Acute kidney injury as a consequence of the use of anesthesia during surgery: causes and approaches to reducing the risk of

A. P. Merkulova[1*], *T.M.* Sadigov[1], *T.T.* Kuliev[1], *G.R.* Kasumov[1], *I.A.* Tarasov[1], and *T.I.* Simonyan[1]

[1]Pirogov Russian National Research Medical University, 117997 Moscow, Russia

Abstract. The article reveals the causes and approaches to reducing the risk of acute kidney injury that occurs as a result of surgical intervention. The authors note that this problem is extremely urgent, since the effect of anesthesia on acute kidney injury may depend on various factors, including the type of anesthesia, the duration of surgery, the patient's condition and the anesthetics used. Some anesthetics and agents used during general anesthesia can cause hypotension (lowering of blood pressure). This can lead to a decrease in blood flow in the kidneys and deterioration of their function. It is important to keep blood pressure at an optimal level during surgery to minimize the risk of kidney damage. Patients with pre-existing kidney problems may be more susceptible to the negative effects of anesthesia. The anesthesiologist should assess the condition of the kidneys before surgery and choose the anesthetics and methods that are least likely to cause additional damage. The effect of anesthesia on acute kidney injury can be complex and depends on many factors. It is important that the anesthesiologist and the surgeon work together to minimize risks to the kidneys and ensure safe operation in patients with acute kidney injury.

1 Introduction

Acute kidney injury (AKI) is a fairly common complication in patients who have undergone surgery. Its consequence is complications that manifest themselves with high frequency, which quite often act as predictors of patient death, and the risk of chronic kidney disease also increases, which is fraught with long-term dialysis and increased health care costs[1]. Most often, such patients have an increase in serum creatinine levels, as well as a decrease in diuresis. According to experts, the frequency of perioperative AKI is affected by the type of surgical intervention, as well as the concomitant diseases diagnosed in the patient. The degree of risk associated with the occurrence of AKI depends on both the type of surgery and the group of patients. At the same time, the highest risk occurs in cardio- and vascular surgery [2].

Experts point out that most often, as a result of extensive cardiovascular surgery, the frequency of AKI can be up to 49%, but this indicator is also influenced by the type of

* Corresponding author: filosoff123@list.ru

surgical intervention - the highest frequency of AKI is observed during operations on the abdominal aorta, it is lower in cases of operations on peripheral vessels [3]. Other researchers point out that with planned endovascular plasty of an aneurysm of the infrarenal abdominal aorta, there is an increased risk of perioperative AKI, which can range from 5% to 18%, if surgical intervention is performed for juktarenal aneurysms, as well as in the case of restoration of a ruptured abdominal aortic aneurysm, cases of AKI can range from 32% to 75%, respectively [4]. Statistics show that the consequence of extensive abdominal surgery can also be AKI, which occurs in 13% of cases [5].

The occurrence of AKI in patients during the perioperative period is influenced by many different factors, including age, body mass index, a decrease in the estimated glomerular filtration rate and anemia [6]. In addition, in patients who had the first signs of AKI upon admission to the hospital, the risk of developing this pathology is higher than in those who previously had no such signs. There is also a possibility of late AKI, which is associated with postoperative aspects, including sepsis, artificial ventilation, positive fluid balance, blood transfusion and exposure to diuretics, as well as nonsteroidal anti-inflammatory drugs [7].

The aim of the study is to investigate the causes and approaches to reducing the risk of acute kidney injury that occurs as a result of the use of anesthesia during surgery.

2 Materials and methods

In the process of writing the study, articles and monographs were studied within the framework of the topic under study, in addition, data from cohort studies of specialists in the field under study were analyzed. When writing the work, comparative and analytical research methods were used.

3 Results

AKI should be understood as "the rapid development of organ dysfunction as a result of direct exposure to renal or extrarenal damaging factors" [8]. It is necessary to trace the mechanism of occurrence of this pathology.

In a healthy state, the kidneys receive 20% of cardiac output. The blood flow inside the kidneys is selectively distributed, with most of the blood in the cortex being directed to glomerular filtration [9]. The main functions of complex peritubular microcirculation consist in the delivery of oxygen and nutrients, the return of reabsorbed solutes and water to the large circulation circle and participation in countercurrent mechanisms that are necessary for water conservation [10]. The pathogenesis of perioperative AKI includes several different processes Table 1.

Table 1. Processes included in the structure of the pathogenesis of perioperative AKI

Mechanism	Characteristic	Variants of pathologies
Hypoperfusion	Reduction of glomerular perfusion	Heart surgery Aortic surgery Hypotension/hypovolemia
Microcirculatory dysfunction	Redistribution of intrarenal blood flow/intrarenal bypass, causing heterogeneous perfusion with areas of microishemia and hyperperfusion.	Sepsis Contrast agents
Endothelial dysfunction	Increased capillary permeability leads to interstitial edema. Release of pro-inflammatory cytokines by endothelial cells Neutrophil migration	Sepsis

Formation of microvascular thrombi	Activation of procoagulant pathways caused by inflammation Activation of the add-on	Sepsis Inflammatory conditions Liver disease
Inflammation	Recruitment of inflammatory cells, including neutrophils	Inflammatory conditions Sepsis
Damage to tubular cells	Ischemic tubular injury due to microcirculatory dysfunction. Direct effect on the tubules of inflammatory substances / toxins / free iron.	Nephrotoxic drugs Contrast agents Hemolysis Sepsis
Obstacle	Internal blockade of the urinary tract. External obstruction Formation of intracanal tides/crystals	Malignant neoplasms of the pelvic organs Urological malignant neoplasms Kidney stone disease
Renal venous congestion	Increased back pressure in the kidneys, which leads to a decrease in the glomerular filtration rate.	Chronic heart failure
Intra-abdominal hypertension	Reduction of venous outflow, which leads to stagnation of the renal veins.	Sharp belly Severe fluid overload

Experts note that there is a connection between intraoperative hypotension and the development of postoperative AKI 19-24 [11]. Thus, a retrospective analysis of the results of 30,000 operations, intraoperative hypotension was an independent risk factor for AKI. An increase in risk was noted with an increase in the duration of hypotension, and its significance was high even for episodes lasting only 1-5 minutes [12].

Some types of surgical operations are especially associated with the risk of hypoperfusion of the kidneys, for example, vascular procedures in which the aorta is squeezed over the renal arteries. Also, in the conditions of cardiac surgery and artificial blood circulation, taking into account hemodynamic instability, non-pulsating flow during artificial blood circulation and hemodilution, kidney ischemia may occur and there may be a risk of AKI Pathogenesis of perioperative AKI, accompanied by systemic inflammation and release of free hemoglobin [13].

The integrity of the intrarenal microcirculation is a key component of kidney health. If there is a dysfunction of microvascular circulation, which occurs with sepsis, then its consequence is heterogeneous blood flow [14]. As a result of this blood flow, focal areas of hypoperfusion appear inside the kidney. Ischemic zones can coexist with intact areas with preserved tissue oxygenation, and the preservation of such changes can occur even with adequate systemic hemodynamics.

Also, in patients with sepsis, endothelial dysfunction may become more active, which plays a central role in microcirculatory dysfunction and can lead to increased capillary permeability, transmigration of leukocytes and the release of pro-inflammatory cytokines. Also, during artificial circulation, blood comes into contact with non-endothelial surfaces, which can also lead to activation of the blood clotting cascade and the formation of microthrombs. The pathogenesis of AKI is directly related to systemic inflammation, so elevated levels of interleukin-6 were associated with the development of AKI in conditions of severe sepsis, artificial circulation, etc. [15].

Periods of microcirculation disorders negatively affect the tubule cells. Their main function involves the filtration of exogenous substances – drugs and iodine-containing contrast agents, as well as cytokines. Thus, in the course of cardiac surgery using artificial circulation, free hemoglobin can be released and cause damage to the tubules through direct toxicity, intracanal crystals can also form. The toxicity of contrast agents for tubular cells has been confirmed by specialists. Damage to the tubules itself may be associated with a significant decrease in the glomerular filtration rate mediated by tubulo-glomerular feedback [16].

In addition, renal venous congestion may occur as a result of surgical operations. The kidney is an encapsulated organ, and increased central venous pressure and, as a consequence, increased pressure along the vascular tree of the kidneys can anticipate kidney stagnation with compression of the tubules, while the net pressure gradient in the glomeruli will decrease, which will reduce the glomerular filtration rate. Experts noted that this phenomenon was noted in patients with congestive heart failure and cardiovascular diseases, it was also noted that compression of the renal veins leads to significant damage to the kidneys.

Obstruction at any level from the tubules to the urethra can cause AKI. In the perioperative period, myoglobinuria or hemoglobinuria as a result of extensive tissue damage, hemolysis or extracorporeal contours can also lead to the formation of intra-tubular casts and tubular obstruction.

In addition, we must not forget that a significant part of the patients undergoing surgical operations are at an advanced age and have a number of concomitant diseases. Comorbid conditions, acute diseases and age-related decrease in physiological reserve led to an increased risk of perioperative AKI in surgical patients. Additional risk factors include dependence on a ventilator, chronic obstructive pulmonary disease, smoking, blood clotting disorders, cancer, obesity and long-term use of steroid drugs [17].

Accordingly, AKI can be the result of a number of surgical interventions, during which the use of anesthesia is inevitable, and the mechanism of its occurrence is quite diverse, and specialists need to take into account all its components in order to prevent the occurrence of this pathology [19].

4 Discussion

Ischemia/reperfusion (IR) of the kidneys is the main cause of preoperative acute kidney injury (AKI), which often complicates major vascular, cardiac, transplant and liver operations. It has been shown that AKI occurs after some major operations, which raises questions about the role of surgical procedures, including the introduction of anesthesia and its effect on kidney function [20].

There are mixed data on the effect of anesthetics on kidney function. Some studies have shown that the use of certain types of anesthesia during surgery, as well as the surgical stress itself, can affect kidney function. Indirect effects are more pronounced than direct ones. However, other experts have indicated that some anesthetics cause anti-inflammatory, anti-necrotic and anti-apoptotic effects that protect against AKI [21].

Volatile anesthetics are administered to many patients undergoing general anesthesia and are an integral part of the perioperative period. Methoxyflurane was the first nonflammable halogenated volatile anesthetic synthesized. Methoxyflurane caused dose-dependent disorders after surgery, including vasopressin-resistant polyuria, serum hyperosmolality, hypernatremia, increased concentrations of serum urea nitrogen and inorganic fluoride, as well as decreased concentrations of potassium, sodium, osmolality and urea nitrogen in urine, with clinical toxicity at certain doses. more than 90 mmol/l. Consequently, the nephrotoxicity caused by methoxyflurane was extended to all halogenated anesthetics. However, most third-generation inhalation anesthetics are effective and safe [22].

Fluorinated anesthetics, especially sevoflurane and enflurane, did not cause deterioration of postoperative renal function in patients with pre-existing renal dysfunction; none of the patients needed dialysis and had no persistent deterioration of renal insufficiency [23]. Moreover, studies on both animals and humans have shown that neither the duration of systemic exposure to fluoride nor the peak values of fluoride correspond to anesthetic nephrotoxicity. In fact, the metabolism of enflurane into inorganic fluoride during and after surgery did not cause a clinically significant level of kidney disease or dysfunction [24].

It is necessary to assess the risk of AKI due to the use of anesthesia. This risk occurs due to the interaction between the patient's preoperative health and susceptibility and the stress associated with the operation. The assessment of this risk is carried out individually, taking into account the characteristics of each patient [25].

In the absence of therapy for perioperative AKI, the most effective strategy for protecting kidney function is to prevent nephrotoxic effects and optimize hemodynamics. Experts believe that intraoperative hypotension should be avoided, and the duration of hypotensive episodes should be as short as possible [26].

In the perioperative period, it is also necessary to optimize the infusion regimen and targeted hemodynamic therapy to prevent AKI [27]. Experts note that when organizing targeted hemodynamic therapy, the intraoperative goal should be to maintain the maximum shock volume at an average blood pressure of > 70 mmHg and a cardiac index of > 2.5 l.min.m-2.. This approach makes it possible to reduce various complications in patients, including AKI, and to reduce the length of hospital stay [28].

In order to avoid AKI during surgery, it is necessary to exclude hypotension. It is necessary that the SAD should be 65 mmHg or higher, however, if patients have a history of chronic hypertension, a higher target indicator is needed [29].

A thorough understanding of the interaction between the type of anesthesia, anesthetics, and kidney function remains fundamental to providing safe perioperative care and optimizing postoperative outcomes. The researchers note that inhaled anesthetics have renal protective properties. It is also believed that fluoride-containing anesthetics may be safe for patients with kidney problems [30]. The sedative effect of propofol or dexmedetomidine may have a renoprotective effect. During the animal experiment, propofol was able to reduce markers of oxidative stress in the kidneys. When dexmedetomidine was used, diuresis occurred due to a decrease in vasopressin secretion and increased renal blood flow and glomerular filtration.

A small randomized controlled trial involving 112 patients who underwent heart valve surgery showed a lower number of AKI in the propofol-treated group compared to sevoflurane. When comparing propofol-based anesthesia with sevoflurane in one of the studies, patients who underwent kidney transplantation from a living donor in the sevoflurane group had higher AKI biomarkers in the urine on the second day after surgery, indicating kidney stress, but there were no differences in the results of transplantation [31].

Confirmation of potential renoprotective effects was carried out in a recent randomized controlled placebo trial involving 200 patients who underwent heart surgery. It was noted that in patients treated with dexmedetomidine, compared with placebo (14% vs. 33%; $p = 0.002$), the frequency of AKI and the totality of the main endpoints of morbidity during the first 48 hours after surgery were significantly lower [32].

Through epidural analgesia, it is possible to ensure effective control of postoperative pain. This occurs by modulating the spinal sympathetic outflow, which allows the vessels to expand and increase visceral perfusion. Thus, the researchers note that among patients who underwent planned restoration of an abdominal aortic aneurysm and received combined epidural and general anesthesia, the risk of mortality was lower, as well as the need for dialysis (OR 0.44; 95% CI 0.23–0.88; $p = 0.02$).) [33].

5 Conclusions

Perioperative AKI acts as a frequent complication after surgery, and it is often underestimated, despite its significant burden on health resources. However, experts note that AKI does not always act as a consequence of the use of anesthesia.

Some anesthetics may have a more beneficial effect on the kidneys than others. For example, intraoperative use of vasoprssors and anesthetics that maintain cardiovascular stability may be a positive factor.

The duration of surgery can also affect the risk of kidney damage. The longer the operation, the more time the kidneys can spend in conditions of insufficient perfusion, which can worsen their function. During surgery, it is important to monitor kidney function using various parameters, such as creatinine concentration in the blood and diuresis (volume of urine excreted). This helps to identify any changes in a timely manner and take the necessary measures.

There is a need to raise awareness of this complication among physicians involved in perioperative care of surgical patients, including anesthesiologists, whose intraoperative strategies have a significant impact on kidney function. For complete and comprehensive kidney protection, a personalized and interdisciplinary approach is needed, which should be implemented during the perioperative period. In this regard, it is necessary to continue comprehensive research on reducing the negative effect of anesthesia on the patient's body and, as a consequence, preventing the occurrence of AKI.

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