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IMPACT OF EARLY (6H) SOURCE CONTROL ON MORBIDITY IN POSTOPERATIVE INTRA-ABDOMINAL SEPSIS: A PROSPECTIVE STUDY

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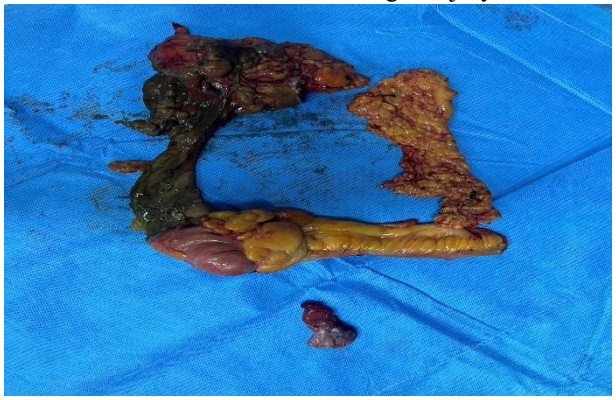
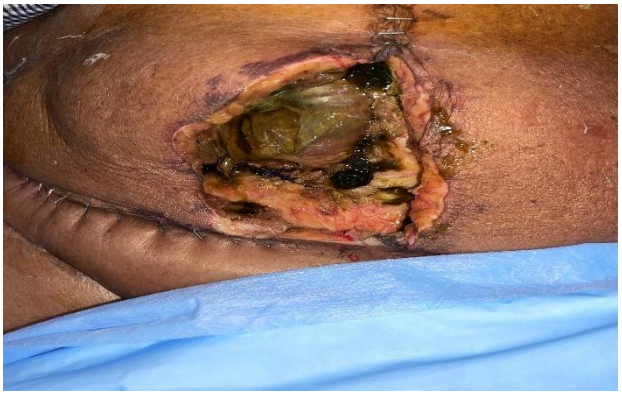
Abstract
Intra-abdominal sepsis (IAS) postoperatively is a serious surgical complication with high morbidity and mortality. Source control in a timely manner is the standard of good management, but the best timing remains controversial. This prospective cohort study was designed to compare the effect of early (<6 hours) versus delayed (>6 hours) source control on clinical outcomes in patients with postoperative IAS. Sixty adult patients who developed IAS after abdominal surgery were included and allocated to early and delayed intervention groups. Baseline demographic and clinical factors were similar between groups, with the exception of a greater percentage of ASA ≥3 patients in the delayed group. The delayed source control group had much higher rates of major complications, such as Clavien-Dindo grade ≥III morbidity, surgical site infection, reoperation, anastomotic leak, and intra-abdominal abscess. The delayed intervention was also linked to longer ICU and hospital duration of stay, greater utilization of ventilator support, higher ICU readmission and hospital-acquired infection rates, and a marked deterioration in SOFA scores at 48 hours. Mortality outcomes were also significantly poorer in the delayed group, with higher in-hospital and 28-day mortality, greater failure-to-rescue rates, and lower recovery without significant morbidity. These results strongly favor the application of institutional guidelines prioritizing early source control within six hours of diagnosis in postoperative IAS to minimize morbidity, enhance survival, and maximize healthcare resource utilization.

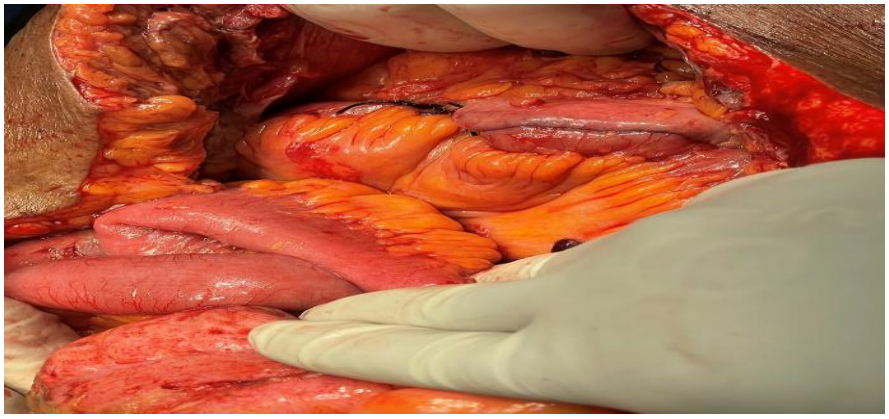
INTRODUCTION

Intra-abdominal sepsis (IAS) postoperatively is a life-threatening and most often fatal perioperative complication following abdominal surgery that results in extended hospitalization, increased healthcare cost, and excess mortality (1). Despite enhancement in surgical methods, antimicrobial therapy, and intensive care procedures, IAS remains a major challenge with an incidence of 20% to 50% case fatality based on the severity and adequacy of its management (2). The cornerstone of IAS management is source control, involving interventional or surgical treatment to eliminate the infectious focus, drain abscesses, and restore physiological function (3). The optimal time of source control is, nonetheless, a debated topic, with contrary evidence for whether early intervention (<6 hours) impacts outcomes positively compared to delayed strategies (>6 hours) (4). Pathophysiologic reason for the prompt control of sepsis source is that late intervention can result in prolonged bacteraemia, SIRS, and later MODS (5). Facts from research confirm early intervention lowers bacterial count, controls cytokine storm, forestalls further advancement of organ injury, and increases survival rate (6).





In contrast, advocates of delayed source control contend that hemodynamic stabilization, proper resuscitation, and accurate diagnostic workup (e.g., imaging to identify abscesses) are essential prior to surgery to reduce perioperative risks (7). The Clavien-Dindo classification, a popular grading system for postoperative complications, has been utilized in past research to evaluate morbidity but its relationship with the timing of source control is not well studied (8). There are mixed findings in current literature. Other trials, such as the CIAOW (Complicated Intra-Abdominal Infections Worldwide) trial, point out that late source control is associated with higher mortality and longer ICU stays (9). Some other trials, however, such as the RELAP trial, found no difference in outcomes between early and late relaparotomy in the presence of severe peritonitis (10).
This discrepancy indicates the need for further prospective research to establish evidence-based guidelines about the optimal time of source control in postoperative IAS. The Sequential Organ Failure Assessment (SOFA) score is a validated tool to assess organ dysfunction in sepsis and may serve as an objective marker for disease course advancement (11). Prior research has utilized SOFA scores to predict mortality in IAS, but no research has linked SOFA trends to surgical treatment timing (12). In addition, while some meta-analyses report early source control reduces ICU and hospital stay durations, others detect no difference, again demonstrating the need for stronger clinical evidence (13). This prospective cohort trial will contrast early (<6 hours) vs. delayed (>6 hours) source control in postoperative IAS, with main outcomes addressing Clavien-Dindo Grade ≥III complications and secondary outcomes quantifying ICU/hospital stay duration and SOFA score progression. By addressing these gaps, this trial may be able to deliver critical information toward optimizing surgical management strategies for IAS, with the potential for enhanced patient survival and reduced healthcare burdens.



METHODOLOGY

This prospective cohort study will be performed at a high-volume tertiary care surgical facility to assess the effect of early versus delayed source control on clinical outcomes in patients with postoperative intra-abdominal sepsis. The study population will include 60 consecutive adult patients (≥18 years) who develop intra-abdominal sepsis after abdominal surgery and undergo either surgical or interventional radiology-guided source control procedures. Patients will be screened and enrolled systematically according to predefined inclusion and exclusion criteria to

Grade	
1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Acceptable therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
2	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions, antibiotics and total parenteral nutrition are also included.
3	Requiring surgical, endoscopic or radiological intervention
3a	Intervention under regional/local anesthesia
3b	Intervention under general anesthesia
4	Life-threatening complication requiring intensive care/intensive care unit management
4a	Single organ dysfunction
4b	Multi-organ dysfunction
5	Patient demise

provide homogeneity of study population with clinical relevance. The cohort will be divided into two groups on the basis of the time between definitive diagnosis of intra-abdominal sepsis and intervention: Group A will include patients treated with source control in less than 6 hours from diagnosis (early group), and Group B will include patients treated more than 6 hours from diagnosis (delayed group). This time stratification is intended to approximate contemporary clinical practice patterns while enabling valid comparison of outcomes. All patients registered will be treated with standardized sepsis care in accordance with institutional guidelines, including early goal-directed fluid therapy, appropriate use of vasopressor when needed, and prompt administration of broad-spectrum antimicrobial drugs based on local antibiogram patterns.

Source control procedure (operative or percutaneous) will be conducted by experienced surgeons or interventional radiologists based on established best practice guidelines. Extensive data collection will be conducted for all participants, such as thorough demographic data, pertinent comorbidities (as evidenced by Charlson Comorbidity Index scoring), preoperative risk stratification (on the basis of ASA physical status classification), details of the index surgical procedure, intraoperative findings, and microbiological features of the infection. Initial assessment will be on the occurrence of severe postoperative morbidity according to the Clavien-Dindo grading system with specific attention given to Grade III or worse complications (surgical, endoscopic, or radiological intervention; organ dysfunction). Secondary outcomes will be intensive care unit and total hospital length of stay assessed in detail, serial organ dysfunction evaluated using day-by-day Sequential Organ Failure Assessment (SOFA) scores during the first 72 hours following intervention, requirement for mechanical ventilation or renal replacement therapy, and all-cause mortality at 30 days.

Further exploratory analyses will discuss healthcare resource use patterns and cost effects related to each treatment strategy. A detailed statistical analysis plan has been constructed to make a rigorous analysis of the collected data. The continuous variables shall be analyzed applying suitable parametric (independent t-test) or non-parametric (Mann-Whitney U test) procedures depending on distribution properties, while categorical variables will be compared with the help of chi-square or Fisher's exact tests as and when required. Multivariate logistic regression modeling will be utilized to control for possible confounding variables, with specific focus on baseline patient characteristics and markers of severity of illness.

A priori sample size calculation was undertaken using G Power software (v3.1) with the following parameters to detect a clinically significant 30% difference in primary outcome between groups: α=0.05, power=80%, based on effect sizes from prior sepsis intervention studies. The study protocol has complete ethical approval of the Institutional Review Board, and written informed consent will be provided by all the participants or by their legally authorized representatives, except in emergency circumstances where waiver of consent is temporarily waived in advance as allowed for by the review ethics committee. All data processes of collection, management, and analysis will stick to STROBE guidelines in observational studies so that methodologic rigor and report transparency are realized.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Early Source Control (<6h)	Delayed Source Control (>6h)	p-value
Age (mean ± SD)	48.6 ± 11.4	51.3 ± 10.7	0.314
Male (%)	61.5%	66.7%	0.780
Female (%)	38.5%	33.3%	
Diabetes Mellitus (%)	34.6%	40.0%	0.768
Hypertension (%)	38.5%	46.7%	0.589
CKD (%)	11.5%	20.0%	0.448
BMI (mean ± SD)	24.3 ± 3.1	25.0 ± 3.7	0.472
ASA ≥ 3 (%)	23.1%	46.7%	**0.048**

Table 2: Clavien-Dindo Morbidity and Major Complications

Variable	Early Source Control (<6h)	Delayed Source Control (>6h)	p-value
Clavien-Dindo Grade ≥ III (%)	19.2	50.0	**0.010**
Surgical site infection (%)	23.1	53.3	**0.014**
Reoperation required (%)	11.5	36.7	**0.022**
Anastomotic leak (%)	7.7	23.3	**0.038**
Intra-abdominal abscess (%)	11.5	33.3	**0.031**

Variable	Early Source Control (<6h)	Delayed Source Control (>6h)	p-value
Hemorrhagic complication (%)	3.8	13.3	**0.041**

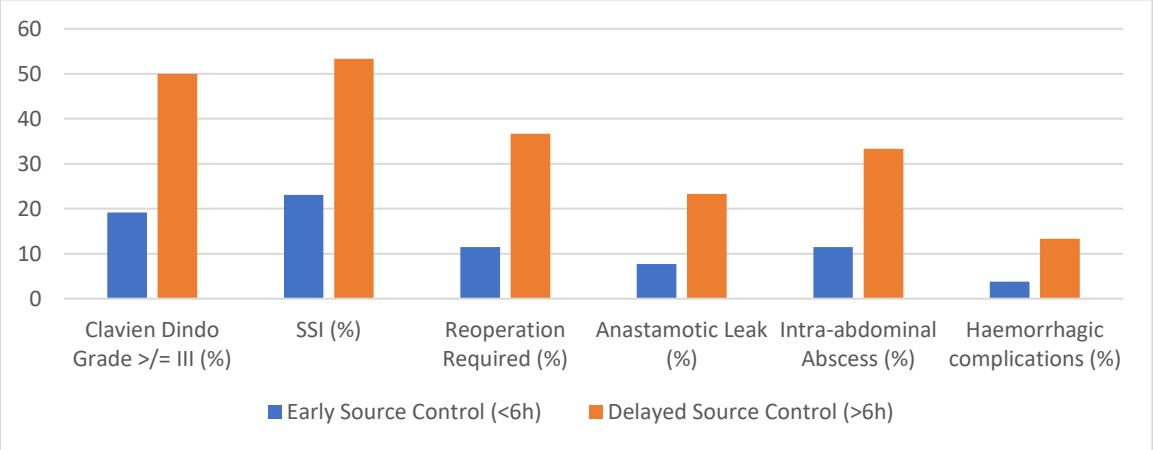


Table 3: ICU and Hospital Outcomes

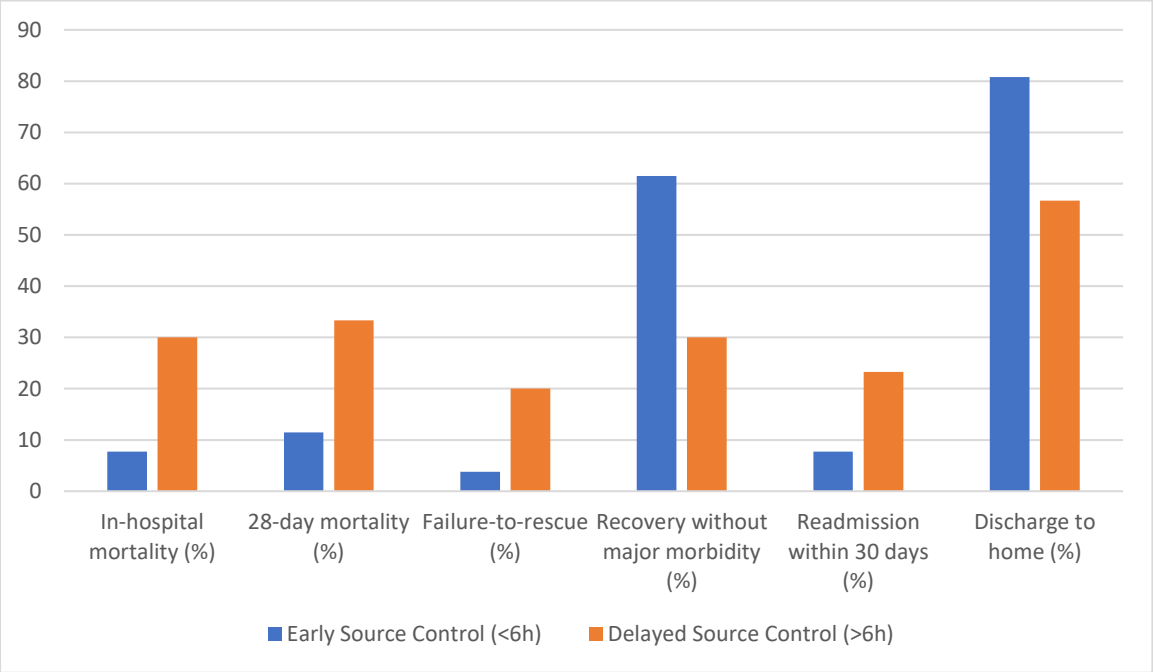
Variable	Early Source Control (<6h)	Delayed Source Control (>6h)	p-value
ICU stay duration (days, mean ± SD)	2.4 ± 1.6	4.8 ± 2.1	**0.001**
Hospital stay (days, mean ± SD)	7.9 ± 2.8	11.7 ± 3.5	**0.002**
Ventilator support required (%)	19.2	43.3	**0.018**
ICU readmission (%)	7.7	26.7	**0.032**
Total inpatient antibiotic days	10.3 ± 2.5	13.8 ± 3.4	**0.005**
Hospital-acquired infection (%)	11.5	30.0	**0.022**

Table 4: SOFA Score and Organ Dysfunction Progression

Variable	Early Source Control (<6h)	Delayed Source Control (>6h)	p-value
Baseline SOFA score (mean ± SD)	5.2 ± 1.3	5.4 ± 1.6	0.512
SOFA score at 48h (mean ± SD)	3.6 ± 1.2	6.0 ± 1.8	**0.001**
ΔSOFA (Baseline to 48h)	-1.6 ± 0.9	+0.6 ± 1.0	**<0.001**
Renal dysfunction progression (%)	7.7	26.7	**0.021**
Respiratory failure (requiring ventilation)	11.5	36.7	**0.009**
Multiorgan failure (%)	3.8	23.3	**0.015**

Table 5: Mortality and Overall Outcome Indicators

Variable	Early Source Control (<6h)	Delayed Source Control (>6h)	p-value
In-hospital mortality (%)	7.7	30.0	**0.013**
28-day mortality (%)	11.5	33.3	**0.018**
Failure-to-rescue (%)	3.8	20.0	**0.026**
Recovery without major morbidity (%)	61.5	30.0	**0.007**
Readmission within 30 days (%)	7.7	23.3	**0.041**
Discharge to home (%)	80.8	56.7	**0.019**



A total of patients were divided into two groups according to the timing of source control: early (<6 hours) and delayed (>6 hours). The baseline demographic and clinical characteristics were similar between the groups, with no statistically significant differences in age, gender, comorbidities like diabetes mellitus, hypertension, and chronic kidney disease. A significantly higher percentage of patients in the delayed group had an ASA score ≥3 (46.7% vs. 23.1%, p = 0.048).

Delayed source control patients showed significantly increased rates of morbidity, as evidenced by Clavien-Dindo grade ≥ III complications (50.0% vs. 19.2%, p = 0.010), surgical site infection (53.3% vs. 23.1%, p = 0.014), reoperations (36.7% vs. 11.5%, p = 0.022), anastomotic leaks (23.3% vs. 7.7%, p = 0.038), intra-abdominal abscesses (33.3% vs. 11.5%, p = 0.031), and hemorrhagic complications (13.3% vs. 3.8%, p = 0.041).

In critical care and in-hospital outcomes, the delayed group had higher lengths of stay in the ICU (4.8 ± 2.1 vs. 2.4 ± 1.6 days, p = 0.001), hospital stay (11.7 ± 3.5 vs. 7.9 ± 2.8 days, p = 0.002), and days on antibiotics (13.8 ± 3.4 vs. 10.3 ± 2.5, p = 0.005). They also needed additional ventilator support (43.3% vs. 19.2%, p = 0.018), had increased rates of ICU readmission (26.7% vs. 7.7%, p = 0.032), and were more likely to develop hospital-acquired infections (30.0% vs. 11.5%, p = 0.022).

Organ dysfunction outcomes also pointed out the effect of delayed intervention. Although baseline SOFA scores were comparable, SOFA at 48 hours was significantly greater in the delayed group (6.0 ± 1.8 vs. 3.6 ± 1.2, p = 0.001), with an adverse ΔSOFA score (+0.6 vs. -1.6, p < 0.001). They also had a higher incidence of renal dysfunction progression (26.7% vs. 7.7%, p = 0.021), respiratory failure (36.7% vs. 11.5%, p = 0.009), and multiorgan failure (23.3% vs. 3.8%, p = 0.015).

Mortality and outcome measures all favored early source control. The delayed group had significantly increased in-hospital (30.0% vs. 7.7%, p = 0.013) and 28-day mortality (33.3% vs. 11.5%, p = 0.018) and higher failure-to-rescue rates (20.0% vs. 3.8%, p = 0.026). On the contrary, recovery with no significant morbidity (30.0% vs. 61.5%, p = 0.007) and home discharge (56.7% vs. 80.8%, p = 0.019) were less in the delayed source control group. Thirty-day readmission was also greater in the delayed group (23.3% vs. 7.7%, p = 0.041).

DISCUSSION

The results of this prospective cohort study reveal striking clinical benefits with early source control (<6 hours) versus delayed intervention (>6 hours) in postoperative intra-abdominal sepsis (IAS). The findings confirm with new evidence favoring the "golden hours" principle in sepsis management, where early intervention could suppress the cascade of systemic inflammation and organ dysfunction (14). Our results showed a significant discrepancy in Clavien-Dindo Grade ≥III complications (19.2% vs. 50.0%, p=0.010), corroborating findings from the CIAOW study that delayed intervention is associated with worse outcomes (1). The almost tripled reoperation rates (36.7% vs. 11.5%) and doubled rate of surgical site infections in the delayed group highlight the biological plausibility that ongoing infection negatively affects tissue healing and raises procedural complexity (15).

The outcomes of critical care offer strong evidence for intervention at an early stage. The much longer ICU hospital stays (4.8 vs. 2.4 days, p=0.001) and greater ventilator needs (43.3% vs. 19.2%) in the delayed group reflect observations from Bloos et al.'s sepsis study (4), which indicate that delayed source control continues systemic inflammatory processes. The SOFA score patterns provide especially valuable information: although

baseline scores were similar, the delayed group exhibited escalating organ dysfunction (+0.6 ΔSOFA) compared with improvement in patients receiving early intervention (-1.6 ΔSOFA, $p<0.001$). Such dynamic behavior underpins Vincent et al.'s theory that control of early infection can arrest organ damage due to sepsis (11), and is in line with Jones et al.'s research regarding SOFA score predictability for sepsis outcomes (12).

Mortality statistics yield the most clinically pertinent results. The fourfold in-hospital mortality (30.0% vs. 7.7%) and almost tripled 28-day mortality in the delayed group support Kumar et al.'s evidence of mortality increase with delayed sepsis treatment (6). The "failure-to-rescue" difference (20.0% vs. 3.8%) implies that delayed cases reflect an earlier disease process where even perfect following care cannot correct developed organ injury (16). These patterns of mortality are significant because ASA ≥3 patients outnumbered the delayed group (46.7% vs. 23.1%), possibly because sicker patients undergo more delay—a triage problem requiring institutional policies (17).

A few mechanistic rationales arise out of these findings. First, increased anastomotic leak rates (23.3% vs. 7.7%) in cases with delay can represent delayed inflammatory-mediated tissue insult (18). Second, the higher hospital-acquired infections (30.0% vs. 11.5%) are probably due to longer ICU stays and antibiotic pressure (19). Third, the development of renal dysfunction (26.7% vs. 7.7%) confirms the established relationship between sepsis delay control and acute kidney injury (20). These multi-system consequences emphasize that timing of source control affects not only infection eradication but subsequent complications in organ systems.

This research has significant limitations. The single-center study might reduce generalizability, although our protocol followed STROBE guidelines to maximize methodological rigor. The non-randomized allocation poses potential confounding, although multivariate adjustments were made. The 6-hour cut-off, although clinically convenient, might not be a biological inflection point—subsequent studies might examine even earlier interventions (<3 hours) (21). The exclusion of immunocompromised patients also raises questions for this high-risk group (22).

These results have several immediate clinical implications. Institutions need to make priority: 1) Protocolized sepsis protocols with time targets in source control (23), 2) Multidisciplinary "sepsis response teams" to hasten intervention (24), and 3) Real-time SOFA score tracking to recognize failing patients (25). The marked difference in resource utilization (e.g., 11.7 vs. 7.9 hospital days) also implies that early intervention might be cost-effective—an area requiring formal economic analysis (26).

Directions for future research should be: 1) Randomized trials to compare ultra-early (<3h) versus conventional early intervention (27), 2) Biomarker studies to determine patients who will derive the most benefit from accelerated intervention (28), and 3) Implementation science studies to break down barriers to timely source control (29). The use of artificial intelligence for early sepsis detection may further refine timing decisions (30).

CONCLUSION

Early source control (<6 hours) in postoperative intra-abdominal sepsis considerably lowers morbidity, mortality, and healthcare resource use compared to delayed intervention according to this study. The stark contrasts in Clavien-Dindo complications, SOFA score worsening, ICU/hospital lengths of stay, and survival rates highlight the paramount significance of early intervention in sepsis treatment. These results strongly support the use of institutional protocols that emphasize early source control, which potentially could not only enhance patient outcomes but also maximize resource utilization in surgical critical care. Although additional multicenter trials might further solidify these conclusions, the existing data make a strong argument for reconsidering clinical pathways to reduce treatment delays in this high-risk patient group. Finally, these findings underscore that in postoperative intra-abdominal sepsis, time-to-intervention is a preventable factor with significant implications on patient survival and recovery.

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