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Renal Implications of Pneumoperitoneum in Laparoscopic Surgery: Mechanisms, Risk Factors, and Preventive Strategies

Gianluca Villa[1,2], Marco Fiorentino[3], Eleonora Cappellini[1],Sergio Lassola[4],Silvia De Rosa[5,6]*

[1] Department of Health Sciences, Section of Anesthesiology Intensive Care and Pain Medicine, University of Florence, Florence, Italy.

[2] Department of Anesthesia and Intensive Care, Section of Oncological Anesthesia, and Intensive Care, AOU Careggi, Florence, Italy.

[3] Dipartimento dell'Emergenza e dei Trapianti di Organi, Sez. di Nefrologia, Università degli Studi di Bari, Piazza Giulio Cesare, 70124 Bari, Italy

[4] Anesthesia and Intensive Care, Santa Chiara Regional Hospital, APSS Trento, Italy

[5] Centre for Medical Sciences - CISMed, University of Trento, Via S. Maria Maddalena 1, 38122 Trento, Italy

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Corresponding author*

Silvia De Rosa, MD.

Centre for Medical Sciences - CISMed,

The University of Trento,

Via S. Maria Maddalena 1,

38122 Trento, Italy

silvia.derosa@unitn.it

mobile: +39 3933098583

email: derosa.silvia@ymail.com

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Gianluca Villa[1,2], MD, Marco Fiorentino[3], MD; Eleonora Cappellini[1], MD ; Sergio Lassola, MD, [4]; Silvia De Rosa, MD [4,5]*

[1] Department of Health Sciences, Anesthesiology Intensive Care and Pain Medicine, University of Florence, Florence, Italy

[2] Department of Anesthesia and Intensive Care, Oncological Anesthesia and Intensive Care, AOU Careggi, Florence, Italy

[3] Department of Emergency and Organ Transplants, Nephrology, University of Bari, Piazza Giulio Cesare, 70124 Bari, Italy

[4] Anesthesia and Intensive Care, Santa Chiara Regional Hospital, APSS Trento, Italy

[5] Centre for Medical Sciences - CISMed, University of Trento, Via S. Maria Maddalena 1, 38122 Trento, Italy

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*** Corresponding author**

Silvia De Rosa, M.D.

Centre for Medical Sciences – CISMed, The University of Trento, Via S. Maria Maddalena 1, 38122 Trento, Italy

Tel: +39 3933098583

E-mail: derosa.silvia@ymail.com; silvia.derosa@unitn.it

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Abstract

Pneumoperitoneum, which is established for laparoscopic surgery, has systemic implications on the renal system and may contribute to acute kidney injury or postoperative renal dysfunction. Specifically, when the pressure exceeds 10 mmHg, pneumoperitoneum decreases renal blood flow, leading to renal dysfunction and temporary oliguria. The renal effects of pneumoperitoneum stem from both the direct effects of increased intra-abdominal pressure and indirect factors such as carbon dioxide absorption, neuroendocrine influences, and tissue damage resulting from oxidative stress. While pneumoperitoneum can exacerbate renal dysfunction in patients with pre-existing kidney issues, preserving the function of the remaining kidney is crucial in certain procedures such as laparoscopic live donor nephrectomy. However, available evidence on the effects of pneumoperitoneum on renal function is limited and of moderate quality. This review focuses on exploring the pathophysiological hypotheses underlying kidney damage, mechanisms leading to oliguria and kidney damage, and fluid management strategies for surgical patients during pneumoperitoneum.

Keywords: Acute kidney injury; Biomarkers; Elective surgical procedure; Pneumoperitoneum; Renal plasma flow; Robot-assisted surgery.

Introduction

Pneumoperitoneum, which is established for laparoscopic surgery, has a systemic impact on the renal system and may contribute to acute kidney injury (AKI) or postoperative renal dysfunction. Specifically, when the pressure exceeds 10 mmHg, pneumoperitoneum can result in reduced renal blood flow, renal dysfunction, and transient oliguria. The mechanisms underlying the renal effects of pneumoperitoneum include both the direct effects of elevated intra-abdominal pressure (IAP) and indirect factors such as carbon dioxide (CO_2) absorption, neuroendocrine influences, and tissue damage secondary to oxidative stress. As patients with preexisting renal dysfunction may experience further deterioration due to pneumoperitoneum, preserving the function of the remaining kidney is crucial in procedures such as laparoscopic live-donor nephrectomy.

Despite extensive research, the mechanisms underlying the renal effects of pneumoperitoneum have not been fully elucidated. Available evidence of its effects on renal function is limited and of moderate quality [1]. Although the adverse effects of pneumoperitoneum on serum creatinine (sCr) levels, renal blood flow, and urine output (UO) are apparent, the reliability and clinical relevance of these findings are not well understood, as the long-term effects of pneumoperitoneum have not been assessed [2].

This review aims to delve into the pathophysiological hypothesis of kidney damage, mechanisms leading to oliguria and kidney damage, and fluid management in surgical patients during pneumoperitoneum.

Epidemiology of AKI for laparoscopic procedures

The incidence of AKI varies considerably, ranging from 0.8% to 22.4% after abdominal surgery [3–6] and and from 3.4% to 8.8 % after laparoscopic surgery [7–13]. This variability stems from differences in AKI diagnostic criteria, study designs, and patient characteristics, which collectively

influence the reported incidence rates and complicate comparisons between studies. The adoption of the Kidney Disease Improving Global Outcomes (KDIGO) criteria [14] has notably affected AKI incidence rates. Studies applying the KDIGO criteria often report higher incidences of postoperative AKI due to its greater sensitivity, which is attributed to the minimal change in sCr required for diagnosis. For instance, in two cohorts of similar patients undergoing laparoscopic abdominal surgery, Sim et al. [7] and Abdullah et al. [8] reported postoperative AKI incidences of 8.8% and 2.9%, respectively, using the KDIGO definition and its modified version. The KDIGO criteria has been found to be inconsistent with other diagnostic criteria, such as the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) or the Acute Kidney Injury Network (AKIN) definitions.

Furthermore, the approach to AKI diagnosis, whether prospective or retrospective, significantly influences the reported incidence rates. The prospective inclusion of both UO and sCr criteria, as per the KDIGO definition, has resulted in higher incidence of AKI than retrospective assessments based on creatinine assessments over time [9-11]. For instance, Srisawat et al. [9] reported an AKI incidence of 35% using the KDIGO criteria in a single-center prospective study, whereas retrospective studies adopting the same criteria reported lower incidences ranging from 3.9% [10] to 9.9% [11], despite enrolling comparable patient cohorts. Moreover, studies focusing solely on sCr for AKI definition have reported even lower incidences of postoperative AKI, such as the 3.4% and 1.6% reported by Park et al. [12] and Moon et al., [13] respectively. These retrospective studies included patients with a high risk of AKI, including those undergoing laparoscopic pancreaticoduodenectomy and liver resection.

Direct effect of CO_2

Carbon dioxide (CO_2), which was introduced to establish pneumoperitoneum in the 1920s, is the most

suitable gas for insufflation into the abdominal cavity (pneumoperitoneum of 8–20 mmHg) [15]. Although CO_2 is non-toxic and non-flammable, its high solubility in blood and tissues, easy elimination through the lungs, and cost-effectiveness make it an optimal choice [16,17]. Direct and indirect physiological changes in the kidneys are associated with CO_2 insufflation, which activates significant mechanical and neurohumoral mechanisms. Regional perfusion of the kidneys occurs in four structurally distinct vascular zones: the cortex, outer stripe of the medulla, inner stripe of the outer medulla, and inner medulla [18]. A pressure of 20 mmHg during insufflation causes a 60% decrease in the renal blood flow, leading to a blood shift from the outer cortex to the juxtamedullary zone. This shift adversely affects filtration because the majority of the glomeruli are located in the cortex [18]. Both robotic and laparoscopic procedures result in a 20%–40% decrease in the glomerular filtration rate (GFR) and a 60%–80% decrease in UO when the pressure exceeds 10 mmHg, as demonstrated in experimental and clinical studies. Fig. 1 illustrates the renal effects of CO_2 pneumoperitoneum. In a systematic review and meta-analysis of animal studies, Wever et al. [2] found robust evidence of harmful effects on renal function and perfusion during pneumoperitoneum; however, data on long-term effects are limited. Another systematic review by Demyttenaere et al. [19] found a transitory reduction in renal blood flow in 17 of the 20 examined studies. Factors such as insufflation pressure, patient positioning (worse in the head-up position), and fluid status were identified as significant contributors to decreased renal blood flow. Long-term effects indicated that sCr normalized 24 h after pneumoperitoneum insufflation at 15 mmHg. Bilgic et al. [20] found a correlation between increased levels of KIM-1 and creatinine, which is consistent with histopathological analyses. Additionally, the IAP was found to significantly increase the degree of kidney injury, even when KIM-1 levels were not significantly increased.

Pathophysiological hypothesis of kidney damage

The pathophysiological hypothesis of kidney damage in surgical patients, particularly those undergoing laparoscopic procedures, encompasses various mechanisms, including renal hypoperfusion, cellular hypoxia, inflammation, and direct toxicity.

The primary mechanism of tubular epithelial cell injury during kidney hypoperfusion involves a mismatch between oxygen and nutrient supplies and the metabolic demand of renal cells. A reduction in the mean arterial pressure (MAP) is a significant cause of decreased renal perfusion pressure, similar to the effect occurring during pneumoperitoneum. Specifically, the pressure applied to the renal parenchyma due to pneumoperitoneum results in reduced renal blood flow [21]. Locally regulated activation of myogenic-induced vasodilation may ensure a transient increase in renal blood flow in patients with physiological renal functional reserve (RFR), thereby maintaining a normal GFR range [22]. Elderly patients with multiple comorbidities, often undergoing laparoscopic surgery, have a limited RFR, making them prone to intraoperative insult to the kidney (Fig. 2). Persistent insults to the kidney can lead to tubular apoptosis, necrosis, and electrolyte imbalance and electrolyte and water homeostasis impairments are associated with reduced waste product elimination [21]. Postoperative AKI is thus typically diagnosed. Prolonged reduction in renal perfusion pressure [19] during pneumoperitoneum in patients with impaired myogenic adaptive mechanisms may further contribute to ischemic reperfusion insults (Fig. 2) [23]. This, in turn, triggers a dysregulated inflammatory response [24], including the activation of neutrophils (as well as macrophages and natural killer, T, and B cells) [25] and the release of reactive oxygen species (ROS) or other inflammatory mediators that promote endothelial cell injury and swelling [26-27].

Patients undergoing laparoscopic or robot-assisted surgery may also experience additional nephrotoxic injuries, including exposure to certain intraoperative agents, promotion of renal vasoconstriction, and direct proximal tubule cytotoxicity (Fig. 2) [28].

Inflammation-derived damage and metabolic abnormalities contribute significantly to kidney

damage triggered by proinflammatory molecules [29-30] during pneumoperitoneum-induced AKI [31]. Notably, the kidneys require a large amount of energy from adenosine triphosphate for active water and solute transport, which is facilitated by its extensive mitochondrial presence [32]. Disruption of physiological proton pumping across the inner mitochondrial membrane can lead to subsequent mitochondrial dysfunction, exacerbating cell damage through the production of ROS and the release of pro-apoptotic or proinflammatory factors, such as mitochondrial DNA (Fig. 2) [33].

Oliguria can develop irrespective of the gas type used for insufflation. An ideal insufflation gas should be cost-effective, colorless, non-flammable, non-explosive, easily eliminated, and non-toxic. CO_2 is a remarkably soluble gas, with a solubility coefficient of 0.570, and is absorbed by the peritoneum, delivered directly to the lungs through circulation, and excreted by the lungs during respiratory exchange [34]. However, CO_2 is not a perfect gas and its absorption can lead to hypercapnia and acidosis, necessitating counteractive hyperventilation [15]. CO_2 is also associated with an increase in the MAP, and in cases of high blood concentrations, it can result in cardiac toxicity. Although the direct effects of CO_2 pneumoperitoneum on renal blood flow have been considered, CO_2-related cardiovascular effects may indirectly affect renal function.

Several gases (e.g., helium, argon, nitrogen, nitrous oxide, and room air) have been introduced as alternatives to carbon dioxide for establishing pneumoperitoneum [35]; however, their use remains controversial. Helium and argon are inert gases but are less soluble than CO_2, potentially increasing the risk of venous gas embolism [36]. Nitrous oxide (i.e., laughing gas) is a mild anesthetic with analgesic properties [35]. However, two cases of explosions using electrocautery during laparoscopy have been reported [37]. Recently, Yu et al. [38] reported no severe side effects related to the use of CO_2, nitrous oxide, or room air, although severe side effects do occur rarely. The effects of nitrous oxide and helium pneumoperitoneum are not well understood compared with those of CO_2 pneumoperitoneum. Evidence from one trial with a small sample size suggested that room-air

pneumoperitoneum may decrease hospital costs for patients undergoing laparoscopic abdominal surgery. The safety of nitrous oxide, helium, and room-air pneumoperitoneum is yet to be established.

Conversely, compared to open procedures, robotic and laparoscopic surgeries offer reduced postoperative pain as they do not suppress the immune system as significantly [39]. They also exhibit a lower elevation of proinflammatory cytokines, such as interleukin-6 (IL-6), IL-1, and tumor necrosis factor-alpha (TNF-α), along with decreased C-reactive protein levels.

Although CO_2 pneumoperitoneum induces a lower release of IL-6 compared to room air, TNF-α levels may vary depending on pneumoperitoneum pressure [40]. Higher plasma TNF-α levels were found in rats undergoing a pneumoperitoneum pressure of 10 mmHg than in those undergoing a pressure of 6 mmHg and control groups [41]. Surgery causes an immediate elevation of stress hormone levels and decreases the immune response [42]. A systemic stress response related to pneumoperitoneum is evoked by an increase in IAP from baseline to 20 mmHg [43]. Remarkably, an increase in IAP increases plasma epinephrine and norepinephrine levels and does not depend on the type of gas used [44]. However, in the open surgical approach, adrenocortical hormone (ACTH), cortisol, norepinephrine, epinephrine, insulin, and blood sugar levels increase and remain elevated during the first 24 h postoperatively [45].

Conversely, in pneumoperitoneum, elevated levels of vasopressin or antidiuretic hormone (ADH) are associated with an increase in systemic vascular resistance [46]. However, intra-abdominal pH changes secondary to pneumoperitoneum can stimulate the activation of peritoneal nerve endings, leading to intra-abdominal pH changes and release of vasopressin via the neurogenic vagal pathway [47]. In addition, decreased venous return stimulates right atrial volume receptors, triggering the release of vasopressin/ADH. This results in decreased UO, although fluid replacement increases the risk of fluid overload [48]. The systemic stress response resolves in the immediate postoperative period, after pneumoperitoneum resolution (Fig. 1).

Risk factors for AKI during pneumoperitoneum

Risk factors for AKI during pneumoperitoneum in minimally invasive surgery include CO_2 insufflation and elevated IAP. While the kidneys are susceptible to pressure changes, risk factors such as dehydration, older age, and pre-existing chronic kidney disease (CKD) affect the RFR [49]. However, assessing changes in renal function during laparoscopic procedures is challenging because no specific markers for monitoring rapid changes in GFR in clinical practice are known. Both pre-clinical and clinical studies have shown transient worsening of renal function with oliguria and reduced GFR (5). Preexisting CKD is a crucial risk factor for AKI in pneumoperitoneum. Cisek et al. [50] investigated the changes in renal function during and after pneumoperitoneum in a swine model with reduced renal mass, suggesting that pneumoperitoneum had an impact on the onset of AKI, with no identified long-term consequences. Abboud et al. [51] found a direct correlation between IAP elevation and AKI development, particularly in diabetic rats, which are sensitive to the deleterious effects of pneumoperitoneum. A case report demonstrated progression to end-stage renal disease in a patient with preexisting CKD after laparoscopic surgery. Moreover, renin-angiotensin-aldosterone system inhibitors pose another risk factor as they affect hemodynamic changes during laparoscopic procedures [52]. Lindstrom et al. [53] reported oliguria and a reduced GFR in rats treated with angiotensin-converting enzyme inhibitors, underscoring the need to discontinue such treatment during conditions characterized by elevated IAP to maintain adequate renal perfusion. Recently, the incidence of postoperative AKI between laparoscopic and open surgery in patients with colorectal cancer has been investigated, with no significant differences in such outcomes reported. At the same time, ICU admission, length of hospital stay, and 1-year mortality were better in the laparoscopic group. Additionally, the same report highlighted that a high body mass index (BMI), preoperative hypoalbuminemia, history of diabetes mellitus, and hypertension were significantly

associated with the onset of postoperative AKI. Table 1 summarizes the risk factors and bundles for AKI. The use of validated risk scores for postoperative AKI is suggested to better stratify patients and facilitate the application of interventions targeting specific modifiable risk factors.

Diagnosis of acute kidney injury

Urinary output and serum creatinine

UO and sCr levels are pivotal for defining and grading AKI according to the KDIGO guidelines [14]. In perioperative settings, changes in the UO or sCr levels signal potential kidney insults and aid in the identification of postoperative AKI [54]. However, although these markers are commonly used, they have limitations as indicators of kidney damage, mainly reflecting alterations in kidney function due to stressors. sCr levels are used to determine the estimated glomerular filtration rate (eGFR); however, confounding factors such as race, sex, age, perioperative malnutrition, sarcopenia, or hydration status can exert an influence [55]. Preoperative sCr levels reflect baseline kidney function, but do not provide information about the presence or amount of renal adaptability to insults (i.e., RFR). Patients with limited RFR may exhibit average sCr levels preoperatively but are vulnerable to acute function reduction post-insult, marked by increased sCr levels and reduced UO. sCr elevation manifests more slowly in kidney dysfunction than reduced UO. In cases of limited RFR, pneumoperitoneum can swiftly induce kidney dysfunction, causing intraoperative oliguria and a subsequent increase in sCr levels postoperatively. According to the KDIGO definition, the severity of AKI should consider the patient's muscle mass and hydration status when using sCr levels. UO is a sensitive kidney function parameter and a tubular injury marker [56]. Intraoperative oliguria due to volume depletion and reduced renal blood flow may not indicate kidney damage, but is crucial for identifying AKI, particularly in patients with limited RFR or pneumoperitoneum-related stressors [57]. In patients with a reduced RFR or multiple stressors related to pneumoperitoneum, this

physiologic reaction may lead to a UO reduction below 0.5 ml/kg/h for at least 6 h, effectively identifying AKI according to the KDIGO criteria [14]. In major abdominal laparoscopic or robot-assisted surgeries, preoperative fasting exacerbates the antidiuretic state caused by manipulation of the viscera and peritoneum [58], along with reflex vasoconstriction mediated by neuroendocrine activation, surgical trauma, blood loss, insensitive fluid loss, and mechanical ventilation [58,59]. Monitoring UO using a urinary catheter is feasible during these procedures, with reports of intraoperative oliguria in both animal models and humans undergoing laparoscopic surgery [60-61]. A systematic review by Demyttenaere et al. [19] found that six human studies revealed decreased renal function during pneumoperitoneum, as indicated by a reduced GFR and UO. Intraoperative UO shows promise as a diagnostic tool during the perioperative period. While intraoperative oliguria may not consistently correlate with postoperative AKI, recent research, such as that conducted by Milder et al. [62], has demonstrated a link between intraoperative oliguria and an increased incidence of postoperative AKI in major abdominal surgeries.

Biomarker levels after robot-assisted laparoscopic and laparoscopic surgery

Minimally invasive surgery is gaining popularity because of its association with oliguria, decreased GFR, and altered renal perfusion [63]. Laparoscopic surgery, aided by advances in anesthesia, reduces surgical trauma, complications, and postoperative pain compared to traditional methods. However, robotic systems featuring 3D imaging and articulated instruments offer advantages over conventional laparoscopy [64]. Various surgical scenarios have been investigated for renal biomarkers during laparoscopic or robotic procedures. This review focuses on neutrophil gelatinase-associated lipocalin (NGAL), a 25-kDa protein primarily generated in neutrophil granules and nephrons in response to tubular epithelium damage [65]. NGAL exhibits a sensitivity of 84% and specificity of 94% in detecting AKI with a cut-off ≥ 150 ng/ml of plasma NGAL [66]. Postoperative

serum NGAL levels were higher after retropubic radical prostatectomy (RRP) than after robot-assisted laparoscopic prostatectomy (RALP), potentially because variances in the surgical approach affected renal physiology. The laparoscopic approach often involves pneumoperitoneum, which induces an IAP exceeding 15 mmHg, thereby reducing the cardiac output and renal blood flow [67].

Additionally, restrictive fluid administration may exacerbate renal impairment [68]. Shalabi et al. [69] demonstrated a negative effect of pneumoperitoneum on kidney function in patients undergoing laparoscopic nephrectomy compared with the open procedure. Although urinary NGAL levels were not affected by increased IAP, these data should be confirmed in a prospective randomized study. In their longitudinal prospective study, Orsolya et al. [70] compared the effects of two anesthetic techniques (general vs. combined) on the plasma levels of NGAL after robotic urogenital surgery. Impairment of renal function and AKI occurred in robot-assisted laparoscopy under both general and combined anesthesia. However, the plasma levels of NGAL were significantly higher at 6 and 12 h in the general anesthesia group than in the combined anesthesia group. The authors did not report pneumoperitoneum levels or possible direct renal effects of CO_2. Consequently, understanding the specific effects of the anesthetic or sedative agents used during surgery is essential, especially in relation to their potential renoprotective roles during procedures involving pneumoperitoneum. This connection underscores the importance of detailed monitoring and reporting of all factors influencing renal function in surgical settings.

Recently, Sun et al. [71] found that dexmedetomidine (DEX) plays a protective role in kidney and other organ functions in patients undergoing elective laparoscopic surgery for colorectal cancer. DEX treatment significantly decreased serum NGAL levels measured 1 and 5 d postoperatively, consistent with preclinical studies that documented the protective role of DEX against ischemia/reperfusion injury in animal kidneys [72]. In 2014, the US Food and Drug Administration (FDA) approved the marketing of a test based on the combination of urine concentrations of urinary tissue inhibitor of

metalloproteinases-2 (TIMP-2) and insulin-like growth factor-binding protein-7 (IGFBP-7) to determine the risk of developing moderate-to-severe AKI [73]. The role of these biomarkers in the diagnosis, management, and prognosis of AKI was analyzed in different clinical settings [74–77]. Although a recent meta-analysis demonstrated that urine TIMP-2 and IGFBP7 levels are promising candidates for the early detection of AKI in different settings [78], it has never been tested in patients undergoing laparoscopic or robotic surgery. Further studies on TIMP-2 and IGFBP7 are needed to assess the effect of pneumoperitoneum and the possible direct renal effects of CO_2 in patients undergoing laparoscopic and robotic surgery.

Prevention of AKI

Preventing AKI is paramount in laparoscopic surgery, and KDIGO bundles have been shown to be essential [55]. Despite it being minimally invasive, laparoscopic surgery introduces challenges such as pneumoperitoneum and nephrotoxic agents. The application of the KDIGO bundle is a potent strategy for mitigating the risk of AKI [55,79]. Preoperative assessment of AKI risk factors, including age, renal conditions, diabetes, and hypertension, is crucial for tailoring prevention strategies. The KDIGO bundle targets potential AKI triggers and emphasizes the need for hemodynamic support for adequate renal perfusion. Maintaining optimal fluid balance, a key component of the bundle, is vital in laparoscopic surgery, balancing hydration and avoiding fluid overload amidst pneumoperitoneum [80]. Renal dysfunction may occur in the context of restrictive fluid administration (with consequent hypotension and renal hypoperfusion) or more liberal fluid approaches (with consequent pulmonary and organ congestion) [81]. Choosing an appropriate fluid solution is crucial, as recent evidence suggests an association between certain solutions and increased risk of AKI [82,83].

Additionally, careful consideration of medications and contrast agents is necessary to avoid nephrotoxic agents whenever possible and to closely monitor sCr levels and UO postoperatively to

detect AKI early [84]. The KDIGO bundle recommends avoiding nephrotoxic agents whenever possible, opting for alternatives or adjusting dosages. The use of bicarbonate or N-acetylcysteine is not supported by strong clinical evidence, and preventive measures continue to be based on hydration therapy [85]. Close monitoring of sCr levels and UO in the postoperative phase is indispensable for early detection of AKI. Furthermore, the use of other potential nephrotoxic drugs should be considered to avoid further insults to renal function [79]. The adequate use of antibiotic treatment and the judicious use of pain management techniques to encourage early mobilization further aid in reducing the risk of AKI. The recent introduction of urinary biomarkers such as TIMP-2 and IGFBP7 has enhanced the early detection and prevention of AKI. Additionally, the application of a biomarker-triggered KDIGO bundle has shown promising results in reducing the incidence of AKI in various surgical settings, emphasizing the importance of these biomarkers in guiding AKI prevention strategies [86–89].

Fluid therapy management plays a pivotal role in patients with AKI by balancing the preservation of intravascular volume and systemic hemodynamics while avoiding hemodilution and fluid overload. The timing and modalities of fluid management require careful consideration, especially in patients with impaired cardiac function, because fluid overload is associated with increased mortality and hinders renal recovery after AKI [90,91]. Individualizing fluid administration based on the patient's condition and the phase of critical illness is crucial, considering factors such as diuretic resistance and the multifactorial nature of AKI [92,93]. Oliguric patients may not respond adequately to fluid therapy despite improvements in systemic hemodynamic parameters, suggesting a dissociation between systemic and renal hemodynamics [94]. Although fluid administration is the first-line treatment for hypotensive conditions during surgery, it may promote hemodilution, induce anemia, and reduce oxygen-carrying capacity. Hemodilution after fluid administration decreases blood viscosity, leading to modifications in capillary density and resulting in reduced oxygen transport at

the tissue level [21]. These changes may reduce renal perfusion and consequently lead to renal hypoxia and AKI, even after optimizing the cardiac output [95]. Several studies have shown that fluid administration significantly improves organ perfusion in patients with microcirculatory dysfunction at baseline, but not in those with normal organ perfusion despite normalization of systemic hemodynamic parameters and cardiac output [96]. In this scenario, the use of specific tools to evaluate microcirculation and tissue oxygen delivery, such as functional capillary density, capillary hematocrit, and red blood cell velocity, may enhance our ability to assess which patients will benefit from fluid administration [97]. In this context, fluid administration should be individualized for each patient based on their condition and the phase of critical illness.

Conclusion

In surgical procedures involving pneumoperitoneum, compromised renal function results from complex pathophysiological mechanisms, including induced abdominal hypertension, varying CO_2 levels, and neuroendocrine activation. These in turn diminish intraoperative renal perfusion, which may not adequately correlate with the loss of renal autoregulation. Future research should focus on elucidating the specific pathophysiological mechanisms and exploring the utility of biomarkers. Such efforts are essential for developing a comprehensive care bundle tailored to preventing renal function decline, particularly in individuals with a diminished RFR.

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Table 1. Risk factors and bundles for acute kidney injury

	Risk factor	Bundle	Preventive anesthesiologic strategies
Preoperative risk factors for AKI	**Dehydration**	Inadequate fluid intake or excessive fluid loss, leading to reduced renal perfusion and function.	Fluid management
	Older age	Advanced age correlates with RFR, heightening susceptibility to AKI.	Geriatric assessment
	Hypertension	Chronic hypertension induces arteriolar sclerosis and renal vascular changes, reducing renal perfusion and function, increasing susceptibility to AKI.	Adequate blood pressure management
	History of diabetes mellitus	Diabetes induces microvascular changes in kidneys, escalating susceptibility to AKI.	Adequate diabetes management
	Pre-existing chronic kidney disease	Patients with pre-existing CKD exhibit impaired renal function, characterized by reduced GFR and nephron loss, increasing vulnerability to AKI.	Chronic kidney disease assessment
	Use of renin-angiotensin	Medications such as ACE inhibitors and ARBs alter renal hemodynamics, causing renal vasodilation and potentially reducing	Medication review

	- aldosterone system inhibitors	renal perfusion, increasing the risk of AKI.	
	High body mass index	Elevated BMI is associated with increased intra-abdominal pressure, impairing renal perfusion and function.	Obesity assessment
	Preoperative hypoalbuminemia	Low serum albumin levels signify compromised nutritional status and may correlate with renal dysfunction, predisposing to AKI.	Nutritional assessment
Intraoperative/post operative risk factors for AKI	**Elevated intra-abdominal pressure**	Increased IAP during laparoscopic procedures compromises renal perfusion, predisposing to AKI.	Maintain adequate intra-abdominal pressure
	Hypovolemia	Reduced blood volume can lead to decreased renal perfusion and function.	Fluid replacement
	Prolonged time of the laparoscopic procedure	Longer duration of surgery may increase the risk of AKI due to prolonged exposure to anesthesia and altered hemodynamics.	Mainysin adequate surgical duration
	Decreased	Reduced heart function leads to decreased	Hemodynami

	cardiac output	blood flow to the kidneys, potentially causing AKI.	c monitoring
	Exposure to nephrotoxic drugs	Drugs with nephrotoxic effects may directly damage renal tissues, increasing the risk of AKI.	Avoidance and minimization of the duration of exposure

RFR: renal functional reserve, AKI: acute kidney injury, CKD: chronic kidney disease, GFR: glomerular filtration rate, ACE: angiotensin-converting enzyme, ARB: angiotensin II receptor blockers, BMI: body mass index, IAP: intra-abdominal pressure.

Figure legends

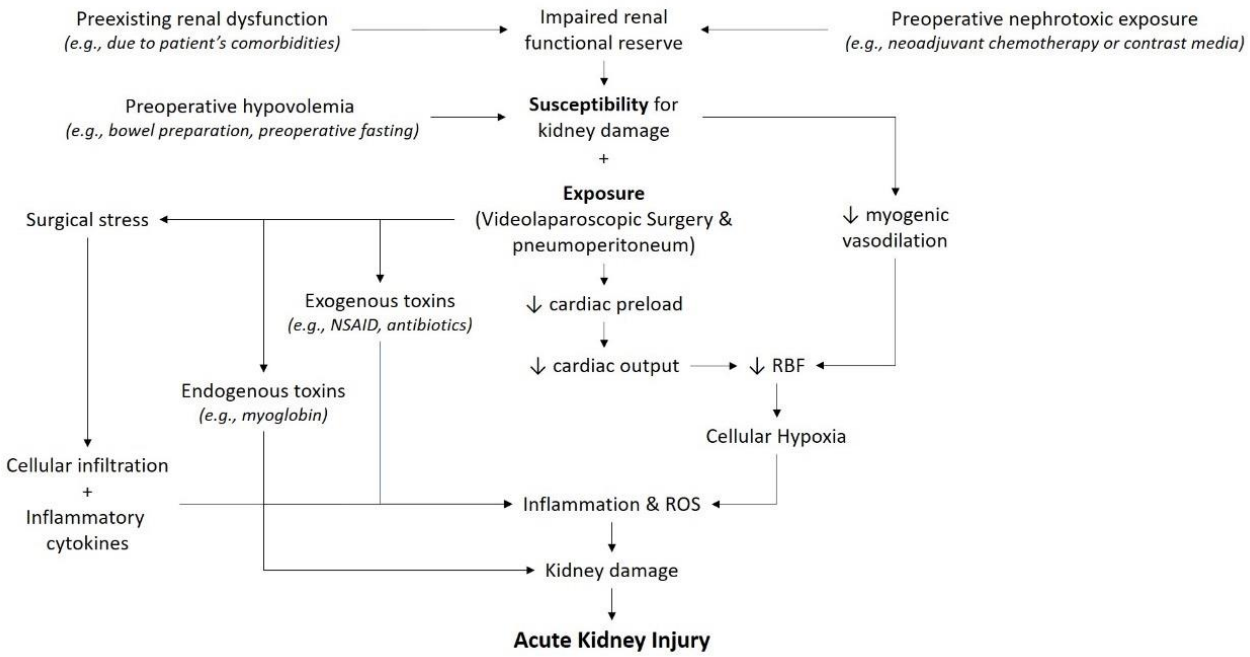

Fig. 1. Neuroendocrine and renal effects of pneumoperitoneum

These figures outline neuroendocrine responses (e.g., sympathetic activation and hormonal fluctuations) and renal changes (e.g., reduced blood flow and altered filtration rates) during pneumoperitoneum. These effects underscore the physiological effects of laparoscopic surgery on the neuroendocrine and renal systems and reflect potential clinical implications.

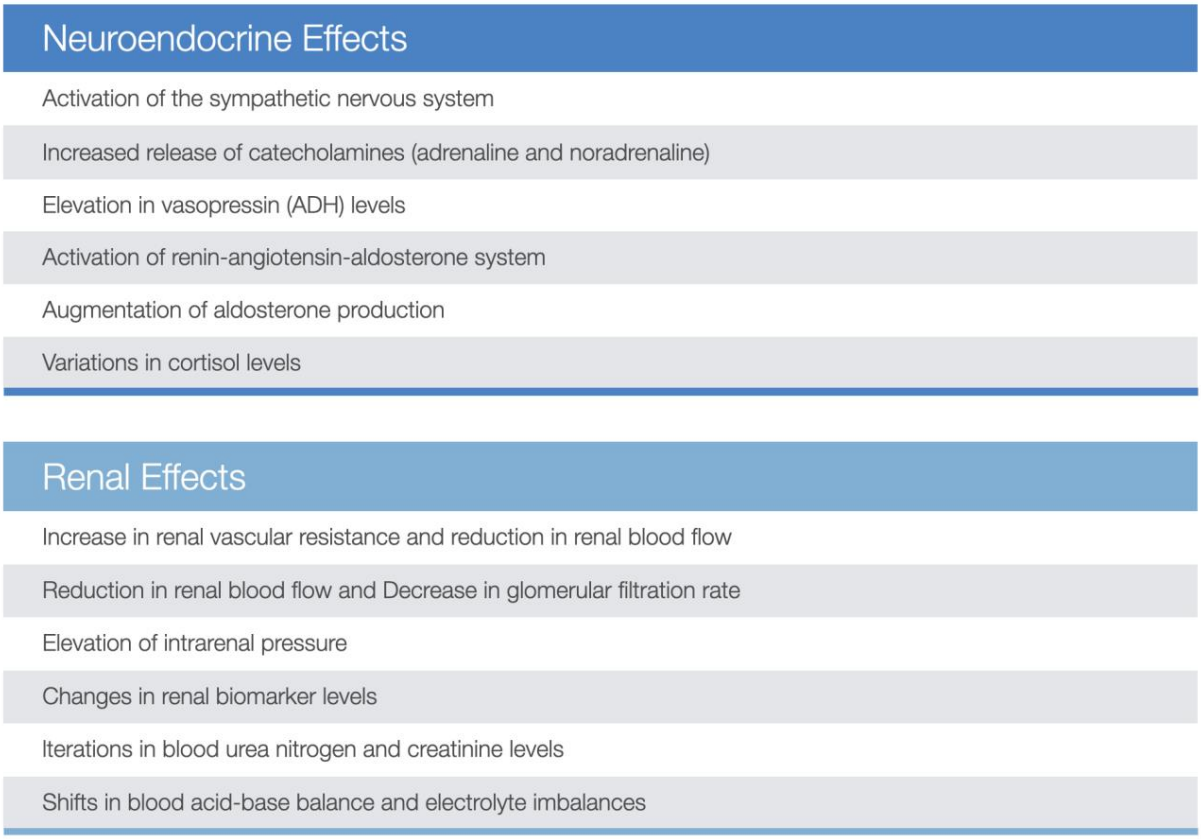

Fig. 2. Pathophysiology of kidney damage during laparoscopic surgery

RFR: renal functional reserve, NSAIDs: non-steroidal anti-inflammatory drugs, RBF: renal blood flow