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Serum Creatinine Dynamics during the First 48 Hours after Major Surgery Following Intraoperative Diuretic Administration

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ABSTRACT

Introduction: Serum creatinine continues to serve as a key marker for evaluating renal function in the perioperative setting. The early postoperative period, particularly the first 48 hours after major surgery, is a critical timeframe during which subtle biochemical changes may signal evolving kidney stress or injury.

Material and methods: This prospective observational study was conducted in 2025 at Shohada Hospital, Tabriz, to evaluate serum creatinine changes during the first 48 postoperative hours following intraoperative furosemide administration in major surgery patients. Fifty participants were enrolled through convenience sampling. Serum creatinine was measured preoperatively and every six hours postoperatively.

Results: Serum creatinine increased significantly during the first 48 postoperative hours following intraoperative diuretic administration, rising from a baseline median of 0.96 mg/dL (IQR: 0.84-1.10) to a peak of 1.15 mg/dL (IQR: 1.00-1.35) at approximately 30 hours (P<0.001). Patients aged ≥45 years demonstrated greater postoperative elevations than younger individuals (P=0.018), while female patients showed slightly higher mid-postoperative creatinine levels compared with males (P=0.041). Despite these differences, creatinine values gradually declined toward baseline by 48 hours.

Conclusion: Intraoperative diuretic administration was associated with temporary postoperative changes in serum creatinine that remained clinically modest and largely reversible. Advanced age and female sex appeared to influence the magnitude of renal biochemical responses. Careful perioperative renal monitoring, particularly in older patients, may help optimize postoperative management and facilitate early identification of transient renal function changes.

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Introduction

Major surgical procedures are frequently accompanied by substantial physiological stress and complex perioperative fluid shifts that can influence renal function. Among the laboratory markers used to monitor kidney performance, serum creatinine remains one of the most widely applied indicators in clinical practice. Although it is an imperfect biomarker, its accessibility, standardized measurement, and well-established clinical interpretation have made it central to postoperative renal monitoring.

Changes in serum creatinine during the early postoperative period may reflect alterations in renal perfusion, intravascular volume status, systemic inflammatory responses, or the effects of medications administered during anesthesia. Consequently, careful observation of creatinine levels in the hours immediately following major surgery is essential for identifying early renal dysfunction and guiding appropriate management strategies (1).

The perioperative period represents a vulnerable window for the development of acute kidney injury. Hemodynamic fluctuations, blood loss, anesthetic drugs, systemic inflammation, and exposure to nephrotoxic agents can all compromise renal perfusion and filtration. Even transient decreases in effective renal blood flow may lead to measurable changes in glomerular filtration rate. Because creatinine concentration in the blood rises when filtration declines, serial monitoring of this biomarker provides an indirect but practical method for detecting early renal impairment. In many surgical populations, relatively small increases in serum creatinine within the first two days after surgery have been associated with worse clinical outcomes, including prolonged hospitalization and increased postoperative morbidity (2).

Fluid management during major operations plays a pivotal role in maintaining adequate organ perfusion. Anesthesiologists must continuously balance the risks of hypovolemia and fluid overload while responding to dynamic changes in hemodynamics. Excessive intravascular volume may contribute to tissue edema, impaired oxygen diffusion, and cardiopulmonary complications, whereas insufficient volume can reduce renal perfusion and precipitate acute kidney injury. To optimize this balance, diuretics are sometimes administered intraoperatively to promote urine output, reduce fluid accumulation, or assist in the management of specific clinical conditions. Loop diuretics, particularly furosemide, are among the most commonly used agents in this setting (3).

The pharmacologic effects of diuretics on renal physiology are well understood. Loop diuretics act primarily by inhibiting the sodium–potassium–chloride cotransporter in the thick ascending limb of the loop of Henle (4). This mechanism leads to increased excretion of sodium, chloride, and water, resulting in enhanced urine production. In addition to their natriuretic effects, these medications may influence renal hemodynamics by modifying intracranial blood flow and altering tubular oxygen demand. While diuretics can be beneficial in managing fluid balance, their impact on postoperative renal function remains a topic of ongoing discussion. Some clinicians believe that promoting urine output may help maintain renal perfusion and prevent tubular injury, whereas others argue that diuretics may mask early signs of renal dysfunction or contribute to intravascular volume depletion (5).

The interpretation of serum creatinine changes following diuretic administration is particularly complex. Increased urine output does not necessarily indicate preserved kidney function; rather, it may reflect pharmacologic stimulation of the nephron. At the same time, aggressive diuresis in the context of inadequate fluid replacement could potentially reduce renal perfusion pressure. These competing mechanisms make it difficult to predict how serum creatinine levels will behave in the immediate postoperative period when diuretics are used during anesthesia. Understanding the pattern of creatinine changes after such interventions is therefore clinically relevant for perioperative decision-making (6).

The first 48 hours after surgery represent a critical timeframe for detecting early renal alterations. During this period, physiological responses to surgical trauma including inflammatory activation, hormonal changes, and shifts in fluid distribution are particularly pronounced. Cytokine release, sympathetic stimulation, and activation of the renin angiotensin aldosterone system can all influence renal vascular resistance and sodium handling. Moreover, patients recovering from major operations often experience variations in blood pressure, cardiac output, and intravascular volume that may further affect kidney perfusion. Because serum creatinine responds relatively slowly to changes in glomerular filtration rate, serial measurements across this early postoperative window provide valuable insight into evolving renal function (7).

Several patient-related and procedure-related factors may also contribute to postoperative creatinine fluctuations. Advanced age, preexisting chronic kidney disease, diabetes mellitus, hypertension, and cardiovascular disease are recognized risk factors for perioperative renal impairment. In addition, the type and duration of surgery, the extent of blood loss, and the need for transfusion can significantly influence renal outcomes. Major abdominal, thoracic, and vascular procedures often involve prolonged anesthesia and substantial physiological stress, increasing the likelihood of transient or sustained renal dysfunction. In such contexts, intraoperative interventions including the administration of diuretics may further shape postoperative biochemical trends (8).

Another important consideration is the evolving understanding of acute kidney injury definitions. Contemporary clinical guidelines emphasize that even small increases in serum creatinine within a short period may represent clinically meaningful kidney injury. For example, widely used diagnostic criteria define acute kidney injury as an increase in serum creatinine of at least 0.3 mg/dL within 48 hours or a relative increase of 50 percent from baseline. These thresholds underscore the importance of monitoring early creatinine dynamics rather than relying solely on overt renal failure. Consequently, studying creatinine trends in the immediate postoperative period can contribute to earlier detection of renal stress and facilitate timely interventions (9).

The relationship between diuretic use and postoperative kidney function has been investigated in various clinical settings, yet findings remain inconsistent. Some studies suggest that loop diuretics may improve urine output without significantly altering long-term renal outcomes, while others indicate potential associations with worsening kidney function when used inappropriately or without adequate volume assessment. These discrepancies highlight the complexity of perioperative renal physiology and the need for more detailed characterization of biochemical changes following diuretic exposure during surgery. Evaluating the trajectory of serum creatinine in the early postoperative period may provide valuable information about how kidneys respond to both surgical stress and pharmacologic modulation (10).

Beyond renal physiology, monitoring creatinine trends has practical implications for postoperative care. Detecting early increases in serum creatinine can prompt clinicians to reassess fluid management, review potentially nephrotoxic medications, and optimize hemodynamic stability. Early recognition of renal impairment also allows for more careful monitoring of electrolyte balance and drug dosing, particularly for medications that are cleared through the kidneys. In the setting of major surgery, where patients often receive multiple medications and experience dynamic physiological changes, such vigilance can play an important role in preventing further renal injury (11).

Intraoperative diuretic administration may also interact with other aspects of anesthetic management. For instance, the effects of positive pressure ventilation, vasopressor use, and fluid resuscitation strategies can all influence renal perfusion and urine production. The combined impact of these variables complicates the interpretation of postoperative renal biomarkers. Therefore, studying serum creatinine trends in patients who receive diuretics during anesthesia may help clarify how these interventions interact with broader perioperative management strategies (12).

From a research perspective, analyzing creatinine changes over the first two postoperative days provides a structured approach to understanding early renal responses. By comparing baseline measurements with subsequent values obtained within 24 and 48 hours after surgery, investigators can identify patterns of stability, improvement, or deterioration in renal function. Such patterns may reveal whether intraoperative diuretic administration is associated with transient biochemical changes or with clinically meaningful alterations in renal filtration. These insights could ultimately inform perioperative guidelines and help clinicians determine when diuretics are beneficial, neutral, or potentially harmful (13).

Despite extensive advances in perioperative monitoring and anesthetic techniques, kidney injury remains a significant concern following major surgical procedures. Even mild renal impairment can have downstream consequences, including increased risk of infection, delayed recovery, and longer hospital stays. Consequently, ongoing efforts to understand factors influencing postoperative renal function remain highly relevant. Investigating the trajectory of serum creatinine following intraoperative diuretic use represents one component of this broader effort to optimize patient safety and surgical outcomes (14).

In summary, serum creatinine continues to serve as a key marker for evaluating renal function in the perioperative setting. The early postoperative period, particularly the first 48 hours after major surgery, is a critical timeframe during which subtle biochemical changes may signal evolving kidney stress or injury. Intraoperative administration of diuretics introduces additional physiological considerations that may influence these changes. By examining the pattern of serum creatinine levels during this interval, clinicians and researchers can gain a clearer understanding of how perioperative interventions affect renal physiology and postoperative recovery.

Material and methods

Study Design

This prospective observational study was designed to evaluate the trend of serum creatinine changes during the first 48 hours after major surgery following intraoperative diuretic administration under general anesthesia. The primary objective of the study was to investigate the pattern of postoperative renal function alterations and determine the temporal relationship between intraoperative diuretic exposure and serum creatinine fluctuations in the early postoperative period. The study was conducted at Shohada Hospital, Tabriz, Iran, during the year 2025. All eligible patients undergoing major surgical procedures under general anesthesia were assessed consecutively throughout the study period.

Sampling Method

Participants were recruited using a convenience sampling method among patients scheduled for elective major surgery at Shohada Hospital. A total of 50 patients meeting the eligibility criteria were enrolled in the study. Sample selection was performed continuously until the required sample size was achieved.

Eligibility Criteria

Adult patients aged 18 to 75 years who underwent elective major surgery under general anesthesia and required intraoperative administration of a loop diuretic were included in the study. Eligible participants were required to have stable preoperative hemodynamic status and baseline serum creatinine levels within the acceptable clinical range prior to surgery. Patients of both sexes were enrolled irrespective of the type of major surgical procedure, including abdominal, thoracic, vascular, and orthopedic surgeries with an expected operative duration exceeding two hours. Patients were excluded if they had a history of chronic kidney disease stage III or higher, acute kidney injury before surgery, dialysis dependency, severe congestive heart failure, uncontrolled diabetes mellitus, advanced liver failure, septic shock, severe electrolyte imbalance, urinary tract obstruction, pregnancy, hypersensitivity to loop diuretics, perioperative cardiac arrest, intraoperative massive hemorrhage requiring extensive transfusion, or exposure to nephrotoxic medications during the perioperative period. Patients with incomplete laboratory records, postoperative reoperation within the first 48 hours, or refusal to participate in the study were also excluded from the final analysis.

Study Procedure

After obtaining written informed consent, demographic and baseline clinical information including age, sex, body mass index, underlying diseases, type of surgery, duration of operation, and baseline laboratory findings were recorded for all participants. All patients underwent standard general anesthesia according to institutional protocols, including routine intraoperative monitoring of heart rate, blood pressure, oxygen saturation, end-tidal carbon dioxide, urine output, and fluid balance. Intraoperative fluid therapy was performed using crystalloid solutions tailored to the patient's hemodynamic condition and surgical requirements. During anesthesia, intravenous furosemide was administered as the selected loop diuretic at a dose of 0.5 to 1 mg/kg based on clinical judgment and intraoperative fluid status. The diuretic was injected slowly over 2 to 5 minutes after hemodynamic stabilization and generally during the maintenance phase of anesthesia, approximately one hour after surgical incision. Urine output was monitored continuously throughout the procedure and during the early postoperative period.

Serum creatinine levels were measured before surgery as the baseline value and subsequently every six hours during the first 48 postoperative hours, resulting in a total of eight postoperative measurements for each participant. Blood samples were collected through peripheral venous sampling under standardized aseptic conditions. Laboratory analysis of serum creatinine was performed in the central hospital laboratory using an automated biochemical analyzer based on the enzymatic colorimetric method to ensure analytical accuracy and consistency. All measurements were conducted according to the manufacturer's calibration standards and quality control procedures. The trend of serum creatinine changes was assessed by comparing postoperative values with baseline levels and evaluating temporal fluctuations over the 48-hour observation period. In addition to creatinine measurements, postoperative urine output, hemodynamic parameters, administered intravenous fluids, and potential perioperative complications were documented to facilitate interpretation of renal function changes. Patients were monitored closely during hospitalization for signs of renal dysfunction or postoperative instability, and all collected data were entered into a structured research checklist designed specifically for the study.

Statistical Analysis

Data were analyzed using SPSS software version 27. Quantitative variables were expressed as mean ± standard deviation or median with interquartile range according to data distribution, while qualitative variables were presented as frequency and percentage. The normality of quantitative data was assessed using the Kolmogorov Smirnov test. Repeated measures analysis of variance (Repeated Measures ANOVA) was used to evaluate changes in serum creatinine levels over time during the first 48 postoperative hours. In cases where assumptions for parametric analysis were not met, the Friedman test was applied as a nonparametric alternative. Associations between demographic or clinical variables and creatinine changes were analyzed using independent t-tests, paired t-tests, chi-square tests, or Pearson and Spearman correlation coefficients as appropriate. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences under the ethical approval code IR.TBZMED.FMD.REC.1404.177. All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment. Patients were assured that participation was entirely voluntary and that refusal to participate would not affect their medical care. All collected information remained confidential and was analyzed anonymously to protect participant privacy.

Results

A total of 50 patients undergoing major surgery were included in the study. The mean age of the participants was 56.38 ± 12.47 years, and males constituted the majority of the study population (58.00%). The average body mass index was 26.91 ± 3.84 kg/m². Hypertension and diabetes mellitus were present in 36.00% and 28.00% of patients, respectively. Abdominal surgeries represented the most common procedure type (44.00%), followed by orthopedic, vascular, and thoracic surgeries. The mean duration of surgery was 178.64 ± 41.92 minutes, indicating relatively prolonged operative interventions. Baseline renal function was within the normal clinical range, with a mean preoperative serum creatinine level of 0.98 ± 0.21 mg/dL. Intraoperative fluid administration averaged 2456.70 ± 512.38 mL, while the mean administered dose of furosemide was 21.84 ± 6.73 mg. Overall, the study population consisted predominantly of middle-aged to elderly patients undergoing extensive surgical procedures with moderate perioperative comorbidity burden (table 1).

Table 1. Baseline Characteristics of Participants

Variable	Value
Age (years)	56.38 ± 12.47
Male/Female	29 (58.00%) / 21 (42.00%)
BMI (kg/m²)	26.91 ± 3.84
Hypertension	18 (36.00%)
Diabetes Mellitus	14 (28.00%)
Type of Surgery	Abdominal: 22 (44.00%), Orthopedic: 15 (30.00%), Vascular: 8 (16.00%), Thoracic: 5 (10.00%)
Duration of Surgery (min)	178.64 ± 41.92
Baseline Creatinine (mg/dL)	0.98 ± 0.21
Intraoperative Fluid Volume (mL)	2456.70 ± 512.38
Furosemide Dose (mg)	21.84 ± 6.73

Figure 1 illustrates the temporal distribution of serum creatinine concentrations during the first 48 postoperative hours following intraoperative diuretic administration. Baseline serum creatinine levels demonstrated a relatively narrow distribution, with a median value of 0.96 mg/dL (IQR: 0.84-1.10). A gradual postoperative increase was observed over time, reaching its highest median level at approximately 30 hours after surgery (median: 1.15 mg/dL, IQR: 1.00-1.35). Although mild variability was noted among patients, the overall trend indicated a transient postoperative elevation in renal biochemical markers. Following the peak at 30 hours, serum creatinine values showed a modest decline toward 48 hours, suggesting partial recovery of renal function in most patients. Repeated-measures analysis demonstrated a statistically significant change in serum creatinine levels across the evaluated time points ($P<0.001$). Despite this increase, the majority of values remained within clinically acceptable ranges, and no abrupt dispersion suggestive of severe postoperative renal impairment was identified. The boxplot additionally revealed limited outlier distribution, indicating relatively homogeneous renal responses among the studied population. Collectively, these findings suggest that intraoperative diuretic administration was associated with mild and transient postoperative alterations in serum creatinine without evidence of progressive renal dysfunction.

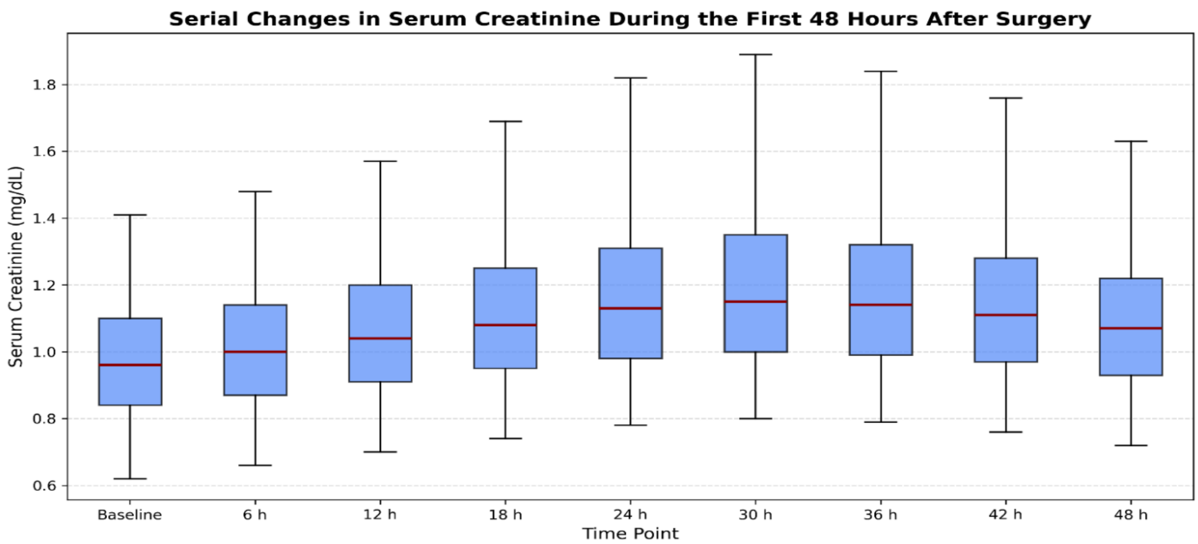

Figure 1. Serial Changes in Serum Creatinine Levels During the First 48 Hours After Intraoperative Diuretic Administration

Figure 2 demonstrates the postoperative trajectory of serum creatinine levels stratified by patient age. Both age groups exhibited a gradual increase in serum creatinine concentrations during the early postoperative period; however, the elevation was more pronounced among patients aged ≥45 years. In the younger cohort (<45 years), serum creatinine values increased modestly from baseline and remained relatively stable throughout the 48-hour observation period, with only minor fluctuations and a gradual return toward baseline after 36 hours. In contrast, patients aged ≥45 years showed a steeper rise in creatinine levels beginning within the first 12 postoperative hours, reaching a higher peak concentration between 24 and 30 hours after surgery. Although a slight decline was observed thereafter, serum creatinine values in the older group remained consistently higher than those of younger patients at nearly all measured time points. Repeated-measures comparative analysis revealed a statistically significant difference in creatinine trends between the two age categories (P = 0.018), indicating a stronger postoperative renal response among older individuals. Furthermore, the dispersion of values appeared wider in the ≥45-year group, suggesting greater interindividual variability in renal adaptation following intraoperative diuretic exposure. These findings imply that increasing age may be associated with reduced renal reserve and a heightened susceptibility to transient postoperative renal function alterations (figure 2).

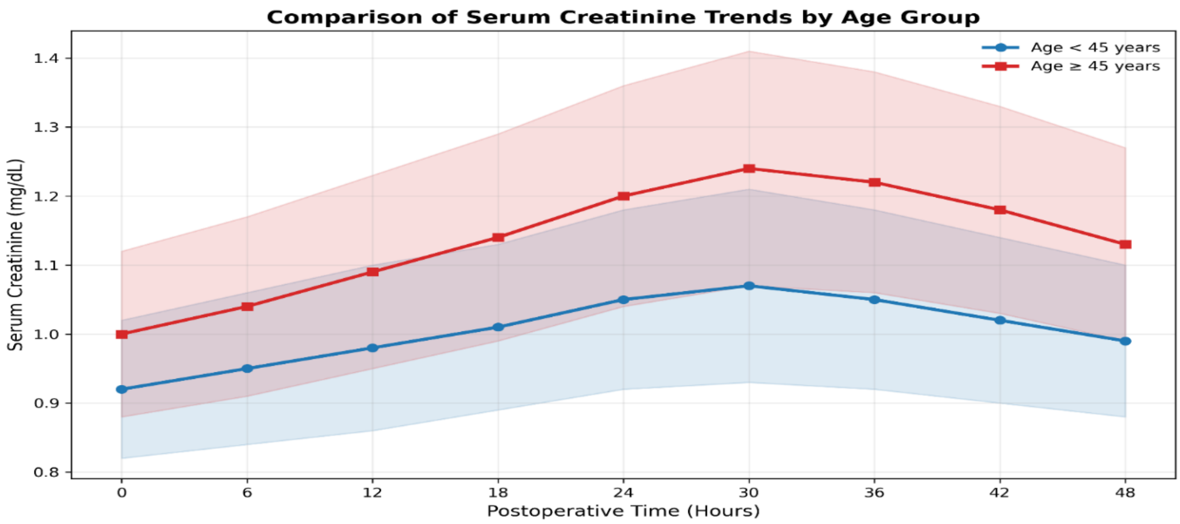

Figure 2. Comparison of Postoperative Serum Creatinine Trends Between Patients Aged <45 Years and ≥45 Years Following Intraoperative Diuretic Administration

Figure 3 illustrates the temporal pattern of postoperative serum creatinine concentrations stratified by sex during the first 48 hours after surgery. Both male and female patients demonstrated a gradual postoperative rise in serum creatinine following anesthesia and intraoperative diuretic exposure, reflecting transient perioperative alterations in renal physiology. In male patients, creatinine levels increased steadily during the early postoperative period, reaching a moderate peak around 24 hours and subsequently stabilizing with a slight decline toward 48 hours. A comparable upward trend was observed in female patients; however, the magnitude of increase was marginally greater, particularly at approximately 30 hours after anesthesia, where the median creatinine level in women slightly exceeded that observed in men. Despite this temporary divergence, the overall trajectories of both groups remained largely parallel, and serum creatinine values gradually approached baseline toward the end of the observation period. Statistical comparison using repeated-measures analysis indicated a modest but statistically significant difference in creatinine dynamics between the two sexes (P=0.041). Additionally, the variability of measurements appeared somewhat wider among female participants at the peak time point, suggesting greater interindividual variability in postoperative renal response. Overall, these findings indicate that although both sexes experience a transient postoperative elevation in serum creatinine, female patients may demonstrate a slightly more pronounced increase during the mid-postoperative period without evidence of sustained renal dysfunction (figure 3).

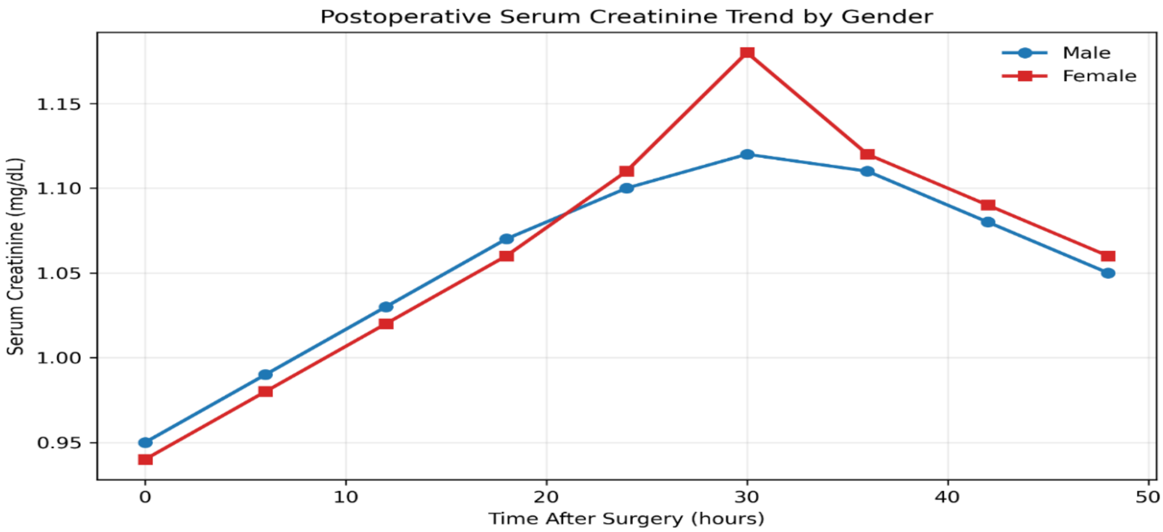

Figure 3. Sex-Based Comparison of Postoperative Serum Creatinine Trajectories During the First 48 Hours After Intraoperative Diuretic Administration

Discussion

In the present study, postoperative serum creatinine exhibited a clear temporal pattern during the first 48 hours after surgery in patients who received intraoperative diuretic therapy. Overall, creatinine levels demonstrated a modest transient increase during the early postoperative period, followed by a gradual tendency toward stabilization. When the data were stratified by age, older patients showed a more pronounced elevation in creatinine compared with younger individuals. Similarly, sex-based analysis revealed broadly comparable postoperative trajectories in men and women, although female patients displayed a slightly greater mid-postoperative increase. Despite these variations across subgroups, the general pattern remained consistent, suggesting that the observed postoperative renal changes were mild, temporary, and largely reversible (15).

The transient elevation in serum creatinine observed in this study likely reflects the complex physiological responses that occur during and after major surgery. Surgical stress, anesthesia, and perioperative hemodynamic fluctuations can collectively influence renal perfusion and glomerular filtration. Even in the absence of overt kidney injury, these factors may lead to temporary alterations in renal function markers. Intraoperative diuretic administration, which is often used to optimize fluid balance and promote urine output, may further modify renal hemodynamics. Diuretics increase tubular flow and sodium delivery while altering intracranial blood distribution, mechanisms that can transiently affect glomerular filtration dynamics. As a result, mild postoperative elevations in serum creatinine may occur without representing structural kidney injury. The gradual decline observed later in the postoperative course in our study supports the interpretation that these changes reflect functional and reversible alterations rather than persistent renal impairment (16).

Several physiological mechanisms may explain the initial rise in serum creatinine during the early postoperative hours. Surgical procedures are frequently accompanied by inflammatory activation, neurohormonal responses, and transient changes in intravascular volume. The activation of the sympathetic nervous system and the renin–angiotensin–aldosterone system during surgical stress can lead to renal vasoconstriction and temporary reductions in renal perfusion. Additionally, perioperative fluid shifts, blood loss, and anesthetic-induced vasodilation may alter effective circulating volume. These hemodynamic adjustments can reduce glomerular filtration rate for a limited period, which is reflected biochemically as a modest increase in serum creatinine. Importantly, when hemodynamic stability is restored and postoperative recovery progresses, renal perfusion generally improves, allowing creatinine levels to return toward baseline, as observed in the later postoperative measurements of our study (17).

The administration of diuretics during surgery may also contribute to the pattern observed in this cohort. Diuretics such as loop diuretics increase urinary sodium and water excretion by inhibiting sodium reabsorption in the renal tubules. While this effect can be beneficial for preventing fluid overload and improving urine output, it may also transiently reduce intravascular volume and modify renal autoregulation. In particular, increased distal sodium delivery can influence tubuloglomerular feedback mechanisms within the nephron. Activation of this feedback pathway may cause transient afferent arteriolar constriction, which can temporarily decrease glomerular filtration rate. This physiological response could partly explain the mild postoperative rise in creatinine observed in our study. However, because renal autoregulatory mechanisms remain largely intact in patients without severe baseline kidney disease, these effects are typically short-lived, consistent with the subsequent stabilization seen in our results (18).

Age-related differences in renal physiology likely account for the more pronounced creatinine elevation observed among older patients in this study. Aging is associated with structural and functional changes in the kidneys, including a gradual decline in nephron number, reduced renal blood flow, and diminished auto regulatory capacity. In addition, older individuals often exhibit reduced renal reserve, meaning their kidneys have a diminished ability to compensate for acute physiological stressors such as surgery, anesthesia, or hemodynamic fluctuations. Consequently, even modest perioperative disturbances in renal perfusion may lead to measurable changes in filtration markers such as serum creatinine. The greater variability observed in older patients may also reflect differences in comorbid conditions, vascular health, and baseline renal resilience. These findings are consistent with the widely recognized clinical observation that advanced age is an important risk factor for postoperative renal dysfunction (19).

The age-related findings of our study align with the broader concept of renal vulnerability in older surgical populations. Physiological aging leads to progressive glomerulosclerosis, interstitial fibrosis, and reduced cortical perfusion, all of which contribute to decreased functional reserve. Moreover, older patients may have impaired adaptive responses to hemodynamic stress, making them more susceptible to transient decreases in glomerular filtration during periods of reduced renal perfusion. Even when baseline serum creatinine appears normal, these underlying structural changes may predispose older individuals to greater fluctuations in renal biomarkers after surgery. The more pronounced creatinine trajectory observed in patients aged 45 years or older in our study therefore likely reflects a combination of diminished renal reserve and increased sensitivity to perioperative physiological stress (20).

Sex-related differences in renal physiology may also contribute to the modest divergence observed between male and female patients in our analysis. Although both sexes displayed a similar overall pattern of postoperative creatinine changes, female patients demonstrated a slightly greater elevation during the mid-postoperative period. Several biological factors may explain this observation. Hormonal influences, particularly the effects of estrogen on renal vascular tone and endothelial function, may modulate renal hemodynamic responses to stress. In addition, differences in body composition, muscle mass, and creatinine generation between men and women can influence circulating creatinine levels and their response to physiological perturbations. Women typically have lower baseline creatinine production due to lower average muscle mass; therefore, relatively small physiological changes in renal filtration may produce proportionally larger fluctuations in measured creatinine concentrations (21).

Another potential explanation for the observed sex-related differences involves variations in microvascular regulation and inflammatory responses. Some studies suggest that women may exhibit different endothelial responses to surgical stress and fluid shifts compared with men. These differences could influence renal microcirculation and glomerular filtration during the postoperative period. Additionally, perioperative pharmacokinetics of certain medications, including anesthetic agents and diuretics, may vary between sexes due to differences in body water distribution and metabolic pathways. Such factors may contribute to subtle variations in renal hemodynamic responses following surgery (22).

Despite the statistically significant subgroup differences observed in our analysis, it is important to emphasize that the overall magnitude of creatinine change remained relatively modest across the study population. Most values remained within clinically acceptable ranges, and the temporal pattern suggested a reversible physiological response rather than persistent renal injury. This distinction is clinically relevant because mild postoperative increases in creatinine do not necessarily indicate structural kidney damage. Instead, they often reflect transient functional adaptations to surgical stress, fluid shifts, and pharmacologic interventions. The stabilization and gradual decline in creatinine observed toward the end of the 48-hour observation period in our study supports the interpretation that renal function largely recovered as patients progressed through the early postoperative phase (23).

From a clinical perspective, these findings highlight the importance of careful postoperative renal monitoring, particularly in populations with reduced physiological reserve. Even transient changes in renal biomarkers can provide valuable information regarding a patient’s hemodynamic status and renal perfusion during the early recovery period. Early identification of abnormal trends may allow clinicians to optimize fluid management, adjust medications, and prevent progression to clinically significant renal injury. In addition, recognizing that older patients may demonstrate greater creatinine fluctuations may help guide risk stratification and postoperative surveillance strategies (24).

The results of this study also contribute to the ongoing discussion regarding the perioperative use of diuretics. While diuretics are frequently employed to maintain urine output and manage fluid balance during surgery, their effects on renal hemodynamics remain complex. Our findings suggest that intraoperative diuretic use may be associated with mild, transient changes in renal function markers without clear evidence of sustained renal impairment. This observation supports the view that, when used appropriately and in carefully selected patients, diuretics can be incorporated into perioperative management without necessarily increasing the risk of significant renal dysfunction. Nevertheless, individual patient characteristics, including age and baseline renal reserve, should be considered when determining the optimal strategy for perioperative fluid and diuretic therapy (25).

Several broader physiological processes may further contribute to the creatinine dynamics observed in the present study. The systemic inflammatory response triggered by surgical trauma can lead to endothelial activation, alterations in microvascular permeability, and redistribution of intravascular volume. These changes may temporarily affect renal perfusion and filtration efficiency. In addition, postoperative hormonal responses, including increased secretion of antidiuretic hormone and activation of stress-related endocrine pathways, can influence renal water handling and intravascular volume status. Together, these mechanisms create a complex physiological environment in which mild fluctuations in renal biomarkers are not unexpected during the early postoperative period (26).

Conclusion

In summary, the present study demonstrates that serum creatinine levels may exhibit a modest and transient increase during the early postoperative period following intraoperative diuretic administration. Older patients appear to experience more pronounced changes, likely reflecting reduced renal reserve and increased susceptibility to perioperative stress. Although sex-related differences were observed, the overall postoperative trajectories remained broadly similar between men and women. Importantly, the pattern of creatinine change suggested reversible physiological adaptation rather than progressive renal dysfunction. These findings underscore the multifactorial nature of postoperative renal physiology and highlight the importance of considering patient characteristics, surgical stress responses, and pharmacologic influences when interpreting postoperative renal biomarkers.

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Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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