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Research Article

PREDICTORS OF PROLONGED ICU STAY AFTER EMERGENCY LAPAROTOMY

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Abstract: ***Introduction:*** Emergency laparotomy (EL) is one of the most frequently performed and high-risk surgeries in the emergency department (ED) around the world. It includes a variety of abdominal surgical procedures for severe acute intra-abdominal conditions, such as intestinal obstruction, perforation of viscus, peritonitis, abdominal trauma and intra-abdominal sepsis. Despite tremendous progress in surgical techniques, peri-operative care and critical care medicine, EL remains intrinsically linked with a significant morbidity and mortality rates, especially in resource-poor areas. **Methodology:** Prospective observational study at the department of surgery in the DHQ Abbottabad during period of 1st March 2024 to 31st August 2024. A total of 100 adult patients (>18 years) who underwent emergency laparotomy and were sent to the postoperative intensive care unit (ICU) were enrolled. Demographic characteristics, pre-operative laboratory parameters (hemoglobin, white blood cell count, serum creatinine, albumin, lactate), ASA grade, surgical factors (operating time, peritoneal contamination grade, requirement for intraoperative blood transfusion, usage of vasopressors), and post-operative complications (surgical site infection, sepsis, acute kidney injury, PONV and need for re-exploration) were recorded. Stay in the (ICU) >72 hours was defined as prolonged ICU stay. Multivariable logistic regression was used to find independent predictors of prolonged ICU stay. **Results:** A total of 100 patients were included, with a mean age of 52.4 ± 16.8 years; 62 (62.0%) were male. 43 (43.0%) patients had a prolonged stay in the ICU. On multivariable analysis, independent predictors of prolonged ICU stay included: ASA grade ≥III (OR: 4.82, 95% CI: 1.92-12.10, p<0.001), preoperative serum lactate >2 mmol/L (OR: 3.45, 95% CI: 1.28-9.30, p=0.014), development of postoperative sepsis (OR: 6.73, 95% CI: 2.41-18.79, p<0.001), need for re-exploration laparotomy (OR: 5.21, 95% CI: 1.69-16.04, p=0.004), and postoperative pulmonary complications (OR: 3.89, 95% CI: 1.38-10.96, p=0.010). Higher ASA grades were associated with longer operating times, longer hospital stays, and more problems (p<0.0001). **Conclusion:** Physiological derangement before surgery (ASA grade, lactate), complexity of surgery and postoperative complications are independent significant factors in relation to prolonged stay in the ICU after emergency laparotomy. These findings highlight the importance of intensive risk stratification prior to surgery, optimization of those at high risk and a systematic method for preventing and managing postoperative complications. Multidisciplinary care models and improved recovery protocols can be used to minimize stay in the ICU and the outcomes of these high risk patients.

Keywords: Emergency Laparotomy, Prolonged ICU Stay, Predictors, ASA Grade, Postoperative Complications, Pakistan

INTRODUCTION

Emergency laparotomy (EL) is one of the most frequently performed and high-risk surgeries in the emergency department (ED) around the world.[1] It includes a variety of abdominal surgical procedures for severe acute intra-abdominal conditions, such as intestinal obstruction, perforation of viscus, peritonitis, abdominal trauma and intra-abdominal sepsis.[2] Despite tremendous progress in surgical techniques, peri-operative care and critical care medicine, EL remains intrinsically linked with a significant morbidity and mortality rates, especially in resource-poor areas.[3]

The recovery phase after EL is sometimes very severe, requiring admission to the intensive care unit (ICU) for careful monitoring and hemodynamic support, mechanical ventilation and organ dysfunction management.[4] In healthcare systems, however, critical care beds are a limited and expensive resource, especially in low- and middle-income countries such as Pakistan, where there is often a shortage of beds to accommodate the demand for critical care. Extended stay in the ICU room by EL patients may result in the late admission of other critically ill patients, higher health care expenditures and worse patient outcome.

Longer duration of stay in the ICU following EL has been shown to be a poor prognosis and risk factors for hospital acquired infections, deconditioning, delirium and death.[5,6] Knowing the factors that make patients at risk for longer ICU stay is therefore important for a number of reasons, including: (1) to help determine early risk stratification and triage of high-risk individuals, (2) to guide perioperative decision making and resource allocation, (3) to help identify potentially modifiable risk factors which may be targeted for preventive interventions, and (4) to facilitate communication with patients and families about likely recovery trajectories.

In the UK, the National Emergency Laparotomy Audit has shown that patient-related factors (age, ASA grade, comorbidity burden),[7] disease-related factors (severity of peritonitis, sepsis)[8] and process-related factors (deferral to surgery, operative complexity) are all associated with postoperative outcomes and the use of ICU resources.[9] A systematic review also revealed that postoperative sepsis/septic shock, severity of illness at admission, emergency operation and comorbidities (renal failure, coronary heart disease) were the most frequently associated risk factors for extended LOS in the ICU.[10]

Delayed presentation, late stage of the disease at the time of laparotomy, limited critical care resources and high burden of emergency laparotomy are seen in Pakistan.[11] There is, however, a lack of local data that specifically focus on factors that predict a longer ICU stay among this patient population. The determinants of the length of stay in the Intensive Care Unit (ICU) have not been studied specifically in Pakistan and most studies have been conducted on the overall length of stay, surgical site infection or re-exploration outcomes.

To fill this gap of knowledge, this study was designed to determine the independent predictors of the long duration of an ICU stay following an emergency laparotomy in a tertiary care hospital in Pakistan. Patient-related factors (ASA grade and comorbidity burden), intraoperative factors (operative duration, contamination, blood transfusion) and postoperative complications were hypothesized to independently predict a prolonged ICU stay. The results of this study will help in creating risk stratification tools, planning around peri-operative management and, planning for critical care resources allocation in Pakistani healthcare environment.

MATERIALS AND METHODS

2.1 Study Design and Setting

This was a prospective observational cohort study which was conducted at the department of surgery in the DHQ Abbottabad during period of 1st March 2024 to 31st August2024. The hospital has 24-bed multidisciplinary intensive care unit (ICU) that is staffed by intensivists, critical care nurses, and respiratory therapists.

2.2 Study Population

Included were patients who fulfilled the following requirements: Every patient over the age of eighteen who was admitted to the emergency department (ED) during the study period and who underwent an emergency laparotomy before being admitted to the intensive care unit (ICU). Any laparotomy conducted within 24 hours of admission for an abdominal condition that required immediate surgical intervention was considered as emergency laparotomy.

Inclusion Criteria:

- Age ≥18 years
- Underwent emergency laparotomy
- Written informed consent acquired

Exclusion Criteria:

Elective laparotomy procedures

- Patients transferred from other hospital >48 hours after initial surgery
- A history of cancer or previous radiotherapy to the abdomen
- Have a do-not-resuscitate (DNR) order on file
- Pregnancy
- Incomplete medical records

Patients who were deceased within 24 hours of admission to the ICU (to eliminate confounding factors) During the study period 100 patients who fulfilled the eligibility criteria were consecutively enrolled. Sample size was determined by the number of expected events that would be included in the multivariable model (rule of thumb 10 events per predictor) and the estimated prevalence of prolonged stay in the ICU (around 40%). Definitions (according to international guidelines): ASA grade: American Society of Anesthesiologists Physical Status Classification. Pulmonary complications: postoperative pneumonia, atelectasis, respiratory failure/ARDS or need for prolonged ventilation. AKI: defined using KDIGO criteria. Sepsis: Sepsis-3 definition (life-threatening organ dysfunction due to dysregulated response to infection). SSI: CDC definition of surgical site infection.

2.3 Data Collection

Data was collected prospectively, and a proforma was developed that was standardized for this study. The data were obtained from patient records, nursing records and patient interviews by two trained research assistants who were not directly involved in patient care. The principal investigator conducted periodic data quality checks and cross-verification.

2.6 Statistical Analysis

The information was coded, imported into Microsoft Excel 2019, and examined using SPSS version 26.0.Categorical data were summarized as frequencies and percentages, and continuous data were summarized as means ± SD for normally distributed data or medians (IQR) for non-normally distributed data.

RESULTS

The research included one hundred patients who had emergency laparotomy and were admitted to the ICU. The mean age of the patients was 52.4 ± 16.8 years (range: 18-85 years), with 62 patients (62.0%) being male. The majority of patients were in ASA class III (n=41, 41.0%), followed by ASA class II (n=29, 29.0%), ASA class IV (n=16, 16.0%), ASA class I (n=10, 10.0%), and ASA class V (n=4, 4.0%). Abdominal trauma (16 cases, 16.0%), intestinal obstruction (38 cases, 38.0%), and perforation peritonitis (34 cases, 34.0%) were the most frequently reported indications for emergency laparotomy. Other indications were complicated appendicitis (6.0%), complicated cholecystitis (4.0%) and mesenteric ischemia (2.0%).

The characteristics of the study population (N=100) are presented in table 1.

Characteristic	Overall (N=100)	Prolonged ICU Stay (n=43)	Non-Prolonged ICU Stay (n=57)	p-value
Demographics				
Age (years, mean ± SD)	52.4 ± 16.8	58.7 ± 15.2	48.1 ± 16.9	0.002
Male sex (n, %)	62 (62.0%)	28 (65.1%)	34 (59.6%)	0.572
BMI (kg/m², mean ± SD)	24.8 ± 4.2	24.2 ± 4.5	25.3 ± 3.9	0.196
Smoking (n, %)	27 (27.0%)	14 (32.6%)	13 (22.8%)	0.274
ASA Grade (n, %)				<0.001
I	10 (10.0%)	1 (2.3%)	9 (15.8%)	
II	29 (29.0%)	6 (14.0%)	23 (40.4%)	
III	41 (41.0%)	21 (48.8%)	20 (35.1%)	
IV	16 (16.0%)	12 (27.9%)	4 (7.0%)	
V	4 (4.0%)	3 (7.0%)	1 (1.8%)	
ASA ≥III (n, %)	61 (61.0%)	36 (83.7%)	25 (43.9%)	<0.001
Comorbidities (n, %)				
Diabetes Mellitus	28 (28.0%)	16 (37.2%)	12 (21.1%)	0.075
Hypertension	35 (35.0%)	19 (44.2%)	16 (28.1%)	0.093
COPD	12 (12.0%)	9 (20.9%)	3 (5.3%)	0.018
CKD	8 (8.0%)	6 (14.0%)	2 (3.5%)	0.056
IHD	10 (10.0%)	7 (16.3%)	3 (5.3%)	0.066
Liver Disease	5 (5.0%)	4 (9.3%)	1 (1.8%)	0.092
Indication for Surgery (n, %)				0.029
Intestinal Obstruction	38 (38.0%)	18 (41.9%)	20 (35.1%)	
Perforation Peritonitis	34 (34.0%)	14 (32.6%)	20 (35.1%)	
Abdominal Trauma	16 (16.0%)	3 (7.0%)	13 (22.8%)	
Complicated Appendicitis	6 (6.0%)	3 (7.0%)	3 (5.3%)	
Complicated Cholecystitis	4 (4.0%)	3 (7.0%)	1 (1.8%)	
Mesenteric Ischemia	2 (2.0%)	2 (4.7%)	0 (0.0%)	
Preoperative Laboratory (mean ± SD)				
Hemoglobin (g/dL)	10.8 ± 2.5	10.1 ± 2.6	11.3 ± 2.4	0.023
WBC (×10⁹/L)	14.6 ± 5.8	16.2 ± 6.1	13.4 ± 5.3	0.016
Creatinine (mg/dL)	1.4 ± 0.9	1.7 ± 1.1	1.2 ± 0.7	0.008
Albumin (g/dL)	3.1 ± 0.7	2.8 ± 0.6	3.3 ± 0.7	0.001
Lactate (mmol/L)	2.8 ± 1.6	3.7 ± 1.8	2.1 ± 1.1	<0.001
Lactate >2 mmol/L (n, %)	48 (48.0%)	30 (69.8%)	18 (31.6%)	<0.001

Time to Surgery (hours, median, IQR)	8.0 (4.0-14.0)	10.0 (5.0-16.0)	6.0 (3.0-12.0)	0.015

The postoperative and operative features are presented in 3.2.The postoperative and operative characteristics are provided in 3.2.

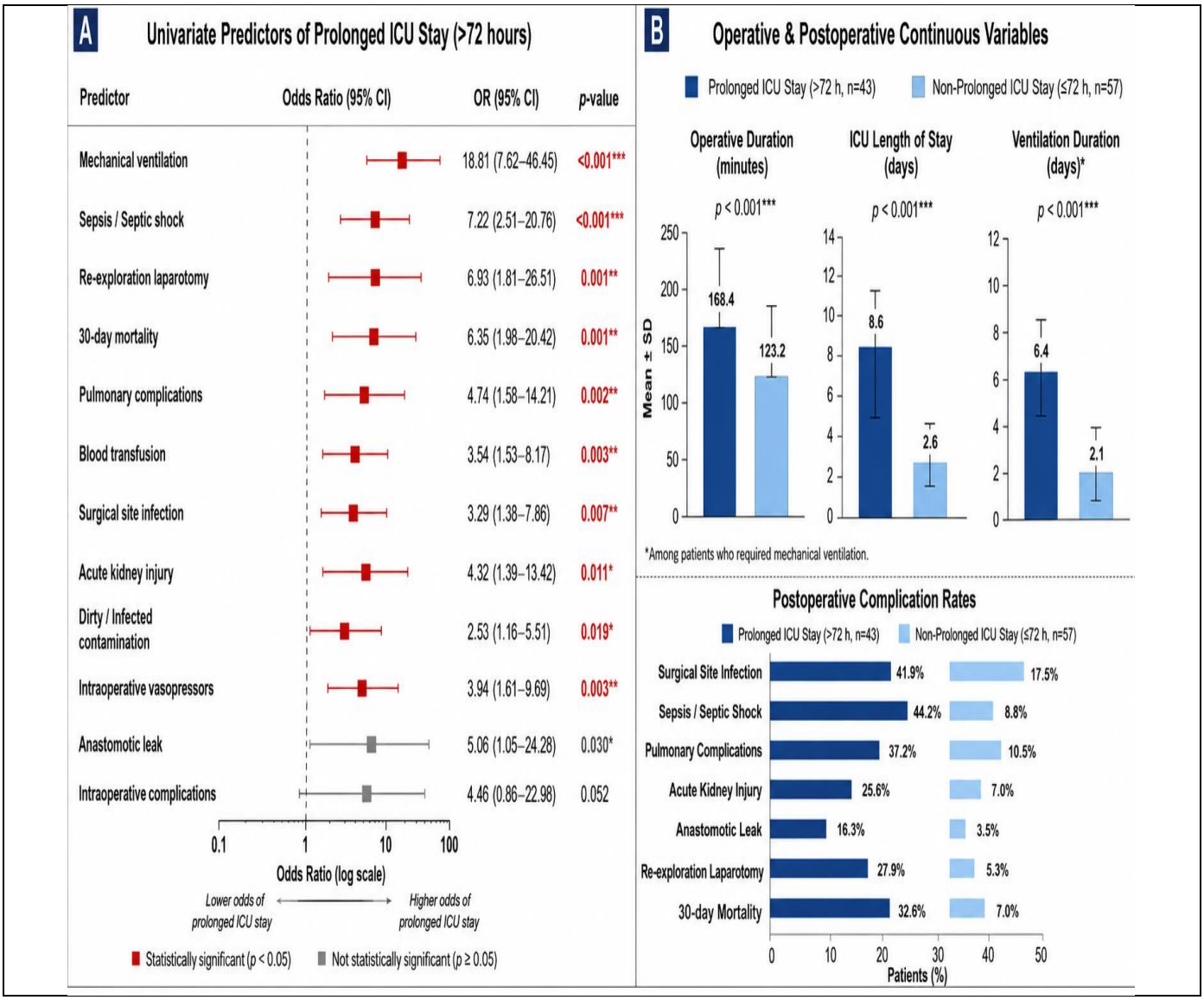
The mean operative duration was 142.6 ± 52.8 minutes (range: 45-310 minutes). Forty one (41.0%) patients had dirty/infected peritoneal contamination, 34 (34.0%) had contaminated, and 25 (25.0%) had clean-contaminated. During the surgery, 39 patients (39.0%) needed to receive a transfusion of blood and 32 patients (32.0%) needed to receive a transfusion of vasopressor. The overall length of the stay in the intensive care unit (ICU) was 5.2 ± 3.8 days (median 4.0, IQR 2.0-7.0 days) postoperatively. Forty-three (43.0%) patients required long-term stays in the ICU (>72 hours). Fifty-four (54.0%) patients required mechanical ventilation, which was used for a mean of 4.8 ± 3.5 days in ventilated patients.Surgical site infection (28.0%), sepsis (24.0%) and pulmonary complications (22.0%) were the most frequent postoperative complications. Re-exploration laparotomy was needed in 15 (15.0%) patients. In-hospital mortality was 18 (18.0%).

The operative and postoperative features of the study group are summarized in Table 2.

Operative and Postoperative Characteristics (N=100)

Characteristic	Overall (N=100)	Prolonged ICU Stay (n=43)	Non-Prolonged ICU Stay (n=57)	p-value
Intraoperative Variables				
Operative Duration (min, mean ± SD)	142.6 ± 52.8	168.4 ± 56.2	123.2 ± 43.1	<0.001
Peritoneal Contamination (n, %)				0.002
Clean-Contaminated	25 (25.0%)	6 (14.0%)	19 (33.3%)	
Contaminated	34 (34.0%)	14 (32.6%)	20 (35.1%)	
Dirty/Infected	41 (41.0%)	23 (53.5%)	18 (31.6%)	
Blood Transfusion (n, %)	39 (39.0%)	24 (55.8%)	15 (26.3%)	0.003
Intraoperative Vasopressors (n, %)	32 (32.0%)	21 (48.8%)	11 (19.3%)	0.002
Intraoperative Complications (n, %)	8 (8.0%)	6 (14.0%)	2 (3.5%)	0.052
Postoperative Variables				
ICU Stay duration (days, mean ± SD)	5.2 ± 3.8	8.6 ± 3.5	2.6 ± 0.8	<0.001
ICU Length of Stay (days, median, IQR)	4.0 (2.0-7.0)	8.0 (6.0-10.0)	2.0 (2.0-3.0)	<0.001
Mechanical Ventilation (n, %)	54 (54.0%)	38 (88.4%)	16 (28.1%)	<0.001
Ventilation Duration (days, mean ± SD)*	4.8 ± 3.5	6.4 ± 3.6	2.1 ± 0.9	<0.001
Postoperative Complications (n, %)				
Surgical Site Infection	28 (28.0%)	18 (41.9%)	10 (17.5%)	0.007
Sepsis/Septic Shock	24 (24.0%)	19 (44.2%)	5 (8.8%)	<0.001
Pulmonary Complications	22 (22.0%)	16 (37.2%)	6 (10.5%)	0.002
Acute Kidney Injury	15 (15.0%)	11 (25.6%)	4 (7.0%)	0.011
Anastomotic Leak	9 (9.0%)	7 (16.3%)	2 (3.5%)	0.030

Cardiac Complications	8 (8.0%)	6 (14.0%)	2 (3.5%)	0.052
Re-exploration Laparotomy (n, %)	15 (15.0%)	12 (27.9%)	3 (5.3%)	0.001
30-day Mortality (n, %)	18 (18.0%)	14 (32.6%)	4 (7.0%)	0.001

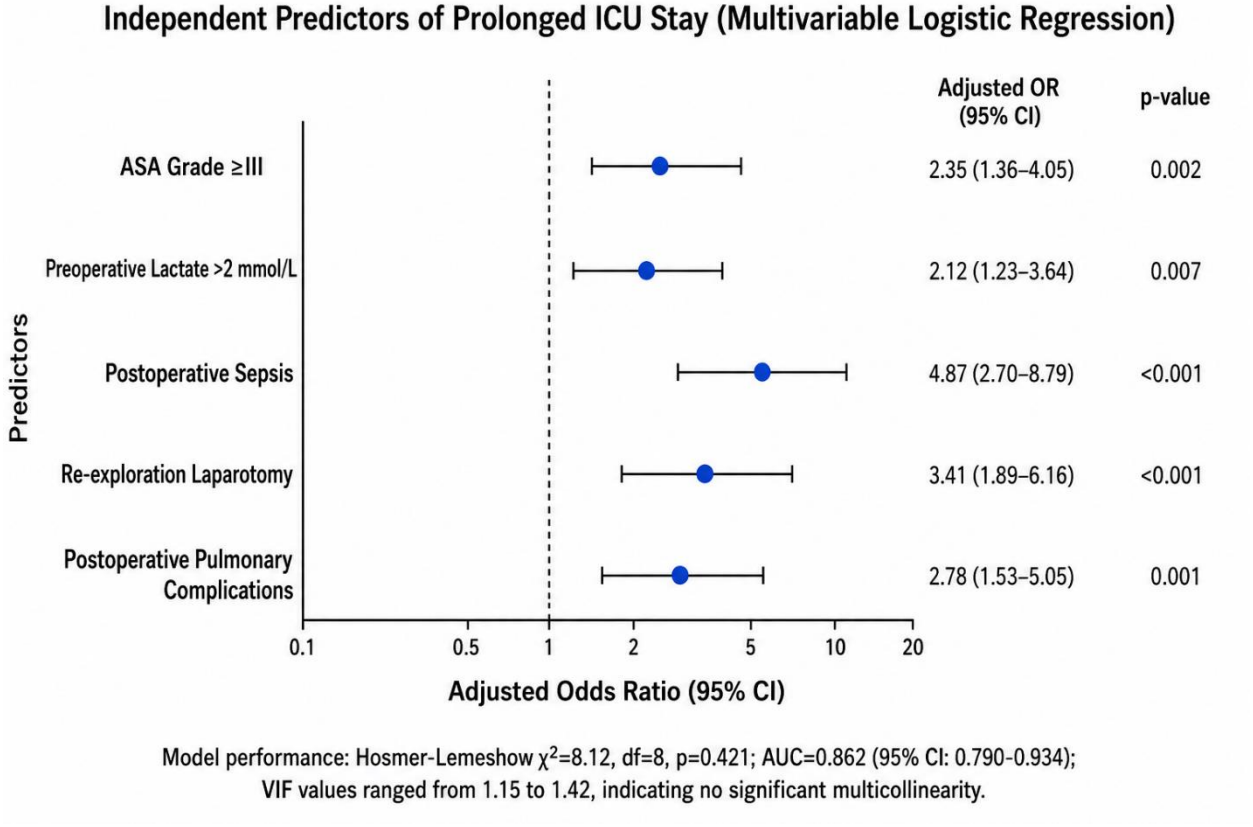


3.3 Independent Predictors of Prolonged ICU Stay

Variables with p<0.10 in univariate analysis were added to the multivariable logistic regression model (age, American Society of Anesthesiologists (ASA) grade ≥III, COPD, diabetes mellitus, hypertension, CKD, IHD, liver disease, preoperative hemoglobin, white blood cell [WBC] count, creatinine, albumin, lactate >2 mmol/L, operative duration, peritoneal contamination grade, blood transfusion, use of intraoperative vasopressors, surgical site infection, sepsis, pulmonary complication, acute kidney injury [AKI], anastomotic leak, re-exploration).Five independent predictors of ICU stay remained after backward stepwise elimination (Table 3). The model demonstrated good fit (Hosmer-Lemeshow χ^2=8.12, df=8, p=0.421) and acceptable discrimination (area under the ROC curve = 0.862, 95% CI: 0.790-0.934). Multivariable Logistic Regression Analysis of Predictors of Prolonged ICU Stay (n=100): Table 3Odds ratio (OR);

Table 3: Multivariable Logistic Regression Analysis for Predictors of Prolonged ICU Stay

Variable	Adjusted OR	95% CI	p-value	VIF
ASA Grade ≥III	4.82	1.92 - 12.10	<0.001	1.28
Preoperative Lactate >2 mmol/L	3.45	1.28 - 9.30	0.014	1.15
Postoperative Sepsis	6.73	2.41 - 18.79	<0.001	1.42
Re-exploration Laparotomy	5.21	1.69 - 16.04	0.004	1.33
Postoperative Pulmonary Complications	3.89	1.38 - 10.96	0.010	1.27



DISCUSSION

This study provides important insights into the factors associated with prolonged intensive care unit (ICU) stay following emergency laparotomy in a tertiary care hospital in Pakistan. Nearly half of the patients (43.0%) required an ICU stay exceeding 72 hours, highlighting the substantial burden of postoperative critical care following emergency abdominal surgery. The independent predictors identified in this study ASA grade ≥III, elevated preoperative lactate levels, postoperative sepsis, re-exploration laparotomy, and postoperative pulmonary complications span the entire perioperative continuum, encompassing preoperative patient status, intraoperative physiological derangements, and postoperative complications. These findings have important implications for perioperative risk stratification, resource allocation, and optimization of critical care services, particularly in low- and middle-income countries where ICU capacity is often limited.

Higher ASA grade (≥III) was the strongest independent predictor of prolonged ICU stay (OR: 4.82, 95% CI: 1.92–12.10). The American Society of Anesthesiologists (ASA) physical status classification remains one of the most widely accepted tools for preoperative risk assessment and has consistently demonstrated good predictive ability for postoperative morbidity and mortality in emergency surgical patients. Patients with higher ASA grades generally have a greater burden of comorbidities, impaired physiological reserve, and reduced ability to tolerate the metabolic stress of emergency surgery, predisposing them to postoperative complications and delayed recovery. Similar findings have been reported in recent emergency laparotomy cohorts, where higher ASA grades were independently associated with postoperative complications and adverse outcomes 12,13

Consistent with previous studies, patients with ASA grade ≥III in our cohort experienced significantly higher

rates of postoperative sepsis, pulmonary complications, and re-exploration. These findings emphasize the importance of careful preoperative assessment and optimization whenever feasible. Although emergency surgery frequently limits opportunities for comprehensive optimization, correction of modifiable factors such as dehydration, electrolyte imbalance, anemia, and hemodynamic instability before surgery may reduce postoperative morbidity and improve recovery.

Elevated preoperative serum lactate was another independent predictor of prolonged ICU stay (OR: 3.45, 95% CI: 1.28–9.30). Serum lactate is a well-established biomarker of tissue hypoperfusion and inadequate oxygen delivery, reflecting global metabolic stress and the severity of circulatory dysfunction. Elevated lactate concentrations commonly occur in patients with hypovolemic shock secondary to hemorrhage, septic shock caused by intra-abdominal infection, and bowel ischemia, all of which are frequent indications for emergency laparotomy.14

Nearly half of our patients (48%) presented with preoperative hyperlactatemia (>2 mmol/L), and these patients experienced significantly longer ICU stays than those with normal lactate concentrations. They also required greater fluid resuscitation, more frequent vasopressor support, and prolonged mechanical ventilation, indicating greater physiological derangement. Previous studies have similarly demonstrated that persistent hyperlactatemia despite initial resuscitation predicts prolonged ICU and hospital stay, postoperative complications, and increased mortality in emergency abdominal surgery.15

Postoperative sepsis was another major determinant of prolonged ICU stay. Approximately one-quarter of our patients developed postoperative sepsis, and nearly 80% of these patients required ICU admission exceeding 72 hours. Management of postoperative sepsis often requires timely source control, broad-spectrum antimicrobial therapy, hemodynamic resuscitation, organ support, and, in selected patients, re-exploration surgery. These complex interventions inevitably increase ICU resource utilization and length of stay.16

The strong association between postoperative sepsis and prolonged ICU stay highlights the importance of prevention and early recognition. Strategies including appropriate perioperative antibiotic prophylaxis, meticulous surgical technique, effective source control during the index operation, prompt identification of anastomotic leakage, and aggressive management of intra-abdominal collections may substantially reduce postoperative infectious complications. Furthermore, implementation of structured screening tools such as the quick Sequential Organ Failure Assessment (qSOFA) facilitates earlier recognition of sepsis and timely initiation of evidence-based treatment, potentially improving clinical outcomes.

Re-exploration laparotomy also independently predicted prolonged ICU stay. Patients requiring reoperation generally have more severe intra-abdominal pathology, ongoing contamination, or postoperative complications such as anastomotic leakage or uncontrolled hemorrhage. Consequently, they frequently require prolonged organ support, repeated surgical interventions, and extended critical care. These findings underscore the importance of meticulous surgical technique, adequate source control during the initial operation, careful hemostasis, and appropriate application of damage-control surgery in physiologically unstable patients. When re-exploration becomes necessary, close collaboration between surgical, anesthesia, and critical care teams is essential to optimize outcomes.

Pulmonary complications, including pneumonia and acute respiratory distress syndrome (ARDS), were independently associated with prolonged ICU stay (OR: 3.89, 95% CI: 1.38–10.96). Postoperative pulmonary complications remain among the most frequent causes of postoperative morbidity following major abdominal surgery and are associated with prolonged mechanical ventilation, increased ICU utilization, and higher mortality18. Multiple factors contribute to respiratory complications after emergency laparotomy, including systemic inflammatory response secondary to sepsis, postoperative pain limiting effective coughing, impaired respiratory mechanics following laparotomy, atelectasis, fluid overload, and prolonged mechanical ventilation.

These findings support implementation of evidence-based preventive strategies including early mobilization, incentive spirometry, adequate analgesia, lung-protective ventilation, judicious perioperative fluid therapy, and prompt diagnosis and treatment of postoperative respiratory infections. Enhanced Recovery After Surgery (ERAS) pathways have also demonstrated reductions in pulmonary complications and hospital length of stay in major abdominal surgery.

Overall, our findings are consistent with international evidence demonstrating that both preoperative physiological status and postoperative complications contribute significantly to prolonged ICU stay after emergency laparotomy. Recognition of high-risk patients before surgery, combined with aggressive perioperative optimization and early management of postoperative complications, may reduce ICU utilization, improve patient outcomes, and facilitate more efficient use of limited critical care resources in resource-constrained healthcare systems.

CONCLUSION

This study confirms that 43.0% of patients in the study developed prolonged stay in the ICU (>72 hours) after undergoing an emergency laparotomy and found five important predictors for prolonged stay in the ICU after

emergency laparotomy in Pakistan: ASA grade ≥III, elevated preoperative lactate levels, postoperative sepsis, re-exploration laparotomy, and pulmonary complications. All these factors are applicable from the very beginning of the care, and are primarily related to the need for a comprehensive perioperative management. These provide the opportunity to identify high-risk patients early and to get them into the Intensive Care Unit and initiate any preventive measures. A key focus of improving the length of stay in the intensive care unit (ICU) is the reduction of postoperative complications, particularly sepsis and pulmonary complications. The key to better outcomes is to focus on multidisciplinary teams, maximising recovery protocols and critical care resource planning within healthcare systems.

Recommendations

Clinically, all patients undergoing laparotomy as part of the emergency department triage should receive routine risk stratification for admission to the intensive care unit and early goal-directed resuscitation, with high-risk patients (ASA ≥ III or lactate >2 mmol/L) identified and treated accordingly. Multidisciplinary team involvement and adapted enhanced recovery elements, along with standardized hospital protocols to prevent infections, pulmonary complications and fluid overload are essential to avoid. System level, capacity planning of ICU units, establishment of validated bedside risk scores and quality improvement audits are key. Further studies are needed to validate multi-center, assess frailty, determine long-term functional outcomes, conduct interventional trials and perform cost-effectiveness analyses for resource allocation.

Limitations

The limited sample size and single-center design (N=100) of the study restrict generalizability of findings and statistical power to examine rare predictors, or to build robust models. The 72-hour cut-off for long hospitalisation in the intensive care unit (ICU), despite being based on literature, is arbitrary, and lack of validated frailty tools may have resulted in residual confounding. Trauma patients (16% of the cohort) and non-tertiary settings are underrepresented and short-term follow-up (in-hospital only) lacks long-term functional and readmission outcomes. Furthermore, the results may be unreplicable because of selection bias, which does not allow the inclusion of non-ICU-admitted patients; potential measurement error for some variables; and seasonal variations over the 6-month study period.

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