Volume 4, Issue 6, 2026

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

ASSOCIATION OF RINGER LACTATE WITH BLOOD GLUCOSE LEVEL IN NON-DIABETICS DURING GENERAL ANESTHESIA.

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DOI: https://doi.org/10.5281/zenodo.21160407

Keywords
Ringer Lactate, blood glucose, general anesthesia, perioperative hyperglycemia, non-diabetic patients, surgical stress response, intraoperative monitoring.

Article History
Received: 17 April 2026
Accepted: 07 June 2026
Published: 21 June 2026

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Abstract

Perioperative glycemic control is especially important in the surgical patient because intra-operative hyperglycemia in non-diabetic patients is linked to adverse outcomes. When surgical stressed trigger, the body releases cortisol, catecholamines and glucagon which stimulate hepatic glycogenolysis and gluconeogenesis regardless of fluid composition. Ringer Lactate is a commonly used balanced crystalloid fluid used in the perioperative period that lacks dextrose, however, its impact on perioperative blood glucose levels in non-diabetic surgical patients undergoing general anesthesia has not been thoroughly examined. Heavy Industry Taxila (HIT) hospital was used for a prospective observational study that lasted for about four months. Patients of ASA physical status I-II aged between 18–60 years who were undergoing elective surgery under general anesthesia were included in the study by convenience sampling and a total of 110 were evaluated. Exclusion criteria included medications that affect blood glucose, impaired glucose tolerance, diabetes, and pre-operative fasting blood glucose >126 mg/dl. Blood glucose level was measured at three times including preoperatively, intraoperatively and postoperatively. Of the preoperatively measured patients 69.1% had glucose levels in the range of 80-90 mg/dl. At the time of surgery, 43.6% were in the 101-110 mg/dl range. Among those who had surgery, 50.9% had a level between 111 and 120 mg/dl and none went below 91 mg/dl. There was a statistically significant correlation between the glucose levels before and during the operation (p = 0.001), before and after the operation (p = 0.001), and during and after the operation (p = 0.008). Ringer Lactate is ineffective at preventing stress-induced hyperglycemia in non-diabetic patients, in general anesthesia. While dextrose-free maintenance fluids are utilized, peri-operative glucose monitoring continues to be clinically important.

INTRODUCTION

A class of metabolic illnesses known as diabetes is defined by hyperglycemia brought on by deficiencies in insulin activity, secretion, or both[1]. Hyperglycemia, which is a common side effect of any kind of surgery and varies depending on the location and length of the procedure, is a key characteristic of all forms of diabetes mellitus[2].A key goal of perioperative patient care is to maintain intravascular volume, adequate tissue

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ISSN: (e) 3007-1607 (p) 3007-1593

perfusion and metabolic homeostasis[3]. IV fluid is a critical part of anesthetic care and is routinely given to replace fluid deficits that occur before anesthesia, to keep blood volume adequate, to replace fluid losses that occur during anesthesia, and to maintain organ perfusion during surgery. Type of IVF can impact not just hemodynamic stability, but metabolic and biochemical response in the peri-op period. Ringer Lactate (RL) is one of the most used crystalloid fluids due to its electrolyte content being similar to extracellular fluid. RL is therefore often used in surgical surgery under general anesthesia.

Surgical procedures trigger a complex physiological stress response which activates the neuroendocrine, metabolic, inflammatory and immunological systems. This is triggered by the injury to the tissues and is exacerbated by preoperative fasting, anxiety, pain, blood loss, hypothermia, anesthetic drugs and surgical trauma. These stimuli trigger the release of stress hormones such as catecholamines, cortisol, glucagon, growth hormone and antidiuretic hormone. During times of stress, these hormones trigger glycogenolysis, gluconeogenesis, lipolysis and protein catabolism to maintain appropriate energy substrate availability[4]. Due to this, blood glucose levels in the patient tend to rise during and after surgery even if the patient is a non-diabetic. There has been a growing appreciation for peri-operative hyperglycemia as an important factor in determining surgical outcomes. Hyperglycemia has been linked to a decrease in immune function, activity of neutrophils, inflammatory reaction, endothelial dysfunction, delayed wound healing, and increased risk of postoperative infection. In addition, hyperglycemia could lead to higher oxidative stress, cardiovascular problems, renal dysfunction, longer hospital stays, and higher health care expenses. Stress induced hyperglycemia has not only been shown to be detrimental to peri-operative outcome in diabetes but also in non-diabetic patients. Thus, it is important to monitor and understand the factors

that affect blood glucose during a surgical procedure. The degree of stress response depends upon the type of anesthesia used during surgery. A general anesthetic has been demonstrated to cause more endocrine and metabolic effects than regional anesthesia (spinal or epidural anesthesia)[5,6].

During general anesthesia, the rise in circulating levels of catecholamines, cortisol and glucagon can lead to greater glucose production in the liver and less use of glucose in the periphery. As a result, blood glucose levels often increase during surgery in general anesthesia, even if a patient has a normal glucose metabolism before surgery. General anesthesia and surgical stress are linked to decreased insulin production and increased insulin resistance in addition to the release of stress hormones. While increased levels of glucagon, cortisol, and catecholamines reduce tissue sensitivity to insulin, increased sympathetic activity inhibits the release of pancreatic insulin[7]. Peripheral tissues absorb less glucose as a result, while the liver produces more glucose through glycogenolysis and gluconeogenesis. Even in individuals without pre-existing diabetes mellitus, this imbalance between glucose production and utilization plays a major role in perioperative hyperglycemia. Apart from the physiological stress-storm, perioperatively, fluid can affect glucose homeostasis. Intravenous fluids are given throughout surgery and may alter metabolic pathways based upon what type of fluid is given[8].

Ringer lactate is composed of sodium chloride, potassium chloride, calcium chloride and sodium lactate. The lactate is a buffering agent and is primarily removed from the blood and metabolized in the liver as it is converted to bicarbonate. But lactate can also enter into gluconeogenic pathways and be utilized as a substrate for the synthesis of glucose. This metabolic characteristic has raised a lot of interest about the effects of RL administration on blood glucose levels during surgery.There are theoretical concerns that the metabolism of lactate could lead to increased blood glucose level, especially in surgical stress patients. RL is not glucose-based, but the production of glucose from lactate to lactate through hepatic gluconeogenesis has raised some questions about its use in circumstances where control of glucose levels is

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ISSN: (e) 3007-1607 (p) 3007-1593

paramount[9].

However, the glucose production by lactate metabolism has been questioned by several investigators and it is unlikely that this process will lead to significant hyperglycemia in most patients. The divergent opinions have led to continued discussion about the effect of RL infusion on metabolism during anesthesia[10].

The results of previous studies that have assessed perioperative changes in glucose levels have been conflicting. The blood glucose level has been reported to increase significantly after RL administration by some researchers and very little or no clinically significant effect by others. In addition, most studies out there have been conducted on diabetic patients or critically ill or cardiac surgical patients. There is comparatively less research on the effect of RL administration on blood glucose in non-diabetic individuals in elective surgeries under general anesthesia. Thus, the role of RL on perioperative glycemic changes in this population is still not known. This is highlighted by the growing focus on better recovery practices and evidence-based perioperative care. The selection of a fluid for an anesthetic is an important part of the practice and knowing the metabolic effects of the fluids used in common anesthetic practice may help optimize patient outcomes. Hence, the impact of RL on blood glucose deserves elucidation for clinical use.In non-diabetic patients, hyperglycemia during the peri-operative period could be easily overlooked as glucose is not monitored as frequently as in diabetic patients[11].

However, even if blood glucose levels are elevated for a short time, they can affect the recovery and rate of complications after surgery. The role of RL administration in these changes may inform anesthesiologists in making the best choice of fluid during surgery, while keeping metabolic control optimal. Hence, this study was proposed to assess the relationship between Ringer Lactate infusion and blood glucose in normal people who are under general anesthesia during surgery. This study will evaluate changes in blood glucose levels preoperatively after RL infusion and the contribution of RL to clinically significant hyperglycaemia. The results could prove useful as evidence of the metabolic effects of RL and help develop better fluid management protocols, patient safety and better surgery.

METHODOLOGY

A prospective observational study design was adopted for this study. The study was conducted at Heavy Industry Taxila (HIT) Hospital over a period of approximately four months after obtaining approval from the Institutional Ethics Review Committee and the University of Haripur. A total sample size of 110 patients was calculated, using a convenience sampling technique. Patients aged 18–60 years with ASA physical status I and II, fasting according to standard preoperative (NPO) guidelines, and without a history of diabetes mellitus were included in the study. Patients with known diabetes mellitus, impaired glucose tolerance, preoperative fasting blood glucose levels greater than 126 mg/dL or random blood glucose levels greater than 200 mg/dL, those receiving medications known to affect blood glucose levels such as corticosteroids and beta-agonists, and patients requiring blood transfusion were excluded from the study.

The study was initiated following ethical approval from the Institutional Ethical Committee of HIT Hospital and the University of Haripur. Data were collected using a slightly modified pre-designed proforma. The reference period for data collection extended from the preoperative phase through the postoperative period. Relevant demographic and clinical information was recorded, and blood glucose measurements were documented according to the study protocol.

Data analysis was performed using SPSS version 27 and Microsoft Excel 2024. Descriptive statistics were used to summarize the collected data, while Chi-square test and crosstabs analysis were applied to assess associations between study variables. A p value is less than 0.05, was considered statistically significant.

RESULT

Demographic Characteristics

Age Distribution:

The study included a total of 110 non-diabetic

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ISSN: (e) 3007-1607 (p) 3007-1593

patients who were undergoing general anesthesia in surgery. The age distribution showed that the largest proportion of patients belonged to the 18–30 years age group (n = 38; 34.5%), followed by the 41–50 years age group (n = 25; 22.7%), the 31–40 years age group (n = 24; 21.8%), and the 51–60 years age group (n = 23; 20.9%). This means that the study population was mainly young adults.

Gender distribution:
As for gender distribution, more females than males were included in the study (n = 62, 56.4% vs. n = 48, 43.6%). This is an indication of the slight predominance of female participants in the study sample.

ASA physical status:
After assessment of ASA physical status, most patients were ASA Class I (n = 62; 56.4%) while ASA Class II patients represented 43.6% of the total. This result suggests that most patients were relatively low risk for anesthetic and good pre-operative physical status.

Preoperative Fasting (NPO):
In terms of the preoperative fasting (NPO) status, the highest number of patients had an NPO time of 6-8 hours (n = 41; 37.3%), followed by less than 6 hours (n = 35; 31.8%) and greater than 8 hours (n = 34; 30.9%). The distribution indicates that most patients followed the usual fasting rules prior to receiving anaesthetic and surgery.

Table 1: Comprehensive Summary of Statistical Results

Comparison	χ^2 Value	df	p-value
Preoperative vs Intraoperative Glucose Levels	61.71	12	0.001
Intraoperative vs Postoperative Glucose Levels	29.52	6	0.001
Preoperative vs Postoperative Glucose Levels	17.28	6	0.008

In the following Table1 the Chi-square analysis was performed to assess the relationship between blood glucose levels measured at different perioperative time points. The results demonstrated a highly significant association between preoperative and intraoperative glucose levels (χ^2 = 61.71, df = 12, p = 0.001), indicating that blood glucose concentrations changed significantly following induction of general anesthesia and administration of perioperative fluids. Similarly, a statistically significant relationship was observed between intraoperative and postoperative glucose levels (χ^2 = 29.52, df = 6, p = 0.001), suggesting that glucose levels continued to vary throughout the surgical and immediate postoperative periods. This finding reflects the ongoing metabolic and hormonal effects of surgical stress and perioperative management. Furthermore, comparison of preoperative and postoperative glucose levels also revealed a significant association (χ^2 = 17.28, df = 6, p = 0.008). This indicates that blood glucose levels measured after surgery differed significantly from baseline preoperative values.

Overall, the Chi-square analysis demonstrates significant variations in blood glucose levels across all three perioperative phases. The strongest association was observed between preoperative and intraoperative glucose levels, as indicated by the highest Chi-square value. These findings suggest that perioperative factors, including surgical stress, general anesthesia, and administration of Ringer Lactate, may contribute to changes in blood glucose concentrations in non-diabetic patients undergoing surgery.

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ISSN: (e) 3007-1607 (p) 3007-1593

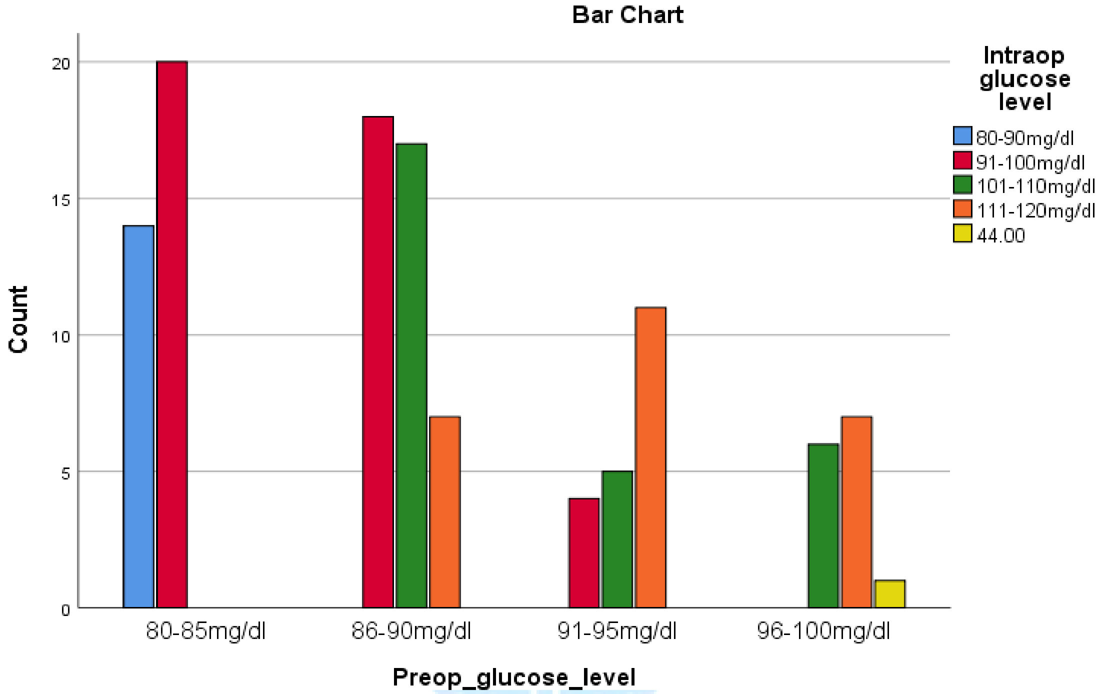

Figure 1 Relationship Between Preoperative and Intraoperative Glucose Level

Figure indicate that a statistically significant association was found between the preoperative baseline glucose level and intraoperative glucose level, X2(12) = 61.71, p=0.001. The Likelihood Ratio is highly significant (68.72, p =0.001) as is the Linear-by-Linear Association (8.20, p = .004) for a sample size of 110 cases. The bar chart shows that the patients with lower preoperative blood glucose levels (80-85 mg/dl) were mostly at lower intraoperative ranges (80-90 mg/dl and 111-120 mg/dl).

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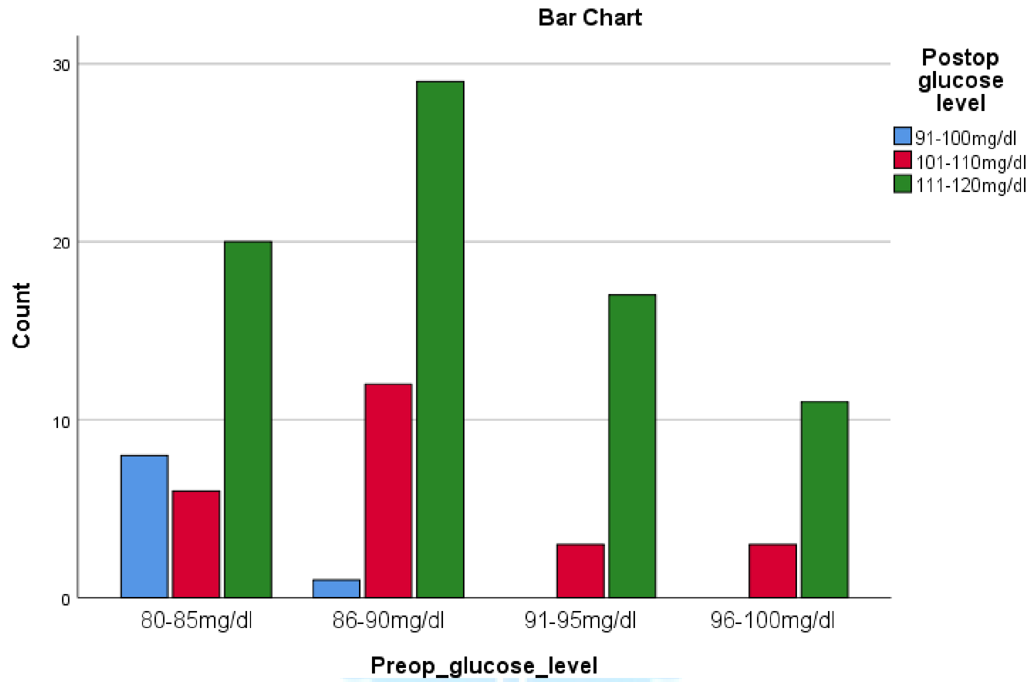
ISSN: (e) 3007-1607 (p) 3007-1593



As seen in table 4.8, a Chi-square test of independence found that there was a statistically significant relationship between pre and post surgery glucose levels, X2(6) = 17.28, p = 0.008. This is clearly reflected by the bar chart of blood sugar levels after surgery for each group of patients (N = 110). The glucose level was seen to be shifting into the highest range, 111-120 mg/dl, in most of the patients, and there was a significant peak in the 86-90 mg/dl, preop, group of patients. On the other hand, the lowest postop range (91-100 mg/dl) completely disappeared for patients with a preop baseline > 90 mg/dl.

DISCUSSION

The study was a prospective observational study that included 110 patients with no diabetes who received Ringer Lactate as the only intravenous fluid during general anesthesia. Three sequential periods of blood glucose level were recorded (pre-, intra-, and postoperatively). The study design was an arm-only design, and the results reflect the effect of glucose on all patients provided Ringer Lactate, and not a comparison of Ringer Lactate with any other fluid.

Patients included in the study were a wide age population ranging from 18 to 60 years. The largest age group was 18–30 years (34.5%), followed by 41–50 years (22.7%), 31–40 years (21.8%), and 51–60 years (20.9%), indicating a relatively even distribution across age categories. Most of the participants were female (56.4%) and the minority was male (43.6%). Regarding ASA physical status, 56.4% of the patients were ASA I, whereas 43.6% were ASA II, and they had relatively few underlying systemic diseases. This distribution is less consistent with pre-existing metabolic dysfunction as a cause of the observed increase in glucose and Favors the contribution of surgical stress to the increase in glucose. In terms of the length of the fast, most patients fasted for 6 to 8 hours (37.3%), then less than 6 hours (31.8%) and more than 8 hours (30.9%). However, prolonged fasting is a known factor for triggering counter-regulatory hormone release and differences in the length of NPO amongst patients may have caused the surgical stress signal that was detected in this study but cannot be separated from the other effects of the single-arm design. (38.2%) of the patients had glucose levels that were in the normal fasting range (86–90 mg/dl), and 30.9% had a glucose level that fell within the 80–85 mg/dl range, which was the combined normal fasting range. This reinforces

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ISSN: (e) 3007-1607 (p) 3007-1593

the fact that all patients had appropriate normoglycemia as was required by the inclusion criteria of the study (non-diabetic and standard NPO)[2].

During the intraoperative stage, a definite increase of glucose distribution was found. The highest percentage of patients (43.6%) was in the 101-110 mg/dl range, and the next highest (38.2%) was in the 91-100 mg/dl range. Only 12.7% remained in the 80–90 mg/dl range, and 5.5% had risen to the 111–120 mg/dl range. This is a statistically significant improvement over the baseline measured in the preoperative period with a Chi-square test (p = 0.001) showed the same pattern and direction of increase in glucose level throughout the surgery.

The glucose distribution shift was even greater to the right as seen in the postoperative reading. Most patients (50.9%) recorded values in the 111–120 mg/dl range, and 40.9% were in the 101–110 mg/dl range. Notably, no patient in this cohort was less than 91 mg/dl at the postoperative time point, meaning that all patients in this cohort had some elevation in glucose level at the end of surgery. The correlation with intraoperative blood glucose level and postoperative blood glucose level was statistically significant (p = 0.001), as was the correlation between preoperative blood glucose level and postoperative blood glucose level (p = 0.008). There was a significant association between the preoperative and postoperative glucose. The increase in blood glucose levels is not due to an exogenous glucose load as Ringer Lactate is a dextrose-free balanced crystalloid solution[12].

The more likely and sound one is that neuroendocrine stress response due to surgery and general anesthesia. Cortisol, catecholamines, glucagon, and adrenocorticotrophic hormone (ACTH) are released with surgical trauma, and all have the effect of promoting hepatic glycogenolysis and gluconeogenesis and at the same time decreasing insulin sensitivity in the periphery[6]. These mechanisms are independent of the composition of the fluid. These results are thus presented as a snapshot of the stress hyperglycaemia response, in a group of patients provided with Ringer Lactate, and not as proof that Ringer Lactate per se leads to hyperglycaemia. This interpretation fits into the previous comparative literature that has always shown less glycemic excursions with Ringer Lactate than with dextrose containing fluids, which it has been attributed to the lack of an exogenous glucose load. In those studies, however, there was still some increase in glucose from the surgical stress response in patients who were given Ringer Lactate[13].

None of the recorded glucose values in this cohort were at or above the 150 mg/dl level suggested in the literature as the glucose level that requires insulin correction, however, the shift from a predominantly 80-90 mg/dl preoperative glucose level to a predominantly 101-120 mg/dl postoperative glucose level is clinically significant. It means that a dextrose-free fluid does not necessarily mean that glucose is stable. Small to moderate increases in glucose during the peri-operative period could play a role in impaired neutrophils function, increased inflammation and delayed wound healing. Thus, for any patient who is not diabetic and gets general anesthesia, intraoperative and postoperative glucose monitoring is still clinically useful, whether they are receiving maintenance fluids with or without glucose[5].

The main drawback of this study is the lack of control fluid. All 110 patients in this study were given Ringer Lactate; the study cannot conclude that any other maintenance fluid would have resulted in a smaller or larger glucose rise or that it would not have produced a glucose rise, even though all the patients were given Ringer Lactate. Furthermore, the blood glucose was not measured in continuous numbers but in intervals, so that a true mean change or before after comparison is not possible. Surgical type and duration, infused total fluid volume, blood loss, and use of vasopressors and/or corticoids were not documented or controlled as systematic factors. This was performed in one center, which limits the generalizability of the results, and glucose monitoring was only performed during the immediate postoperative period, and no information was provided about the length of the

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ISSN: (e) 3007-1607 (p) 3007-1593

glucose elevation or the clinical effects.

CONCLUSION

This study concluded that blood glucose levels increased significantly from the preoperative to the intraoperative and postoperative periods in non-diabetic patients undergoing elective surgery under general anesthesia. The findings demonstrated statistically significant associations between glucose levels at all three perioperative stages ($p < 0.05$), indicating that perioperative metabolic changes occur despite the use of dextrose-free Ringer Lactate solution. These results suggest that the observed rise in blood glucose is more likely related to the physiological stress response of surgery and general anesthesia rather than the composition of Ringer Lactate itself. Although none of the patients developed severe hyperglycemia requiring intervention, a consistent upward trend in glucose levels was observed throughout the perioperative period. Therefore, routine perioperative blood glucose monitoring should be considered even in non-diabetic patients receiving Ringer Lactate during general anesthesia. Early identification of glucose fluctuations may help optimize patient management, reduce potential postoperative complications, and improve overall surgical outcomes. Further comparative studies with different intravenous fluids and larger multicenter populations are recommended to better clarify the independent effect of Ringer Lactate on perioperative glycemic control.

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