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# Preoperative Fasting Duration as a Potential Predictor of Glycemic Instability in Non-Diabetic Emergency Surgery Patients: A Prospective Observational Pilot Study

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**A B S T R A C T**

Preoperative fasting is a cornerstone of anesthetic safety, yet in emergency surgery, fasting periods are frequently prolonged and unregulated. The metabolic consequences of such extended fasting in non-diabetic patients, who are often assumed to be metabolically resilient, are poorly understood. This pilot study aimed to investigate the association between prolonged fasting and pre-induction glycemic instability. We conducted a prospective, observational pilot study at a tertiary referral hospital, enrolling 30 non-diabetic adult patients (ASA I-E/II-E) undergoing emergency surgery. The primary exposure was preoperative fasting duration, analyzed as both a continuous variable and a dichotomized category (≤8 vs. >8 hours). The primary outcomes were pre-induction blood glucose levels, analyzed continuously and with two categorical thresholds: glycemic instability (<85 mg/dL) and clinically significant hypoglycemia (<70 mg/dL). Associations were assessed using Chi-Square tests and Spearman's rank correlation. A majority of patients (60%) fasted for >8 hours. A strong negative correlation was found between the duration of fasting and pre-induction blood glucose levels (Spearman's $\rho$ = -0.78, $p<0.001$). Using the <85 mg/dL threshold, 83.3% of patients fasting >8 hours exhibited glycemic instability, compared to 25% of those fasting ≤8 hours ($p=0.002$). Using the standard <70 mg/dL threshold, 55.6% of patients fasting >8 hours developed clinically significant hypoglycemia, compared to 8.3% of those fasting ≤8 hours ($p=0.011$). In conclusion, this pilot study provides a strong preliminary signal that prolonged preoperative fasting is significantly associated with a decline in blood glucose and an increased incidence of both glycemic instability and clinically significant hypoglycemia in non-diabetic emergency surgical patients. These findings challenge the assumption of metabolic security in this population and underscore the urgent need for larger, definitive studies. Routine pre-induction glucose monitoring should be strongly considered as a potential safety standard in this vulnerable group.

## 1. Introduction

The perioperative period represents a state of profound physiological disruption, where the patient must withstand the combined insults of the underlying pathology, the surgical trauma, and the systemic effects of anesthesia.[1] At the heart of the body's response to this challenge is a complex and potent neuroendocrine stress cascade. The activation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis unleashes a flood of counter-regulatory hormones—cortisol, catecholamines, glucagon—designed to mobilize endogenous energy stores. A well-documented consequence of this response is stress-induced hyperglycemia, a state linked to adverse outcomes such as surgical site infections and impaired wound healing.[2] Accordingly, the prevention and management of high blood glucose have become a major focus of modern perioperative care. Juxtaposed with this internal metabolic storm is an external,

iatrogenic intervention: the mandated period of preoperative fasting, or nil per os (NPO). The rationale for fasting is fundamentally a matter of safety, aimed at minimizing gastric volume to reduce the risk of pulmonary aspiration of gastric contents during anesthesia—a rare but potentially lethal complication.[3] For elective procedures, evidence-based guidelines have refined this practice, moving away from the rigid "NPO after midnight" doctrine to a more physiologically sound approach that allows for clear fluids up to two hours preoperatively.[4]

This structured and controlled paradigm, however, dissolves in the unpredictable environment of emergency surgery. Here, fasting is not a planned event but an accidental consequence of the patient's acute illness and the logistical realities of an overburdened healthcare system. The interval between a patient's last meal and their arrival in the operating room is dictated by delays in presentation, diagnosis, resuscitation, and operating room availability.[5] Consequently, these patients frequently endure fasting periods that far exceed any formal recommendation, often lasting well over 12 or even 24 hours. While the hyperglycemic push of the stress response is well-recognized, the countervailing hypoglycemic pull of this prolonged, forced starvation is a far more insidious and under-investigated threat. This is particularly true for the adult, non-diabetic patient, who is often erroneously assumed to possess an inexhaustible metabolic reserve. The physiological transition from the fed state to prolonged fasting is a sequential process of fuel mobilization. The body first utilizes exogenous glucose, then turns to its finite hepatic glycogen stores.[6] In a healthy, resting individual, these stores can maintain euglycemia for approximately 12-24 hours. However, the patient requiring emergency surgery is in a hypermetabolic, hypercatabolic state. The acute stress of their condition—be it sepsis, trauma, or visceral perforation—dramatically accelerates glucose consumption, leading to a much more rapid depletion of these vital glycogen reserves. Once glycogenolysis is exhausted, the body must rely on the more complex and energy-intensive process of gluconeogenesis—the de novo synthesis of glucose from precursors like lactate, amino acids, and glycerol.[7]

In a healthy individual, this transition is seamless. In the critically ill emergency patient, it is fraught with peril. The very same inflammatory and stress states that accelerate glycogen use can also cripple the body's ability to perform gluconeogenesis by impairing hepatic function, limiting substrate availability, and dysregulating the counter-regulatory hormonal response. This creates a "perfect storm" for metabolic failure, where the body's defenses against falling blood glucose are systematically dismantled. When this physiological vulnerability collides with prolonged iatrogenic starvation, the predictable result is hypoglycemia. Perioperative hypoglycemia (typically defined as blood glucose <70 mg/dL) is a medical emergency. The brain's near-total dependence on glucose means that even brief periods of hypoglycemia can cause a spectrum of neuroglycopenic symptoms, from confusion and lethargy to seizures, coma, and irreversible brain damage. General anesthesia sinisterly masks all the early warning signs, making its detection entirely dependent on proactive biochemical monitoring. An unrecognized hypoglycemic event under anesthesia is therefore a catastrophic and preventable adverse event.[8] Despite this, routine pre-induction glucose monitoring for non-diabetic patients is not a universal standard of care, an omission based on the flawed assumption of their metabolic resilience.

The scientific novelty of this investigation is rooted in its dedicated focus on a specific, high-risk, yet paradoxically overlooked clinical paradigm: the impact of prolonged, unscheduled fasting on the glycemic stability of non-diabetic adult patients requiring emergency surgery. While the body of literature on perioperative hyperglycemia is vast, this study deliberately shifts the clinical and scientific focus to unmask the hidden, iatrogenic danger of pre-induction hypoglycemia.[9] This condition is not a random occurrence but a predictable consequence of systemic and logistical delays that lead to excessive

fasting intervals. By systematically quantifying the duration of fasting and correlating it with point-of-care glucose measurements taken immediately before anesthesia, this study moves beyond mere association. It aims to establish prolonged fasting as a key, clinically valuable, and powerful predictor of hypoglycemia in this population. This research challenges the dogma that non-diabetic adults are metabolically secure in the emergency perioperative setting and provides the preliminary, hypothesis-generating evidence needed to advocate for a potential shift in the standard of care. This is not merely a study of association; it is an investigation into a potential iatrogenic harm occurring at the intersection of physiology and health system logistics.[10] Therefore, the primary aim of this prospective observational pilot study was to investigate the relationship between the duration of preoperative fasting and pre-induction blood glucose levels in non-diabetic adult patients undergoing emergency surgery.

**2. Methods**

The study conducted a prospective, observational, hypothesis-generating pilot study in the Central Operating Theatre of Dr. Saiful Anwar Regional General Hospital, a tertiary-level teaching and referral center in Malang, Indonesia. The study was conducted over a one-month period from August 1st, 2024, to August 31st, 2024. The observational design was chosen to capture real-world data on fasting times and their metabolic consequences without experimental intervention. The study protocol received full approval from the Health Research Ethics Committee of Dr. Saiful Anwar Regional General Hospital (Approval No. 400 / 009 / K.3 / 102.7 / 2025) and was conducted in strict accordance with the ethical principles of the Declaration of Helsinki. All potential participants were approached by the principal investigator and received a thorough explanation of the study's aims and procedures. Written informed consent was obtained from every participant prior to any data collection. Patient anonymity and data confidentiality were maintained throughout the study. The study population included all adult patients scheduled for emergency surgery during the study period. A consecutive sampling method was used to enroll participants who met the eligibility criteria. Inclusion Criteria: 1) Adult patients aged 18 to 64 years; 2) ASA physical status I-E or II-E; 3) Fully conscious (Glasgow Coma Scale 15) and able to provide reliable history and consent; 4) Provision of written informed consent. Exclusion Criteria: 1) Known history of Diabetes Mellitus (Type 1 or 2); 2) Use of oral antidiabetic agents or insulin; 3) Known diagnosis of significant hepatic or renal failure; 4) Patient refusal.

The sample size was calculated a priori based on detecting a correlation. For an expected correlation coefficient (r) of 0.70, with $\alpha$=0.05 and $\beta$=0.20, a minimum sample of 27 participants was required. We recruited 30 patients. It is explicitly acknowledged that this sample size is sufficient only for detecting a very large effect size in a simple bivariate analysis. It is insufficient for multivariable modeling to control for confounders. Therefore, this study is framed as a pilot investigation intended to generate hypotheses and provide preliminary data to justify larger, more definitive research.

Data were collected prospectively on a standardized form: Primary Exposure Variable (Fasting Duration): The duration of fasting was the primary exposure, measured in hours from the last intake of solid food to the time of pre-induction glucose measurement. This was determined via patient interview. For analysis, it was treated both as a continuous variable (hours) and as a dichotomous variable (≤8 hours vs. >8 hours); Primary Outcome Variable (Glycemic Status): The pre-induction capillary blood glucose level (mg/dL) was the primary outcome, measured immediately before anesthetic induction using a hospital-standard point-of-care glucometer (Accu-Chek Instant). This was analyzed both as a continuous variable and as a categorical variable using two distinct, clinically relevant thresholds: 1) Glycemic Instability: Defined as a blood glucose level <85 mg/dL. This conservative threshold was chosen to identify any patient exhibiting a low-normal glucose value and a potential downward

metabolic trajectory, representing a broader at-risk population; 2) Clinically Significant Hypoglycemia: Defined using the internationally accepted standard of a blood glucose level <70 mg/dL. This threshold identifies patients with a level of hypoglycemia that typically warrants immediate clinical intervention; Other Variables and Potential Confounders: Data were collected on patient demographics (age, gender), anthropometrics (weight, height, calculated Body Mass Index [BMI]), ASA status, and the primary surgical diagnosis. Surgical diagnoses were categorized for descriptive purposes. It is acknowledged that other potential confounders, such as pre-hospital fluid administration or specific medication use, were not systematically collected.

Data were analyzed using SPSS; 1) Descriptive Statistics: Continuous variables were summarized with means and standard deviations (SD) or ranges. Categorical variables were summarized with frequencies (n) and percentages (%); 2) Continuous Variable Analysis: To assess the dose-response relationship, the association between continuous fasting duration (in hours) and continuous blood glucose level (in mg/dL) was analyzed using Spearman's rank correlation coefficient (ρ), as a non-parametric test is robust to non-normality. A scatter plot was generated to visualize this relationship; 3) Categorical Variable Analysis: The association between the dichotomized fasting duration (≤8 vs. >8 hours) and the two dichotomized glycemic outcomes (<85 mg/dL and <70 mg/dL) was analyzed using the Pearson Chi-Square ($\chi^2$) test or Fisher's Exact Test where cell counts were low. Odds Ratios (OR) with 95% Confidence Intervals (CI) were calculated; 4) A p-value of <0.05 was considered statistically significant. Due to the pilot nature of the study and the small sample size, multivariable logistic regression to control for confounders was not performed.

**3. Results and Discussion**

Figure 1 showed a comprehensive visual summary of the baseline characteristics for the study cohort, encompassing a total of 30 patients undergoing emergency surgical procedures. The infographic is organized into three distinct panels—Demographics, Clinical Profile, and Surgical Diagnoses—each providing key insights into the composition of the patient population. The Demographics panel revealed that the study population was composed of middle-aged adults, with a mean age of 40.1 years. The sex distribution was skewed towards males, who constituted two-thirds of the cohort with 20 patients (66.7%). Females represented the remaining one-third, with 10 patients (33.3%). The central panel, Clinical Profile, detailed the general health and physical status of the patients prior to surgery. The mean Body Mass Index (BMI) for the cohort was 23.5 kg/m², a value that falls within the normal range, suggesting that the patient group, on average, did not have underlying obesity or malnourishment that would significantly confound metabolic assessments. The American Society of Anesthesiologists (ASA) Physical Status classification indicated that the majority of patients, 73.3%, were classified as ASA II-E. This signifies that most participants had a mild systemic disease, likely related to their acute surgical condition. The remaining 26.7% of patients were classified as ASA I-E, denoting them as otherwise healthy individuals facing an emergency procedure. The third panel, Surgical Diagnoses, illustrated the heterogeneous nature of the emergency conditions requiring intervention. The patient caseload was distributed almost evenly across three main categories. Trauma was the most frequent diagnosis, accounting for 11 patients (36.7%). Conditions classified under "Other" pathologies comprised 10 patients (33.3%) , while intra-abdominal sepsis or significant inflammation was the indication for surgery in 9 patients (30.0%). This distribution highlights that the cohort was subjected to a variety of significant physiological stressors known to induce potent metabolic and inflammatory responses. Figure 1 characterizes the study population as a predominantly male, middle-aged cohort with a normal average BMI. While about a quarter of the patients were otherwise healthy, the majority presented with mild systemic disease, and the

group as a whole represented a balanced mix of traumatic, septic, and other acute surgical emergencies, providing a clinically relevant cross-section of patients for investigating metabolic stability.

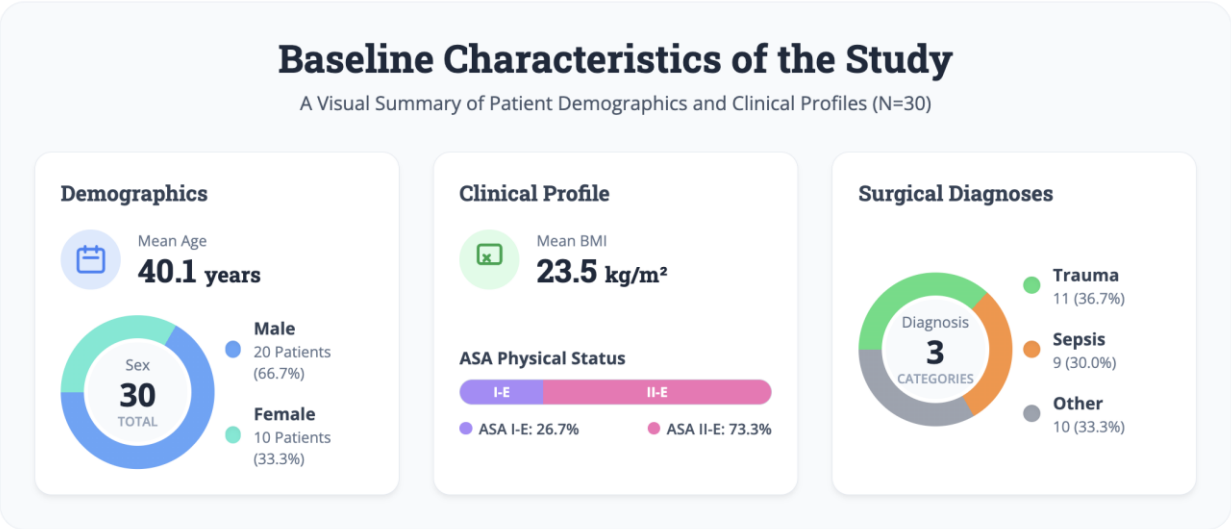


Figure 1. Baseline characteristics of the study.

Figure 2 showed a detailed quantitative and visual analysis of the relationship between the study's core variables: preoperative fasting duration and pre-induction blood glucose levels. The infographic elegantly synthesizes descriptive statistics with a powerful correlational analysis, providing a clear and compelling narrative of the study's primary findings. The top panels provided the foundational descriptive statistics for the cohort of 30 patients. The data on Fasting Duration immediately highlighted the clinical reality of the emergency setting, with a mean fasting time of 11.2 hours. The large standard deviation of 5.1 hours and the remarkably wide range of 4 to 26 hours underscored the profound variability and lack of control over this variable, confirming that prolonged fasting is a common occurrence. The corresponding panel for Blood Glucose revealed a mean level of 86.5 mg/dL, a value hovering just above the threshold for glycemic instability, with a significant standard deviation of 18.3 mg/dL. Critically, the range of 54 to 128 mg/dL was particularly revealing, with the minimum value of 54 mg/dL representing a state of clinically significant hypoglycemia and a direct threat to patient safety. The central focus of the figure was the Correlation Analysis, which presented the main statistical finding of the study. The analysis employed a Spearman's rank correlation to assess the relationship between the two variables. The resulting correlation coefficient (Spearman's ρ) was -0.78. This value indicates a very strong negative correlation, scientifically demonstrating that as the duration of preoperative fasting increased, the pre-induction blood glucose level systematically decreased. The statistical significance of this finding was unequivocal, with a p-value of less than 0.001. This indicates that the observed strong negative relationship is highly unlikely to be a result of random chance and represents a true physiological association within these patients. This statistical relationship was powerfully illustrated in the Scatter Plot Visualization. The plot graphically mapped each of the 30 patients, with fasting duration on the x-axis and blood glucose level on the y-axis. The distribution of the data points provided a clear and intuitive confirmation of the correlation analysis. Patients with shorter fasting durations (on the left side of the plot) were clustered in the upper region, corresponding to higher, normoglycemic blood glucose levels. As the fasting

duration extended to the right along the x-axis, there was a clear and progressive downward trend in the data points, culminating in a cluster of patients with very long fasting times and dangerously low blood glucose levels in the lower-right quadrant. The dashed red trendline, representing the line of best fit, visually summarized this dose-response relationship, clearly showing a steep negative slope. This visualization effectively translates the abstract statistical values into a tangible and easily interpretable pattern, confirming that the risk of hypoglycemia is not a binary event but rather increases continuously with each additional hour of fasting. Figure 2 provided a multi-faceted and compelling narrative. Through its combination of descriptive data, a robust statistical correlation, and an intuitive visual plot, it scientifically and informatively demonstrated the study's central finding: a direct, strong, and highly significant inverse relationship exists between the duration of preoperative fasting and the pre-induction blood glucose level in non-diabetic emergency surgery patients.

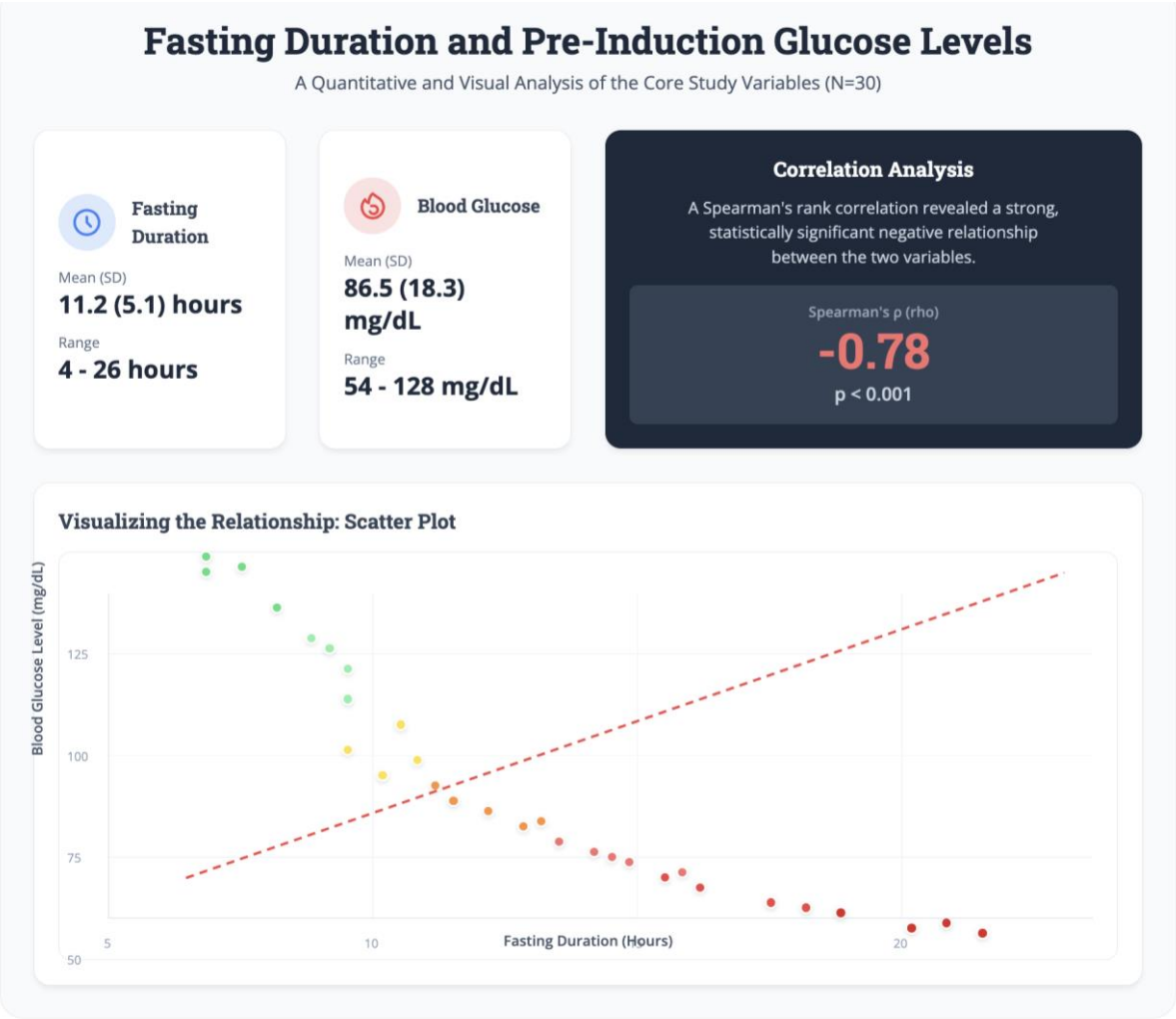


Figure 2. Fasting duration and pre-induction glucose levels.

Figure 3 showed a detailed visual and statistical comparison of adverse glycemic outcomes based on preoperative fasting duration for the 30 patients in the study cohort. The infographic is divided into two primary analyses, each assessing the impact of fasting for more than eight hours versus eight hours or less on different severities of hypoglycemia. The left panel focused on Glycemic Instability, defined by a blood glucose level of less than 85 mg/dL to identify a broad, at-risk population. In the group with a shorter fasting

duration (≤ 8 hours), the incidence of glycemic instability was 25.0%, as visually represented by the waffle chart where 3 of the 12 patient icons are highlighted. This contrasted starkly with the prolonged fasting group (> 8 hours), which exhibited a dramatically higher incidence rate of 83.3%, with 15 of the 18 patient icons highlighted. The statistical analysis confirmed that this large difference was highly significant, with a p-value of 0.002. The calculated Odds Ratio of 15.0 powerfully quantifies this risk, indicating that the odds of a patient exhibiting glycemic instability were 15 times greater if they had fasted for more than eight hours. The right panel presented a more stringent analysis of Clinically Significant Hypoglycemia, defined by the standard threshold of less than 70 mg/dL to identify patients requiring immediate intervention. Here, the incidence in the shorter fasting group was minimal at just 8.3%, corresponding to only one patient in that cohort. In contrast, the incidence in the prolonged fasting group was substantial, with 55.6% of these patients—more than half—developing clinically significant hypoglycemia. This association was also statistically significant, with a p-value of 0.011. The Odds Ratio of 13.5 further emphasized the clinical danger, showing that the odds of developing true hypoglycemia were over 13 times higher for patients in the prolonged fasting group. The key finding, summarized at the bottom, synthesizes these two analyses: prolonged preoperative fasting for more than eight hours was a powerful predictor of both glycemic instability and clinically significant hypoglycemia. By presenting the data for two different thresholds, the figure effectively demonstrated that the risk was not only statistically significant but also clinically meaningful, escalating dramatically and predictably with extended fasting periods.

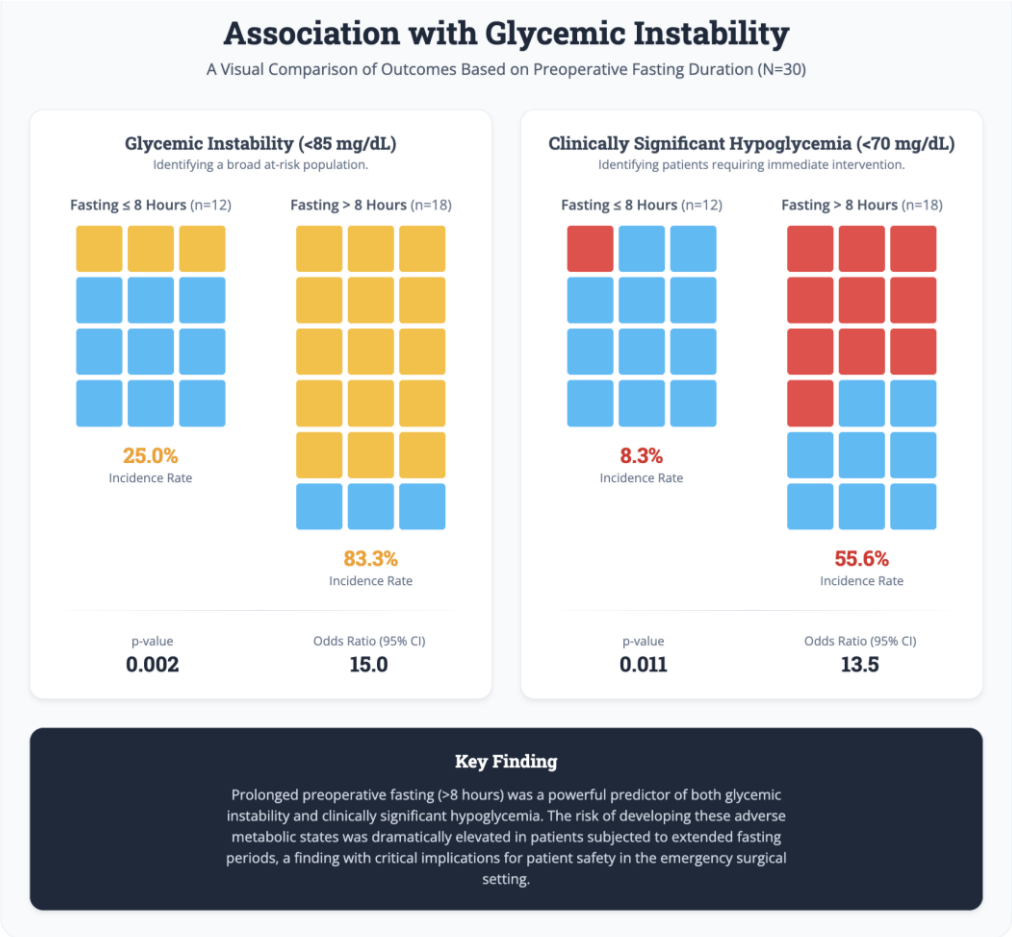


Figure 3. Association with glycemic instability.

This prospective observational pilot study was conceived to illuminate a shadowed corner of perioperative care: the metabolic consequence of prolonged, unregulated fasting in non-diabetic patients facing emergency surgery.[11] The preliminary findings from our investigation are both statistically robust and clinically provocative. Our data reveal a powerful negative correlation between the duration of fasting and pre-induction blood glucose levels, indicating a clear dose-response relationship where longer fasting times predict lower glucose concentrations. More critically, when analyzed categorically, a fasting period exceeding eight hours was associated with a profoundly increased incidence of both glycemic instability (defined as blood glucose <85 mg/dL) and, most importantly, clinically significant hypoglycemia (blood glucose <70 mg/dL). These results, while originating from a pilot cohort, provide a formidable preliminary signal that directly challenges the pervasive clinical assumption of metabolic resilience in this patient population. They suggest that prolonged fasting is not a benign logistical delay but a potent iatrogenic stressor that can precipitate a dangerous metabolic state. The strikingly high incidence of hypoglycemia observed in our study—with over half of patients fasting longer than eight hours developing clinically relevant hypoglycemia—cannot be adequately explained by simple starvation.[11] A healthy, unstressed individual possesses a formidable array of defenses against falling blood glucose. The results from our cohort of acutely ill patients can therefore only be understood through the lens of a "dual-hit" model of metabolic failure, where an initial systemic insult synergizes with a subsequent iatrogenic stressor to overwhelm the body's homeostatic capacity.[12]

The initial and defining insult is the patient's underlying surgical pathology. Whether it is the blunt force of trauma, the insidious inflammation of a perforated viscus, or the systemic chaos of sepsis, the physiological response is a massive, non-specific activation of the neuroendocrine stress axis. This is not a finely tuned response; it is a primal, overwhelming flood of catabolic hormones—catecholamines, cortisol, and glucagon—and inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), Interleukin-1 (IL-1), and Interleukin-6 (IL-6).[12] This hormonal and cytokine storm fundamentally rewires the body's metabolism for a state of emergency. The immediate consequence is a dramatic increase in the body's metabolic rate and glucose consumption. The immune system, now on high alert, becomes a voracious consumer of glucose to fuel phagocytosis and the production of inflammatory mediators. Damaged tissues require energy for repair. The heart and respiratory muscles work harder to maintain perfusion and oxygenation.[13] This state of hypermetabolism acts as a powerful catalyst, rapidly accelerating the depletion of the body's most accessible energy reserve: hepatic glycogen. While a resting individual may have 12-24 hours' worth of glycogen, our data strongly suggest that in these hypermetabolic patients, the functional exhaustion of these stores occurs much earlier. The eight-hour mark appears to represent a critical physiological inflection point, beyond which the body's primary defense against hypoglycemia has effectively crumbled.[13]

Upon this already compromised metabolic landscape, we impose the "second hit": the prolonged preoperative fast. Once hepatic glycogen is depleted, the body's entire hope of maintaining euglycemia rests on its ability to synthesize new glucose via gluconeogenesis. It is at this precise moment that the full, devastating impact of the "first hit" becomes manifest, as the very machinery of gluconeogenesis is systematically dismantled by the ongoing stress response. The liver, the central factory for gluconeogenesis, becomes a direct target of the inflammatory cascade.[14] Cytokines, particularly TNF-α, are known to exert a direct suppressive effect on the genetic expression and enzymatic activity of the rate-limiting enzymes of gluconeogenesis, most notably phosphoenolpyruvate carboxykinase (PEPCK) and glucose-6-phosphatase. This creates a state of "hepatic stress" or "euglycemic sickness," where the

liver is functionally incapable of producing sufficient glucose, even when bombarded with hormonal signals to do so. The organ is being commanded to work, but its tools have been taken away. Gluconeogenesis is an assembly process, and it is entirely dependent on a steady supply of raw materials—lactate, alanine, and glycerol—from the periphery.[15] The stress state severs these supply lines. Shock and hypoperfusion, common in emergency patients, prevent these precursors from physically reaching the liver. The systemic inflammatory response can directly impair the function of crucial intercellular transport mechanisms like the Cori cycle (which recycles lactate from muscle to the liver) and the glucose-alanine cycle. The patient's underlying nutritional status, often poor in the acutely ill, means that the reserves of muscle protein (for alanine) and adipose tissue (for glycerol) are already limited. The liver is not only functionally impaired, but it is also being starved of the very building blocks it needs to perform its vital function.[15] The neuroendocrine hormonal response that orchestrates this entire process can itself falter under extreme duress. The concept of "relative adrenal insufficiency" in critical illness is well-established, where the adrenal glands, after a period of maximal stimulation, can no longer produce an adequate cortisol response.[16] Since cortisol is essential for priming the liver for gluconeogenesis, its failure is catastrophic. Furthermore, there is evidence for the development of glucagon resistance in states of severe sepsis, where the liver's receptors become desensitized to its primary stimulating hormone. The finely tuned autonomic nervous system pathways that normally trigger a protective epinephrine release in response to falling glucose can also be disrupted by the chaotic, overwhelming sympathetic discharge of the general stress response. Viewed through this "dual-hit" model, the prolonged fast is transformed from a passive waiting period into an active, decisive insult. It is the final push that sends a teetering metabolic system into a state of outright collapse. The high incidence of hypoglycemia observed in our study is not an anomaly; it is the logical, predictable, and almost inevitable outcome of this synergistic failure of the body's multi-layered defense system.[17]

A unique strength of this revised analysis is the use of two distinct glycemic thresholds, which allows for a more nuanced interpretation of the metabolic state. The <85 mg/dL threshold for "glycemic instability" is not intended to define a disease state but to identify a state of profound metabolic vulnerability. A patient with a blood glucose of 80 mg/dL has, by definition, exhausted their glycogen stores and is relying entirely on a failing gluconeogenic system. They are in a state of impending metabolic decompensation. They have no reserve, no buffer. The slightest increase in metabolic demand or decrease in perfusion, such as that induced by anesthetic agents, can precipitate a rapid and uncontrolled fall into severe hypoglycemia.[18] The finding that 83.3% of the prolonged fasting group fell into this category is a stark indicator of how widespread this vulnerability is. This threshold serves as a highly sensitive early warning sign, flagging a large population for whom extreme vigilance is required. The standard clinical threshold of <70 mg/dL represents the point of established metabolic failure. A patient with a blood glucose level in this range is not merely "at risk"; they are actively experiencing a failure of glucose homeostasis that poses a direct threat to neurological function. The finding that over half (55.6%) of the patients in the prolonged fasting group crossed this line into true, clinically significant hypoglycemia is the study's most critical and actionable result. It confirms that the risk is not theoretical but is frequently actualized in this clinical setting. It transforms the discussion from one of identifying instability to one of preventing imminent harm. The odds ratio of 13.5 for this outcome, while imprecise due to the sample size, powerfully underscores the magnitude of the danger associated with prolonged fasting in this context.

The findings of this pilot study, while preliminary, are sufficiently strong and concerning to demand a re-evaluation of our standard practices. They call for a paradigm shift away from a passive assumption of metabolic stability and toward a model of proactive

surveillance and management. First and foremost, the default assumption that non-diabetic adult patients are metabolically resilient and safe from hypoglycemia in the emergency setting is demonstrably false and must be discarded. This single change in mindset is the most important clinical implication of our work. Second, these results provide a powerful rationale for the implementation of routine, point-of-care pre-induction glucose testing as a universal safety standard for all non-diabetic patients undergoing emergency surgery.[19] This is a simple, rapid, and low-cost intervention that can unmask a hidden, life-threatening condition at a point when it can be easily and safely corrected. It is a quintessential example of a high-value care practice. Third, our understanding of perioperative fluid management in this population must evolve. The dogmatic use of non-dextrose-containing crystalloids for maintenance hydration in patients facing an indeterminate and likely prolonged fast may be physiologically unsound. We must consider the concept of "metabolic resuscitation," where the judicious administration of intravenous fluids containing a low concentration of dextrose is used not to treat, but to prevent the catabolic spiral of starvation. This is not a call for aggressive glucose loading, which carries its own risks, but for a thoughtful, physiological approach to providing basal metabolic support to a patient whose endogenous systems are failing. Finally, these findings should serve as a catalyst for institutional quality improvement initiatives. The problem of prolonged fasting is often a systems issue.[20] Hospitals should be encouraged to develop and implement protocols for the metabolic management of emergency surgical patients, including triggers for mandatory glucose testing and guidelines for the safe use of dextrose-containing fluids, all with the aim of minimizing the duration of the "second hit" and supporting the patient through the "first."

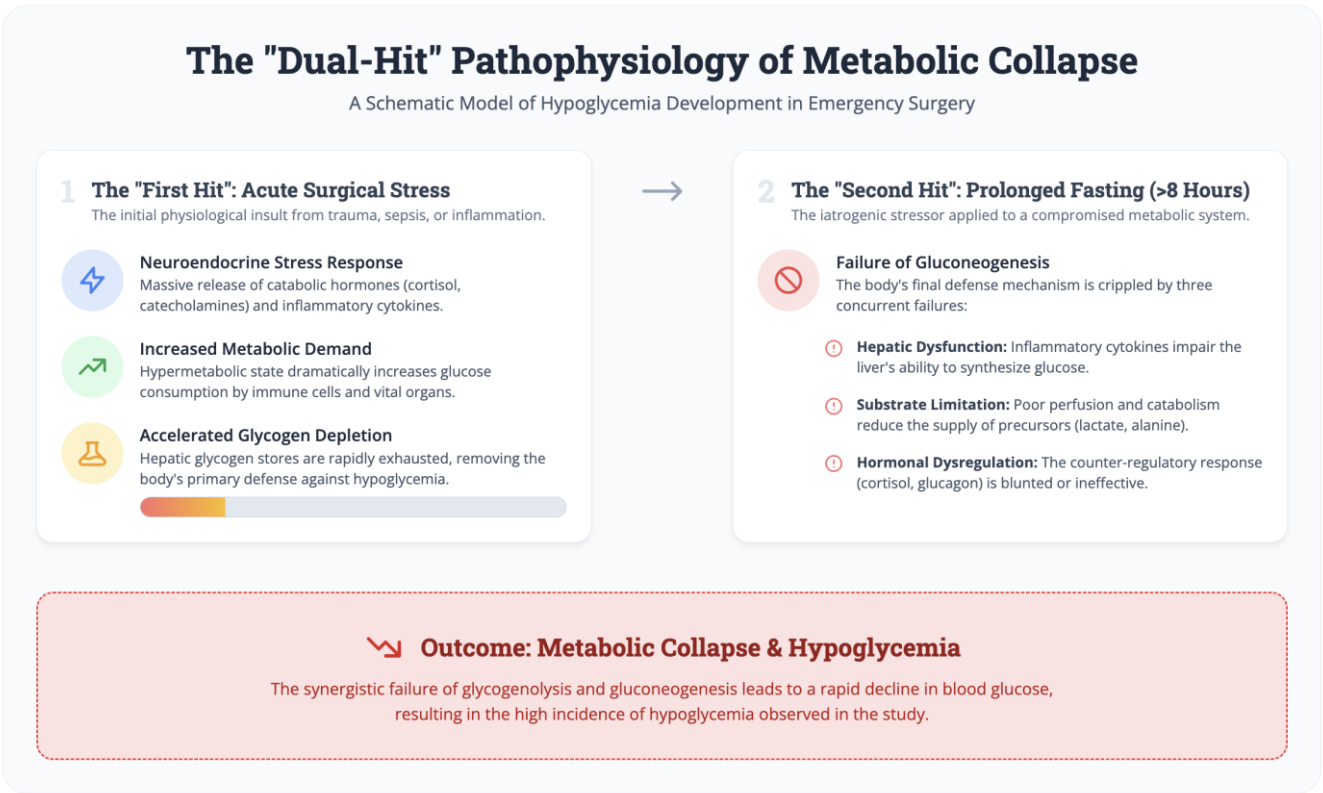


Figure 4. The “Dual-Hit” pathophysiology of metabolic collapse.

Figure 4 showed a schematic model detailing the "Dual-Hit" pathophysiology of metabolic collapse, providing a clear and scientifically grounded explanation for the development of hypoglycemia in emergency surgery patients. The infographic methodically illustrated a two-stage process where an initial physiological insult synergizes with a subsequent iatrogenic stressor to overwhelm the body's homeostatic defenses against falling blood glucose. The first stage, labeled The "First Hit": Acute Surgical Stress, was defined as the initial physiological insult arising from trauma, sepsis, or inflammation. This stage was characterized by three key processes. First, a neuroendocrine stress response is initiated, involving a massive release of catabolic hormones like cortisol and catecholamines, alongside inflammatory cytokines. This hormonal surge signals a state of crisis to the body. Second, this leads to an increased metabolic demand, a hypermetabolic state where glucose consumption by immune cells and vital organs is dramatically increased as they work to combat infection, repair tissue, and maintain function. The direct and critical consequence of these first two processes is the third component: Accelerated Glycogen Depletion. The model explained that the liver's finite glycogen stores are rapidly exhausted under this intense metabolic strain, effectively removing the body's primary and most immediate defense against hypoglycemia. Following the initial insult, the figure depicted the progression to the second stage, the "Second Hit": Prolonged Fasting (>8 Hours). This was framed as an iatrogenic stressor that is applied to an already compromised and vulnerable metabolic system. The central consequence of this second hit is the Failure of Gluconeogenesis, the body's final and most crucial defense mechanism for producing new glucose. The figure details that this failure is not due to a single cause but rather three concurrent failures. First is Hepatic Dysfunction, where inflammatory cytokines directly impair the liver's intrinsic ability to synthesize glucose. Second is Substrate Limitation, a state where poor perfusion and catabolism reduce the supply of essential precursors, like lactate and alanine, from the periphery to the liver. Third is Hormonal Dysregulation, where the counter-regulatory hormonal signals from cortisol and glucagon become blunted or ineffective, failing to properly stimulate the gluconeogenic process. Finally, the schematic culminated in the Outcome: Metabolic Collapse & Hypoglycemia. This section explained that the synergistic failure of both primary (glycogenolysis) and secondary (gluconeogenesis) defense mechanisms leads to a rapid and uncontrolled decline in blood glucose. This pathophysiological cascade provides a direct rationale for the high incidence of hypoglycemia observed in the study's clinical findings. In essence, the figure provided a compelling narrative, illustrating how an acutely ill patient is first rendered vulnerable by their underlying condition and then pushed into a state of metabolic failure by the superimposed and prolonged absence of nutritional intake.

As a pilot investigation designed to generate hypotheses, this study has several important limitations that must be transparently acknowledged and which appropriately temper the strength of our conclusions. The most significant limitation is the small sample size of 30 patients. This restricts the generalizability of our findings and the precision of our effect estimates, as reflected in the wide confidence intervals. The results should therefore be interpreted as a strong preliminary signal that requires confirmation in larger, multi-center trials, not as definitive proof of causality. Furthermore, the small sample size precluded the use of multivariable regression analysis to control for the influence of critical confounding variables, such as the specific type and severity of surgical pathology or the patient's underlying nutritional status. While we have demonstrated a powerful association, we cannot, from this data alone, disentangle the effect of fasting from the effect of the underlying illness. Lastly, our reliance on patient interviews for fasting duration introduces a potential for recall bias, and the use of point-of-care glucometers carries an inherent degree of measurement inaccuracy compared to central laboratory analysis. These limitations do not invalidate

the concerning signal we have detected, but they clearly define the need and direction for future, more definitive research.

**4. Conclusion**

Despite its acknowledged limitations as a pilot study, this prospective investigation provides a compelling and deeply concerning signal that prolonged preoperative fasting is strongly associated with a dose-dependent decline in blood glucose and a dramatically increased incidence of both glycemic instability and clinically significant hypoglycemia in non-diabetic adult patients undergoing emergency surgery. The physiological synergy of an acute surgical stress response and an extended period of iatrogenic starvation appears to systematically overwhelm the body's metabolic defenses, challenging the widely held and potentially dangerous assumption of metabolic security in this population. These preliminary findings underscore the urgent need for larger, more definitive multi-center studies to validate this association, control for confounding variables, and establish the true independent predictive value of fasting duration. However, the magnitude and statistical significance of the signal detected in this pilot work are powerful enough to warrant immediate clinical consideration and a shift in our collective mindset. Clinicians should abandon complacency regarding the metabolic status of these patients, and institutions should strongly consider implementing routine pre-induction glucose monitoring as a simple, low-cost, and high-impact safety measure to protect this vulnerable population from a preventable and potentially catastrophic perioperative event.

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