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Association between timing of operative interventions and mortality in emergency general surgery

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ABSTRACT

Background Emergency general surgery (EGS) often demands timely interventions, yet data for triage and timing are limited. This study explores the relationship between hospital arrival-to-operation time and mortality in EGS patients.

Study design We performed a retrospective cohort study using an EGS registry at four hospitals, enrolling adults who underwent operative intervention for a primary American Association for the Surgery of Trauma-defined EGS diagnosis between 2021 and 2023. We excluded patients undergoing surgery more than 72 hours after admission as non-urgent and defined our exposure of interest as the time from the initial vital sign capture to the skin incision timestamp. We assessed the association between operative timing quintiles and in-hospital mortality using a mixed-effect hierarchical multivariable model, adjusting for patient demographics, comorbidities, organ dysfunction, and clustering at the hospital level.

Results A total of 1199 patients were included. The median time to operating room (OR) was 8.2 hours (IQR 4.9–20.5 hours). Prolonged time to OR increased the relative likelihood of in-hospital mortality. Patients undergoing an operation between 6.7 and 10.7 hours after first vitals had the highest odds of in-hospital mortality compared with operative times <4.2 hours (reference quintile) (adjusted OR (aOR) 68.994; 95% CI 4.608 to 1032.980, p=0.002). A similar trend was observed among patients with operative times between 24.4 and 70.9 hours (aOR 69.682; 95% CI 2.968 to 1636.038, p=0.008).

Conclusion Our findings suggest that prompt operative intervention is associated with lower in-hospital mortality rates among EGS patients. Further work to identify the most time-sensitive populations is warranted. These results may begin to inform benchmarking for triaging interventions in the EGS population to help reduce mortality rates.

Level of evidence IV.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Timely source control improves outcomes in sepsis. Delays are associated with increased mortality, but specific data on emergency general surgery (EGS) patients are limited.

WHAT THIS STUDY ADDS

⇒ This study shows that increasing time to operating room is associated with in increases in odds of mortality in EGS patients, highlighting the importance of prompt surgical intervention.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings support the development of guidelines for timely surgical interventions in EGS, which can improve patient outcomes and inform hospital policies on resource allocation and triage.

INTRODUCTION

Reducing the time to intervention by focusing on prompt recognition and treatment is paramount for enhancing outcomes in critically ill patients with time-sensitive conditions. Trauma,[1–3] ST-segment elevation myocardial infarction,[4–7] and ischemic stroke[8–10] have improved mortality by benchmarking timing for triage and resource coordination. In the same disciplines, time to intervention is a criterion for center verification and performance metrics. Prior work attributes gains in sepsis-related mortality to early recognition and protocolized management.[11 12] Recent research underscores the importance of achieving source control within 6 hours to reduce mortality in patients with intra-abdominal and soft tissue infections.[13 14]

Emergency general surgery (EGS) is responsible for approximately 10% of hospital admissions, but it accounts for nearly 50% of surgical mortality.[15] EGS presents distinctive timing and triage challenges. At the individual patient level, challenges arise from the variability in life-limiting comorbidities, difficulty in assessing surgical risk, inherent uncertainty surrounding the onset of acute disease processes, and symptom presentation. These factors collectively restrict the availability of data for informed surgical decision-making in the acute setting. From the standpoint of the healthcare system, factors such as the immediate availability of operating rooms (ORs), competing elective obligations, and the availability of other specialties, like anesthesia and OR staff, can significantly affect the start time of a surgical procedure. Striking a balance between the constrained resources of ORs and surgical staff and the pressing needs of other

time-sensitive conditions poses a considerable challenge when executing expedient operative management of EGS patients.[16] While deferring cases to an urgent or 'next day' may be appropriate in many situations, inappropriate delay may have significant consequences for patients.

With that, our objective was to determine if time from first contact to operation start is associated with mortality in EGS. We hypothesize that increasing time will be associated with increased odds of adjusted mortality.

METHODS

Study population

We analyzed our local EGS registry that captures retrospective electronic health record (EHR) information on primary and consulting patients seen by EGS surgeons. The registry includes patients who underwent surgery and those who received non-operative treatment. The data also link admission comorbidities, vital signs, laboratory results, procedural records, and all encounter-associated *International Clinical Diagnosis* (ICD) codes of the 10th revision, providing a comprehensive view of patient care and outcomes. The registry draws on mortality data from hospital discharge information and the state vital statistics to capture deaths outside the primary admission. We included patients from our quaternary academic referral center and three additional high-volume regional hospitals within a single, multi-hospital healthcare payer-provider institution receiving regional referrals and interfacility patient transfers from both within and outside of the institution.

We considered patients for analysis if they had an American Association for the Surgery of Trauma (AAST)-defined EGS diagnosis and underwent a procedure in an OR in the first 72 hours of their hospital encounter.[17 18] We limited our analysis to this timeframe to reduce the influence of other medical treatments and events that could affect the results, allowing us to focus specifically on the effect of the timing of the surgery. Prior work characterizes patients as urgent or emergent from within 48 hours to 72 hours.[19 20] We deemed it crucial to extend the hospital stay to 72 hours, as numerous patients need additional preoperative investigations, trials of non-operative management, or further optimization and discussion of care goals. Furthermore, procedures performed beyond this initial 3-day period could have varying levels of urgency, introducing further uncertainty. The clinical conditions include soft tissue infections, acute diverticulitis of the colon or small bowel, bowel perforation, internal or abdominal wall hernia, colitis, intestinal obstruction, intestinal ischemia, acute pancreatitis, perforated ulcer disease, and complications of other procedures including surgical site infection.

We excluded patients who underwent a procedure with gastroenterology before surgery to isolate the effect of time on OR better. We also excluded laparoscopic appendectomy or cholecystectomy as the primary initial procedure as marginal delays in operative intervention have proven to be a non-inferior strategy and therefore timing is commonly based on scheduling logistics rather than acuity and have a very low mortality risk overall.[21 22] We assessed all EGS conditions in the primary model to evaluate common operational practices. At our facility, unless a patient is critically hemodynamically unstable, prioritization of transfer priority and OR availability does not distinguish based on the underlying EGS diagnosis and receive a relatively uniform urgency. Consequently, the EGS population in practice is not stratified based on the clinical diversity of underlying pathologies for pragmatic purposes.

Missing data

We evaluated missing data in our model covariates and observed minimal missingness within our sample, ranging from 0% to 8% across analysis variables, affecting 90 patients. Notably, we observed the highest rate of missingness in laboratory data. Despite considering imputation techniques such as multiple imputations by chained equations, we found their predictive performance for missing values to be poor, likely due to the non-random nature of the missingness. Consequently, we excluded patients with missing covariates from the final models.

Statistical analysis

Our primary outcome was in-hospital mortality. Our secondary outcome was 30-day mortality given the incorporation of this metric in the National Surgical Quality Improvement Program. We examined the association between time to OR and our mortality outcomes. We express continuous data as median and IQR, comparing unadjusted continuous variables with Wilcoxon rank-sum and categorical variables using χ^2 tests. We applied a significance threshold of $p \leq 0.05$.

We define time to the OR as the hours between the earliest recorded vital sign recording during the hospital encounter and the timestamp when the initial surgical procedure begins with skin incision. This measurement provides a comprehensive view of how our hospital manages surgical emergencies and urgencies, encompassing the entire process from the patient's initial evaluation and surgical consultation to the time between requesting an OR and the actual start of the surgery. While this duration may not represent the onset of the patient's disease process, it is a practical interval that can be examined and optimized at both the hospital and system levels.

We categorized time to OR into quintiles using percentiles, a common strategy when dealing with limited data.[23] This approach helps address the non-normal distribution and potential non-linear associations with mortality. There are no widely accepted clinical cut points or timing benchmarks to use. Using percentiles also enhances result interpretability and allows us to capture threshold effects and non-proportional relationships that linear analysis might overlook. Moreover, along with the described risk adjustment, it mitigates the impact of survival bias for patients receiving later surgery. Analyzing it as a continuous variable at the individual patient level could accentuate this bias. Finally, it allowed evenly distributed patients among the quintiles to permit comparative analysis rather than using predefined thresholds that would result in small groups or such wide timeframes to include enough patients for analysis to limit the clinical utility of the findings.

To explore the relationship between mortality and intervention timing, we used risk-adjusted mixed-effects logistic regression models clustered at the hospital level. We selected a priori risk adjustments based on existing EGS-specific risk models[24 25] and clinical expertise. We include age, frailty, interfacility transfer status, vital signs on presentation, markers of preoperative sepsis and organ failure, and procedure completed. We capture frailty using the validated Risk Analysis Index (RAI)[26] and organ damage by the Sequential Organ Failure Score.[27] The RAI is a validated frailty index specifically designed for use in surgical populations. It includes variables such as age, unintentional weight loss, renal failure, heart failure, shortness of breath, cognitive function, living situation, activities of daily living, and cognitive scoring. The score also considers the presence of active malignancy, providing a comprehensive assessment of a patient's frailty and associated surgical risk. The Sequential Organ Failure

Assessment (SOFA) score assesses each organ system to determine the extent of a patient's organ failure and predicts mortality in critically ill patients.

Transfer status in our primary model is binary; however, we included total transfer time in our sensitivity analyses. We calculated a c-statistic and used calibration curves to evaluate model discrimination and calibration.

We employed generalized additive mixed models (GAMM), as detailed in the online supplemental methods (Supplementary Digital Content 1 (SDC 1)), to better understand the non-linear correlation between time and mortality. GAMM facilitates exploring non-linear relationships by using smoothing splines for independent variables.

We used Stata V.18 (StataCorp, College Station, TX) and R V.4.2.0 (R Foundation for Statistical Computing, Vienna, Austria) for data analysis. Data reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines (SDC 2).[28]

Subgroup analyses

We performed exploratory subgroup analyses. We first looked at mortality in patients with varying SOFA scores. An initial SOFA score of greater than 1 confers a 5% mortality in patients in the critical care setting, going up to 20% with scores between 2 and 3.[27 29 30] We then examined patients meeting criteria for frailty. We define frailty as an RAI score greater than or equal to 24 because of known decreases in physiologic reserve and higher rates of complications among elective and emergent procedures.[31]

As an additional subgroup analysis, we examined patients who had a diagnosis requiring an operation related to intra-abdominal pathology based on ICD codes and procedure performed. This effectively excludes soft tissue infection, both necrotizing (NSTI) and non necrotizing, from our study population, given these patients have highly variable diagnostic criteria and presentations with wide range of clinical findings. Often patients with a life-threatening necrotizing infection appear similar in the ICD diagnosis coding to patients with large abscesses, despite different clinical courses. Additionally, early debridement is considered within 12 hours while more recent evidence suggests source control within 6 hours, adding a wide range of timing targets.[32]

Sensitivity analyses

We conducted sensitivity analyses to test our assumptions and the strength of our results. First, if the patient underwent interfacility transfer prior to admission at our center, we incorporated the time elapsed from patient acceptance to arrival into the model to see how this impacted our assumptions and odds of mortality. Second, we calculated an E-value to assess the magnitude of association needed for hypothetical unmeasured confounders to nullify the observed relationship between the timing of OR procedures and mortality (online supplemental methods, SDC 1). While the E-value does not suggest unmeasured confounding does not exist, it helps assess the robustness of the findings by considering whether unmeasured confounding of the magnitude needed to nullify or reverse the study results is plausible or likely. Third, we completed spline analyses using evenly spaced knots and our institutional triage guidelines for all surgical procedures based on stakeholder consensus to approximate more rounded timeframes that may be used clinically. Finally, we revised our original model to test our assumptions regarding comorbidities by using the Emergency Surgery Score (ESS) instead of the RAI and SOFA. This allowed us to incorporate a broader range of comorbidities to validate our assumptions. The ESS includes factors such as age, ascites, body mass index, chronic obstructive pulmonary disease, hypertension, steroid use, cancer, weight loss, dyspnea, functional dependence, and other laboratory values indicating organ damage.[25]

Table 1 Demographics and characteristics of study population and time to operating room

n	1199
Age, median (IQR)	63 (49–73)
Sex, female, n (%)	617 (51.5)
Frailty, n (%)	523 (43.7)
SOFA score, median (IQR)	1 (1–3)
Initial HR, median (IQR)	90 (75–103)
Initial white cell count, median (IQR)	9.6 (7–13.3)
SBP low, median (IQR)	83 (74–92)
Temperature high, median (IQR)	37.11 (36.83)
Temperature low, median (IQR)	35.4 (34–36)
RR high, median (IQR)	26 (22–32)
Laparotomy, n (%)	615 (51.4)
Transfer, n (%)	384 (32.1)
Sepsis, n (%)	190 (15.9)
Ventilator, n (%)	65 (5.4)
EGS diagnosis, n (%)	
Incarcerated hernia	218 (21.2)
Volvulus	25 (2.4)
Toxic *Clostridium difficile*	42 (4.1)
Perforated SB	96 (9.3)
Ischemic bowel	75 (7.3)
NSTI	171 (16.6)
Perforated LB	99 (9.6)
Bowel obstruction	59 (5.7)
Surgical rescue	148 (14.4)
In-hospital mortality, n (%)	75 (6.27)
30-day mortality, n (%)	87 (7.27)

EGS, emergency general surgery; HR, heart rate; LB, large bowel; NSTI, Necrotizing soft tissue infection; RR, respiratory rate; SB, small bowel; SBP, systolic blood pressure; SOFA, Sequential Organ Failure Assessment.

RESULTS

Of the 10 201 patients in the EGS registry, 1199 underwent operative intervention and met the criteria for inclusion in this study. Patients were predominantly female, with signs of mild organ damage and low systolic blood pressure (table 1). In-hospital and 30-day mortality was 6.3% and 7.3%, respectively. Of the patients who had a 30-day mortality, the median days to death was 2 days (IQR 1–9 days). The median time to the OR was 490 minutes (IQR 294–1227 minutes). The time to OR quintiles were as follows: 1–252 minutes (0–4.2 hours), 253–399 minutes (4.2–6.7 hours), 400–641 minutes (6.7–10.7 hours), 642–1465 minutes (10.8–24.4 hours), and 1467–4257 minutes (24.5–70.9 hours; online supplemental eTable 1, SDC 1). We used the exact number of minutes for improved precision in our analysis but have converted them to hours for ease of interpretation in the remainder of our reporting.

The distribution of age, sex, and proportion of frail patients was consistent across quintiles. However, there were distinct differences in diagnoses between groups, with NSTI accounting for 14% in group 1 and 22% in group 4. Notably, the primary admitting service varied, with general surgery being predominant

Table 2 Adjusted OR and 95% CI for in-hospital mortality from logistic regression model

	aOR	95% CI lower bound	95% CI upper bound	P value
Time to OR				
0–4.2 (reference)				
4.2–6.7	6.124	0.308	121.857	0.235
6.7–10.7	68.994	4.608	1032.980	0.002
10.8–24.4	15.725	0.686	360.689	0.085
24.5–70.9	69.682	2.968	1636.038	0.008
Age	1.072	1.002	1.147	0.044
Frailty	1.619	0.302	8.683	0.574
Initial HR	0.987	0.955	1.019	0.415
White cell count	0.986	0.897	1.083	0.767
SBP low	0.950	0.895	1.007	0.085
Laparotomy	1.358	0.243	7.590	0.727
SOFA score	1.617	1.302	2.007	0.000
Temperature high	0.204	0.068	0.611	0.005
Temperature low	1.115	0.875	1.420	0.379
RR high	1.013	0.994	1.033	0.185
Transfer	2.238	0.473	10.591	0.310
Sepsis	7.337	1.584	33.993	0.011

Time in minutes.
aOR, adjusted OR; HR, heart rate; OR, operating room; RR, respiratory rate; SBP, systolic blood pressure; SOFA, Sequential Organ Failure Assessment.

at 75% in group 1 but decreasing to 56% in group 3, where hospitalist and critical care medicine approached 20% together.

Increasing time to OR significantly increased the likelihood of in-hospital mortality. The 24.5–70.9 hour quintile had the highest odds of in-hospital mortality compared with the reference (adjusted OR (aOR) 69.682; 95% CI 2.968 to 1636.038, p=0.008, table 2). This effect is observed in 6.7–10.7 hours as well (aOR 68.994; 95% CI 4.608 to 1032.980, p=0.002, table 2) and nears significance in 10.8–24.4 hours (aOR 15.725; 95% CI 0.686 to 360.689, p=0.085, table 2). The model demonstrated acceptable discrimination and calibration (online supplemental eFigure 1, SDC 1). For our secondary outcome, the likelihood of 30-day mortality was not significantly increased by time to OR. 6.7–10.7 hours approached significance (aOR 3.540; 95% CI 0.858 to 14.602, p=0.080, online supplemental eTable 2, SDC 1).

When evaluating patients with signs of organ damage, we found similar results. The likelihood of in-hospital mortality compared with the reference was significantly elevated for the 3rd (6.7–10.7 hours), 4th (10.8–24.4 hours), and 5th (24.5–70.9 hours) OR time quintiles among patients with a SOFA score >1 (online supplemental eTable 3, SDC 1). We did, however, find in patients with a SOFA score ≥3 that 6.7–10.7 and 24.5–70.9 hours had a significantly increased odds of 30-day mortality relative to the reference group, (aOR 10.138; 95% CI 1.403 to 73.251, p=0.022, table 3) and (aOR 15.016; 95% CI 1.312 to 171.831, p=0.029, table 3).

When we examine gastrointestinal pathology and exclude necrotizing soft tissue infections, all OR time quintiles demonstrated significantly increased adjusted odds of mortality relative to the reference group (online supplemental eTable 4, SDC 1).

We completed an analysis examining patients who met criteria for frailty with an RAI score >24 and similarly found significance across all time intervals relative to the reference (table 4).

Using time as a continuous variable, results of GAMM illustrate a steady rising in-hospital mortality rate that peaks around 10 hours (figure 1). Mortality rates also increase with time yet peak around 1200 minutes when modeling for 30-day mortality (online supplemental eFigure 3, SDC 1). Subsequently, the rate experiences a decline, reaching a relative plateau until approximately 20.8 hours. Beyond this point, there is a renewed increase in mortality, aligning with the observed quintiles.

As a sensitivity analysis, we added total transfer time to time to OR variable. Reference in this analysis was <260 minutes. The 25.8–149.4 hour (aOR 69.6708; 95% CI 2.968 to 1635.382, p=0.008, online supplemental eTable 5, SDC 1) and 6.9–11.1 hour quintiles (aOR 68.985; 95% CI 4.608 to 1032.657, p=0.002, online supplemental eTable 5, SDC 1) had the highest odds of in-hospital mortality relative to the reference population.

As an additional sensitivity analysis, we conducted a spline model with evenly spaced intervals[23] and another model using rounded time thresholds. Both models demonstrated statistically significant increased odds of mortality in similar intervals. (online supplemental table 6 SDC 1)

We calculated the E-value for the point estimate of our primary analysis, which was determined to be 137.488 for 6.7–10.7 hours. This value signifies a very large magnitude of association that an unmeasured confounding variable would need to have to eliminate the observed relationship, suggesting a robust association between increasing time to OR and in-hospital mortality (online supplemental eFigure 2, SDC 1). This robustness indicates that the impact of potential confounders not considered or able to be captured in our analysis would need to be substantial to completely nullify the observed association between time to operation and mortality.

We reconfigured our model to consider the ESS score in place of RAI and SOFA with similar results. The likelihood of in-hospital mortality compared with the reference was bimodal again, significantly elevated for the 3rd (6.7–10.7 hours) and 5th (24.5–70.9 hours) OR time quintiles among patients (online supplemental eTable 7, SDC 1).

DISCUSSION

These results suggest an association between time to OR and mortality rates among EGS patients. In our primary

Table 3 Adjusted OR and 95% CI for 30-day mortality from logistic regression model for SOFA score >3

	aOR	95% CI lower bound	95% CI upper bound	P value
Time to OR				
0–4.2 (reference)				
4.2–6.7	1.000	0.088	14.967	0.916
6.7–10.7	10.138	1.403	73.251	0.022
10.8–24.4	10.7295	1.040	110.688	0.046
24.5–70.9	15.01557	1.312	171.831	0.029
Age	1.074	0.999	1.113	0.055
Frailty	1.008	0.275	4.658	0.864
Initial HR	0.973	0.969	1.024	0.780
White cell count	0.989	0.906	1.079	0.800
SBP low	0.977	0.949	1.052	0.969
Laparotomy	2.189	0.752	20.025	0.105
SOFA score	1.753	1.162	1.725	0.001
Temperature high	0.182	0.137	0.857	0.022
Temperature low	1.174	0.917	1.294	0.330
RR high	1.003	0.983	1.022	0.822
Transfer	2.693	0.523	7.256	0.321
Sepsis	11.064	1.203	16.102	0.025

Time in minutes.
aOR, adjusted OR; HR, heart rate; OR, operating room; RR, respiratory rate; SBP, systolic blood pressure; SOFA, Sequential Organ Failure Assessment.

analysis, the third OR time quintile, representing time intervals of 6.7–10.7 hours, showed significantly higher mortality odds than the reference category (0–4.2 hours). Notably, these findings are pronounced for patients displaying organ damage and experiencing prolonged transfer times but were only evident when modeling for 30-day mortality in SOFA scores greater than 3. The association is more robust in subgroup analyses, excluding patients with necrotizing soft tissue infections and examining patients who meet criteria for frailty. When modeling for non-linear relationships, there is a positive relationship with increasing mortality and time for in-hospital and 30-day mortality. We tested our assumptions with various sensitivity analysis including different sets of comorbidities and found similar results held across various conditions and model iterations.

As noted above, we only saw 30-day mortality risk increase in the more critically ill with signs of severe organ dysfunction. There are several potential reasons for this. First, after the index operation, numerous interventions, complications, and other unmeasured confounders impact survival. Specifically, in a heterogenous EGS population, factors such as frailty and multimorbidity independently predict outcomes.[19 31 33 34] We suggest that early operative intervention is significant for early mortality but further work is needed to isolate the impact on long-term

Table 4 Adjusted OR and 95% CI for in-hospital mortality from logistic regression model with RAI score >24 (frail)

	aOR	95% CI lower bound	95% CI upper bound	P value
Time to OR				
0–4.2 (reference)				
4.2–6.7	64.796	1.370	147.520	0.026
6.7–10.7	85.482	5.460	798.267	0.001
10.8–24.4	80.522	2.346	786.248	0.011
24.5–70.9	216.851	3.271	1005.998	0.006
Age	1.094	1.002	1.129	0.042
Frailty	0.997	0.271	6.535	0.725
Initial HR	0.974	0.952	1.017	0.337
White cell count	0.932	0.881	1.051	0.397
SBP low	1.267	0.910	1.012	0.129
Laparotomy	1.763	0.585	9.013	0.234
SOFA score	0.427	1.288	1.924	0.000
Temperature high	1.165	0.159	0.853	0.020
Temperature low	1.014	0.907	1.349	0.320
RR high	4.173	0.998	1.036	0.075
Transfer	1.396	0.346	5.625	0.639
Sepsis	64.796	1.370	147.520	0.026

Time in minutes.
aOR, adjusted OR; HR, heart rate; OR, operating room; RAI, Risk Analysis Index; RR, respiratory rate; SBP, systolic blood pressure; SOFA, Sequential Organ Failure Assessment.

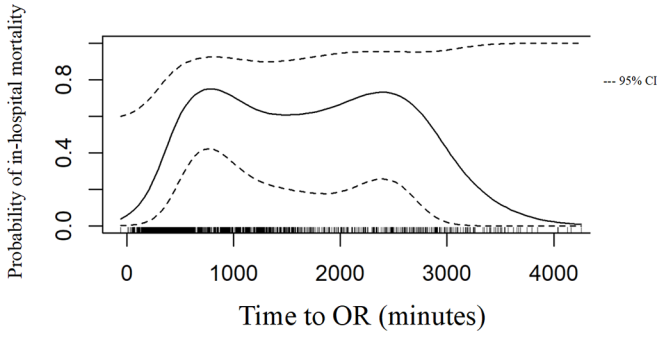

Figure 1 Generalized additive mixed model (GAMM) of probability of in-hospital mortality versus time to operating room (OR). Solid line represents effect estimates, dotted lines represent 95% CI.

survival among different populations. Furthermore, our data warehouse identifies 30-day mortality by incorporating the vital statistics at the Pennsylvania state level. There is potential for patients to die after we acquired the data. We may also miss mortalities from out-of-state patients.

Our findings align with prior studies highlighting reduced mortality in early intervention among necrotizing soft tissue infections, cholangitis, and intra-abdominal sepsis.[35–38] The Surviving Sepsis Campaign recommends rapid source control as soon as medically and logistically practical. Further, the recommendations detail the mixed data in terms of timing. While 6–12 hours is described, there is minimal literature demonstrating a mortality benefit to source control less than 6 hours.[39] Recent work by Reitz *et al* has highlighted a mortality benefit among patients with sepsis as defined by end-organ failure and provider concern for infection, which was especially apparent among those who underwent intra-abdominal and soft tissue source control procedures who undergo a source control procedure within 6 hours.[13] Our present study finds similar data with an inflection point around 6 hours but also builds on these findings and contributes to the existing literature in several significant ways.

Our results demonstrate an unexpected bimodal timing and mortality pattern in logistic modeling and GAMM. Despite consistent age, sex, and frailty proportions across quintiles, we observed significant differences in diagnoses and primary admitting teams. Notably, NSTI prevalence ranged from 14% in group 1 to 22% in group 4. The primary admitting service also shifted, with general surgery dominating at 75% in group 1 but decreasing to 56% in group 3, where hospitalist and critical care medicine reached 20%. Our hypothesis suggests that a potential delay in diagnosis or involvement of acute care surgery may lead to this later spike in mortality risk. The findings therein present an opportunity for further exploration.

The timeliness of intervention is critical, particularly in frail populations. While these results are consistent with previous research, they indicate a potential uniqueness in the population's sensitivity to the timing of operations. Although prior work emphasizes intervention delays in patients with sepsis, our study involves a substantial proportion of EGS patients who do not meet sepsis criteria. Further, our subgroup analyses focusing on frailty indicate that patients with limited reserve face an elevated risk of poor outcomes after procedural delays. Further exploration can determine whether time significantly affects mortality risk or if frailty independently predicts mortality, irrespective of intervention timing.

Multiple sensitivity analyses challenge our assumptions and demonstrate that our main findings hold true even with changing conditions. Of note, our sensitivity analysis had a considerable E-value. The E-value is advantageous for several reasons. It requires no assumptions from investigators, which makes it a robust alternative or addition to our standard sensitivity analysis. A strong, unmeasured confounder or combination of confounders would negate the observed association. With the large value, coupled with multiple sensitivity analyses, we demonstrate the strength of our association findings while acknowledging that further work is needed to identify other important factors related to timing and operative intervention.

Additionally, our findings suggest an opportunity to integrate objective measures of frailty into existing risk stratification systems, enhancing our understanding of the potential trajectory for these patients.

Consensus studies suggest timing guidelines, yet this is one of the few studies to quantify the associated mortality with time from first contact to the procedure start.[40–42] Our data can serve as a launching point to begin developing benchmark and timing goals for EGS cases and quantifying the risk of delay.

This study is one of only a few to employ a locally developed EGS registry, which helps us critically assess our own timing and triage practices. Although our sample size is relatively small, as centers seek AAST/American College of Surgeons EGS verification, we aspire to collaborate with other institutions in the future to bolster our statistical power and validate our findings.

Our study treats all EGS procedures as one group. This strategy is aligned with prior work on the topic and our approach is perhaps even more focused than prior retrospective investigations. Reitz *et al* included all forms of community-acquired sepsis and a wide variety of source control procedures, whereas our study looks at patients going to the OR with a specific set of EGS conditions. While we recognize the variations in urgency and risk among these procedures, our approach aims to mirror everyday decision-making processes at a system level, especially in triage situations. While the individual surgeon certainly can risk stratify and triage individual EGS patients, our system transfer priority and OR triage processes do not distinguish with high granularity among EGS patients and use broad priority categories. One of the reasons we grouped EGS patients in this manner was to assess this approach and whether improvements can be made based on these data to our system. Our findings highlight the importance of efficiently allocating resources, particularly within specific timeframes for EGS cases. Despite acknowledging limitations, we anticipate that future research will shed light on the most sensitive diseases and patient populations. Our approach underscores the ongoing need for investigation to enhance our understanding and management of EGS cases.

We also include dwell time after acceptance to transfer at the outside hospital and total transfer time in our models, using the rich data available in our local registry. This additional information can further enhance our understanding of the system factors that impact patient outcomes. Future work should examine whether the increased odds of mortality is proportional to the increase in time to OR.

Our exploratory subgroup analyses demonstrate stronger signals when necrotizing soft tissue infections are excluded. The findings align with prior work and show the need for a more precise definition with varying presentation and acuity. In the current data, differences between large abscesses requiring extensive debridement are challenging to separate from necrotizing infections. Future work may focus on developing a

standard definition because there may be time-to-intervention relationships in the NSTI population we are not fully capturing with current approaches to define this group.

We recognize that time to OR and mortality do not have a linear relationship. Our approach allows us to examine outcomes across various time categories that correspond to potentially actionable time thresholds. The second and third OR time quintiles likely represent urgent and priority operations. The increased odds of mortality represent the cost of delaying intervention for these groups.

Our study has several limitations. Our existing registry needs more power to stratify based on specific disease processes. With this, we recognize the heterogeneity in diseases included. Our primary aim was to highlight the associations and patterns to inform future research questions. Consequently, we cannot identify which conditions with these data are particularly sensitive to the relationship under investigation. Focusing on specific diagnosis can provide more precise insights and should be considered in future research projects when more data with this level of detail are available. Nevertheless, it is worth noting that there are scenarios in which the specific EGS diagnosis is identified after surgical intervention (eg, pneumoperitoneum from perforated peptic ulcer disease vs. diverticulitis vs. other bowel pathology) and, therefore, may present challenges to disease-specific OR prioritization. While we acknowledge this constraint, we view our findings as the initial step toward providing general guidance on the importance of prompt operative management and generating avenues for future research inquiries. Second, this is a retrospective study on EHR data not necessarily designed for this study question. The data are, however, readily available in most health systems, so there is an opportunity for validation and similar future iterative designs. Third, there is potential survivor bias. The longer the patients survive to get into the OR, the higher the likelihood they will ultimately survive. We do not know or have data on patients who died either at an outside hospital or in one of our facilities before being able to get into an OR which biases the relationship between time and mortality toward the null. Third, there may be unobserved delays, such as goals of care discussions, that we cannot capture in our data, although this would likely be a minority of patients. Non-surgical procedures, such as interventional radiology or initial non-operative management strategies, may have contributed to time delays from hospital arrival to operation. Regardless of the strategy, the 'clock' starts at admission to measure the time to operative intervention. Small bowel obstructions were included in our analysis for several reasons. We use hypertonic oral contrast within 6 hours of admission for diagnostic and therapeutic purposes. This approach often resolves the issue, excluding such cases from our study, or identifies patients likely to fail non-operative management, indicating surgery within our studied timeframe.

Additionally, while different from our local practice, according to Eastern Association for the Surgery of Trauma guidelines, a 5-day marker for surgery typically places these patients outside our study criteria.[43] Therefore, our findings underscore the importance of early identification and intervention, regardless of the chosen management strategy. Our analysis focused solely on patients who had surgery at the beginning of their hospital stay.

Our practice also cares for a significant number of surgical rescue and other high-risk patients who have been hospitalized for various reasons, like transplants, and are several days into their hospital stay. We understand that specific populations, such as those in medical intensive care, face an exceptionally high risk of mortality when they have a complex EGS-related diagnosis and maybe even more sensitive to prompt intervention.[44] For instance, our study included only three patients with pancreatitis who required decompressive laparotomies. Typically, pancreatitis can be managed by medical intensive care unit for days or weeks before EGS involvement. Consequently, our study does not capture the impact of timing for these cases, even though it is an important aspect of EGS that warrants further investigation. As a result of the mentioned limitations, these findings should be interpreted cautiously, but they can still provide insights for future efforts to guide triage of EGS cases. Despite these limitations, these findings offer descriptive insights into the importance of timing and should generate more hypotheses for targeted multicenter collaborative research efforts. The use of quintiles as noted above preserved power and allowed the data to define thresholds but may be awkward to implement as clinically relevant timeframes. As we grow our registry, we plan to explore different time thresholds with increasing power. It is also reasonable to round current quintile boundaries to the nearest practical thresholds for potential implementation.

Our findings have several implications. First, the absence of established, evidence-based triaging systems for prioritizing EGS cases underscores the need for further research.[45] Our study can provide a foundational starting point for developing such systems, helping healthcare providers make more informed decisions regarding case prioritization and resource allocation. Second, the substantial variation in EGS practices highlights the importance of our findings. Mortality is also rare and long-term functional outcomes may provide a better picture of the implications of delayed intervention. The results reported can serve as a starting point to shape benchmarks, assisting systems facilities in standardizing their approach to EGS care. These data can also offer guidance, potentially prompting consideration of patient interfacility transfers to ensure timely intervention and improved outcomes.

CONCLUSION

Increased time to the OR for EGS patients is associated with higher in-hospital mortality rates. This information should guide future research in pinpointing the most time-critical medical conditions and patient groups, as well as establishing standardized benchmarks. Existing nationwide quality improvement initiatives for EGS, along with robust data collection procedures, can enhance our comprehension of timing issues and elevate the quality of EGS care throughout the USA.

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based study. The investigators have access to medical records for clinical purposes, and the use of this information for research does not impact the rights and welfare of the subjects.

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Supplementary Digital Content 1

Supplemental Methods

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eFigure 1: Calibration curve and C statistic for primary model

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eTable 6: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality with ESS included in model

Supplemental Methods

1. Generalized Additive Model (GAM)

   GAM is an extension of GLM. Unlike Generalized Linear Model (GLM), GAM does not assume a linear relationship between outcome variable and predicted variable. As shown in the mathematical representation $y = \alpha + f(X)$, GAM does not specify anything about the shape of the function connect X and y; it only allows so-called smooth terms $f(X)$ which can be "loess", "splines" or other very flexible link functions. The smoothing parameters are decided based on cross-validation or maximum likelihood estimation.
2. Generalized Additive Mixed Model (GAMM)

   GAMM is to GAM as Generalized Linear Mixed Model (GLMM) to GLM. GAMM allows random effects and random smooths by group random variation. Random smooth is like random slope, but random smooth is more flexible. Random smooth can deal with by group variation in non-linear effect while random slope can account for by group variation in linear form.
3. E-Value

   The e-value is defined as the minimum strength of association that an unmeasured confound would need to have to explain away the exposure-outcome association. An e-value of 137.488 implies considerable unmeasured confounding would be required to explain away the timing and mortality association.

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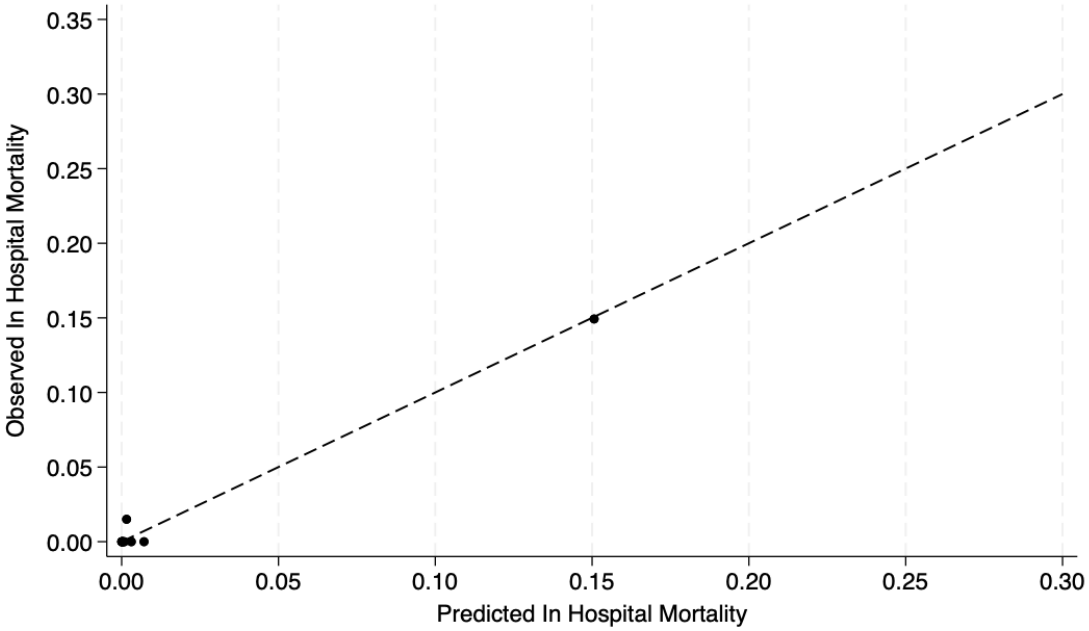
eTable 1: Demographics and characteristics of study population and time to operating room quintiles

Time Quintile		All Groups	1-252 minutes	253-399 minutes	400-641 minutes	642-1465 minutes	1467-4257 minutes
N		1,199	242	237	240	239	239
Age, median (IQR)		63 (49-73)	63 (50-73)	64 (54-75)	62.5 (47.5-73)	61 (44-71)	62 (47-73)
Sex, female, No.(%)		617 (51.5%)	128 (52.9%)	118 (49.8%)	134 (55.8%)	113 (47.3%)	124 (51.9%)
Frail, No.(%)		523 (43.7%)	66 (27.3%)	102 (43%)	97 (40.4%)	112 (46.9%)	146 (61.1%)
SOFA Score, median (IQR)		1 (1-3)	2 (1-6)	1 (1-3)	1 (1-3)	1 (0-3)	1 (0-2)
Initial HR, median (IQR)		90 (75-103)	90 (78-109)	90 (74-105)	85 (71-97)	92 (79-104)	86 (73-102)
Initial WBC, median (IQR)		9.6 (7-13.3)	10.75 (7.8-15.8)	10.3 (7.3-14.3)	9.75 (6.9-13.5)	9.3 (6.9-12.2)	8.75 (6.5-12.2)
SBP Low, median (IQR)		83 (74-92)	81 (70-90)	83 (75-92)	83 (74-92)	84 (74-93)	84.5 (75.5-92)
Temperature High, median (IQR)		37.11 (36.83)	37.11 (36.88-37.5)	37.1 (36.83-37.44)	37.1 (36.78-37.5)	37.11 (36.83-37.5)	37.11 (36.89-37.5)
Temperature Low, median (IQR)		35.4 (34-36)	35.2 (33.6-35.8)	35.5 (34.1-36)	35.5 (34.25-36)	35.4 (33.9-36)	35.3 (34-36)
RR High, median (IQR)		26 (22-32)	27.5 (23-35)	27 (22-33)	26 (22-32)	25 (21-30)	25 (21-31)
Laparotomy, No.(%)		615 (51.4%)	173 (71.5%)	154 (65.0%)	124 (51.7%)	75 (31.4%)	89 (37.2%)
Transfer, No.(%)		384 (32.1%)	151 (62.4%)	67 (28.3%)	52 (21.7%)	55 (23.0%)	59 (24.7%)
Sepsis, No.(%)		190 (15.9%)	66 (27.3%)	34 (14.3%)	34 (14.2%)	27 (11.3%)	29 (12.1%)
Ventilator, No.(%)		65 (5.4%)	25 (10.3%)	10 (4.2%)	10 (4.2%)	12 (5.0%)	8 (3.3%)
EGS Diagnosis, No.(%)	Incarcerated Hernia	218 (21.2%)	23 (10.2%)	39 (18.9%)	48 (22.3%)	61 (31.0%)	47 (25.3%)
	Volvulus	25 (2.4%)	5 (2.2%)	9 (4.4%)	10 (4.7%)	1 (0.5%)	0 (0.0%)
	Toxic C Diff	42 (4.1%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	3 (1.5%)	3 (1.6%)
	Perforated SB	96 (9.3%)	7 (3.1%)	4 (1.9%)	11 (5.1%)	12 (6.1%)	8 (4.3%)
	Ischemic Bowel	75 (7.3%)	39 (17.3%)	26 (12.6%)	16 (7.4%)	7 (3.6%)	8 (4.3%)
	NSTI	171 (16.6%)	26 (11.6%)	12 (5.8%)	19 (8.8%)	9 (4.6%)	9 (4.8%)
	Perforated LB	99 (9.6%)	32 (14.2%)	32 (15.5%)	34 (15.8%)	44 (22.3%)	29 (15.6%)
	Bowel Obstruction	59 (5.7%)	22 (9.8%)	25 (12.1%)	18 (8.4%)	12 (6.1%)	22 (11.8%)
	Surgical Rescue	148 (14.4%)	13 (5.8%)	13 (6.3%)	16 (7.4%)	8 (4.1%)	9 (4.8%)
In-hospital Mortality, No. (%)		75 (6.27%)	32 (13.2%)	13 (5.49%)	11 (4.58%)	9 (3.77%)	10 (4.18%)
30-day Mortality, No. (%)		87 (7.27%)	34 (14.05%)	16 (6.75%)	15 (6.25%)	11 (4.6%)	11 (4.6%)

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; C Diff, clostridium difficile; SB, Small Bowel; LB Large Bowel; Time in Minutes

eFigure 1: Calibration Curve



Calibration graph for the primary outcome of in-hospital mortality logistic regression model depicting predicted mortality from the model versus observed mortality across deciles of predicted mortality. The dotted line indicates a perfect association between predicted and observed mortality. The C-statistic of 0.971 indicates excellent discrimination.

eTable 2: Adjusted odds ratio and 95% Confidence Interval for 30-day mortality from logistic regression model

Adjusted odds ratio and 95% Confidence Interval for 30-day mortality from logistic regression model				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.2 (Reference)				
4.2-6.7	1.835	0.391	8.619	0.442
6.7-10.7	3.540	0.858	14.602	0.080
10.8-24.4	2.244	0.428	11.764	0.339
24.5-70.9	2.373	0.470	11.979	0.296
Age	1.028	0.989	1.069	0.163
Frailty	2.128	0.695	6.519	0.186
Initial HR	1.001	0.980	1.022	0.948
WBC	0.994	0.928	1.065	0.864
SBP Low	0.974	0.940	1.009	0.144
Laparotomy	1.599	0.575	4.448	0.369
SOFA Score	1.338	1.172	1.528	0.000
Temperature High	0.477	0.244	0.931	0.030
Temperature Low	0.977	0.900	1.062	0.589
RR High	1.021	0.996	1.046	0.102
Transfer	3.928	0.514	30.024	0.187
Sepsis	8.163	1.302	51.186	0.025

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes

eTable 3: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with varying SOFA score

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with SOFA $\geq$ 1				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.2 (Reference)				
4.2-6.7	5.691	0.643	522.583	0.089
6.7-10.7	62.981	6.890	6108.439	0.002
10.8-24.4	14.463	1.692	4168.549	0.026
24.5-70.9	65.197	4.012	11571.530	0.008
Age	1.072	1.002	1.177	0.046
Frailty	1.586	0.399	27.482	0.268
Initial HR	0.987	0.948	1.021	0.389
WBC	0.986	0.839	1.066	0.359
SBP Low	0.951	0.861	0.999	0.047
Laparotomy	1.310	0.125	9.557	0.936
SOFA Score	1.603	1.346	2.283	0.000
Temperature High	0.210	0.018	0.340	0.001
Temperature Low	1.112	0.849	1.444	0.451
RR High	1.013	0.996	1.046	0.102
Transfer	2.213	0.514	30.024	0.187
Sepsis	7.040	1.302	51.186	0.025
SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes				

eTable 4: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model including only intraabdominal pathology

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model including only intraabdominal pathology				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.2 (Reference)				
4.2-6.7	18.337	0.643	522.583	0.089
6.7-10.7	205.157	6.890	6108.439	0.002
10.8-24.4	83.974	1.692	4168.549	0.026
24.5-70.9	215.451	4.012	11571.530	0.008
Age	1.086	1.002	1.177	0.046
Frailty	3.310	0.399	27.482	0.268
Initial HR	0.984	0.948	1.021	0.389
WBC	0.945	0.839	1.066	0.359
SBP Low	0.928	0.861	0.999	0.047
Laparotomy	1.092	0.125	9.557	0.936
SOFA Score	1.753	1.346	2.283	0.000
Temperature High	0.079	0.018	0.340	0.001
Temperature Low	1.108	0.849	1.444	0.451
RR High	1.021	0.996	1.046	0.102
Transfer	3.928	0.514	30.024	0.187
Sepsis	8.163	1.302	51.186	0.025
SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes				

eTable 5: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality including interfacility transfer time

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with added total transfer time				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.3 (Reference)				
4.4-6.9	6.124	0.308	121.828	0.235
6.9-11.1	68.985	4.608	1032.657	0.002
11.2-25.7	15.723	0.686	360.582	0.085
25.8-149.4	69.670	2.968	1635.382	0.008
Age	1.072	1.002	1.147	0.044
Frailty	1.619	0.302	8.683	0.574
Initial HR	0.987	0.955	1.019	0.415
WBC	0.986	0.898	1.083	0.768
SBP Low	0.950	0.895	1.007	0.085
Laparotomy	1.358	0.243	7.589	0.727
SOFA Score	1.617	1.302	2.007	0.000
Temperature High	0.204	0.068	0.611	0.005
Temperature Low	1.115	0.875	1.420	0.379
RR High	1.013	0.994	1.033	0.185
Transfer	2.238	0.473	10.587	0.310
Sepsis	7.336	1.584	33.986	0.011
SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes				

eTable 6a: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality with 4 knot spline model

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with splines				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
Spline 1[1]	1.017	1.005	1.028	0.005
Spline 2	0.770	0.622	0.954	0.017
Spline 3	1.489	1.066	2.080	0.020
Age	1.058	0.994	1.126	0.078
Frailty	2.056	0.391	10.806	0.394
Initial HR	0.991	0.960	1.024	0.597
WBC	0.961	0.871	1.059	0.418
SBP Low	0.963	0.909	1.020	0.202
Laparotomy	2.399	0.487	11.804	0.282
SOFA Score	1.679	1.330	2.119	0.000
Temperature High	0.209	0.072	0.604	0.004
Temperature Low	1.134	0.920	1.399	0.238
RR High	1.017	0.997	1.038	0.101
Transfer	2.235	0.500	9.999	0.293
Sepsis	7.145	1.620	31.510	0.009

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes
[1] 4 evenly spaced knot model with knots at 2.1, 5.1, 13.5, 48.1 hours.

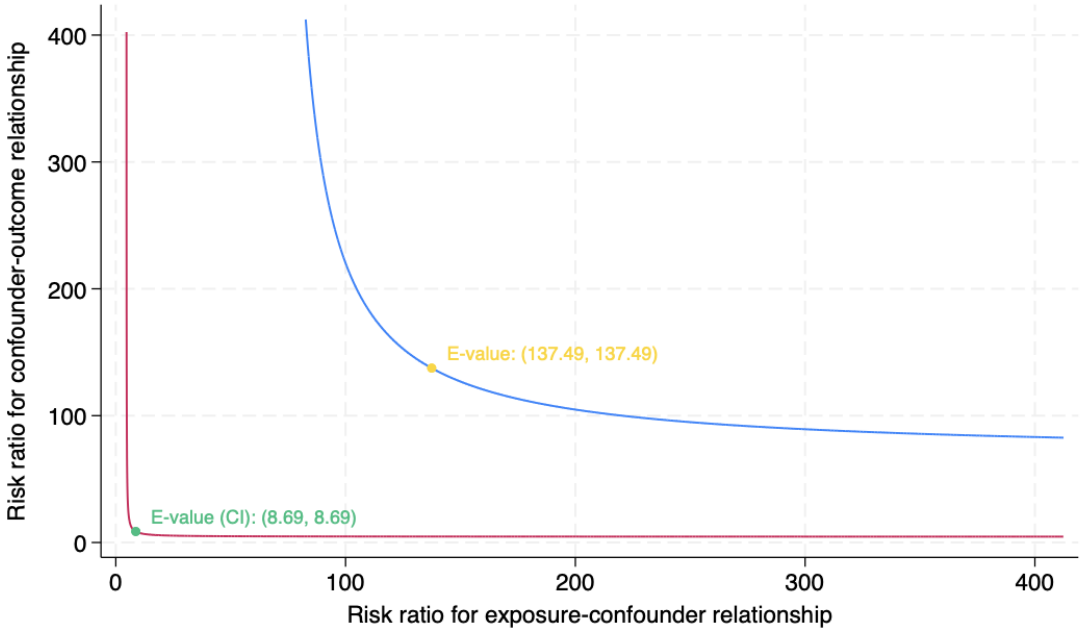
eTable 6b: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality with clinical splines

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with splines				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
Spline 1[2]	0.950	0.887	1.017	0.140
Spline 2	1.726	1.050	2.837	0.031
Spline 3	0.413	0.189	0.901	0.026
Age	1.065	0.997	1.137	0.062
Frailty	2.856	0.513	15.899	0.231
Initial HR	0.992	0.960	1.024	0.610
WBC	0.968	0.881	1.063	0.495
SBP Low	0.948	0.890	1.011	0.104
Laparotomy	2.297	0.478	11.034	0.299
SOFA Score	1.650	1.309	2.080	0.000
Temperature High	0.242	0.089	0.660	0.006
Temperature Low	1.157	0.926	1.446	0.200
RR High	1.019	1.000	1.039	0.052
Transfer	2.417	0.526	11.100	0.257
Sepsis	8.033	1.780	36.252	0.007

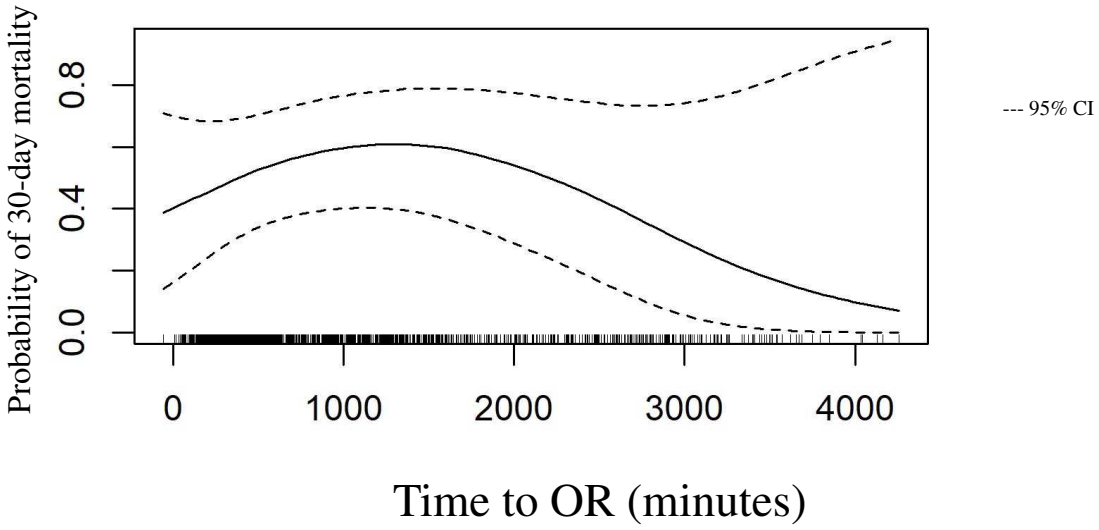
SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes
[2] 4 knot model derived from institutional guidelines at 1, 2, 4, 8 hours.

eFigure 2: E-value calculation for primary analysis

E-value (point estimate): 137.488
E-value (CI): 8.686



eFigure 3: Generalized additive mixed model (GAMM) of probability of 30-day mortality versus time to operating room. Solid line represents effect estimates, dotted lines represent 95% confidence interval.



eTable 7: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality with ESS included in model

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.3 (Reference)				
4.4-6.9	2.067	0.131	32.583	0.606
6.9-11.1	31.992	2.994	341.901	0.004
11.2-25.7	7.638	0.437	133.512	0.164
25.8-149.4	23.638	1.594	350.581	0.022
Age	1.077	1.005	1.155	0.035
Initial HR	1.005	0.972	1.039	0.783
WBC	0.927	0.838	1.026	0.142
SBP Low	0.924	0.872	0.979	0.008
Laparotomy	1.805	0.339	9.622	0.489
Temperature High	0.159	0.049	0.514	0.002
Temperature Low	1.016	0.870	1.186	0.842
RR High	1.009	0.996	1.022	0.168
Transfer	1.342	0.315	5.726	0.691
Sepsis	18.454	4.374	77.856	0.000
ESS Score	1.950	1.389	2.737	0.000
HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; ESS, Emergency Surgery Score; Time in Minutes				