hours of surgery. We identified 2 SR limited to patients with gynecologic malignancies[38,39] and 1 MA[40] including

TABLE 3
Summary of guidelines supporting Improving Surgical Care and Recovery protocol components in gynecologic surgery

Intervention	Guideline	Year	Recommendation
Preoperative			
Patient education	ERAS Society[85]	2016	Patients should routinely receive dedicated preoperative counseling
Immediate preoperative			
Bowel preparation	ERAS Society[85]	2016	Routine oral mechanical bowel preparation should not be used in gynecologic/oncology surgery including patients with planned enteric resection
	ASER[84a]	2017	Not used routinely
Intraoperative			
Minimize drains			
a. No routine nasogastric intubation	ERAS Society[85]	2016	Routine nasogastric tube should be avoided; if inserted during surgery, it should be removed before reversal of anesthesia
b. No routine peritoneal drains	ERAS Society[86]	2016	Not recommended routinely in gynecologic/oncology surgery including cases with lymphadenectomy or bowel surgery
Postoperative			
Early mobilization	ERAS Society[86]	2016	Patients should be encouraged to mobilize within 24 h of surgery
	ASER[84a]	2017	Out of bed on day of surgery, then for 6 h/d beginning postoperative day 1; ambulation 4 times/d
Early alimentation	ERAS Society[86]	2016	Regular diet within first 24 h after gynecologic/oncology surgery is recommended
	ASER[84a]	2017	Bland diet started on day of surgery; adult Boost Breeze supplement (Nestle HealthScience, Epalinges, Switzerland) with each meal
Early urinary bladder catheter removal	ERAS Society[86]	2016	Urinary catheters should be used for postoperative bladder drainage for short period, preferably $<$24 h postoperatively
	HICPAC[87]	2009	Remove catheter as soon as possible postoperatively, preferably within 24 h
Prevention of ileus			
a. Laxatives	ERAS Society[86]	2016	Use of postoperative laxatives should be considered
	ASER[84a]	2017	Docusate sodium, Milk of Magnesia
b. Chewing gum	ERAS Society[86]	2016	Chewing gum should be considered
	ASER[84a]	2017	Chewing gum is supported
c. Alvimopan	Not included in guidelines		
Early IV fluid discontinuation	ERAS Society[86]	2016	IV fluids should be terminated within 24 h after surgery; balanced crystalloid solutions are preferred to 0.9% NS
	ASER[84a]	2017	IV fluids (D5NS or D5LR) at 125 mL/h until patient drinks at least 500 mL
Additional evidence-based perioperative interventions			
SSI bundle	Not included in guidelines yet		
Glucose management	ERAS Society[86]	2016	Perioperative maintenance of blood glucose levels ($<$180–200 mg/dL) results in improved perioperative outcomes; glucose levels above this range should be treated with insulin infusions and regular blood glucose monitoring to avoid risk of hypoglycemia
	ASER[84a]	2017	Monitor blood glucose every 6 h for 24 h after surgery
	ACS/SIS SSI[88]	2016	Target perioperative blood glucose between 110–150 mg/dL is recommended for all patients regardless of diabetic status to reduce SSI

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TABLE 3
Summary of guidelines supporting Improving Surgical Care and Recovery protocol components in gynecologic surgery *(continued)*

Intervention	Guideline	Year	Recommendation
Preoperative venous thromboembolism prophylaxis	American College of Chest Physicians[89]	2012	Risk-stratified recommendations based on patient- and procedural-specific risk factors Gynecologic surgery for malignant indications: preoperative pharmacologic prophylaxis is recommended in addition to mechanical
	American Congress of Obstetricians and Gynecologists[90]	2007	Risk-stratified recommendations based on patient- and procedural-specific risk factors Highest risk level: preoperative pharmacologic prophylaxis is recommended in addition to mechanical
	ERAS Society[85]	2016	Patients at risk of venous thromboembolism should receive prophylaxis with either low molecular weight or unfractionated heparin, commenced preoperatively, combined with mechanical methods
	American Society of Clinical Oncology[91]	2015	Patients undergoing major cancer surgery should receive low molecular weight or unfractionated heparin starting before surgery and continuing for at least 7–10 d
Postoperative venous thromboembolism prophylaxis	American College of Chest Physicians[89]	2012	Risk-stratified recommendations based on patient- and procedural-specific risk factors Gynecologic surgery for malignant indications: extended-duration pharmacologic prophylaxis (4 wk) with low molecular weight heparin is recommended over limited-duration prophylaxis
	American Congress of Obstetricians and Gynecologists[90]	2007	Risk-stratified recommendations based on patient- and procedural-specific risk factors Highest risk level: consider continuing pharmacologic prophylaxis for 2–4 wk after discharge
	ERAS Society[86]	2016	Patients should receive both mechanical and pharmacologic prophylaxis; extended prophylaxis (28 d) should be given to patients after laparotomy for abdominal or pelvic malignancies
	American Society of Clinical Oncology[91]	2015	Patients undergoing major cancer surgery should receive low molecular weight or unfractionated heparin starting before surgery and continuing for at least 7–10 d
	European Society for Medical Oncology[92]	2011	Cancer patients undergoing elective major abdominal or pelvic surgery should receive in-hospital and postdischarge prophylaxis with low molecular weight heparin for up to 1 mo after surgery
	National Institute for Health and Care Excellence[93]	2010	At-risk patients should receive both mechanical and pharmacologic prophylaxis until patient no longer has significantly reduced mobility (general 5–7 d); extend pharmacological prophylaxis to 28 d postoperatively for patients who have had major cancer surgery in abdomen or pelvis

5-HT3, 5-hydroxytryptamine 3; *ACS*, American College of Surgeons; *ASER*, American Society of Enhanced Recovery; *ASHP*, Americal Society of Health-System Pharmacists; *COX*, cyclooxygenase; *D5LR*, 5% dextrose in lactated ringers; *D5NS*, 5% dextrose in normal saline; *ERAS*, Enhanced Recovery after Surgery; *HICPAC*, Healthcare Infection Control Practices Advisory Committee; *IDSA*, Infectious Diseases Society of America; *IV*, intravenous; *n/a*, not applicable; *NS*, normal saline; *PO*, per os; *SHEA*, Society for Healthcare Epidemiology of America; *SIS*, Surgical Infection Society; *SSI*, Surgical Site Infection.

[a] Guidelines from ASER are currently based off of only 1 enhanced recovery protocol presented in ASER website specific to gynecologic oncology.

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both benign and malignant gynecologic surgery that compared early oral intake to traditional postoperative feeding. In 1 SR that included 7 RCT of 947 oncology patients and 1 observational study, early feeding (as early as 4 hours after surgery) shortened time to flatus and length of stay.[38] The second SR included a different collection of 7 RCT and reported that early oral feeding decreased length of stay in patients undergoing surgery for gynecologic malignancies.[39] Importantly, although early oral feeding was occasionally associated with more nausea in these studies, it did not increase the frequency of vomiting. In the Cochrane MA, the authors concluded that early feeding did not increase gastrointestinal or other complications, was associated with earlier return of bowel function, lower infectious complications, earlier hospital discharge, and improved patient satisfaction following major gynecologic surgery.[40]

Summary: Evidence strongly suggests that early oral feeding is safe, well tolerated, and results in earlier return of bowel function and shorter hospital length of

TABLE 4
Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery protocol in gynecologic surgery

Preoperative	
Patient education	• Routine preoperative patient education is recommended Level of evidence: low
Immediate preoperative	
Preoperative diet	
a. Reduce fasting	• May ingest solids until 6 h prior to induction and clear liquids until 2 h prior to induction Level of evidence: high
b. Carbohydrate loading	• Routine carbohydrate loading is recommended • May ingest 2–3 h (up to 5 h) before induction • Options to be considered (~50 g of carbohydrate): 500-mL apple juice or cranberry cocktail; 200 mL Ensure Clear (Abbot Laboratories, Chicago, IL); 355mL Clearfast (ClearFast Laboratories, Atlanta, GA) Level of evidence: moderate
Bowel preparation	• Minimally invasive gynecologic surgery: no bowel preparation • Major abdominal gynecologic surgery (with or without expected bowel surgery): no bowel preparation is acceptable within enhanced recovery pathways protocol with SSI reduction bundle; if bowel preparation is desired, choice between mechanical bowel preparation plus oral antibiotics or oral antibiotics alone Level of evidence: moderate
Skin preparation	• 4% Chlorhexidine gluconate shower night before and morning of surgery • Chlorhexidine cloths morning of admission Level of evidence: high
Multimodal preanesthesia medication	
a. Analgesia	• Combination of acetaminophen, COX-2 inhibitors (ie, celecoxib), and/or gabapentinoids (ie, gabapentin) Level of evidence: high
b. Postoperative nausea and vomiting prophylaxis	• Choice between scopolamine, midazolam, and/or gabapentinoids Level of evidence: high
Prokinetics	• Alvimopan 12 mg PO once 2 h before induction (only if large bowel resection is anticipated) Level of evidence: moderate
Intraoperative	
Antibiotic prophylaxis	• Prophylactic antibiotics should be given within 1 h prior to incision per CDC, ACOG, and ASHP/IDSA/SHEA guidelines[94–96] • Redose prophylactic antibiotics for long procedures (ie, cefazolin within 3–4 h after incision) Level of evidence: high
Skin preparation	• 2% Chlorhexidine gluconate and 70% isopropyl alcohol solution for entire broader incisional area Level of evidence: high
Blood transfusion	• Judicious use of blood transfusion during surgery for hemoglobin of 6–10 g/dL is recommended, taking clinical context into account Level of evidence: high
Fluids/goal-directed fluid therapy	• Goal to maintain intraoperative euvolemia • Decrease crystalloid and increase colloid administration as needed • Use goal-directed fluid therapy when available Level of evidence: high

Kalogera. Enhanced recovery and gynecologic surgery. Am J Obstet Gynecol 2018. *(continued)*

TABLE 4
Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery protocol in gynecologic surgery *(continued)*

Normothermia	• Maintain intraoperative normothermia Level of evidence: high
Pain management — liposomal bupivacaine	• Wound infiltration with liposomal bupivacaine at time of incision closure in extensive laparotomy cases Level of evidence: moderate
Minimize drains	
a. No routine nasogastric intubation	• If nasogastric tube is used intraoperatively, remove at time of extubation Level of evidence: high
b. No routine peritoneal drains	• Consider only when high risk of postoperative pelvic collections or after low anterior resection with anastomosis within 6 cm from anal verge and no concurrent prophylactic bowel diversion Level of evidence: moderate
Standard intraoperative anesthesia pathway	• Use of standardized intraoperative anesthesia pathway is recommended Level of evidence: n/a
Postoperative nausea and vomiting prophylaxis	• Use combination of following classes of antiemetics: 5-HT3 receptor antagonists (ie, ondansetron), corticosteroids (ie, dexamethasone), butyrophenones (ie, droperidol and haloperidol), antihistamines, anticholinergics (eg, transdermal scopolamine), and neurokinin-1 receptor antagonists Level of evidence: moderate
Postoperative	
Early mobilization	• Out of bed (walks and sitting in chair) for at least 1 time night of surgery (total ~2 h) and ≥4 times/d after surgery until discharge (total ~6–8 h) • Up in chair for all meals Level of evidence: moderate
Early alimentation	• Encourage oral intake as early as 4 h following surgery and advance as tolerated per patient • Focus on encouraging intake of oral fluids, especially night of surgery Level of evidence: high

Early urinary bladder catheter removal	• Urinary catheter should be removed:
	  • Immediately after minimally invasive gynecologic surgery
	  • Within 6 h if not immediately after uncomplicated abdominal hysterectomy
	  • By 8:00 AM morning after surgery after debulking surgery for gynecologic malignancies in absence of specific indications for prolonged urinary catheter use (ie, partial bladder resection)
	Level of evidence: low

Early IV fluid discontinuation	• IV maintenance fluids should be discontinued within 12–24 h following surgery, or earlier if adequate oral intake has been achieved Level of evidence: low

Kalogera. Enhanced recovery and gynecologic surgery. Am J Obstet Gynecol 2018. *(continued)*

stay. Oral intake should be initiated as early as 4 hours following gynecologic surgery with or without bowel resection.

Level of evidence: high

Early urinary bladder catheter removal. Rationale: Prolonged urinary bladder catheter use may result in higher incidence of catheter-associated urinary tract infections, prolonged immobilization, and delayed postoperative recovery.

Evidence: We identified 1 MA of 10 RCT comparing immediate (in the operating room at the end of the case) vs delayed urinary catheter removal (defined as removal ≥24 hours) following uncomplicated benign hysterectomy.[41] Immediate urinary catheter removal lowered rates of asymptomatic bacteriuria and symptomatic urinary tract infection but increased risk for recatheterization (relative risk, 3.32; 95% confidence interval [CI], 1.48–7.46). Delayed urinary catheter

TABLE 4
Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery protocol in gynecologic surgery *(continued)*

Prevention of ileus	

a. Laxatives	• Use of postoperative laxatives is recommended
	  • Options include senna with docusate, docusate, magnesium oxide, magnesium hydroxide, bisacodyl
	  • If rectosigmoid resection has been performed avoid suppositories
	Level of evidence: low

b. Chewing gum	• Chewing gum is recommended (3 times daily, for at least 30 min, starting few hours after surgery until return of bowel function) Level of evidence: high
c. Alvimopan	• Alvimopan 12 mg PO twice daily, until bowel movement or maximum of 7—10 d (if bowel resection performed) Level of evidence: moderate

Standard postoperative multimodal analgesic regimen	• Use of multimodal postoperative analgesic regimen is recommended
	  • Scheduled acetaminophen and nonsteroidal anti-inflammatory drugs
	  • May consider gabapentinoids and tramadol as needed
	  • Opioid medications should be avoided when possible except in patients with chronic opioid dependence
	Level of evidence: high

Additional evidence-based perioperative interventions	
SSI bundle	• Incorporation of surgical site intervention bundles is recommended; in addition to interventions included above, important elements consist of: • Sterile closing tray, staff regloving for fascia and skin closure, removal of incision dressing within 24—48 h after surgery, daily showering with 4% chlorhexidine gluconate, and enhanced attention and early follow-up by providers or nurses Level of evidence: high
Glucose management	• Goal to control perioperative blood glucose between 110—180 mg/dL Level of evidence: high
Preoperative venous thromboembolism prophylaxis	• Minimally invasive surgery or surgery for benign gynecologic conditions: intermittent pneumatic compression alone as preoperative prophylaxis is sufficient • Gynecologic surgery for malignant indications: preoperative pharmacologic prophylaxis with low molecular weight or unfractionated heparin in addition to intermittent pneumatic compression is recommended Level of evidence: moderate

Postoperative venous thromboembolism prophylaxis	• Adherence to established societal guidelines such as American College of Chest Physicians and American Congress of Obstetricians and Gynecologists (Table 3) is recommended to assess level of risk for venous thromboembolism and appropriate prophylaxis strategy
	  • Inpatient prophylaxis: all gynecologic surgical patients should receive mechanical prophylaxis; pharmacologic prophylaxis should be considered based on level of risk for thrombosis; gynecologic oncology surgical patients should receive mechanical and/or pharmacologic prophylaxis
	  • Postdischarge prophylaxis: extended pharmacologic prophylaxis for 4 wk is recommended for gynecologic oncology surgical patients
	Level of evidence: high

This comprehensive Agency for Healthcare Research and Quality protocol for Improving Surgical Care and Recovery (ISCR) protocol for Gynecologic Surgery includes elements reviewed in this article as well as relevant elements reviewed in Agency for Healthcare Research and Quality review for ISCR for colorectal surgery as well as anesthesia.

ACOG, American Congress of Obstetricians and Gynecologists; *CDC*, Centers for Disease Control and Prevention; *IV*, intravenous; *SSI*, Surgical Site Infection.

Kalogera. Enhanced recovery and gynecologic surgery. Am J Obstet Gynecol 2018.

removal was associated with longer time to first ambulation and no difference in the length of hospital stay. Importantly, a recent RCT compared outcomes following immediate, intermediate (after 6 hours), or delayed (after 24 hours) urinary catheter removal following uncomplicated total abdominal hysterectomy.[42] They observed that immediate catheter removal increased rates of urinary retention requiring recatheterization compared to intermediate and delayed removal (16.4% vs 2.5% vs 0%, $P < .001$). In agreement with prior findings, delayed catheter removal increased rates of urinary tract infection, delayed mobilization and, in this study, prolonged hospital stay. A Cochrane MA including RCT across a range of surgical specialties including gynecologic surgery suggested that there may be a benefit in midnight (intermediate) urinary catheter removal over early morning (delayed) removal.[43]

Summary: The evidence suggests that urinary catheters should be used for <24 hours following gynecologic surgery to minimize the risk of urinary tract infection. Removal at 6 hours appears to optimally balance low rates of both urinary infection and retention, especially for uncomplicated gynecologic cases. Removal of the urinary catheter the morning after surgery may be a more suitable option for complicated cases such as urogynecologic or gynecologic oncology procedures. Importantly, urine output and the potential for fall risk should be considered when removing catheters <24 hours.

Level of evidence: moderate

Prevention of ileus.

a. *Laxatives*

Rationale: Early laxative use may accelerate return of bowel function.

Evidence: We found 3 RCT and 3 prospective nonrandomized trials investigating the use of various laxatives across the spectrum of gynecologic surgery.

In a RCT of patients undergoing abdominal hysterectomy for benign indications within a previously established fast-track pathway, patients were randomized to either receive a maximum of 3 doses of magnesium oxide with disodium phosphate (at 6 hours after surgery, morning and evening of postoperative day 1) or placebo.[44] There was a significantly shorter time to first bowel movement with no differences in postoperative complications, postoperative nausea and vomiting, or need for antiemetics, and a nonstatistically significant reduction in hospital length of stay.

Two RCT focused on patients undergoing urogynecologic procedures. Patients undergoing pelvic reconstructive surgery were randomized to receive either senna with docusate starting the night of postoperative day 1 or placebo with all patients being expected to take magnesium citrate if they did not have a bowel movement on postoperative day 4.[45] There was 1 day earlier return of bowel function (4.05 vs 3.0 days, $P < .002$) and decrease in the need to use magnesium citrate to initiate a bowel movement (43.6% vs 7%, $P < .001$). In a second RCT, the addition of polyethylene glycol 3350 to a bowel regimen consisting of docusate sodium twice daily starting on postoperative day 1 following surgery for pelvic organ prolapse or stress urinary incontinence did not reduce the time to first bowel movement with median time being <3 days for both groups.[46]

In 1 prospective trial, 20 consecutive patients undergoing radical hysterectomy with pelvic and paraaortic lymphadenectomy received magnesium hydroxide and bisacodyl suppositories.[47] When compared to a cohort of patients who did not receive postoperative bowel stimulation, patients treated with laxatives had an earlier return of bowel function and a 50% reduction of length of stay (8 vs 4.3 days, $P = .001$) with no change in complication rates. The same investigators subsequently compared the combination of Phospho-Soda (Fleet, Lynchburg, VA) along with early oral feeding to the prior bowel regimen and observed a further reduction in length of stay (4.3−3.5 days, $P < .001$) with no intestinal complications.[48]

No studies specifically focused on bowel regimens after gynecologic surgeries involving bowel resection. In a nonrandomized trial of 707 patients undergoing minimally invasive and open gynecologic surgery, patients were fed immediately postoperatively along with bowel stimulation with magnesium hydroxide (Milk of Magnesia).[49] The ileus rate was <1% with no increase in postoperative complications or adverse events. Similar to the conclusions of this study, there is no evidence of safety concerns with the use of laxatives in the CRS literature, including colon-stimulating laxatives such as bisacodyl.[50,51]

Summary: Standardized use of postoperative laxatives (eg, senna with docusate, docusate, magnesium oxide or magnesium hydroxide, and bisacodyl) is recommended in gynecologic surgery to accelerate return of bowel function.

Level of evidence: low

Chewing gum. Rationale: Chewing gum postoperatively may decrease the incidence of ileus.

Evidence: We identified 5 RCT that studied postoperative use of chewing gum following laparotomy for gynecologic malignancies,[52] laparotomy for benign gynecologic indications,[53] a mixture of abdominal gynecologic surgeries,[54] and laparoscopic gynecologic surgery.[55,56] The perioperative chewing gum protocols most commonly involved chewing sugarless gum for 15−30 minutes at least 3 times daily starting a few hours following surgery. Use of gum in the postoperative setting was demonstrated to lead to earlier time to flatus,[52,55,56] earlier time to first bowel movement,[52,54] better tolerance of diet,[52] less nausea,[53] and decreased ileus rates.[52,53] In patients undergoing surgery for gynecologic malignancies, its use reduced mean length of stay by 1 day ($P < .05$).[52] No safety concerns were identified in any study.

Summary: Postoperative use of chewing gum is recommended as a safe and low-cost intervention to hasten return of gastrointestinal function following gynecologic surgery.

Level of evidence: high

Alvimopan. Rationale: Alvimopan, a novel peripheral mu receptor antagonist,

may prevent postoperative ileus after abdominal surgery.

Evidence: We found 1 MA studying the efficacy of alvimopan in accelerating gastrointestinal function recovery after major abdominal surgery, defined as bowel surgery or total abdominal hysterectomy,[57] and 1 RCT published after the MA focusing on the use of alvimopan in patients undergoing laparotomy for ovarian cancer (published abstract).[58]

Five RCT reporting on 2195 patients were included in the MA.[59] Oral use of 12 mg of alvimopan perioperatively with the first dose at least 2 hours before surgery, and then twice daily starting on postoperative day 1 until hospital discharge or a maximum of 7−10 days postoperatively, significantly accelerated return of bowel function, as measured by time to flatus, time to bowel movement, and time to tolerance of solid food, with no difference in adverse events compared to placebo groups. Time to discharge was shorter with a hazard ratio of 1.26 ($P <$ .001). However, only 1 of the 5 RCT was limited to patients undergoing benign total abdominal hysterectomy[60] and only 1 of the remaining 4 RCT that included both bowel surgery and hysterectomy patients analyzed these groups separately.[61] In the first RCT, perioperative use of alvimopan reduced the time to first bowel movement by 22 hours in 408 patients undergoing simple total abdominal hysterectomy.[60] The second RCT found no difference in time to gastrointestinal recovery compared to placebo irrespective of the alvimopan dose (6 or 12 mg) among the hysterectomy cohort.[61]

In a RCT of perioperative use of 12 mg of alvimopan among patients undergoing laparotomy for ovarian cancer, its use significantly shortened time to first bowel movement (1 day).[58] Although differences did not reach statistical significance, the ileus rate was 10.6% in the alvimopan group compared to 19.1% in the placebo group. Of note, 16.4% of patients in this cohort underwent bowel resection. The use of alvimopan is also supported by the evidence review conducted for the CRS pathway that concluded its use prior to and following CRS reduces postoperative ileus and length of stay.

Summary: The existing evidence suggests that while perioperative use of alvimopan may not be beneficial in benign gynecologic surgery, it may result in earlier return of bowel function and decrease in ileus rates for patients undergoing surgery for ovarian cancer. Alvimopan should be considered for patients expected to undergo bowel resection during gynecologic surgery.

Level of evidence: moderate

Early intravenous fluid discontinuation. Rationale: Administration of excess fluids may increase the risk of pulmonary, cardiac, renal, gastrointestinal, and wound complications.[62,63]

Evidence: There were no studies focusing on the isolated effect of early intravenous (IV) fluid discontinuation postoperatively in gynecologic surgery or CRS.[3] Based on the evidence review conducted for the CRS pathway and expert opinion, the final recommendation was for maintenance IV fluid to be discontinued by postoperative day 1 unless the patient has difficulty with oral intake and/or evidence of kidney injury. Of note, per standardized protocols, the maintenance rate for IV fluids is 1.2 mL/kg for adults.[64]

Although not specifically examining the effect of early IV fluid discontinuation following gynecologic surgery, a recent study investigated the impact of fluid status on surgical outcomes for patients undergoing surgery for advanced ovarian cancer.[65] The authors observed a median perioperative weight change in this population of 7.3 kg. A positive fluid status was significantly associated with unscheduled reoperation, anastomotic leak, SSI, and length of hospital stay >5 days on univariate analysis; the association between positive fluid status and SSI remained significant in the multivariate analysis.

Summary: In agreement with the CRS recommendations and based on expert opinion, maintenance IV fluids should be discontinued within 12−24 hours following surgery, especially in the setting of early oral fluid and solid intake. Urine output as low as 20 mL/h should be recognized as a normal response to perioperative stress without the need for intervention.

Level of evidence: low

Additional evidence-based perioperative interventions sentinel to ERP in gynecologic surgery

SSI bundle. Rationale: Use of care bundles, which represent a structured approach of implementing at least 3−5 evidence-based interventions, has improved patient outcomes. A perioperative surgical bundle after gynecologic surgery could reduce rates of SSI.

Evidence: We identified 3 interventional studies implementing SSI reduction bundles in patients undergoing surgery for gynecologic malignancies[13,16,66] and 1 consensus statement on SSI prevention consensus bundle after major gynecologic surgery.[17]

In 1 investigation, addition of a SSI prevention bundle to an established ERP decreased in the SSI rate from 6.0−1.1% ($P <$ .01) among patients undergoing laparotomy for advanced gynecologic malignancies, including bowel resection.[16] In another study, the 30-day SSI rate in gynecologic cancer patients undergoing colon surgery decreased from 37−12% using a SSI reduction bundle.[66] Finally, in patients undergoing surgery for ovarian cancer, implementation of a bundle in women undergoing surgery for ovarian cancer decreased SSI rate from 20−3% (33−7% among women undergoing bowel resection).[13] Although specific interventions varied between these bundles, most focused on patient education, preoperative and intraoperative prophylactic OA prophylaxis, preoperative and intraoperative skin preparation with 4% chlorhexidine gluconate, use of a sterile closing tray, regloving and regowning for fascia and skin closure, tight perioperative glycemic control, appropriate postoperative wound care including removal of incision dressing between 24−48 hours after surgery, daily showering with 4% chlorhexidine gluconate, good hand hygiene, and early follow-up by providers or nurses postdischarge.

Only 1 of these 3 studies reported on the type of vaginal preparation used (4% chlorhexidine solution).[13] Although only povidone-iodine preparations are approved for surgical preparation of the vagina, there are published reports on the off-label use of chlorhexidine gluconate with low alcohol concentration solutions.[67–69] Notably, Culligan et al[67] demonstrated in a randomized trial that chlorhexidine gluconate was more effective in decreasing the bacterial colony counts found in the operative field compared to povidone-iodine following vaginal hysterectomy for benign indications. In 2013, the American Congress of Obstetricians and Gynecologists (ACOG) published the following committee opinion on surgical preparation of the vagina: "solutions of chlorhexidine gluconate with low concentrations of alcohol (eg, 4%) are both safe and effective for off-label use as vaginal surgical preparations and may be used as an alternative to iodine-based preparations in cases of allergy or when preferred by the surgeon."[70] The Council on Patient Safety in Women's Health Care, a collaborative network convened by the ACOG, published a consensus bundle for prevention of SSI after major gynecologic surgery to help guide institutions to implement bundled interventions to decrease infection rates.[17]

Summary: SSI bundles lead to decreased rates of SSI and should be included in an evidence-based pathway for gynecologic surgery. While the efficacy of the SSI bundles has been investigated in open gynecologic surgery due to the significantly higher rates of SSI compared to minimally invasive gynecologic surgery, incorporating SSI bundles in minimally invasive gynecologic surgery should be considered given their low cost and low risk.

Level of evidence: high

Glucose management. Rationale: Approximately 2% of all hysterectomies are complicated by SSI[71] with perioperative hyperglycemia (defined as blood glucose >180–200 mg/dL) being a known risk factor.[72] Perioperative blood glucose control may decrease the risk of SSI.

Evidence: There are no MA or SR in gynecologic surgery examining the impact of blood glucose management on SSI reduction. A recent MA of 15 RCT in mostly cardiac and abdominal surgery patients compared intensive glucose management (<150 mg/dL) vs conventional glucose management (≤220 mg/dL). The intensive protocol reduced the rate of SSI (odds ratio [OR], 0.43; 95% CI, 0.29–0.64).[73] These results were consistent in patients with and without a diagnosis of diabetes. Two observational studies of merit were identified within the gynecologic oncology literature. The first, a retrospective study of 372 patients, showed a 35% reduction in SSI (OR, 0.5) for hyperglycemic patients managed with an insulin infusion compared to those who received subcutaneous insulin.[74] In the second study of 462 patients, a multidisciplinary referral to discharge perioperative glycemic control initiative (including rigorous preoperative/intraoperative/postoperative glucose monitoring with a target blood glucose ≤180 mg/dL) led to a 55% reduction in SSI.[75]

Summary: Perioperative blood glucose control with a goal of ≤180 mg/dL is recommended to reduce the risk of SSI.

Level of evidence: high

Preoperative venous thromboembolism prophylaxis. Rationale: Venous thromboembolism (VTE) may occur intraoperatively; preoperative VTE prophylaxis (vs postoperative alone) may reduce VTE events in the perioperative period.

Evidence: Two SR including multiple RCT have demonstrated that preoperative and perioperative VTE prophylaxis using intermittent pneumatic compression, alone or in combination with low molecular weight or unfractionated heparin, is efficacious with no significant increase in adverse events.[76,77] VTE events are rare (<1%) in patients undergoing minimally invasive surgery for any indication or surgery for benign gynecologic conditions, and intermittent pneumatic compression alone as preoperative prophylaxis is sufficient.[77,78] In contrast, patients with gynecologic malignancies have a postoperative VTE rate as high as 35% and may benefit from combined mechanical venous thromboembolism prophylaxis and chemoprophylaxis. Observational and case-control studies have specifically evaluated the effect of adding preoperative chemoprophylaxis to intermittent pneumatic compression in patients undergoing gynecologic surgery for malignant indications, confirming a reduction in VTE events ($P = .04$), fewer deep vein thrombosis-attributable deaths ($P < .001$), and no increase in adverse bleeding events.[79,80]

Summary: Evidence from RCT and the low overall rate of VTE supports the use of preoperative intermittent pneumatic compression alone for patients undergoing minimally invasive surgery for any indication or laparotomy for benign disease. Weak evidence from observational studies supports the addition of preoperative pharmacologic prophylaxis for patients undergoing laparotomy for gynecologic malignancies, particularly considering the high rate of VTE in this population. This practice is supported by multiple societal guidelines.

Level of evidence: moderate

Postoperative VTE prophylaxis. Rationale: Timely administration of VTE chemoprophylaxis is thought to reduce VTE events. Extended VTE chemoprophylaxis may be beneficial for patients with gynecologic malignancies.

Evidence: We identified 1 SR of 14 RCT evaluating the use of mechanical and/or pharmacologic prophylaxis in gynecologic surgery for both benign and malignant indications; 1 SR of 11 RCT specifically focused of patients with gynecologic malignancies and 1 MA of 7 RCT (overlapping with 4 of the RCT from the 2011 SR) evaluated the use of mechanical prophylaxis (intermittent pneumatic compression) in gynecologic surgery.[76,77,81] For benign gynecologic surgery, the SR was inconclusive on whether there was a benefit to the use of chemoprophylaxis when compared to usual care (early ambulation) alone, however, there was no increase in adverse bleeding events.[77] For patients

with gynecologic malignancies, the 2 SR concluded that the use of mechanical or pharmacologic prophylaxis was superior to usual care, but was inconclusive as to whether there was a benefit to pharmacologic compared to mechanical prophylaxis.[77,81] The 1 SR also identified high-risk patients to be those aged ≥60 years, with a history of VTE or cancer, or with a hypercoagulable state.[77] The recommendation was that these high-risk patients warrant the use of pharmacologic prophylaxis, either in addition to or instead of mechanical prophylaxis. The MA concluded that the use of mechanical prophylaxis (5 days or until full ambulation/discharge) was superior to usual care (relative risk, 0.33; 95% CI, 0.16−0.66) and was effective in reducing VTE complications in gynecologic surgery; recommendations were inconclusive on the topic of pharmacologic compared to mechanical prophylaxis.[76]

Examining at the role of extended chemoprophylaxis in the gynecologic oncology population, we identified 1 Cochrane SR and 2 pre-post interventional studies addressing this topic. The Cochrane SR evaluated RCT of prolonged VTE chemoprophylaxis with low molecular weight heparin for 4 weeks after surgery compared to VTE chemoprophylaxis during the admission period only for patients undergoing major abdominal and pelvic surgery for malignancy.[82] The incidence of clinical and symptomatic VTE at 30 days after surgery was significantly lower in those receiving prolonged VTE chemoprophylaxis (OR, 0.41; 95% CI, 0.26−0.63; $P < .001$) as well as the incidence of symptomatic VTE alone (OR, 0.22; 95% CI, 0.06−0.80; $P = .02$).[82] In a pre-post study in women undergoing complex gynecologic surgery specifically, the expanded use of VTE chemoprophylaxis beginning preoperatively and continued for 14 days postoperatively led to a decrease in VTE events in a time-to-event analysis ($P = .049$).[79] In a second pre-post study in women undergoing laparotomy for a gynecologic malignancy, a protocol was implemented with VTE chemoprophylaxis beginning within 24 hours of surgery and continued for 28 days. Although they reported a significant reduction in the incidence of VTE at 30 days ($P = .040$), they failed to identify a difference in VTE at 90 days postsurgery ($P = .619$), with a change in median time between surgery and VTE diagnosis from 12 days pre-intervention to 57 days post-intervention.[83] It is unclear whether this finding is due to delayed VTE development with the use of extended duration VTE chemoprophylaxis or if other factors such as the initiation of chemotherapy contributed.

Summary: Evidence from RCT supports the use of mechanical prophylaxis for the duration of hospitalization in all gynecologic surgical patients and the use of mechanical and/or pharmacologic prophylaxis for gynecologic oncology surgical patients. Extended VTE chemoprophylaxis for 4 weeks following surgery is recommended in gynecologic oncology patients, which is supported by multiple societal guidelines. However, the long-term benefit of this practice requires further investigation.

Level of evidence: high

Comment

A growing body of literature demonstrates that ERP are safe and effective in accelerating postoperative recovery following gynecologic surgery. Dissemination, however, is still lagging in the United States with a marked lack of uniformity among implemented pathways. This study is published in conjunction with the AHRQ Safety Program for ISCR reviews in CRS and anesthesiology and examines the most current evidence supporting 16 individual interventions sentinel to the ERP in gynecologic surgery. Relevant elements from the CRS and anesthesiology review are also presented (Table 4). These recommendations are in agreement with guidelines endorsed by the Enhanced Recovery after Surgery Society and the American Society of Enhanced Recovery.[84−86] This review and pathway for gynecologic surgery is intended to serve as the most up-to-date frame of evidence-based perioperative care following gynecologic surgery. Successful implementation requires a multidisciplinary effort from surgeons, anesthesiologists, nursing, pharmacists, physicians in training, advanced medical providers, and clinical assistants, while keeping the patient informed and actively engaged in their recovery. Hospitals participating in the AHRQ Safety Program for ISCR will be supported expeditiously and sustainably translating this evidence base into practice over the next few years with the goal of improving surgical outcomes throughout the United States. ■

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SUPPLEMENTAL TABLE
Search terms

Preoperative	
Patient education	"patient education" "preoperative education" "preoperative education"
Immediate preoperative	
Bowel preparation	"bowel preparation" "oral antibiotic bowel preparation"
Intraoperative	
Minimize drains	
a. No routine nasogastric intubation	"drain" "nasogastric"
b. No routine peritoneal drains	"suction drain" "peritoneal drain"
Postoperative	
Early mobilization	"early mobilization" "early ambulation" "ambulation" "mobilization"
Early alimentation	"early feeding"
Early urinary bladder catheter removal	"Foley removal" "urinary catheter removal" "catheter-associated urinary tract infection" "urinary tract infection"
Prevention of ileus	
a. Laxatives	"laxative"
b. Chewing gum	"gum" "gum chewing"
c. Alvimopan	"alvimopan"
Early IV fluid discontinuation	"IV fluid discontinuation" "intravenous fluid discontinuation" "fluid therapy" "fluid management"
Additional evidence-based perioperative interventions	
Surgical site infection bundle	"surgical site infection" "bundle" "surgical site infection bundle"
Glucose management	"glucose" "glucose management"
Preoperative venous thromboembolism prophylaxis	"preoperative" "venous thromboembolism prophylaxis" "VTE prophylaxis" "thromboprophylaxis"
Postoperative venous thromboembolism prophylaxis	"preoperative" "venous thromboembolism prophylaxis" "VTE prophylaxis" "thromboprophylaxis"
General search terms: "gynecologic surgery" "fast track" "enhanced recovery" "meta-analysis" "systematic review" "randomized controlled trial" "randomized trial"	

Kalogera. Enhanced recovery and gynecologic surgery. Am J Obstet Gynecol 2018.