

Outcomes of early versus delayed surgical intervention for critically ill patients in the intensive care unit: A systematic review

Tameem Alhomaid ^{1*}, Mohammed Hassan Albarakati ², Saud Derbash Alzahrani ³, Layla Abdashaheed Al Julaih ⁴, Fatimah Abdashaheed Al Julaih ⁵, Nasser ayidh Alruwaythi ⁶, Wurayf Fahad Alharbi⁷, Wijdan Salem Almatrafi ⁸, Sameera M Refaie Felemban⁹

¹Family medicine and mental health consultant, Qassim Health Cluster

²Ministry of Health, Makkah heath cluster, Ibn sina extended care hospital

³King Fahad Medical City, Riyadh

⁴ Medical intern, Eastern Health Cluster

⁵ Medical intern ,Eastern Health Cluster

⁶ Student at Dar Al Uloom University

⁷Taibah university, AL Madinah, Medicine and Surgery.

⁸College of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia

⁹King Fahd Hospital Jeddah

Corresponding author:

Tameem Alhomaid

Affiliation: Family medicine and mental health consultant, Qassim Health Cluster

Email ID: tameem@missionacademy.sa

ABSTRACT

The timing of surgical intervention in critically ill ICU patients remains a pivotal yet complex decision, balancing the urgency of source control against the risks of operative stress. This systematic review synthesizes evidence from 20 studies to compare outcomes of early versus delayed surgical intervention across various conditions, including abdominal emergencies, trauma, and neurological cases.

Findings reveal that optimal timing is highly condition-specific. Time-critical conditions such as acute intestinal ischemia, necrotizing soft tissue infections, and free intestinal perforation demonstrate significantly reduced mortality with early intervention (within 4–12 hours), while delays beyond these thresholds are associated with poorer outcomes. On the other hand, conditions like necrotizing pancreatitis with persistent organ failure and blunt carotid injury show increased mortality with early surgery, emphasizing the need for initial physiological stabilization.

Early intervention consistently reduced ICU and hospital length of stay (LOS) and complications such as ventilator-associated pneumonia (e.g., tracheostomy ≤ 10 days) and pressure ulcers (e.g., hip fractures < 48 hours). However, premature surgery in high-risk scenarios, such as necrotizing enterocolitis or pancreatitis with organ failure, paradoxically worsens outcomes. Resource utilization improved with early laparoscopic cholecystectomy (reduced costs and LOS) and decompressive craniotomy for malignant MCA infarction (better functional recovery).

The review underscores that the therapeutic window for surgery depends on disease pathophysiology, patient stability, and procedural risks. While early intervention benefits time-sensitive conditions, delayed surgery after optimization is preferable for systemic inflammatory or organ failure-dominated cases. Future research should refine condition-specific timing thresholds and integrate dynamic physiological markers to guide decision-making. Clinicians must tailor surgical timing to individual patient and disease profiles to optimize outcomes and resource use

Keywords: Surgical timing, critically ill, ICU outcomes, early intervention, delayed intervention, mortality, morbidity.

How to Cite: Tameem Alhomaid, Mohammed Hassan Albarakati, Saud Derbash Alzahrani, Layla Abdashaheed Al Julaih, Fatimah Abdashaheed Al Julaih, Nasser ayidh Alruwaythi, Wurayf Fahad Alharbi, Wijdan Salem Almatrafi, Sameera M Refaie Felemban, (2025) Outcomes of early versus delayed surgical intervention for critically ill patients in the intensive care unit: A systematic review, *Journal of Carcinogenesis*, *Vol.24*, *No.8s*, 699-713

1. INTRODUCTION

The timing of surgical intervention for critically ill patients in the intensive care unit represents one of the most complex and consequential decisions in modern critical care medicine. The delicate balance between the urgency of surgical treatment and the patient's capacity to withstand operative stress creates a persistent clinical dilemma that directly impacts patient outcomes.¹ Current evidence suggests that the optimal timing of surgery for critically ill patients can significantly influence mortality rates, with studies showing that delayed surgical intervention beyond certain thresholds is associated with increased morbidity and mortality across various surgical conditions.^{1–3}

Critically ill patients often present with multi-organ dysfunction, hemodynamic instability, and varying degrees of physiological derangement, all of which influence surgical risk and recovery.⁴ The decision to proceed with early versus delayed surgery frequently hinges on clinical factors, including the patient's overall stability, the nature and severity of the underlying pathology, and the availability of supportive therapies.⁵ Early intervention has the advantage of mitigating complications by addressing the source of critical illness at the earliest moment. However, premature surgical intervention without adequate resuscitation may exacerbate morbidity and mortality.^{3,6} Delayed surgical timing, in contrast, allows for optimization of the patient's hemodynamic status, correction of coagulopathy, and stabilization of organ function before operative intervention but risks progression of sepsis, tissue damage, or other disease complications.^{5,6} Recent studies have demonstrated that mortality rates can increase significantly when surgical delays exceed specific time thresholds, with some research identifying critical inflection points at 12-16 hours for certain conditions.^{1,7} The complexity is further compounded by the heterogeneity of critically ill surgical patients, who may present with diverse pathophysiology, varying degrees of organ dysfunction, and different underlying conditions requiring surgical management.^{1,8,9}

This systematic review aims to synthesize the current evidence regarding the comparative outcomes of early versus delayed surgical intervention in critically ill Intensive Care Unit (ICU) patients. By examining mortality rates, morbidity patterns, ICU length of stay, and long-term functional outcomes across different surgical conditions and patient populations, this analysis seeks to provide evidence-based guidance for clinicians making these time-critical decisions. The ultimate goal is to establish clearer parameters for optimal surgical timing that can improve patient outcomes while informing clinical practice guidelines and resource allocation strategies in intensive care settings.

2. METHODS

This was a systematic review guided by following search question: In critically ill patients admitted to the intensive care unit (Population), how does early surgical intervention (within a defined early time window after ICU admission or diagnosis) compared to delayed surgical intervention (surgery performed after initial stabilization or beyond the early time window) (Intervention versus Comparator) affect clinical outcomes such as mortality, morbidity, length of ICU and hospital stay, and long-term functional recovery (Outcomes)?

Database Search

Electronic searches were performed at PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and Scopus to identify peer-reviewed articles. Manual searches of reference lists from included studies and relevant reviews supplemented database queries.

Search Strategy

The PICO framework guided search term development: Population terms ("critically ill," "ICU," "multi-organ failure"), Intervention/Comparator terms ("early surgery," "delayed surgery," "surgical timing"), and Outcomes ("mortality," "length of stay," "complications"). Boolean operators (AND/OR) combined terms, with database-specific syntax adjustments. For instance, this is one of the PubMed search strings used: ("critically ill"[tiab] OR "critical illness"[tiab]) AND ("early surgery"[tiab]) OR "immediate surgery"[tiab]) AND ("delayed surgery"[tiab]) AND ("mortality"[tiab] OR "length of stay"[tiab]).

Eligibility Criteria

Studies were included if they were peer-reviewed, involved critically ill patients admitted to the ICU requiring surgical intervention, and explored outcomes of early versus delayed surgical interventions for patients in the ICU. Early intervention was defined as surgery within condition-specific time thresholds, while delayed intervention involved surgery after initial stabilization or beyond early thresholds. Eligible designs included randomized controlled trials (RCTs), prospective/retrospective cohort studies, and observational studies. English-language publications from January 2014 to July 2025 were considered. Exclusions comprised case reports, animal studies, non-comparative designs, non-peer-reviewed studies, studies without explicit timing definitions, reviews, and non-surgical interventions.

Study Selection Process

Two independent reviewers screened titles/abstracts, with conflicts resolved via consensus or a third reviewer. Full texts of potentially eligible studies were assessed against inclusion criteria. The PRISMA flow diagram below documented

screening stages (Figure 1).

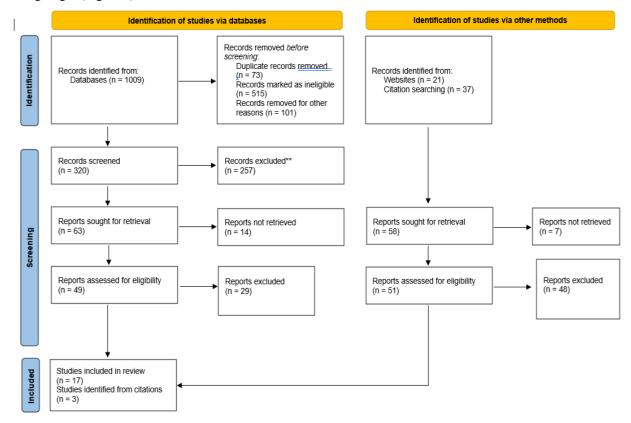


Figure 1. PRISMA Flow chart showing the study selection process

Data Extraction

We recorded study characteristics (author, year, design, sample), population (diagnosis, age, comorbidities), intervention/comparator details (timing thresholds, procedures), and outcomes (mortality, complications, LOS). Data were extracted independently by two reviewers, with discrepancies resolved through discussion.

Quality Assessment

Risk of bias was evaluated using the Cochrane Risk-of-Bias tool for RCTs¹¹ and the Newcastle-Ottawa Scale (NOS)¹² for observational studies. Domains included selection bias, confounding, outcome measurement, and attrition. Studies were rated as low, moderate, or high risk, with ratings informing evidence synthesis.

Data Synthesis and Reporting

Data synthesis was performed using a structured narrative approach, stratifying findings by clinical condition to reflect the heterogeneity of patient populations and surgical pathologies. Outcomes were categorized into primary endpoints (mortality, morbidity/complications, ICU and hospital length of stay) and secondary endpoints (functional recovery, infection rates, healthcare resource utilization). Extracted data from included studies were organized into summary tables detailing study characteristics, definitions of early versus delayed intervention, and main findings. Comparative patterns and differences in outcomes were analyzed within and across conditions, highlighting disease-specific therapeutic windows and the influence of physiological stabilization versus urgency of source control. Where applicable, the direction and magnitude of effect were reported alongside relevant statistical significance. Reporting adhered to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) reporting guidelines, ¹⁰ ensuring transparent documentation of study selection, quality assessment, and synthesis methods to allow reproducibility and facilitate interpretation by clinicians and researchers.

3. RESULTS

Characteristics of included studies

The systematic review synthesized 20 studies evaluating surgical timing in critically ill ICU patients, revealing notable variability in design, populations, and definitions of "early" intervention (Table 1). Most studies (13/20) were retrospective observational, with few prospective observational, and randomized controlled trials. Sample sizes ranged from

small cohorts (<50)²⁸ to large datasets (>9000).²³

Populations were condition-specific, including abdominal emergencies (e.g., **necrotizing soft tissue infection**, bowel perforation, cholecystitis, pancreatitis), orthopedic trauma (hip fractures), neurological emergencies (malignant MCA infarction), vascular trauma (blunt carotid injury), and airway management (tracheostomy). Age varied from neonates with necrotizing enterocolitis¹⁹ to elderly hip fracture patients.³¹

Definitions of "early" surgery ranged from ultra-urgent (<6–12 hours for perforated appendicitis, necrotizing soft tissue infection, bowel ischemia) to urgent (<48–72 hours for fractures or cholecystitis) and delayed (weeks for pancreatitis). The "delayed" intervention was consistently defined as surgery performed after the specified "early" threshold, often involving initial medical stabilization (e.g., antibiotics/fluids for cholecystitis or appendicitis) or simply occurring later due to logistical/clinical reasons. Procedures reflected the underlying pathology, such as debridement, bowel resection, craniotomy, or tracheostomy.

Primary clinical outcomes

Early interventions are beneficial in time-critical conditions (e.g., intestinal ischemia, necrotizing soft tissue infections, intestinal perforation, hip fractures) but increases risks in others (e.g., necrotizing pancreatitis with organ failure, blunt carotid injury, necrotizing enterocolitis) (Table 1).

Mortality

Time-sensitive surgical conditions consistently demonstrate reduced mortality with early intervention. For Acute intestinal ischemia, early surgery (within 4-12 hours of shock onset) yielded a 95.24% survival rate compared to 4.76% with non-surgical management. Similarly, early intervention (<6 hours) for necrotizing soft tissue infections led to lower mortality (7.5% vs. 12.5%), though this difference was not statistically significant. In hip fractures, reduced time-to-surgery (<48 hours) significantly decreased in-hospital mortality (from 9.6% to 6.8%) and 1-year mortality. Early intervention (<9 hours) for free intestinal perforation resulted in an 80% survival rate versus 73% with later intervention. However, conflicting evidence exists for other conditions. In necrotizing pancreatitis, early intervention (≤30 days) was associated with higher mortality compared to delayed intervention (>30 days), except in patients without persistent organ failure. Zhang et al. found that intervention within 4 weeks did not worsen mortality compared to later intervention in patients with persistent organ failure. For necrotizing enterocolitis, early surgical intervention was paradoxically associated with higher mortality. In blunt carotid injury, early intervention (<24 hours) was associated with increased mortality compared to delayed intervention (>24 hours), particularly with endovascular approaches.

Morbidity and complications

Early intervention reduced complications in specific conditions. For perforated appendicitis, immediate surgery significantly reduced postoperative complications compared to delayed surgery. Surgery within 72 hours for fragility hip fractures significantly reduced pressure ulcers, pneumonia, and urinary tract infections. Surgery within 72 hours for fragility hip fractures significantly reduced pressure ulcers, pneumonia, and urinary tract infections. Surgery decompressive craniotomy (<6 hours) for malignant middle cerebral artery (MCA) Infarction significantly improved neurological/functional outcomes and reduced mortality. Effects varied in other conditions. For acute cholecystitis, early laparoscopic cholecystectomy (ELC) consistently reduced hospital stay and costs, Surgery and potentially higher (though often non-significant) complication rates in some studies; overall morbidity was lower with ELC in randomized controlled trials. Surgery In Unperforated Appendicitis, delayed appendectomy (≥8 hours) did not increase complications or length of stay compared to early appendectomy. For necrotizing pancreatitis, early intervention (≤30 days) was associated with higher re-intervention rates, while Zhang et al. found comparable complication rates (e.g., fistula, bleeding) between early and late intervention groups. For necrotizing enterocolitis, early surgical intervention was paradoxically associated with more bowel resection compared to delayed intervention, suggesting benefit from medical optimization first.

Length of stay (ICU & hospital)

Significant reductions in length of stay (LOS) were observed with early intervention across several conditions. Early surgery for necrotizing soft tissue infections reduced both ICU and hospital LOS. ¹³ Early surgery for hip fractures reduced hospital LOS. ^{20,24,31} ELC for acute cholecystitis reduced hospital LOS. ^{25,29,30} Early tracheostomy (<10 days of mechanical ventilation) reduced ICU LOS and mechanical ventilation duration, ^{22,32} with very early percutaneous dilatational tracheotomy (PDT) (<2 days) in the elderly also reducing ICU LOS. ³² Early emergency laparoscopic gi surgery reduced hospital LOS. ¹⁸ However, an increased stay with early intervention was noted in one specific instance of acute cholecystitis: early laparoscopic cholecystectomy (LC) (<24 hours) prolonged hospitalization compared to delayed LC (6-8 weeks post-conservative therapy), attributed to higher conversion rates and potentially sicker patients selected for early surgery. ¹⁵

Table 1. Characteristics of included studies

Authors, Year*	Title	Study design	Sample	Population characteristics	Intervention	Main findings
Hadeed et al. ¹³ 2016	Early surgical intervention and its impact on patients presenting with necrotizing soft tissue infections: A single academic center experience	Retrospective observational study	87	62% males and 38% females Age and comorbidities were comparable between groups (no specific details provided)	Surgical debridement within the first 6 hours after diagnosis (early intervention group) or after 6 hours (late intervention group)	Early surgical intervention within 6 hours of diagnosis significantly reduced hospital and ICU length of stay. The early intervention group had a lower mortality rate (7.5%) compared to the overall mortality rate (12.5%), although this difference was not statistically significant. Early surgery improves in-hospital outcomes for patients with necrotizing soft tissue infections.
Bukhari and Kumar ¹⁴ 2021	Early Surgical Intervention Improves Survival in Acute Intestinal Ischemia in the Intensive Care Unit	Retrospective observational study	- Surgery group: 60 - No surgery group: 3 - Total: Not explicitly mentioned, but at least 63 (60 + 3)	Patients with acute mesenteric ischemia (AMI) and septic shock Critically ill patients admitted to the intensive care unit	Early surgical intervention involving the removal of ischemic bowel; mean time to surgery: 17.7 hours; 65 patients had surgery between 4 and 12 hours from the onset of hypotension.	Early surgical intervention significantly improves survival in patients with acute mesenteric ischemia and septic shock, with a survival rate of 95.24% in the surgery group compared to 4.76% in the nonsurgery group. The timing of surgical intervention is critical, with a statistically significant survival benefit observed when surgery is performed early (P_<0.001). Early removal of ischemic bowel is associated with improved survival outcomes in patients with AMI-related surgery.
Acar et al. ¹⁵ 2017	Laparoscopic cholecystectom y in the treatment of acute cholecystitis:	Retrospective comparative study	66 patients (33 early LC, 33 late LC)	Early LC group: Mean age 63.5 yrs, 51.5% male, 78.8% comorbidities, higher rates of	Early LC group: Surgery within 24h of admission. Late LC group: Conservative	Hospitalization: Longer in early LC group (5.03 vs. 2.36 days; p=0.006). Conversion to open surgery: Higher in early LC (48.5% vs. 21.2%; p=0.020). Complications: Non-significantly higher in early LC (18.2% vs. 3%; p=0.105).
	comparison of results between early and late cholecystectom y			rebound tenderness (60.6%), Murphy's sign (69.7%), and pericholecystic fluid (54.5%). Late LC group: Mean age 53.7 yrs, 33.3% male, 48.5% comorbidities.	therapy (IV antibiotics/fluids/ana lgesics) followed by LC after 6–8 weeks. Early LC group: Surgery within 24h of admission. Late LC group: Conservative therapy (IV antibiotics/fluids/ana lgesics) followed by LC after 6–8 weeks.	Operation duration: No difference (p=0.529). 5. Early LC is cost-effective but requires careful patient selection.
Naveen et al. ²⁶ 2025	Delayed versus immediate surgical intervention for perforated appendicitis	Prospective observational study; controlled study with two groups (immediate vs. delayed surgery)	Total: 100 Immediate surgery: 50 Delayed intervention: 50	Patients with radiologic and clinical proof of perforated appendicitis	Immediate surgery (6 hours after diagnosis), Delayed intervention (within 24-72 hours)	Early surgery significantly reduced postoperative complications and hospital stay in patients with perforated appendicitis. Prompt surgical intervention enhances outcomes and lowers healthcare costs.
Hecker et al. 16 2015	The impact of early surgical intervention in free intestinal perforation: a time-to- intervention pilot study.	Retrospective cohort analysis, observational study, single- site study	Total: 76 Under 3 h: 25 3 to 9 h: 36 Longer than 9 h: 15	76 septic patients - Mean age: 59.64 years (range 21-88 years) Gender: 45 males, 31 females All patients had intestinal perforation confirmed by	Surgical source control: Segmental resection with side- to-side anastomosis for small intestine perforations, resection for sigmoid colon perforations, Hartmann operation, descendorectostomy,	The study found that immediate surgical intervention might be advantageous for septic emergency patients, with an improved overall survival rate of 80% in the early intervention group compared to 73% in the late intervention group. More than 80% of patients underwent surgical source control within the first 9 hours after hospital admission, aligning

				radiographic imaging and surgery	ileotransversostomy for ascending colon perforations. Antibiotics: Administered to 97% of patients. Revision: Performed in 38% of cases.	with recommendations for early intervention. The study suggests that early surgical intervention may lead to lower rates of peritonitis, but further multicenter studies are needed to confirm these findings.
Zhang et al. ¹⁷ 2022	Early versus delayed intervention in necrotizing acute pancreatitis complicated by persistent organ failure.	Retrospective observational study	Total: 131 Early intervention: 100 Delayed intervention: 31	Patients with necrotizing acute pancreatitis (NAP) complicated by persistent organ failure (POF)	Invasive intervention for pancreatic necrosis: 100 patients (76.3%) received intervention within 4 weeks. 31 patients (23.7%) received delayed intervention beyond 4 weeks Specific nature of intervention not specified	Intervention within 4 weeks did not worsen clinical outcomes in NAP patients complicated by POF. Mortality rates were not significantly different between early and delayed intervention groups. Other clinical outcomes, such as new-onset multiple organ failure, gastrointestinal fistula, bleeding, length of ICU stay, and hospital stay, were comparable between the two groups.
Guo et al. ³³ 2024	Timing of Intervention in Necrotizing Pancreatitis.	Observationa 1 study; prospective database review; subgroup analysis	Total: 223 Early intervention: 136 Delayed intervention: 87	Patients with necrotizing pancreatitis	Surgical intervention; median timing of intervention was 32 days; early intervention ≤30 days; delayed intervention >30 days	The median timing of intervention was 32 days. Mortality rates were higher in the early intervention group compared to the delayed intervention group. Early intervention in patients without persistent organ failure showed similar outcomes to delayed intervention.
Subramania	ThTP5.8 Single	Retrospectiv,	Total: 172	Patients	Colorectal	Early laparoscopic surgery within 48 hours
n et al. ¹⁸ 2023	centre, single surgeons	observationa, single centre	Colorectal resections	undergoing laparoscopic	resections: 41 performed within 48	of admission is associated with shorter
2023	Surgeons	single centre	rescenons	пригозсоріс	performed within 10	
Rauh et al. 19	experience of laparoscopic emergency surgery from a tertiary care NHS hospital: delay in surgery is associated with higher mortality and morbidity.	Retrospective	within 48 hours (Group A): 41 Colorectal resections after 48 hours (Group B): 50 Small bowel resections within 48 hours (Group C): 20 Small bowel resections after 48 hours (Group D): 6 Laparoscopic adhesiolysis: 28 Laparoscopic hernia repair: 20 Total: 118	emergency gastrointestinal surgery Various types of surgical procedures: colorectal resections, small bowel resections, laparoscopic adhesiolysis, hernia repair	hours, 50 performed after 48 hours Small bowel resections: 20 performed within 48 hours, 6 performed after 48 hours Laparoscopic adhesiolysis: performed in 28 patients Laparoscopic hernia repair: performed in 20 patients	hospital stays and lower mortality rates compared to delayed surgery. Lower morbidity rates are also observed in patients who undergo surgery within 48 hours. Early surgery is associated with better surgical outcomes in various procedures such as colorectal resections, small bowel resections, laparoscopic adhesiolysis, and hernia repair.
Rauh et al. 19 2024	Does the Timing of Surgical Intervention Impact Outcomes in Necrotizing Enterocolitis?	Retrospective study	Total: 118 Early intervention: 92 Late intervention: 26	Infants with surgical necrotizing enterocolitis (sNEC) Diagnosed at different ages: early intervention group diagnosed younger (DOL: 8), late intervention group diagnosed older (DOL: 20)	Peritoneal drain (PD): 22 in early intervention, 2 in late intervention Laparotomy (LAP): 62 in early intervention, 20 in late intervention PD with subsequent LAP (PD + LAP): 8 in early intervention, 4 in late intervention	a higher mortality rate compared to those with late intervention. Early intervention was associated with more bowel resection and a higher incidence of pneumoperitoneum. The study suggests that medical optimization before surgery may improve outcomes in infants with NEC.

Bohm et al. ³¹ 2015	Reduced time to surgery improves mortality and length of stay following hip fracture: results from an intervention study in a Canadian health authority.	Intervention study Before-and- after design Observationa 1 study Non- randomized Non- controlled	Pre- intervention: 3525 Post- intervention: 3007 Total: 6525	Patients aged 50 years or older Adjusted for age, sex, comorbidities	Coordinated, region- wide efforts to improve timeliness of hip fracture surgery, aiming to meet a 48-hour benchmark.	The proportion of patients receiving surgery within 48 hours increased from 66.8% to 84.6%. Median length of stay decreased from 13.5 to 9.7 days. Crude in-hospital mortality decreased from 9.6% to 6.8%, with adjusted analyses showing reduced mortality in hospital and at 1 year.
Elkbuli et al. ²⁰ 2018	Isolated hip fracture in the elderly and time to surgery: is there an outcome difference?	Retrospectiv, stratified, observationa, prognostic cohort study	Total: 485 Surgery <48 hours: 460 Surgery >48 hours: 25	Patients aged 65 years and older Majority female (75% in <48 hours group, 76% in >48 hours group) Majority Caucasian (98% in <48 hours group, 96% in >48 hours group) Average age: 84 years in <48 hours group, 85 years in >48 hours group Similar Injury Severity Score (ISS) in both groups	Surgery for isolated hip fractures: - Group 1: Surgery within 48 hours of admission (460 patients) Group 2: Surgery after 48 hours of admission (25 patients) Standard venous thromboembolism (VTE) prophylaxis at admission and for 35 days postoperatively	Time to surgery significantly affects ICU-LOS, with surgeries within 48 hours resulting in shorter stays compared to those after 48 hours. Time to surgery does not affect complication rates, 30-day readmission, or mortality.
Kao et al. ²⁹ 2018	Evidence-based Reviews in	Randomized controlled	Total: 86 Early LC: Not	Patients with symptoms of acute	Early laparoscopic cholecystectomy	Early laparoscopic cholecystectomy (ELC) resulted in lower overall morbidity
	Surgery: Early		mentioned	cholecystitis lasting	(ELC)	compared to delayed cholecystectomy.
	Cholecystectom y for Cholecystitis.	trial, single center	Delayed LC: Not mentioned	more than 72 hours before admission	Delayed laparoscopic cholecystectomy (delayed LC)	Median total length of stay and duration of antibiotic therapy were significantly shorter in the ELC group. Total hospital costs were lower in the ELC group compared to those of delayed cholecystectomy.
Seudeal et al. ²¹ 2018	Early versus delayed appendectomy: A comparison of outcomes.	Retrospective observational study	Total: 116 Group 1: 75 Group 2: 41	Adult patients with acute appendicitis	Appendectomy: within 8 hours (group 1) or after 8 hours (group 2)	Delayed appendectomy performed more than 8 hours was not associated with increased perioperative complications. There were no significant differences in postoperative length of stay or 30-day readmission rate between early and delayed appendectomies. No deaths occurred in either group, indicating safety of delayed appendectomy.
Yadav et al. ³⁰ 2023	A randomized comparative study of early and delayed laparoscopic cholecystectom y in acute cholecystitis: a tertiary center experience and review of literature.	Prospective, randomized, comparative, hospital- based study	Total: 60 Early laparoscopic cholecystectom y: 30 Delayed laparoscopic cholecystectom y: 30	Adults aged over 18 years Diagnosed with acute cholecystitis	Early laparoscopic cholecystectomy: performed within 72 hours of hospital admission (Group 1) Delayed laparoscopic cholecystectomy: performed 6-8 weeks after the acute episode (Group 2) Conservative management (Group 2): intravenous fluids and antibiotics (doses and duration not specified)	Early laparoscopic cholecystectomy significantly reduced the duration of surgery and hospital stay compared to delayed surgery. Early surgery had a lower conversion rate to open cholecystectomy, although not statistically significant. Early laparoscopic cholecystectomy offers advantages such as shorter hospital stays and lower conversion rates without increasing postoperative morbidity.

Jeon et al. ²² 2014 Blitzer et	Effect of Tracheostomy Timing on Clinical Outcome in Neurosurgical Patients: Early Versus Late Tracheostomy. Timing of	Retrospective observational study	Total: 125 Early group (group E): 39 Late group (group L): 86 Total: 9190	Neurosurgical patients Mechanically ventilated for ≥7 days Adult BCI patients	Tracheostomy performed within 10 days of mechanical ventilation (early group, n=39) or after 10 days of mechanical ventilation (late group, n=86) Antithrombotic	Early tracheostomy significantly reduced the total mechanical ventilation duration and ICU length of stay compared to late tracheostomy. The incidence of ventilator-associated pneumonia was lower in the early tracheostomy group. Early tracheostomy did not reduce ICU or hospital mortality rates. Operative management did not differ from
al. ²³ 2020	intervention may influence outcomes in blunt injury to the carotid artery.	observational study, multi- site, propensity score matching	Operative intervention: 812 Open: 288 - Endovascular: 481 Both: 43		therapy (some participants) Open surgery (n = 288) - Endovascular surgery (n = 481) - Both open and endovascular surgery (n = 43) Early intervention: within 24 hours Delayed intervention: after 24 hours	nonoperative management in terms of mortality but was associated with a higher risk of stroke and longer hospital stays. Early intervention (within 24 hours) was associated with higher mortality rates compared to delayed intervention, particularly in the endovascular cohort. The study suggests that intervention should be delayed for at least 24 hours if possible.
Tud et al. ²⁴ 2024	A Comparison of Complication Rates between Early and Delayed Surgery among Filipino Patients with Fragility Fractures of the Hip.	Retrospective observational study, single- site study	Total: 96 Early intervention: 41 Delayed intervention: 55	Predominantly female (79.2%) Elderly (mean age: 77.2 to 81.6 years) Majority with intra- capsular fractures (61.5%) Higher number of comorbidities in the delayed	Early intervention: Surgery within 72 hours Partial hip arthroplasty (59.4%) - Fixation (33.33%) Total hip arthroplasty (7.3%)	Early intervention (surgery within 72 hours) resulted in a significantly lower incidence of pressure ulcers, pneumonia, and urinary tract infections compared to delayed intervention. Early intervention led to shorter hospital stays, with a mean length of stay of 8.85 days compared to 14.6 days for delayed intervention.
				intervention group (mean: 2.5 ± 0.7 vs. 2.89 ± 1.2)	Delayed intervention: Surgery beyond 72 hours Partial hip arthroplasty (59.4%) - Fixation (33.33%) Total hip arthroplasty (7.3%)	Overall, early intervention showed a significantly lower incidence of in-hospital complications and reduced length of confinement for patients with fragility fractures of the hip.
Elsawaf and Galhom ²⁸ 2018	Decompressive Craniotomy for Malignant Middle Cerebral Artery Infarction: Optimal Timing and Literature Review.	Prospective, randomized, controlled study	Total: 46 Group I: 27 Group II: 19	Patients with malignant middle cerebral artery territory infarction	Decompressive craniotomy performed prophylactically within 6 hours of presentation (group II, 19 patients)	Early decompressive craniotomy within 6 hours of ictus showed statistically significant improvements in neurological and functional outcomes compared to delayed surgery. There was a significant difference in mortality rates, with more than half of the delayed group dying due to delays in surgery or related complications. Early intervention has a significant impact on prognosis, despite potential surgical complications.
Minutolo et al. ²⁵ 2014	Laparoscopic cholecystectom y in the treatment of acute	Retrospective analysis	Total: 91 Early surgery: 32 Delayed surgery: 59	91 patients in total: 52 female, 39 male Mean age: 55	Laparoscopic cholecystectomy: Early surgery in 32 cases, delayed surgery in 59 cases.	Early laparoscopic cholecystectomy has comparable outcomes to delayed cholecystectomy in terms of operative time, conversion rate, and complications. Total hospital stay was significantly

Li et al.32	Association	Descriptive	Total: 235	Critically ill elderly	Percutaneous	Performing percutaneous dilatational
2024	Between	study,	Very Early	patients	dilatational	tracheotomy (PDT) very early (within 2
	Timing of	retrospective,	PDT: 161	Average age over	tracheotomy (PDT)	days of mechanical ventilation) resulted in
	Percutaneous	observationa,	Early PDT: 41	60 years	performed bedside	a significantly shorter length of stay in the
	Dilatational	single-site	Late PDT: 33	Patients with	using Ciaglia	intensive care unit (ICU).
	Tracheotomyan			cardiac diseases	technique with	The hospital mortality rate was
	d Clinical			Patients with	dilating forceps	significantly lower in the very early PDT
	Outcomes of			chronic obstructive	(PORTEX) and	group compared to the early and late
	Critically-ill			pulmonary disease	Seldinger guidewire.	groups.
	Elderly Patients.			(COPD)	Timing varied: very	The very early PDT group had a better
				Similar severity of	early PDT group (≤2	postoperative survival rate compared to the
				illness across	days), early PDT	other groups.
				groups as indicated	group (3-5 days),	
				by Apache II	late PDT group (≥6	
				scores	days) after	
				ICU patients	endotracheal	
				requiring	intubation.	
				prolonged		
				mechanical		
				ventilation		

*Year of publication, AMI: Acute Mesenteric Ischemia, BCI: Blunt Carotid Injury, DOL: Day of Life (used for infants), ELC: Early Laparoscopic Cholecystectomy, h: Hours, ICU: Intensive Care Unit, ISS: Injury Severity Score, IV: Intravenous, LAP: Laparotomy, LC: Laparoscopic Cholecystectomy, LOS: Length of Stay (often ICU-LOS or Hospital LOS), MCA: Middle Cerebral Artery, NAP: Necrotizing Acute Pancreatitis, NHS: National Health Service (UK), PD: Peritoneal Drain, PDT: Percutaneous Dilatational Tracheotomy, POF: Persistent Organ Failure, sNEC: Surgical Necrotizing Enterocolitis, VTE: Venous Thromboembolism

Condition specific optimal timing

As shown by Table 2, optimal timing is condition-specific, and outcomes depend on balancing physiological stabilization against disease progression risks. Time-sensitive conditions like intestinal ischemia, perforations, and necrotizing soft tissue infections consistently demonstrate reduced mortality with early intervention (<12 hours), where delays exceeding 12 hours are frequently fatal. ^{13,14,16,26} Then, for non-emergent conditions such as uncomplicated appendicitis, delayed intervention results in comparable outcomes to early surgery when combined with medical optimization. ²¹

Outcomes remain inconsistent for certain pathologies: In cholecystitis, early laparoscopic cholecystectomy reduces length of stay (LOS) and costs^{25,29,30} but increases conversion-to-open rates,¹⁵ while for pancreatitis, early intervention elevates mortality unless performed without persistent organ failure.²⁷ Critically, premature intervention carries significant risks, including increased mortality in blunt carotid injury,²³ necrotizing enterocolitis,¹⁹ and pancreatitis with organ failure.²⁷

Special populations exhibit distinct benefits: Elderly/fragile patients experience fewer complications and shorter LOS with early hip surgery, ^{20,24,31} and neurological patients show reduced ICU stays with early tracheostomy. ^{22,28,32}

Table 2. Condition-specific outcomes of early vs. delayed surgical intervention in critically ill ICU patients

Condition	Intervention Timing	Mortality	Morbidity/Complications	Length of Stay (LOS)	Key Remarks
Acute Intestinal Ischemia ¹⁴	Early: Surgery within 4–12h of shock onset Delayed: Non- surgical/unknown timing	Decreased mortality (95.24% survival vs. 4.76% non- surgery; P<0.001)	_	1	Early surgery critical for survival; delayed intervention fatal.
Necrotizing Soft Tissue Infections ¹³	Early: Surgery <6h of diagnosis Delayed: Surgery >6h	Decreased mortality (7.5% vs. 12.5% overall; Not statistically significant)	_	Decreased ICU & Hospital LOS	Mortality reduction not statistically significant.
Hip Fractures ^{24,31}	Early: Surgery <48h ³¹ Early: Surgery <72h ²⁴ Delayed: Beyond thresholds	Decreased mortality (Decreased In-hospital mortality: 9.6%→6.8%) ³¹	Decreased complications (Decreased pressure ulcers, pneumonia, UTIs) ²⁴	Decreased hospital LOS (Decreased Median LOS: 13.5 to 9.7 days) ³¹	Early intervention consistently beneficial.
Free Intestinal Perforation ¹⁶	Early: Surgery <9h	Decreased mortality (80% vs. 73% survival)	Decreased peritonitis risk (observed)	_	Supports source control within 9h.

	Delayed: Surgery >9h				
Acute Cholecystitis ^{15,30}	Early: LC ≤24h– 72h Delayed: LC after 6–8 weeks	No change in mortality	Increased conversion to open surgery (48.5% vs. 21.2%) ¹⁵ No change in complications	Decreased hospital LOS ³⁰ Increased hospital LOS if early ¹⁵	Conflicting LOS data; early LC reduces costs despite higher conversion rates.
Perforated Appendicitis ²⁶	Early: Immediate surgery Delayed: Delayed surgery	_	Decreased complications Decreased hospital stay	Decreased hospital LOS	Prompt intervention lowers costs & complications.
Malignant MCA Infarction ²⁸	Early: Decompression <6h Delayed: >6h	Decreased mortality	Increased neurological/functional recovery	_	Half of delayed group died; early intervention critical.
Necrotizing Pancreatitis ^{17,27}	Early: ≤4 weeks ²⁷ Early: ≤30days ¹⁷	No change in mortality Increased mortality if early ²⁷	No change in omplications ¹⁷ Increased re- interventions ²⁷	No change in ICU/Hospital LOS	Conflict: Early intervention harmful except in patients without persistent organ failure ²⁷
Necrotizing Enterocolitis ¹⁹	Early: Surgery at younger age Delayed: Surgery after stabilization	Increased mortality if early	<u>Increased_howel</u> resection	-	Medical optimization before surgery improves outcomes.
Blunt Carotid Injury ²³	Early: Intervention <24h Delayed: >24h	Increased mortality (esp. endovascular)	Increased stroke risk	Increased hospital LOS	Delay intervention ≥24h if possible.
Tracheostomy ^{22,32}	Early: ≤2-10 days of MV Delayed: >10 days	No change in mortality	Decreased ventilator- associated pneumonia Decreased MV duration	Decreased ICU LOS	Very early tracheostomy (≤2d) decreased
					mortality in elderly ³²

h: Hours, ICU: Intensive Care Unit, LOS: Length of Stay (Hospital or ICU), UTIs: Urinary Tract Infections, LC: Laparoscopic Cholecystectomy, MCA: Middle Cerebral Artery, MV: Mechanical Ventilation, d: Days, PDT: Percutaneous Dilatational Tracheotomy

Secondary clinical and healthcare resource utilization outcomes

Early intervention generally improved other secondary outcomes. Resource utilization was reduced, with lower costs for acute cholecystitis, ^{25,29} and shorter antibiotic duration. ²⁹ Functional outcomes improved significantly with early decompressive craniotomy for malignant MCA infarction. ²⁸ Infection rates decreased, as early tracheostomy reduced ventilator-associated pneumonia incidence. ²² Table 3 below shows further details of secondary outcomes identified.

Table 3. Clinical and Healthcare Resource Utilization Outcomes

Study Outcome		Effect on Outcomes	Condition
Elsawaf & Galhom ²⁸	Functional Outcomes	Increased neurological recovery	Malignant MCA Infarction
Minutolo ²⁵ and Kao ²⁹	Costs	Decreased total hospital costs	Acute Cholecystitis
Jeon et al. ²²	Infection Rates	Decreased ventilator-associated pneumonia	Tracheostomy
Kao et al. ²⁹	Antibiotic Duration	Decreased duration of antibiotic therapy	Acute Cholecystitis

MCA: Middle Cerebral Artery

4. DISCUSSION

The evidence from this systematic review underscores a fundamental paradigm: the optimal timing of surgical intervention in critically ill ICU patients is not a universal constant but a dynamic variable dependant on the specific pathophysiology of the underlying condition, the patient's physiological reserve, and the inherent risks of the disease progression versus operative stress. This complexity is reflected in the contrasting outcomes observed across different surgical emergencies. Our findings reveal that time-critical conditions (characterized by rapidly escalating tissue damage, ischemia, or contamination) demonstrate considerable benefits from early intervention. For instance, acute intestinal ischemia mandates surgery within 4-12 hours of shock onset to achieve survival rates exceeding 95%, contrasting with near-universal mortality in non-operative management or delayed intervention¹⁴ Similarly, necrotizing soft tissue infections, ¹³ free intestinal perforations, ¹⁶ and fragility hip fractures^{24,31} consistently show reduced mortality and morbidity with early surgical interventions. This aligns with the broader surgical principle that "source control" is vital in managing sepsis and ischemic emergencies, where delays allow irreversible damage or systemic inflammatory cascades to escalate. ^{34,35}

In contrast, conditions where the primary threat is the systemic inflammatory response or where organ failure dominates the clinical picture often exhibit poor outcomes with early interventions. Early intervention (≤30 days) in patients with persistent organ failure was associated with significantly higher mortality compared to delayed intervention (>30 days) in our included studies, ^{17,27} a finding also reported by other previous large-scale analyses. ^{36,37} This reinforces the concept that operating on a patient with severe systemic inflammation and organ dysfunction adds an intolerable physical and physiological stress, leading to poor outcomes. Similarly, blunt carotid injury demonstrated increased mortality with intervention within 24 hours, particularly endovascular approaches, ²³ likely reflecting increased risk of manipulating an acutely injured, unstable vessel amidst trauma-induced coagulopathy and inflammation. Necrotizing enterocolitis in infants also paradoxically showed higher mortality with earlier surgery, ¹⁹ emphasizing the potential benefit of medical stabilization to mitigate the inflammatory burden before operative insult. ³⁸

Our review noted reduced ICU length of stay and ventilator days with early tracheostomy, consistent with previous metaanalyses, ^{39,40} which found significant reductions in ICU stay and ventilator duration. However, the impact on mortality
remains mixed. While some RCTs and meta-analyses ^{41,42} suggested potential long-term mortality benefits of early
tracheostomy in specific subgroups like brain injury, others found no difference. ^{43,44} This ambiguity agrees with our
findings for other procedures and underscores that while resource utilization (ventilator days, ICU stay) is consistently
improved by early intervention in stable airway management, the effect on survival depends heavily on the reason for
prolonged ventilation (e.g., neurological injury vs. acute respiratory distress syndrome and baseline patient prognosis. Our
finding of reduced mortality with very early percutaneous dilatational tracheotomy (≤2 days) in the elderly³² further
complicates the picture, hinting at population-specific thresholds.

Despite the variable mortality impact, a consistent finding is the association of early intervention with reduced ICU and hospital LOS, ventilator duration, and specific complications in appropriately selected scenarios. Beyond tracheostomy, this was evident for early laparoscopic cholecystectomy (reduced LOS and costs), ^{25,29,30} hip fracture surgery (reduced pressure ulcers, pneumonia, UTIs, LOS), ^{24,31} and emergency GI surgery (reduced LOS). ¹⁸ The literature supports our findings showing that early surgical intervention shows benefits in reducing ICU stays, hospital length, and resource utilization. ^{39,44,45} This reduction in resource burden is clinically significant, decreasing risks of hospital-acquired infections, such as VAP, as noted with early tracheostomy, ^{22,45} pressure injuries, and functional deconditioning, while also having positive healthcare economic implications.

The identified divergence in outcomes can be conceptualized through the lens of disease-specific therapeutic windows. ⁴⁶ Conditions like intestinal ischemia or necrotizing fasciitis operate on a narrow window where rapid source control is the primary determinant of survival, and consequently, delay inevitably leads to catastrophic progression. Here, physiological derangement, while significant, is secondary to the uncontrolled primary insult, and operative risk, though high, is outweighed by the consequences of inaction. In contrast, conditions like severe pancreatitis with persistent organ failure or severe blunt carotid injury involve a primary pathological process (intense systemic inflammation, unstable vascular injury) where the immediate operative stress itself can be the tipping point into irreversible organ failure or death. The therapeutic window here necessitates a period of active physiological optimization (resuscitation, coagulopathy correction, and inflammatory modulation) to narrow the gap between physiological reserve and operative stress before proceeding. ^{4,34} For "intermediate" conditions like hip fractures or uncomplicated cholecystitis, the window is broader, allowing for safe optimization within hours to days, but still showing clear morbidity and resource utilization benefits with earlier intervention once stable.

Our findings provide several insights for consideration. Early intervention in physiologically unstable patients might not necessarily cause more complications inherently, but may occur in patients with such diminished reserve that any complication (e.g., anastomotic leak, bleeding) becomes fatal. Delaying intervention for optimization aims to build a sufficient physiological buffer to withstand potential complications. Future research should analyze timing data further, considering these dynamics.

During the pre-surgery stabilization period, relying solely on traditional vital signs normalization is insufficient.

Incorporating dynamic measures of resuscitation adequacy, such as lactate clearance, central venous oxygen saturation (ScvO2), bedside echocardiography assessing fluid responsiveness, or even microcirculatory parameters (using sidestream dark field imaging),⁴⁷ could provide more objective physiological thresholds for safe surgical timing in non-time-critical emergencies.^{6,46}

Refining patient stratification within conditions is crucial. In pancreatitis, distinguishing infected necrosis from sterile inflammation and identifying biomarkers predicting response to medical therapy (e.g., procalcitonin kinetics, CRP trajectories, interleukin profiles) could better define who benefits from early drainage versus prolonged medical management. Similarly, in sepsis requiring source control, biomarkers like presepsin or cell-free DNA might help identify patients deteriorating despite antibiotics, necessitating earlier intervention than standard clinical parameters suggest.

Timing isn't just about *when* but also *what* and *how*. Minimally invasive approaches (laparoscopic, percutaneous, endovascular) lower the physiological cost of intervention, potentially widening the therapeutic window for earlier intervention in some scenarios (e.g., percutaneous drainage preceding necrosectomy in pancreatitis, or laparoscopic vs. open repair for perforation) without the full stress of open surgery (van Grinsven et al., 2016).⁵⁰ Thus, the optimal timing might differ for the initial step (drainage) versus definitive procedure. System-level factors significantly impact achievable timing. Delays often stem from logistical constraints (operating room availability, imaging delays, inter-hospital transfer) or diagnostic uncertainty. Research should explore how optimizing these pathways impacts outcomes, especially for time-critical conditions.

Some limitations may influence the interpretation of our findings. Overall, evidence shows heterogeneity in timing definitions, patient populations, and study design. The definition of "Early" varied drastically across studies (e.g., 1.5 hours for cancer patients, 6 hours for necrotizing soft tissue infections, 48 hours for hip fractures, 4 weeks for pancreatitis), making direct comparisons difficult and highlighting that the optimal window is highly condition-specific. Condition heterogeneity means outcomes are tightly linked to the specific pathophysiology. This leads to time-critical conditions (ischemia, perforation, necrotizing soft tissue infections) favoring early intervention, while others (uncomplicated appendicitis, some pancreatitis presentations) allow for optimization or delay without harm. This makes it challenging to distinguish beneficial physiological optimization vs. harmful delay, allowing disease progression. Finally, evidence presented in this review relies predominantly on observational studies introducing potential bias, and randomized controlled trials.

CONCLUSION

This review demonstrates that "early" is not universally superior, nor is "delayed" inherently safer. The optimal timing for surgical intervention in critically ill ICU patients exists within a condition-specific, pathophysiology-defined therapeutic window, balancing the escalating risk of disease progression against the physiological burden of operative stress. Time-critical conditions demand expedited source control, while conditions dominated by severe systemic inflammation or organ failure often mandate a period of intensive physiological optimization before intervention. The consistent reduction in ICU/hospital stay and specific complications (like VAP) with appropriately timed early intervention across many conditions highlights a crucial opportunity to mitigate secondary morbidity and resource burden. Future progress hinges on moving beyond simple dichotomies.

Clinicians must balance the urgency of surgery against the risks of operating on physiologically deranged patients, using evidence-based windows tailored to each clinical scenario. Careful patient selection and condition-specific protocols are necessary as the definition of "early" varies substantially, necessitating disease-specific guidelines. Future research should focus on defining precise, validated time thresholds for different surgical emergencies and high-quality RCTs where feasible.

REFERENCES

- [1] Lee J, Im C. Time-to-surgery paradigms: wait time and surgical outcomes in critically III patients who underwent emergency surgery for gastrointestinal perforation. BMC Surg. 2024;24(1):159. doi:10.1186/s12893-024-02452-w
- [2] Meschino MT, Giles AE, Rice TJ, et al. Operative timing is associated with increased morbidity and mortality in patients undergoing emergency general surgery: a multisite study of emergency general services in a single academic network. CJS. 2020;63(4):E321-E328. doi:10.1503/cjs.012919
- [3] Silver DS, Lu L, Beiriger J, et al. Association between timing of operative interventions and mortality in emergency general surgery. Trauma Surg Acute Care Open. 2024;9(1):e001479. doi:10.1136/tsaco-2024-001479
- [4] Scott MJ, APSF Hemodynamic Instability Writing Group. Perioperative Patients With Hemodynamic Instability: Consensus Recommendations of the Anesthesia Patient Safety Foundation. Anesth Analg. 2024;138(4):713-724. doi:10.1213/ANE.00000000000006789
- [5] Franklin KN, Nishtala M, McCracken A, Berian JR, Zarzaur B. Does delayed operation increase morbidity

- and mortality? An analysis of emergency general surgery procedures. J Trauma Acute Care Surg. 2024;97(2):266-271. doi:10.1097/TA.0000000000004339
- [6] Dünser MW, Noitz M, Tschoellitsch T, et al. Emergency critical care: closing the gap between onset of critical illness and intensive care unit admission. Wien Klin Wochenschr. 2024;136(23-24):651-661. doi:10.1007/s00508-024-02374-w
- [7] Warren M, Bretherton C, Parker M. Delay to surgery beyond 12 hours is associated with increased hip fracture mortality. Eur J Orthop Surg Traumatol. 2024;34(6):2973-2980. doi:10.1007/s00590-024-03997-5
- [8] Martini V, Lederer AK, Laessle C, et al. Clinical Characteristics and Outcomes of Surgical Patients with Intensive Care Unit Lengths of Stay of 90 Days and Greater. Crit Care Res Pract. 2017;2017:9852017. doi:10.1155/2017/9852017
- [9] Park CM, Chun HK, Lee DS, Jeon K, Suh GY, Jeong JC. Impact of a surgical intensivist on the clinical outcomes of patients admitted to a surgical intensive care unit. Ann Surg Treat Res. 2014;86(6):319. doi:10.4174/astr.2014.86.6.319
- [10] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. Published online March 29, 2021:n71. doi:10.1136/bmj.n71
- [11] Nejadghaderi SA, Balibegloo M, Rezaei N. The Cochrane risk of bias assessment tool 2 (RoB 2) versus the original RoB: A perspective on the pros and cons. Health Science Reports. 2024;7(6):e2165. doi:10.1002/hsr2.2165
- [12] Lo CKL, Mertz D, Loeb M. Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. BMC Med Res Methodol. 2014;14(1):45. doi:10.1186/1471-2288-14-45
- [13] Hadeed G, Smith J, O'Keeffe T, et al. Early surgical intervention and its impact on patients presenting with necrotizing soft tissue infections: A single academic center experience. J Emerg Trauma Shock. 2016;9(1):22. doi:10.4103/0974-2700.173868
- [14] Bukhari HA, Kumar A. Early Surgical Intervention Improves Survival in Acute Intestinal Ischemia in the Intensive Care Unit. Ledda C, ed. BioMed Research International. 2021;2021(1):6672591. doi:10.1155/2021/6672591
- [15] Acar T, Kamer E, Acar N, et al. Laparoscopic cholecystectomy in the treatment of acute cholecystitis: comparison of results between early and late cholecystectomy. Pan Afr Med J. 2017;26:49. doi:10.11604/pamj.2017.26.49.8359
- [16] Hecker A, Schneck E, Röhrig R, et al. The impact of early surgical intervention in free intestinal perforation: a time-to-intervention pilot study. World J Emerg Surg. 2015;10(1):54. doi:10.1186/s13017-015-0047-0
- [17] Zhang H, Gao L, Mao WJ, et al. Early versus delayed intervention in necrotizing acute pancreatitis complicated by persistent organ failure. Hepatobiliary & Pancreatic Diseases International. 2022;21(1):63-68. doi:10.1016/j.hbpd.2020.12.019
- [18] Subramanian A, Swaminathan C, Siby J, Singh A, Sajid M. ThTP5.8 Single centre, single surgeons' experience of laparoscopic emergency surgery from a tertiary care NHS hospital: delay in surgery is associated with higher mortality and morbidity. British Journal of Surgery. 2023;110(Supplement_6):znad241.291. doi:10.1093/bjs/znad241.291
- [19] Rauh JL, Reddy MN, Santella NL, et al. Does the Timing of Surgical Intervention Impact Outcomes in Necrotizing Enterocolitis? The American SurgeonTM. 2024;90(9):2279-2284. doi:10.1177/00031348241256054
- [20] Elkbuli A, Eily A, Polcz V, et al. Isolated hip fracture in the elderly and time to surgery: is there an outcome difference? Trauma Surg Acute Care Open. 2018;3(1):e000212. doi:10.1136/tsaco-2018-000212
- [21] Seudeal K, Abidi H, Shebrain S. Early versus delayed appendectomy: A comparison of outcomes. The American Journal of Surgery. 2018;215(3):483-486. doi:10.1016/j.amjsurg.2017.10.057
- [22] Jeon YT, Hwang JW, Lim YJ, Lee SY, Woo KI, Park HP. Effect of Tracheostomy Timing on Clinical Outcome in Neurosurgical Patients: Early Versus Late Tracheostomy. Journal of Neurosurgical Anesthesiology. 2014;26(1):22-26. doi:10.1097/ANA.0b013e31829770a0
- [23] Blitzer DN, Ottochian M, O'Connor JV, et al. Timing of intervention may influence outcomes in blunt injury to the carotid artery. Journal of Vascular Surgery. 2020;71(4):1323-1332.e5. doi:10.1016/j.jvs.2019.05.059
- [24] Tud AR, Claudio RS. A Comparison of Complication Rates between Early and Delayed Surgery among Filipino Patients with Fragility Fractures of the Hip. Acta Med Philipp. 2024;58(3):34-39. doi:10.47895/amp.vi0.6799

- [25] Minutolo V, Licciardello A, Arena M, et al. Laparoscopic cholecystectomy in the treatment of acute cholecystitis: comparison of outcomes and costs between early and delayed cholecystectomy. Eur Rev Med Pharmacol Sci. 2014;18(2 Suppl):40-46.
- [26] J Naveen B, Rhea K, Department of Internal Medicine, Sparsh Hospital Bengaluru, Karnataka, India, et al. Delayed versus immediate surgical intervention for perforated appendicitis. Bioinformation. 2025;21(06):1612-1615. doi:10.6026/973206300211612
- [27] Guo Q, Li A, Xia Q, et al. Timing of Intervention in Necrotizing Pancreatitis. Journal of Gastrointestinal Surgery. 2014;18(10):1770-1776. doi:10.1007/s11605-014-2606-1
- [28] Elsawaf A, Galhom A. Decompressive Craniotomy for Malignant Middle Cerebral Artery Infarction: Optimal Timing and Literature Review. World Neurosurgery. 2018;116:e71-e78. doi:10.1016/j.wneu.2018.04.005
- [29] Kao LS, Ball CG, Chaudhury PK. Evidence-based Reviews in Surgery: Early Cholecystectomy for Cholecystitis. Annals of Surgery. 2018;268(6):940-942. doi:10.1097/SLA.00000000000002867
- [30] Yadav R, Rao H, Goel G. A randomized comparative study of early and delayed laparoscopic cholecystectomy in acute cholecystitis: a tertiary center experience and review of literature. Int J Curr Pharm Sci. Published online September 15, 2023:78-82. doi:10.22159/ijcpr.2023v15i5.3059
- [31] Bohm E, Loucks L, Wittmeier K, Lix LM, Oppenheimer L. Reduced time to surgery improves mortality and length of stay following hip fracture: results from an intervention study in a Canadian health authority. cjs. 2015;58(4):257-263. doi:10.1503/cjs.017714
- [32] Li C, Wang T, Sheng D, Zhang M, Zheng M, Li X. Association Between Timing of Percutaneous Dilatational Tracheotomyand Clinical Outcomes of Critically-ill Elderly Patients. J Coll Physicians Surg Pak. 2024;34(2):222-225. doi:10.29271/jcpsp.2024.02.222
- [33] Paramythiotis D, Karlafti E, Tsavdaris D, et al. When to Intervene in Acute Necrotizing Pancreatitis: A Narrative Review of the Optimal Timing for Intervention Strategies. Medicina. 2024;60(10):1592. doi:10.3390/medicina60101592
- [34] De Waele JJ, Girardis M, Martin-Loeches I. Source control in the management of sepsis and septic shock. Intensive Care Med. 2022;48(12):1799-1802. doi:10.1007/s00134-022-06852-5
- [36] Van Santvoort HC, Besselink MG, Bakker OJ, et al. A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis. N Engl J Med. 2010;362(16):1491-1502. doi:10.1056/NEJMoa0908821
- [37] Schepers NJ, Hallensleben NDL, Besselink MG, et al. Urgent endoscopic retrograde cholangiopancreatography with sphincterotomy versus conservative treatment in predicted severe acute gallstone pancreatitis (APEC): a multicentre randomised controlled trial. The Lancet. 2020;396(10245):167-176. doi:10.1016/S0140-6736(20)30539-0
- [38] McQueen K, Coonan T, Ottaway A, et al. Anesthesia and Perioperative Care. In: Debas HT, Donkor P, Gawande A, Jamison DT, Kruk ME, Mock CN, eds. Essential Surgery: Disease Control Priorities, Third Edition (Volume 1). The International Bank for Reconstruction and Development / The World Bank; 2015. Accessed August 9, 2025. http://www.ncbi.nlm.nih.gov/books/NBK333510/
- [39] Andriolo BN, Andriolo RB, Saconato H, Atallah ÁN, Valente O. Early versus late tracheostomy for critically ill patients. Cochrane Emergency and Critical Care Group, ed. Cochrane Database of Systematic Reviews. 2015;2018(12). doi:10.1002/14651858.CD007271.pub3
- [40] Griffiths J, Barber VS, Morgan L, Young JD. Systematic review and meta-analysis of studies of the timing of tracheostomy in adult patients undergoing artificial ventilation. BMJ. 2005;330(7502):1243. doi:10.1136/bmj.38467.485671.E0
- [41] Terragni PP, Antonelli M, Fumagalli R, et al. Early vs Late Tracheotomy for Prevention of Pneumonia in Mechanically Ventilated Adult ICU Patients: A Randomized Controlled Trial. JAMA. 2010;303(15):1483. doi:10.1001/jama.2010.447
- [42] McCredie VA, Alali AS, Scales DC, et al. Effect of Early Versus Late Tracheostomy or Prolonged Intubation in Critically Ill Patients with Acute Brain Injury: A Systematic Review and Meta-Analysis. Neurocrit Care. 2017;26(1):14-25. doi:10.1007/s12028-016-0297-z
- [43] Young D, Harrison DA, Cuthbertson BH, Rowan K, TracMan Collaborators FT. Effect of Early vs Late Tracheostomy Placement on Survival in Patients Receiving Mechanical Ventilation: The TracMan Randomized Trial. JAMA. 2013;309(20):2121. doi:10.1001/jama.2013.5154

- [44] Chorath K, Hoang A, Rajasekaran K, Moreira A. Association of Early vs Late Tracheostomy Placement With Pneumonia and Ventilator Days in Critically Ill Patients: A Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2021;147(5):450. doi:10.1001/jamaoto.2021.0025
- [45] Koch T, Hecker B, Hecker A, et al. Early tracheostomy decreases ventilation time but has no impact on mortality of intensive care patients: a randomized study. Langenbecks Arch Surg. 2012;397(6):1001-1008. doi:10.1007/s00423-011-0873-9
- [46] Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y
- [47] Treu CM, Lupi O, Bottino DA, Bouskela E. Sidestream dark field imaging: the evolution of real-time visualization of cutaneous microcirculation and its potential application in dermatology. Arch Dermatol Res. 2011;303(2):69-78. doi:10.1007/s00403-010-1087-7
- [48] Tarján D, Szalai E, Lipp M, et al. Persistently High Procalcitonin and C-Reactive Protein Are Good Predictors of Infection in Acute Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis. IJMS. 2024;25(2):1273. doi:10.3390/ijms25021273
- [49] Seymour CW, Kennedy JN, Wang S, et al. Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis. JAMA. 2019;321(20):2003. doi:10.1001/jama.2019.5791
- [50] Van Grinsven J, Van Santvoort HC, Boermeester MA, et al. Timing of catheter drainage in infected necrotizing pancreatitis. Nat Rev Gastroenterol Hepatol. 2016;13(5):306-312. doi:10.1038/nrgastro.2016.23.