Surgical Technical Evidence Review for Acute Cholecystectomy Conducted for the AHRQ Safety Program for Improving Surgical Care and Recovery

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Enhanced recovery pathways (ERPs) bundle evidence-based perioperative care processes that aim to decrease the physiologic stress response to surgical procedures and maintain postoperative physiologic function. Use of ERPs has reduced complication after operation and decreased length of hospital stay across multiple surgical procedure areas.[1-3]

The AHRQ Safety Program for Improving Surgical Care and Recovery (ISCR) was initiated in September 2016 through collaboration among the AHRQ (funder), the American College of Surgeons, and the Johns Hopkins Medicine Armstrong Institute for Patient Safety and Quality. This 5-year program aims to provide tools and support to participating hospitals to accelerate adoption of ERPs in select surgical areas. Materials to support implementation of the ISCR program include prototype pathways with strategies for local adaptation, patient education, a data registry for benchmarking process and outcomes measures, and other components. The first cohort was focused on colorectal surgery and details of the colorectal pathway have been published previously.[4] With subsequent cohorts, the program has added additional services, including orthopaedics and gynecology.

The benefits of ERPs have been well-documented in various elective procedures. As hospitals have gained experience with ERP, the basic principles have become the standard of care for broader groups of elective surgery patients. However, applying these principles in complementary emergency general surgery is less defined, but might be an opportunity to further improve surgical care. In the US, approximately 300,000 cholecystectomies are performed annually.[5] Use of some ERP principles in elective laparoscopic cholecystectomy (LC) has improved surgical quality and patient care, but little is described with regard to urgent or emergent cholecystectomy.[6-8] Although there are differences in the preoperative presentation of elective vs nonelective laparoscopic cholecystectomies, postoperative management can be similar and ERPs can be considered for nonelective LC.

The objective of this article was to provide a comprehensive review of the evidence to support ERP processes for LC for acute cholecystitis in a nonelective setting. The surgical components for acute appendicitis,[9] other emergency general surgery procedures, and anesthesiology components were reviewed in parallel and will be reported separately.

METHODS

A review protocol was developed with input from stakeholders. The components of this emergency cholecystectomy ERP were identified through an iterative process that involved the review of existing ERPs for other

Disclosure Information: Nothing to disclose.

Support for this study: This study was supported by the AHRQ, US Department of Health and Human Services (contract number HHSP233201500020I). The study authors received salary (Drs Hu, Liu, Ko, and Wick) or a consultant fee (Drs Gibbons, Reinke, and Peden) from the AHRQ for the completion of this review.

Disclaimer: The AHRQ specified evidence review to identify essentials of enhanced recovery pathways as part of the contract, and reviewed and provided comments on a draft of this manuscript. The findings and opinions in this article are those of the authors and do not reflect the official position of AHRQ or the US Department of Health and Human Services.

Received September 2, 2019; Revised November 11, 2019; Accepted November 11, 2019.

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https://doi.org/10.1016/j.jamcollsurg.2019.11.014
ISSN 1072-7515/19

Abbreviations and Acronyms

ERP = enhanced recovery pathway
ISCR = AHRQ Safety Program for Improving Surgical Care and Recovery
LC = laparoscopic cholecystectomy
LOS = length of stay
MA = meta-analysis
OR = odds ratio
RAC = robotic-assisted cholecystectomy
RCT = randomized controlled trial
RR = relative risk
SR = systematic review
VAS = visual analog scale
VTE = venous thromboembolism

relevant procedures, such as colorectal, and elicited input from national and international leaders in enhanced recovery and emergency general surgery (Table 1). We derived many of the pathway components that formed the basis of this review from existing ERPs, and noted whether the evidence came from cholecystectomy or a related procedure. The emergency cholecystectomy ERP spans the continuum of care from preoperative to discharge and includes questions such as the timing of urgent cholecystectomy. Individual literature reviews for each pathway component were performed in PubMed for English-language articles published before July 2018 (Fig. 1; eTable 1). Additional citations were identified through reference mining of included studies and by technical experts. Importantly, as the ISCR work has evolved through previous evidence reviews for other procedures (eg colorectal and acute appendectomy[4,9]), we have identified core components (principles and processes) of an ERP that hospitals should consider for all surgical patients. These core components represent an opportunity for improvement in urgent and emergent cases, as much of the ERP work at hospitals have so far excluded this population.

The American Association for the Surgery of Trauma developed a grading scale that is helpful with risk stratification and is commonly used to classify severity of individual cases (Table 2). Our classification of uncomplicated acute cholecystitis aligns with American Association for the Surgery of Trauma grade I, and more complicated cholecystitis aligns with American Association for the Surgery of Trauma grade II to V. Unless otherwise specified, the processes of care described here apply to uncomplicated acute cholecystitis.

We used the hierarchy of evidence and preferentially included systematic reviews (SR) with or without a meta-analysis (MA), randomized controlled trials (RCT), observational cohort design if the study was not in an SR/MA, and clinical guidelines from professional societies or the US Department of Health and Human Services, where applicable. We excluded editorials, case reports, and articles reporting interventions or outcomes that were not applicable to US hospitals. Given the limited body of literature on ERP use in LC for acute cholecystectomy, some of the data summarized were based on observational data instead of RCTs. We did summarize the quality of evidence in our review. The results are presented in narrative format.

RESULTS

We identified 13 components for cholecystectomy for review beyond basic best practices in perioperative care (Table 1). The processes are organized by perioperative phase, and each process includes the rationale, evidence review, summary of guidelines (if available), and a summary of the evidence with our recommendation for or against inclusion in the ERP. Table 3 summarizes the evidence for each component, the strength and consistency of the evidence, and the level of guideline support. Table 4 summarizes the guideline recommendations for each component and the corresponding strength of evidence.

Preoperative management

Patient education and counseling

Rationale. Preoperative education is theorized to set expectations for the patient and family members about the operation, postoperative course, anticipated recovery time to return to baseline function, and possible complications. This helps the patient and family understand these expectations and play an active role in recovery.

Evidence. We identified 1 prospective study that examined patient education for urgent cholecystectomy and 1 Cochrane SR evaluated preoperative education for patients undergoing elective LC. We think it is reasonable that the evidence for patient education in elective cholecystectomy is applicable in urgent/emergent cholecystectomy, as the hospital course and recovery are similar.

The prospective study by King and colleagues[10] studied patients undergoing urgent cholecystectomy or appendectomy and identified 4 key areas lacking in education, including alternatives to operation, return to work, driving, and lifting weights. Researchers developed written education materials and, after implementation, 12 of 14 patients (86%) reported that the education provided valuable information. In addition, information retention significantly improved for returning to driving (2% pre-patient education to 57% post;

Table 1. Improving Surgical Care and Recovery: Cholecystectomy Components Evaluated—Surgery

Enhanced recovery pathway component
Preoperative management
Education and counseling
Preoperative antibiotics
Venous thromboembolism prophylaxis
Early laparoscopic cholecystectomy within 7 d of diagnosis
Avoid type and screen/cross before the operating room
Intraoperative management
Surgical technique
Avoid intra-abdominal drain placement
Avoid urinary catheter placement
Intraoperative skin antisepsis
Postoperative management
Same-day discharge for uncomplicated cholecystitis
Early oral alimentation
Restrictive IV fluids with early discontinuation
Minimizing routine labs

$p < 0.05$) and for lifting weights (4% pre to 36% post; $p < 0.05$).

The Cochrane SR (4 RCTs, n = 431) compared deliberate preoperative patient education with the standard of care.[11] Patient satisfaction was higher in the preoperative education group (standardized mean difference 0.34; 95% CI, 0.04 to 0.65). No group differences were found in mortality, pain, or patient knowledge; no harms were found from performing the education.

Summary and recommendations. There was limited evidence to support patient education in urgent cholecystectomy and some data that suggested a benefit for elective cholecystectomy. However, patient education did increase patient satisfaction and is still recommended because patient and family engagement is beneficial and education is one strategy to promote engagement.

Preoperative antibiotics

Rationale. The use of prophylactic antibiotic administration can reduce the incidence of infectious complication after LC.

Evidence. We identified 2 professional society guidelines that address prophylactic antibiotic use in nonelective LC for acute cholecystitis. Given that the guidelines were updated recently and have been broadly adopted, we summarized the guideline recommendations.

The American Society of Health-System Pharmacists, Infectious Diseases Society of America, Surgical Infection Society, and Society for Healthcare Epidemiology of America released joint guidelines for antimicrobial prophylaxis in operations. Antimicrobial prophylaxis is recommended in patients undergoing nonelective LC for acute cholecystitis.[12] In their guideline evidence review (2013), they cite a large multicenter RCT (1998, n = 4,477) that found decreased rate of infectious complication (0.6% and 0.8% with prophylaxis vs 3.3% without prophylaxis) and decreased rate of surgical site infection (0.1% and 0.2% with prophylaxis vs 1.6% without prophylaxis). Their recommendations stress that antibiotic selection should be guided by local susceptibility patterns.

The Tokyo Guidelines (2018) recommend that antibiotics should only be administered at the time of incision and redosed intraoperatively, if necessary, based on half-life of antibiotic and operative duration in the average nonelective LC patient following source control with surgical management.[13] Antibiotics should not be continued after the operation. The guidelines cite 2 RCTs that evaluated for noninferiority with regard to postoperative antibiotic administration and were unable to prove noninferiority (risk difference 0.01; 95% CI, −0.04 to 0.06); however, they found significant risk associated with extended antibiotic therapy. Therefore, the guidelines recommend not continuing antibiotics after the conclusion of the operation. These guidelines also stressed the importance of considering local susceptibility patterns when selecting an antibiotic.

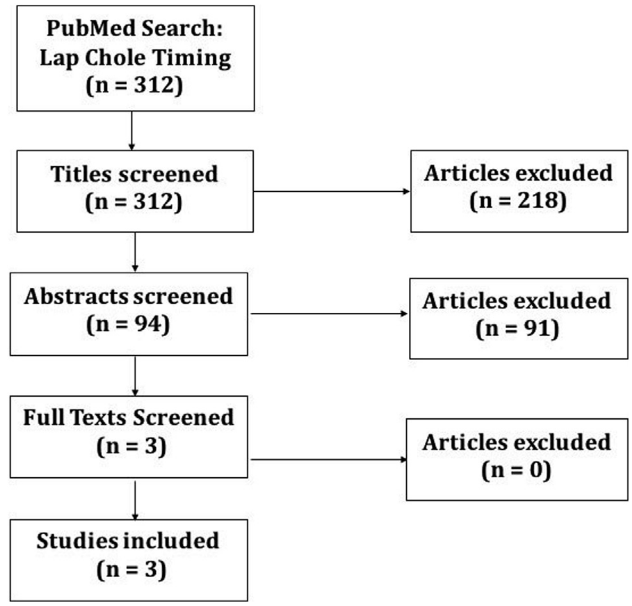

Figure 1. Visual representation of the search methodology. This summarizes the flow of studies for the evidence review on timing of laparoscopic cholecystitis (early laparoscopic cholecystectomy [lap chole] within 7 days of diagnosis). This same flow was used for all 13 components evaluated in this evidence review.

Table 2. American Association for the Surgery of Trauma Grading Scale for the Severity of Cholecystitis

AAST grade	Description	Clinical criteria	Imaging criteria	Operative criteria	Pathologic criteria
I	Acute cholecystitis	RUQ or epigastric pain; Murphy's sign; leukocytosis	Wall thickening; distention; gallstones or sludge; pericholecystic fluid; nonvisualization of GB on hepatobiliary iminodiacetic acid HIDA scan	Inflammatory change localized to GB; wall thickening; distention; gallstones	Acute inflammatory change in the GB wall without necrosis or pus
II	GB empyema or gangrenous cholecystitis or emphysematous cholecystitis	RUQ or epigastric pain; Murphy's sign; leukocytosis	Above, plus air in GB lumen, wall or in the biliary tree; focal mucosal defect without frank perforation	Distended GB with pus or hydrops; necrosis or gangrene of wall; not perforated	Above, plus pus in the GB lumen; necrosis of GB wall; intramural abscess; epithelial sloughing; no perforation
III	GB perforation with local contamination	Localized peritonitis in RUQ	HIDA with focal transmural defect, extraluminal fluid collection or radiotracer but limited to RUQ	Perforated GB wall (non-iatrogenic) with bile outside the GB but limited to RUQ	Necrosis with perforation of the GB wall (non-iatrogenic)
IV	GB perforation with pericholecystic abscess or gastrointestinal fistula	Localized peritonitis at multiple locations; abdominal distention with symptoms of bowel obstruction	Abscess in RUQ outside GB; bilio-enteric fistula; gallstone ileus	Pericholecystic abscess; bilio-enteric fistula; gallstone ileus	Necrosis with perforation of the GB wall (non-iatrogenic)
V	GB perforation with generalized peritonitis	Above, with generalized peritonitis	Free intraperitoneal bile	Above, plus generalized peritonitis	Necrosis with perforation of the GB wall (non-iatrogenic)

AAST, American Association for the Surgery of Trauma; GB, gallbladder; HIDA, hepatobiliary iminodiacetic acid; RUQ, right upper quadrant.

Summary and recommendations. All patients undergoing nonelective LC for acute cholecystitis should receive prophylactic antibiotics before the procedure. The type of antibiotic prophylaxis prescribed should be based on local susceptibility patterns. Additionally, evidence suggests that continuation of prophylactic antibiotics postoperatively does not reduce infectious complication and is unnecessary.

Venous thromboembolism prophylaxis

Rationale. The rate of venous thromboembolism (VTE) after cholecystectomy is low and the benefit of chemoprophylaxis needs to be weighed against the risk of bleeding associated with chemoprophylaxis.

Evidence. We identified 1 SR/MA and 1 RCT that met inclusion criteria. We believed that the evidence for VTE chemoprophylaxis use in elective cholecystectomy was still applicable in urgent/emergent cholecystectomy.

The SR by Rondelli and colleagues[14] (15 studies) found a lower incidence of VTE in patients after laparoscopic compared with open cholecystectomy (odds ratio [OR] 0.47; 95% CI, 0.40 to 0.56) with an overall incidence of symptomatic VTE appearing in 9 of 1,672 patients (0.6%). They were unable to detect any significant reduction in VTE in patients who received VTE chemoprophylaxis after LC (OR 0.86; 95% CI, 0.12 to 5.82), given the low incidence rate of VTE events in the cohort. In those receiving VTE prophylaxis, the incidence of bleeding reported was 0.9%.

For more complex patients with independent risk factors for VTE, such as prolonged immobility or medical comorbidity, risk-stratified VTE prophylaxis should be considered. The Society of American Gastrointestinal and Endoscopic Surgeons guidelines include a list of risk factors for VTE (Table 5) and recommend that VTE prophylaxis is not always necessary for shorter and less complex cases in patients with 0 to 1 risk factor, but is recommended in

Table 3. Summary of Reviewed Cholecystectomy Protocol Components, Outcomes, and Guideline Support

Component	Outcomes	Study	Population studied	Evidence*	Guideline support†
Preoperative management					
Education and counseling	No measurable effect	1 SR, 1 obs	Elective cholecystectomy	+	NA
Preoperative antibiotic	↓ infectious complication	2 society guidelines and 1 federal guideline	Nonelective cholecystectomy	++	√√
VTE chemoprophylaxis	Can reduce VTE in moderate to high-risk patients; consider risk-stratified approach with mechanical and/or chemical prophylaxis	1 SR/MA, 1 RCT	Elective cholecystectomy	+	√
Early LC within 7 d of diagnosis	↓ postoperative complication with no ↑ in injury	3 SR/MAs	Nonelective cholecystectomy for acute cholecystitis	++	√√
Type and screen/cross before operating room	No need for routine blood product/lab	6 obs	All cholecystectomy	+	NA
Intraoperative management					
Surgical technique	↑ operative time and cost with robotic operation compared with LC; no change in outcomes	2 SR/MAs	All cholecystectomy	+	NA
Intra-abdominal drain placement	No benefit, can ↑ morbidity and pain	4 SR/MAs	Elective cholecystectomy	++	√√
Avoid urinary catheter placement	↓ UTI	1 RCT, 1 obs	Elective cholecystectomy	++	NA
Intraoperative skin antisepsis	↓ SSI	4 SR/MAs	All cholecystectomy	++	√√
Postoperative management					
Same-day discharge	Safe in selected elective patients; unknown for nonelective	3 SR/MAs	Elective cholecystectomy	+	√
Early oral alimentation	No evidence of complication with early feeding	1 RCT, 1 obs	All cholecystectomy	++	NA
Restricted IV fluid with early discontinuation	No harm compared with liberal fluid therapy, no ↑ in complication with use	3 RCTs	Elective cholecystectomy	++	NA
Minimizing routine lab	No change in safety without	3 obs	All cholecystectomy	+	NA

↑, increase; ↓, decrease; LC, laparoscopic cholecystectomy; MA, meta-analysis; obs, observational study; NA, not applicable; RCT, randomized controlled trial; SR, systematic review; SSI, surgical site infection; UTI, urinary tract infection; VTE, venous thromboembolism.

*Evidence grading: ++, consistent evidence across studies showed benefit (intervention) or impact (risk assessment); +, evidence was either mixed, with the majority favoring benefit/impact or little evidence existed in only one direction; +/−, evidence either did not exist or existed in both directions without one direction being favored; −, evidence showed no effect of a given practice or the intervention's harm outweighed its benefit.

†Consistency with clinical guidelines: √√, all guidelines supported a given practice or the guidelines cited strong evidence of support; √, guidelines cited weak evidence or expert opinion.

Table 4. Summary of Guidelines Supporting the Reviewed Components

Component, society	Year	Recommendation/statement
Preoperative management		
Education and counseling	—	Not available
Preoperative antibiotics		
WSES	2016	In complicated cholecystitis, the antimicrobial regimens depend on presumed pathogens involved and risk factors for major resistance patterns (level III, grade B); results of microbiologic analysis are helpful to customize antibiotic treatment and ensure adequate antimicrobial coverage in patients with complicated cholecystitis and at high risk for antimicrobial resistance (level III, grade C)
SAGES	2010	Antibiotics are not required in low-risk patients undergoing laparoscopic cholecystectomy (level I, grade A); antibiotics can reduce the incidence of wound infection in high-risk patients (aged older than 60 y, presence of diabetes, acute colic within 30 d of operation, jaundice, acute cholecystitis, or cholangitis) (level I, grade B); antibiotics should be limited to a single preoperative dose given within 1 h of skin incision (level II, grade A)
ASHP/SIS/IDSA/SHEA	2013	No antibiotics are indicated for laparoscopic low-risk cases; high-risk laparoscopic and open cases should receive antibiotics (cefazolin, cefoxitin, cefotetan, ceftriaxone, or ampicillin-sulbactam and, if β-lactam allergy, consider clindamycin or vancomycin plus aminoglycoside or aztreonam or fluorquinolone; metronidazole plus aminoglycoside or fluoroquinolone)
CDC	2017	Parenteral antibiotics should be administered before incision when appropriate; parenteral antibiotics should be discontinued after operation.
VTE prophylaxis		
SAGES	2010	In patients with 0 to 1 risk factors: none indicated, PCDs, UH, or LMWH (level II/III, grade C); in patients with 2 or more risk factors: PCDs, UH, or LMWH (level II/III, grade C)
ACCP	2012	Caprini score 0: none; Caprini score 1 to 2: PCDs; Caprini score >3: PCDs, UH, or LMWH
ELC within 7 d of diagnosis		
WSES	2016	ELC is preferable to DLC in patients with ACC within 10 d of onset of symptoms (level I, grade A); in patients with more than 10 d of symptoms, delaying cholecystectomy for 45 d is better than immediate operation (level II, grade B); ELC should be performed as soon as possible, but can be performed up to 10 d of onset of symptoms; earlier operation is associated with shorter hospital stay and fewer complications (level I, grade A)
SAGES	2010	ELC (within 24 to 72 h of diagnosis) can be performed; does not lead to increased rates of conversion or risk of complications; can decrease cost and total LOS (level I, grade A); in critically ill patients with acute cholecystitis, percutaneous cholecystostomy is an effective temporizing measure until the patient recovers sufficiently to undergo cholecystectomy (level II, grade B)
Type and screen/cross before the operating room	—	Not available
Intraoperative management		
Surgical technique	—	Not available
Intra-abdominal drain placement		
SAGES	2010	Drains are not needed after elective laparoscopic cholecystectomy, and their use can increase complication rates (level I, grade A); drains can be useful in complicated cases, particularly if choledochotomy is performed (level III, grade C)
Avoidance of urinary catheter placement		
CDC	2009	Foley catheter should be avoided for procedures shorter than 2 h and removed within 24 h of operation if placed

(Continued)

Table 4. Continued

Component, society	Year	Recommendation/statement
Intraoperative skin antisepsis		
CDC SSI prevention guideline, ACS and SIS	2017	Skin preparation with alcohol-containing agent is recommended; if alcohol-containing agent cannot be used, chlorhexidine is favored over iodine
Postoperative management		
Same-day discharge		
SAGES	2010	Patients undergoing uncomplicated laparoscopic cholecystectomy for symptomatic cholelithiasis can be discharged home on the day of operation (level II, grade B); patients older than 50 y can be at increased risk for admission (level II, grade B); time to discharge after operation for patients with acute cholecystitis, bile duct stones, or in patients converted to an open procedure should be determined on an individual basis (level III, grade A)
Early oral alimentation	—	Not available
Restricted fluid therapy with early discontinuation	—	Not available
Minimizing routine lab	—	Not available

ACC, acute cholecystectomy; ACCP, American College of Chest Physicians; ACS, American College of Surgeons; ASHP, American Society of Health-System Pharmacists; DLC, delayed laparoscopic cholecystectomy; ELC, early laparoscopic cholecystectomy; IDSA, Infectious Diseases Society of America; LMWH, low-molecular-weight heparin; LOS, length of stay; PCD, pneumatic compression device; SAGES, Society of American Gastrointestinal and Endoscopic Surgeons; SHEA, Society for Healthcare Epidemiology of America; SIS, Surgical Infection Society; SSI, surgical site infection; UH, unfractionated heparin; VTE, venous thromboembolism; WSES, World Society of Emergency Surgery.

patients with 2+ risk factors.[15] Their recommendation includes starting unfractionated heparin within 2 hours before operation or low-molecular-weight heparin either the night before operation or 2 hours before operation, and continuing until patients are fully mobile or until discharge from the hospital. American College of Chest Physicians guidelines use a combination of VTE incidence and surgical and patient factors to risk-stratify patients and guide prophylaxis.[16] Laparoscopic procedure longer than 45 minutes is included as part of the Caprini risk score and counts as 2 points. In patients with Caprini risk score 1 to 2, mechanical prophylaxis is recommended.

Summary and recommendations. There is a very low incidence of VTE events after LC and the evidence on whether VTE chemoprophylaxis is necessary remains unclear. Therefore, mechanical prophylaxis is likely sufficient for LC in straightforward patients. For more complex patients, risk-stratified VTE prophylaxis should be considered for LC using a national guideline (Society of American Gastrointestinal and Endoscopic Surgeons or American College of Chest Physicians).

Timing of operation

Rationale. Controversy exists about the optimal timing for LC for acute cholecystitis, with concerns of increased technical difficulty, greater complication rate, and higher conversion to open cholecystectomy. The 2 main approaches include early operation vs initial conservative treatment with antibiotics until resolution of inflammation, followed by delayed operation.

Evidence. We identified 3 SR/MAs that met our inclusion criteria; all studies focused on patients with acute cholecystitis. Of note, timing of cholecystectomy in patients managed with cholecystostomy drain/tube was not addressed. Early cholecystectomy was defined that performed during the index hospital admission and usually within 7 days of diagnosis. Delayed cholecystectomy was defined that performed on a second admission after initial nonoperative management.

An SR/MA by Cao and colleagues[17] (14 RCTs, $n = 1,608$) compared early and delayed LC. The severity of the degree of acute cholecystitis in these patients was not disclosed. The number of patients with complication was 15% in the early group compared with 30% in the delayed group (relative risk [RR] 0.66; 95% CI, 0.42 to 1.03; $p = 0.07$), but did not reach statistical significance. Ten studies reported total complication events (with a single patient being able to have more than 1 complication event) and there were fewer total complication events in the early group (158 vs 273; $p = 0.03$). Early operation had a lower risk of wound infections (4.2% vs 6.2%, RR 0.57; 95% CI, 0.35 to 0.94; $p = 0.02$) and shorter hospital length of stay (LOS) (4.1 days vs 7.3 days; $p < 0.001$). No difference between groups was found in bile duct leak or injury, mortality, conversion from laparoscopic to open procedure, or duration of procedure.

Additionally, Cao and colleagues[18] conducted an MA from case-control studies of early compared with delayed cholecystectomy for urgent indication (77 case-control studies, $n = 40,910$). They found lower

Table 5. Risk Factors for Venous Thromboembolism

Risk factor
Procedure-specific
Duration >1 h
Pelvic procedure
Patient-specific
History of venous thromboembolism
Age older than 40 y
Immobility
Varicose vein
Cancer
Chronic renal failure
Obesity
Peripartum
Congestive heart failure
MI
Hormone therapy
Oral contraceptive use
Multiparity (n = 3)
Inflammatory bowel disease
Severe infection

For inherited or acquired thrombophilias, hematology consult is recommended, where available.

mortality rates for early operation (0.47% vs 0.78%; OR 0.46; 95% CI, 0.33 to 0.62; $p < 0.001$), lower complication rates (8% vs 11.5%; OR 0.59; 95% CI, 0.50 to 0.69; $p < 0.001$), shorter LOS (5.1 days vs 11.3 days; $p < 0.001$), and decreased rate of bile duct injury, bile duct leak, wound infection, conversion from laparoscopic to open procedure, and blood loss (all were $p < 0.05$). In the delayed management group, 15.7% of patients failed nonoperative management and required an urgent cholecystectomy, and 22.9% had an acute presentation to the hospital related to gallstone disease.

Finally, Wu and colleagues[19] conducted an MA (15 RCTs, n = 1,625 patients) addressing the cost-effectiveness, quality of life, and safety and effectiveness in early compared with delayed cholecystectomy. Again, the severity of the degree of acute cholecystitis was not disclosed. Early operation was associated with lower hospital costs, fewer work days lost (mean difference −11.07 days; 95% CI, −16.21 to −5.94 days; $p < 0.001$), and higher patient satisfaction and quality of life.

The Tokyo Guidelines recommend early cholecystectomy in grade I (mild) acute cholecystitis at any facility and early cholecystectomy in grade II (moderate) acute cholecystitis at experienced centers.[20]

Summary and recommendations. Early LC (index hospitalization and fewer than 7 days after diagnosis) for acute cholecystitis, especially mild and moderate degrees, appears to be beneficial with decreased rate of complication, mortality, and other important outcomes metrics. Additionally, it is not associated with any increase in bile duct injury, duration of operation, or other harm and is supported by a surgical guideline.

Type and screen/cross before the operating room

Rationale. Routine use of type and screen/type and cross labs for blood matching before the procedure might be unnecessary.

Evidence. We identified 5 retrospective observational studies that met the inclusion criteria (Table 6). We believed that the evidence for routine type and screen/type and cross use in elective cholecystectomy was still applicable in urgent/emergent cholecystectomy.

Tandon and colleagues[21] (n = 2,079) found that the incidence of significant bleeding requiring transfusion was uncommon after elective LC. A type and screen occurred in 907 patients (43.6%) and a type and cross in 28 patients (3.1%). None of these patients required perioperative blood transfusion and 12 (0.58%) required a postoperative blood transfusion. Of these 12 patients, 10 (0.48%) required transfusion secondary to significant hemorrhage, a transfusion risk of 1:200. Hamza and colleagues[22] (n = 913) found a similarly low transfusion rate among elective LC in a multi-institutional cohort. Only 8 patients (0.9%) received blood transfusion, with a median time to transfusion of 10 hours (range 3 hours to 240 hours), and 3 of 8 patients had an additional type and screen collected again, despite already having a routine sample that was still valid. Thomson and colleagues[23] (n = 293) found that 256 patients (87%) underwent type and screen and 8 patients (3%) underwent type and cross, with 0 patients transfused perioperatively. Ghirardo and colleagues[24] (n = 1,137) found a transfusion rate of 4 (0.35%). Quinn and colleagues[25] (n = 4,462) found that 2,461 patients (55.2%) underwent a type and screen and 455 patients (10.2%) underwent a type and cross, with only 48 patients (1.1%) requiring blood transfusion.

Summary and recommendations. The majority of evidence is from retrospective observational studies and the quality of evidence is low. However, all studies suggest a low rate of transfusion (<1.1%) with most cases requiring nonemergent transfusions. Although high-risk populations can still benefit from preoperative blood tests, the current evidence recommends against routine type and screen or type and cross blood tests for LC, and instead recommends that O-negative blood be

Table 6. Summary of Studies on Use of Type and Screen/Type and Cross and Transfusion Rates

	Study, first author, year				
Variable	**Tandon, 2017[21]**	**Hamza, 2015[22]**	**Thomson, 2016[23]**	**Ghirardo, 2010[24]**	**Quinn, 2011[25]**
Patient, n	2,079	913	293	1,137	4,462
Type and screen, %	43.6	Not studied	87	Not studied	55.2
Type and cross, %	3.1	Not studied	3	Not studied	10.2
Transfused, %	0.6	0.9	0	0.35	1.1

available in the operating room for emergency hypovolemic situations.

Intraoperative management

Laparoscopic vs robotic surgical technique

Rationale. Robotic surgery has been implemented at some centers and clinical outcomes might be comparable with a laparoscopic approach.

Evidence. We identified 2 SR/MAs comparing a robotic approach for LC. There was significant overlap between the 2 articles and 1 was excluded. The evidence found was for elective cholecystectomy, but we believed it was still applicable in urgent/emergent cholecystectomy.

An SR/MA by Han and colleagues[26] (5 RCTs and 21 non-RCTs, n = 4,004) found a longer operative time in robotic-assisted cholecystectomy (RAC) compared with LC for benign disease (mean difference 12.04 minutes; 95% CI, 7.26 to 16.82 minutes) with no significant difference in rate of intraoperative complication (pooled RR 0.87; 95% CI, 0.42 to 1.80). There was no difference in estimated blood loss, conversion to open rate, hospital LOS (mean difference 0.05; 95% CI, −0.10 to 0.21), readmission rate (RR 1.21; 95% CI, 0.62 to 2.35), and postoperative complication (RR 1.76; 95% CI, 0.41 to 7.53). Of the RCTs, 10% (3 of 30) in the RAC group had incisional hernia vs 0% in the LC. Of the non-RCTs, the RAC and LC groups had a 5.5% (37 of 671) and 1.1% (9 of 818) rate of incisional hernia, respectively. A significantly higher rate of incisional hernia was found in the RAC group (pooled RR 3.06; 95% CI, 1.42 to 6.57). Our findings are summarized in Table 7.

There were no guideline recommendations found on surgical approach.

Summary and recommendations. Robotic-assisted cholecystectomy has a longer operative time compared with LC and a higher incisional hernia rate compared with LC. Aside from these, there were no additional differences in operative parameters and intraoperative or postoperative complication objectively measured in these studies. Robotic-assisted cholecystectomy was not found to be safer or more effective than LC for cholecystectomy. It should be considered a developing procedure and should not currently be deemed a replacement for the gold standard of LC.

Routine intra-abdominal drain placement

Rationale. Routine prophylactic intra-abdominal drain use is likely unnecessary for cholecystectomy and should be inserted only as needed based on clinical indication.

Evidence. We identified 4 articles that met the inclusion criteria and believed the evidence for routine intraoperative drain use in elective cholecystectomy was still applicable in urgent/emergent cholecystectomy.

A Cochrane SR (12 RCTs, n = 1,831) found no significant difference between those with and those without drains relative to short-term mortality (RR 0.41; 95% CI, 0.04 to 4.37), serious adverse events (RR 2.12; 95% CI, 0.67 to 7.40), quality of life, LOS, return to normal activity, and return to work.[6] Additionally, drain placement prolonged operative time (5.00 minutes; 95% CI, 2.69 to 7.30 minutes) and fewer patients with drains were discharged as a same-day procedure (RR 0.05; 95% CI, 0.00 to 0.75).

Additionally, an SR/MA by Bugiantella and colleagues[27] (7 RCTs, n = 1,310) found that abdominal collections were more frequent when routine drains were left (OR 1.56; 95% CI, 1.00 to 2.43; p = 0.048), and found no difference in the need for percutaneous drainage or reintervention between patients without drainage and those with drainage (OR 1.22; 95% CI, 0.23 to 6.60; p = 0.816). Picchio and colleagues[28] (12 RCTs, n = 1,939) found a lower morbidity rate (OR 1.97; 95% CI, 1.26 to 3.10; p = 0.003), a lower wound infection rate (OR 2.35; 95% CI, 1.22 to 4.51; p = 0.01), and less severe abdominal pain 24 hours after operation (standardized mean difference 2.30; 95% CI, 1.27 to 3.34; p < 0.001) in the no drain group. Wong and colleagues[29] (12 RCTs, n = 1,763) found no difference in the overall incidence of nausea/vomiting (RR 1.10; 95% CI, 0.90 to 1.36; p = 0.36).

The Society of American Gastrointestinal and Endoscopic Surgeons guidelines recommend that drains are not necessary after elective LC and their use can increase complication rates.[30]

Summary and recommendations. There is evidence to suggest that routine intraoperative abdominal drain use does not prevent postoperative complications or decrease postoperative pain or discomfort. Drain use can increase the incidence of intra-abdominal collections, wound infection, and abdominal pain. The current evidence does not support the routine use of drain after LC. The evidence suggests against the use of routine intraoperative abdominal drain use.

Urinary catheter insertion

Rationale. Urinary catheter insertion before LC allows for measurement of urinary output and can be especially beneficial for long or difficult operative cases. However, its use can increase complication of urinary tract infection and urethral stricture and can increase costs.

Evidence. We identified 1 RCT and 1 observational study that met the inclusion criteria. Both studies were specific to elective LC, but we believed that the evidence for elective cholecystectomy was still applicable in urgent/emergent cholecystectomy.

An RCT by Liu and colleagues[31] (n = 261) found higher rate of urinary tract complication in those with routine Foley placement compared with no placement (4 complications vs 1). There was no significant difference in length of operation and perioperative complication between the 2 groups.

Additionally, Hata and colleagues[7] conducted a prospective observational study (n = 282) and found that urinary

Table 7. Robotic vs Laparoscopic Cholecystectomy

Variable	Data source	Robotic vs laparoscopic
Operative time	5 RCTs and 16 NRCSs	Increase
Intraoperative complication	4 RCTs and 9 NRCSs	No change
Estimated blood loss	2 RCTs and 3 NRCSs	No change
Conversion rate	4 RCTs and 18 NRCSs	No change
Postoperative complication	3 RCTs and 13 NRCSs	No change
Length of hospital stay	3 RCTs and 14 NRCSs	No change
Readmission rate	6 NRCSs	No change
Incisional hernia	1 RCT and 5 NRCSs	Increase
Hospitalization cost	7 studies	Increase
Subgroup		SIRC vs MILC
Operative time	2 RCTs and 5 NRCSs	Increase
Intraoperative complication	2 RCTs and 5 NRCSs	No change
Estimated blood loss	2 RCTs and 5 NRCSs	No change
Conversion rate	2 RCTs and 5 NRCSs	No change
Postoperative complication	2 RCTs and 5 NRCSs	No change
Length of hospital stay	2 RCTs and 5 NRCSs	No change
Incisional hernia	2 RCTs and 5 NRCSs	Increase
Subgroup		SIRC vs SILC
Operative time	6 NRCSs	No change
Intraoperative complication	6 NRCSs	No change
Estimated blood loss	6 NRCSs	No change
Conversion rate	6 NRCSs	No change
Postoperative complication	6 NRCSs	No change
Length of hospital stay	6 NRCSs	No change
Subgroup		MIRC vs MILC
Operative time	3 RCTs and 10 NRCSs	Increase
Intraoperative complications	3 RCTs and 10 NRCSs	No change
Estimated blood loss	3 RCTs and 10 NRCSs	No change
Conversion rate	3 RCTs and 10 NRCSs	No change
Postoperative complication	3 RCTs and 10 NRCSs	No change
Length of hospital stay	3 RCTs and 10 NRCSs	No change

MILC, multi-incision laparoscopic cholecystectomy; MIRC, multi-incision robotic cholecystectomy; NRCS, nonrandomized comparative studies; RCT, randomized controlled trial; SILC, single-incision laparoscopic cholecystectomy; SIRC, single incision robotic cholecystectomy.

complication occurred at a lower rate in the noncatheterized group than in the control (catheterized) group (1.6 vs. 7.8%, respectively; $p = 0.0137$), and that the postoperative hospital stay was slightly shorter for the noncatheterized group (3.7 vs. 4.0 days; $p = 0.0185$). Although the operation and anesthesia times did not differ between the 2 groups, the volume of intraoperative IV infusion was greater in the catheterized group than the noncatheterized group (1,389.3 vs 1,003.7 mL; $p < 0.0001$). Three patients in the noncatheterized group experienced urinary retention, which resolved after temporary intermittent straight catheterization.

Urinary catheter insertion for LC is not mentioned in any of the professional society guidelines.

Summary and recommendations. Avoiding routine Foley catheterization has been demonstrated to be safe, well tolerated, and can reduce the incidence of postoperative urinary tract complications. The evidence suggests not placing routine Foley catheters in LC, and Foley use only in select patients.

Intraoperative skin antisepsis

Rationale. Skin preparation with antiseptic agents just before incision decreases rates of surgical site infection. Different types of agents are available and particular skin preparation types can be more effective.

Evidence. We identified 4 SR/MAs that compared chlorhexidine gluconate and povidone-iodine in clean and clean contaminated procedures, of which LC falls into this category. Two articles had significant overlap and were not included in our review. No articles were found that addressed skin antisepsis in LC alone.

An SR/MA from Zhang and colleagues[32] (13 RCTs, n = 6,997) found a lower incidence of surgical site infrection with chlorhexidine gluconate use compared with povidone-iodine (RR 0.70; 95% CI, 0.60 to 0.83). There was no difference in adverse events between the 2 groups. Additionally, an SR/MA by Privitera and colleagues[33] (19 RCTs/observational studies, n = 7,700) found decreased bacterial skin colonization from chlorhexidine gluconate use vs povidone-iodine (RR 0.45; 95% CI, 0.36 to 0.55).

Guideline recommendations from the American College of Surgeons, Surgical Infection Society, and CDC recommend skin preparation before operation with an alcohol-containing agent.[34] If an alcohol-containing agent is contraindicated, then chlorhexidine is favored over iodine.

Summary and recommendations. Evidence supports preoperative skin antisepsis with alcohol-based solutions. In the event of an allergy to alcohol, chlorhexidine should be used.

Postoperative management

Same-day operation protocols (fast-track)

Rationale. Same-day operation is increasing in popularity for elective LC. The concern is that postoperative complications can be missed if the patient is discharged before these occur.

Evidence. We identified 3 SR/MAs that met the inclusion criteria and addressed elective LC; no evidence addressed nonelective LC. There was significant overlap with 2 of the SR/MAs, which presented similar evidence[35,36] and were excluded from our evidence review.

A Cochrane SR/MA (6 RCTs, n = 492) found no mortality and no significant difference in serious adverse events (RR 3.24; 95% CI, 0.74 to 14.09) when comparing same-day operation with overnight-stay operation for symptomatic gallstones.[37] When analyzing secondary outcomes, they also found no significant difference between the 2 groups in quality of life (standardized mean difference −0.11; 95% CI, −0.33 to 0.10), pain (mean difference 0.02 cm on visual analogue scale [VAS] score; 95% CI, −0.69 to 0.73), time to return to activity, time to return to work, hospital readmission (rate ratio 1.25; 95% CI, 0.43 to 3.63), and number of people requiring readmission (RR 1.09; 95% CI, 0.33 to 3.60).

Summary and recommendations. There is little to no evidence currently available on same-day operations in nonelective laparoscopic cholecystectomies. However, there is evidence to suggest that same-day operation in an elective LC population is safe in select patients. It is unclear how the data on elective cases applies to nonelective, and the safety of same-day LC on a nonelective basis is still unknown and requires additional study.

Early oral alimentation

Rationale. Early oral alimentation after LC has been proposed to improve postoperative outcomes and reduce LOS, enhancing patient experience and diminishing hospital resource use.

Evidence. We identified 2 RCTs and 1 observational study that met the inclusion criteria. Although some of the evidence presented was for elective procedures, we believed the evidence for early oral alimentation after elective procedures was still applicable in urgent/emergent cholecystectomy.

An RCT by Çalişkan and colleagues[38] (n = 60) in patients undergoing LC, which did not report any information on urgency of procedure or indication, found that early oral intake of 200 mL warm water 4 hours after procedure had first flatulence earlier compared with those who did not receive early oral intake (11 ± 4.2 hours vs 18.6 ± 6 hours; $p < 0.05$). However, no difference was found in time to first stool (35.4 ± 12.5 hours vs 38.1 ± 12.7 hours; $p > 0.05$).

An observational study by Shah and colleagues[8] (n = 294) conducted in elective LC found that on average oral fluids were started 5.5 hours after operation (range 4 hours to 9 hours). Postoperative nausea and vomiting occurred in 76 patients (25.9%), and 285 patients (97%) tolerated early discontinuation of IV fluids within 6 hours of operation when oral intake was started, without requiring reinitiation of IV fluids.

An RCT by Klappenbach and colleagues[39] (n = 295) studied early oral alimentation in patients undergoing emergency abdominal surgical procedure and found no difference in complication rate (45.3% vs 37.4%, OR 1.3; 95% CI, 0.8 to 2.2; $p = 0.1$) or ileus when comparing early oral feeding with traditional postoperative care. Early alimentation was associated with more postprandial vomiting (13.5% vs 6.1%; OR 2.4; 95% CI, 1.05 to 5.40; $p = 0.03$); however, there was no difference in the need for nasogastric tube insertion. Early alimentation patients consumed less food in their first 3 meals and reported less hunger (both $p < 0.01$).

Early oral alimentation for LC is not mentioned in any of the professional society guidelines.

Summary and recommendations. Early oral feeding has been demonstrated to be safe, well tolerated, and beneficial after abdominal emergency operation, and is likely also beneficial after LC. The evidence supports early introduction of oral intake after LC.

Restrictive fluid therapy

Rationale. Avoidance of hypervolemia with early postoperative discontinuation of IV fluids and restrictive fluid therapy is thought to reduce postoperative complication and improve return of bowel function.

Evidence. We identified 3 RCTs that met the inclusion criteria. Although these articles included patients undergoing elective LC, we believe the evidence remains applicable to those undergoing average-risk LC for urgent or emergent indication.

An RCT by Henriques and colleagues[40] (n = 100) compared patients receiving restrictive fluids (mean 1,600 mL) with a control group receiving standard fluid (mean 3,000 mL) and found increased urinary output (1,257 ± 736 mL vs 888 ± 392 mL, respectively; $p < 0.05$), weight, and extracellular water through bioimpedence analysis. There were no differences found in nausea, vomiting, creatinine level, hemodynamic stability, thirst, hunger, or return of bowel function.

Another RCT by Belavic and colleagues[41] (n = 120) that randomized patients to receive restrictive fluid at 1 mL/kg/h lactated Ringer's solution vs liberal fluids at 5 mL/kg/h found no sign of global hypoperfusion in either of the groups, and no significant difference in the duration of operation and anesthesia. However, the consumption of volatile anesthetics (34.4 mL [range 30.6 to 46 mL] sevoflorane vs 46 mL [range 38.2 to 46 mL]; $p = 0.017$), and opioids (150 μg [range 100 to 200 μg] fentanyl vs 175 μg [range 150 to 250 μg]; $p < 0.01$) were significantly lower in the restrictive group compared with the liberal group.

Another RCT by Yao and colleagues[42] (n = 100) compared restrictive fluid infusion at 5 mL/kg/h vs liberal fluid infusion at 30 mL/kg/h lactated Ringer's solution and found no difference in VAS pain scores at 1 and 24 hours. However, patients in the restrictive group were found to have higher VAS pain scores at 6 hours after operation compared with those in the liberal group (3.34 ± 2.58 vs 2.00 ± 1.80; $p < 0.01$). X-rays showed a higher incidence of subdiaphragmatic residual gas in the restrictive group compared with the liberal group (62% vs 42%; $p = 0.045$), and higher VAS pain scores were observed in those with residual gas in the restrictive group. There were no significant differences found in abdominal distention, hypovolemia, nausea, vomiting, or time to return of bowel function between the 2 groups.

Summary and recommendations. The evidence from RCTs suggests that intraoperative restrictive fluid therapy and early discontinuation of IV fluids are beneficial.

Minimizing routine labs

Rationale. Minimizing postoperative blood testing has the potential to reduce hospitalization time, expense, and inconvenience to the patient and family. There is concern that this practice can increase the rate of undetected postoperative complication.

Evidence. We identified 2 observational studies that met the inclusion criteria. Although these articles included patients undergoing elective LC, we believe the evidence remains applicable to those undergoing average-risk LC for urgent or emergent indication.

A retrospective case-control study from Ben-Ishay and colleagues[43] (n = 532) in elective LC found that postoperative blood labs were not independently associated with increased rate of complication ($p = 0.44$) and did not change patient management or predict complication. Older age, prolonged operation, drain placement, and more than 1 day of hospitalization were associated with increased use of postoperative blood work (all $p < 0.05$).

A retrospective observational study by Kaldor and colleagues[44] (n = 199) of both elective and emergent LC found no difference between pre- and postoperative levels of total bilirubin and aminotransferase ($p > 0.05$ for both), but did find a difference in alanine aminotransferase and alkaline phosphatase (31 vs 50 U/L; p = 0.003 and 95 vs 90 U/L; p = 0.001, respectively). Of those with postoperative hyperbilirubinemia, 87.5% had no postoperative intervention and no diagnosed complication. From the cohort that had no hyperbilirubinemia, 5 patients underwent ERCP based on clinical suspicion and 4 were found to have retained common bile duct stones. Of the 9 patients (4.5%) with postoperative complications (8 with retained common bile duct stones and 1 with a cystic duct leak), only 4 had postoperative hyperbilirubinemia, and all complications were diagnosed with postoperative ERCP.

Minimizing labs postoperatively for LC is not mentioned in any of the professional society guidelines.

Summary and recommendations. A moderate level of evidence (observational comparative studies) supports the safety and benefit of minimizing laboratory tests after average-risk LC. Routine postoperative blood tests might be unnecessary and could be carried out, but only in select cases when clinically indicated.

DISCUSSION

This evidence review covers 13 components that are potentially relevant to developing an ERP for patients undergoing nonelective LC for acute cholecystitis. ERPs have demonstrated success in multiple fields of elective surgery; however, their use in emergency surgery remains undefined. Although the evidence compiled in this review varies in strength, it does support some components that could be combined to develop an ERP for nonelective LC.

The evidence we used for the components to develop the ERP was drawn from cohorts undergoing nonelective LC whenever possible. However, this patient population is difficult to study, especially in a prospective randomized fashion. In situations where evidence was not available for nonelective patients only, evidence from elective LC was also included when appropriate. While the applicability of evidence for elective to nonelective LC varies by component, we believed that in most situations the clinical management of an average, nonelective patient did not differ significantly from the management of an elective patient, especially in the postoperative period, providing the procedure was performed without significant intraoperative complication.

Compared with traditional elective ERP protocols, some common preoperative components for elective ERP pathways, such as patient bathing at home, will not be possible for patients presenting with acute cholecystitis for urgent procedures. We chose to focus instead on perioperative intervention that can be performed in the hospital, such as the use of preoperative antibiotics and reducing routine blood labs. Although patient education might be more effective in an elective setting, the use of patient education still applies in a nonelective situation, as the patient and their family members can still benefit from a clear description of what to expect from the surgical procedure and the postoperative recovery period. In other service lines, such as colorectal surgery, ERP has improved patient outcomes significantly by reducing LOS and decreasing complication rate after colorectal operation.[2] Patients undergoing LC and other emergency general surgery represent a different patient population, however, the benefits of ERP are likely to be present in this population as well. The greatest room for improvement in this population is focused on decreasing complication rate and decreasing readmission, and although there is less room to improve on LOS, for those that do not undergo same-day operation, we believe these ERP components can contribute significantly to decreasing LOS as well. Both ERP process measures adherence and routine postoperative outcomes captured by the NSQIP are being collected by the hospitals participating in the ISCR program and are metrics that will undergo national benchmarking with data reports to allow for iterative improvement from participating hospitals.

There are a few topics worthy of discussion that are not in our evidence review. With acute cholecystitis, there are various forms of preoperative imaging modalities, such as ultrasound, CT scan, and hepatic iminodiacetic acid scans; however, these are related to the ultimate diagnosis of disease, and the imaging modality used for diagnosis is not appropriate for a clinical pathway for ERP and was excluded from our review.

Although surgical approach (robotic vs laparoscopic) was discussed from a safety standpoint with intraoperative use, it is worth noting that one of the main drawbacks to robotic surgery is the significantly increased cost associated with RAC compared with laparoscopic procedures.[45] There is a high capital cost for equipment and annual maintenance of the robots used for RAC, and RAC is distinctly higher in cost for cholecystectomy than laparoscopy. However, with RAC, there is the possible benefit of better visualization and precision, and the use of RAC is subject to surgeon preference. Our evidence found no clear demonstration of significant benefit between RAC and LC in outcomes, and the higher cost of RAC can lead the evidence to favor using LC in cholecystectomy over RAC; however, we would advocate using the technique that is the preference of the operating surgeon to optimize for safety and outcomes.

Additionally, the use of intraoperative cholangiogram is an important decision point for patients undergoing

LC, and its routine use remains heavily debated. However, with the wide variation in indication and clinical scenarios that influence this decision, this technique was believed to fall under intraoperative patient management rather than an aspect of a clinical pathway for an ERP, and was believed to be beyond the scope of our evidence review.

To our knowledge, this is the first literature review to cover ERP components related to nonelective LC. The components are supported in the literature and expand on guideline and society recommendations when available. The anesthesiology components for ERP in emergency general surgery are being reviewed in parallel, and together they serve as a framework for developing a standardized pathway for this patient population that can help ensure that consistent practice is applied to all patients with the goal of improving patient outcomes, improving patient satisfaction, and reducing healthcare use. It is likely that improving time to the operating room, appropriate use of antibiotics, standardized skin preparation, as well as avoidance of Foley catheters, are the processes most likely to be associated with improvement in patient outcomes and experience.

CONCLUSIONS

We identified 13 overall components to consider for a nonelective LC for acute cholecystitis ERP. The evidence base and guideline support for each component are described in detail in this review. These components, combined with the anesthesia components, should be delivered consistently for optimal care delivery for the patient undergoing cholecystectomy. The ISCR cholecystectomy pathway components span the preoperative, intraoperative, and postoperative phases of care and will require transdisciplinary collaboration among surgeons, nursing staff, anesthesia providers, hospital leadership, and patients. Hospitals participating in the AHRQ ISCR will be supported in carrying out practices that enhance care for patients and gathering data to support continuous quality improvement around the ERP. The ultimate goal is to raise the bar for surgical care nationally.

Author Contributions

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Acknowledgment: We would like to acknowledge Christine G Holzmueller, Senior Technical Writer at the Johns Hopkins Armstrong Institute for Patient Safety and Quality, who copyedited the manuscript and Q Eileen Wafford, MSt, MLIS, Research Librarian at Northwestern University Feinberg School of Medicine, who aided with the identification of search terms.

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eTable 1. Search Criteria for Improving Surgical Care and Recovery Components Evaluated for Cholecystectomy

Component	Operation	Component	Qualifier
Preoperative management			
Patient education and counseling	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	(Patient education as topic [MeSH] or “preoperative education”[tiab] or “preoperative education” [tiab])	NA
Timing of operation	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	(“Failure to return”[tiab] or “time to OR”[tiab] or “initial hospitalization”[tiab] or (early[tiab] and delayed[tiab]) or timing[tiab])	NA
Preoperative antibiotics	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	(Antibiotic*[tiab])	(Urgent[tiab] or acute[tiab] or emergent[tiab] or nonelective [tiab]))
Perioperative VTE prophylaxis	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	(“Thromboembolism”[MeSH] OR “thromboembolism”[tw] OR “thromboprophylaxis”[tw] OR “chemoprophylaxis”[tw] or “VTE”[tw] or “venous thrombosis”[tw] or “venous thromboembolism”[tw])	NA
Type and screen/cross before the operating room	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	(Typing[tw] or screen[tw] or “type and screen”[tw] or “type and cross”[tw] or “blood transfusion”[tw] or “blood group”[tw])	NA
Intraoperative management			
Intraoperative skin antisepsis	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	(“Skin antiseptic”[tiab] OR “skin antisepsis”[tiab] OR “skin antiseptics”[tiab] OR chlorhexidine[tiab] OR antisep*[tiab] OR “skin prep*”[tiab])	NA
Surgical approach	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab]	(Robotic[tiab] or “robotic-assisted”[tiab])	NA
Intraoperative drain use	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	(Drain(tiab) AND (abdominal(tiab) OR routine(tiab) OR intraperitoneal(tiab) OR prophylac*(tiab)))	NA
Intraoperative Foley use	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	(Foley[tiab] or “urinary catheter*”[tiab])	NA
Postoperative management			
Same-day operation protocol (fast-track)	((“Cholecystectomy”[MeSH]) OR cholecyst*[tiab])	“Same day discharge”[tiab] OR “early discharge”[tiab] OR “day surgery”[tiab] OR “day case surgery”[tiab] OR “ambulatory surgical procedures”[tiab]”	NA
Early alimentation	(("Cholecystectomy"[MeSH]) OR cholecyst*[tiab])	(Nutrition[tiab] or feeding[tiab] or alimentation[tiab] or enteral[tiab])	("Postoperative period"[mesh]) OR ("postoperative"[tiab] OR "postop"[tiab] OR "post-operative"[tiab] OR "post-op"[tiab])
Restrictive fluid therapy and early discontinuation	(("Cholecystectomy"[MeSH]) OR cholecyst*[tiab])	("IV fluid"[tiab] OR "intravenous fluid"[tiab] OR "fluid therapy"[tiab])	NA
Minimizing routine labs	(("Cholecystectomy"[MeSH]) OR cholecyst*[tiab])	(Labs[tiab] or "blood work"[tiab] or "routine blood tests"[tiab] or "postoperative blood tests"[tiab] or "blood tests"[tiab] or (("liver function test"[tiab] or "liver enzyme"[tiab]) and postoperative[tiab]))	NA

MeSH, medical subject headings; NA, not applicable; VTE, venous thromboembolism.