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Strategies for prevention of acute kidney injury in cardiac surgery: an integrative review

Estratégias de prevenção da lesão renal aguda em cirurgia cardíaca: revisão integrativa

ABSTRACT

Acute kidney injury is a common complication after cardiac surgery and is associated with increased morbidity and mortality and increased length of stay in the intensive care unit. Considering the high prevalence of acute kidney injury and its association with worsened prognosis, the development of strategies for renal protection in hospitals is essential to reduce the associated high morbidity and mortality, especially for patients at high risk of developing acute kidney injury, such as patients who undergo cardiac surgery. This integrative review sought to assess the evidence available in the literature regarding the

most effective interventions for the prevention of acute kidney injury in patients undergoing cardiac surgery. To select the articles, we used the CINAHL and MedLine databases. The sample of this review consisted of 16 articles. After analyzing the articles included in the review, the results of the studies showed that only hydration with saline has noteworthy results in the prevention of acute kidney injury. The other strategies are controversial and require further research to prove their effectiveness.

Keywords: Acute kidney injury/ prevention & control; Thoracic surgery/ complications

INTRODUCTION

Acute kidney injury (AKI) is a fairly common serious complication after cardiac surgery that is associated with increased morbidity and mortality and with the need for an increased length of stay in the intensive care unit (ICU).^(1,2)

The severity of AKI is variable; however, when renal replacement therapy is needed, the mortality rate exceeds 60%.⁽³⁾ Several authors have shown that increases >0.3mg/dL in serum creatinine (Cr) values compared to baseline are an independent predictor of mortality.⁽⁴⁾

AKI is a complex phenomenon in which hemodynamic, cellular, molecular and metabolic factors interact. Hemodynamic changes, including vasoconstriction and decreased renal perfusion, play a central role in the pathogenesis of AKI. Despite considerable progress on understanding the pathophysiology, definition and treatment of AKI using different types of renal replacement therapy, the morbidity and mortality of this syndrome remain significantly high.⁽⁵⁾

The incidence of renal dysfunction associated with cardiovascular surgery varies greatly among studies. According to Hobson et al.,⁽⁶⁾ the condition may

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affect 37% of patients who undergo coronary surgery, 49% in the case of valve surgery, and 55% in the case of aortic surgery. The condition is also more common when cardiopulmonary bypass (CPB) is used. The prevalence of AKI after cardiac surgery with CPB reaches 35% in some series, and among patients who develop AKI after surgery, approximately 1.5% require dialysis.⁽⁷⁾

The prevention of AKI essentially depends on the maintenance of adequate renal perfusion. It is known that hydration reduces the patient's risk of developing AKI.⁽⁸⁾ However, hypotension is an important issue and requires aggressive correction to maintain renal perfusion and thus preserve its function.⁽⁹⁾

Despite the use of routine measures that aim to control certain risk factors in the postoperative period of cardiac surgery, the incidence of renal dysfunction remains high, especially in high risk-patients. For this reason, there is a need to seek more effective alternatives to prevent this complication.

Due to the high rates of morbidity and mortality found in AKI, preventive and mitigation measures must be widely studied. The careful evaluation of patients at high risk for developing this syndrome, such as patients who undergo invasive procedures, major surgery and the use of nephrotoxic drugs, allows early identification with the possibility of intervention to achieve better outcomes.

In light of these facts and considering the high prevalence and evident association of acute kidney injury with worsened prognosis, the development of strategies for renal protection becomes essential, especially for patients at a high risk of developing AKI, such as patients who undergo cardiac surgery, to minimize the incidence of AKI in hospitals and thereby reduce the associated high morbidity and mortality. Thus, we aimed to evaluate the evidence available in the literature on the most effective interventions for the prevention of AKI in adult patients who undergo cardiac surgery.

METHODS

To guide the integrative review,⁽¹⁰⁻¹²⁾ the following question was formulated: what are the most effective strategies available in the literature for the prevention of AKI in patients who undergo cardiac surgery? Scientific articles were searched in the Medical Literature Analysis and Retrieval System Online (MedLine) and in the Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases.

The inclusion criteria defined for the selection of the articles were as follows: articles published in Portuguese and English, with abstracts available in these databases, with randomized controlled trials (RCT) that addressed strategies for prevention of AKI in open chest cardiovascular surgeries. Articles that addressed preventive measures for AKI in contrast-induced nephropathy (CIN), studies performed in the pediatric population, and retrospective studies were excluded.

To search for articles, the following keywords and their combinations in Portuguese and English were used: "cirurgia cardíaca", "prevenção", and "lesão renal aguda"; "thoracic surgery", "preventive", and "acute kidney injury". The search was performed using online access, and after the inclusion criteria were applied, the final sample for the integrative review consisted of 16 articles. All articles found that met the inclusion criteria between 1999 and 2013 were included.

To collect data from the articles included in the study, we adapted an instrument⁽¹³⁾ developed for the evaluation of integrative reviews, which was previously validated by other authors. The instrument includes the following items: identification of the original article and authors; methodological characteristics of the study; evaluation of methodological rigor, interventions measured and results found; and conclusions and recommendations for practice.

The articles found were organized according to the selection order, and the data were analyzed according to their content using descriptive statistics.

RESULTS

After searching the selected databases, 386 articles were found in MedLine; however, using the selected descriptors, no articles were found in the CINAHL database.

Of the total articles found, 301 were excluded after reading the abstract because their content was not relevant to this study. Three researchers reviewed 85 abstracts that met the inclusion criteria by reading the full text. Based on reading the abstracts, 69 articles were excluded because (1) the procedure evaluated was not cardiac surgery (n=48); (2) the full text of the article was not available (n=11); (3) the study participants were children (n=5); (4) the article was not a randomized clinical trial (n=3); or (5) the text was in another language (n=2). The 16 articles remaining were included in the integrative review (Figure 1).

All studies were published between 1999 and 2013. Three studies were conducted in England,⁽¹⁴⁻¹⁶⁾ two in

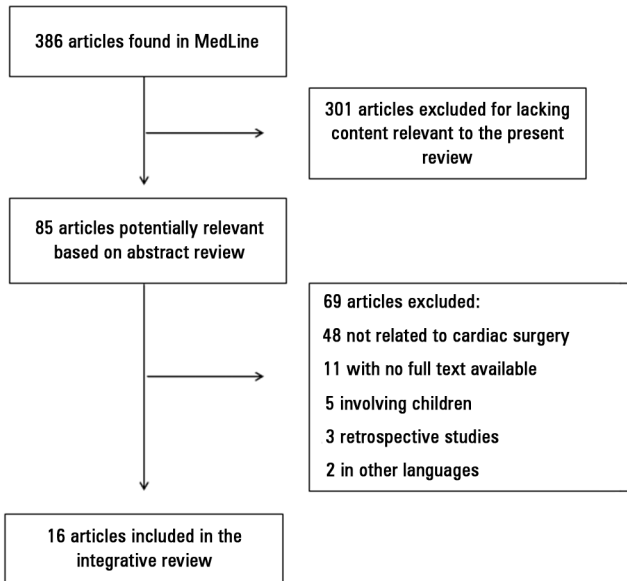


Figure 1 - Flowchart of selection of studies included in the integrative review.

Australia,^(17,18) two in South Korea,^(19,20) two in Iran,^(21,22) two in Italy,^(23,24) one in Austria,⁽²⁵⁾ one in the United States,⁽²⁶⁾ one in Finland,⁽²⁷⁾ one in Greece,⁽²⁸⁾ and one in Turkey.⁽²⁹⁾

In 10 of the 16 studies, the patients included had a heightened risk for developing AKI.^(14,15,17,19-21,24,26-28) Several authors have shown that the presence of preoperative renal dysfunction is an important risk factor for the development of AKI. The incidence of this injury requiring renal replacement therapy in surgical patients may reach 20% in patients with preoperative Cr values between 2 and 4mg/dL and approximately 30% in patients with Cr >4mg/dL.^(1,30,31) According to Palomba et al.,⁽³²⁾ patients with Cr >1.2mg/dL have twice the risk of developing AKI after cardiac surgery. Moreover, it has been shown that an increase in Cr >0.5mg/dL in the postoperative period of cardiac surgery contributes to increased mortality 30 days after surgery.⁽⁴⁾

In the majority of the studies (n=9), the only surgical procedure evaluated was coronary artery bypass grafting.^(14,16,19-24,29) For the other studies (n=7), the surgical procedures evaluated were combined surgeries, in which replacement or repair of the valve was performed in association with coronary artery bypass grafting.^(15,17,18,25-28)

The 16 RCTs included a total of 1,904 patients, of whom 1,357 (71.3%) were male with a mean age of 65±8 years, and most of them (62.5%) had previous renal dysfunction.

Among the studies reviewed, there were various strategies to prevent AKI, including the use of drugs that act in the inhibition of the expression of reactive oxygen species (ROS), such as antioxidants; strategies that increase renal blood flow, thereby increasing the glomerular filtration rate (GFR); strategies that promote hydration through the use of bicarbonate or sodium chloride; and strategies that use pulsatile CPB. We divided the presentation of the selected studies into categories for easy understanding of the results.

Antioxidants as nephroprotective substances

Oxidative stress is defined as an imbalance between excessive generation of oxidant compounds and insufficient antioxidant defense mechanisms. This imbalance results in the accumulation of ROS, which act as mediators between oxidative stress and tissue injury. ROS are also important in the pathogenesis of AKI. Therefore, it is of interest to assess whether the use of strategies that reduce ROS levels is associated with improved renal function under these conditions.^(33,34)

In table 1, we present a synthesis of the studies that used drugs with antioxidant effects aimed at decreasing the expression of ROS, thereby reducing the incidence of AKI. The studies presented below show that none of the strategies used was effective in reducing the incidence of AKI.

Nouri-Majalan et al.⁽²¹⁾ used the association between allopurinol and vitamin E. Allopurinol inhibits xanthine oxidase (XO), which is an enzyme associated with ischemia-reperfusion injury,⁽³⁵⁾ while the use of vitamin E prevents the sudden reductions in renal function induced by ischemia, contrast or drugs.⁽³⁶⁾ However, there was no renoprotective effect from the use of this strategy. Pentoxifylline, like allopurinol, is a drug able to inhibit the expression of XO and of certain pro-inflammatory cytokines.⁽³⁷⁾ A study⁽²²⁾ included in this review that used pentoxifylline to reduce the incidence of AKI failed to demonstrate the beneficial effect of this drug on renal function.

In two other studies,^(19,20) the authors used erythropoietin (EPO), a hormone that regulates the production of blood cells and that is mainly produced by the fibroblasts of the renal cortex. EPO production is increased when ischemia is present, facilitating oxygen supply and erythropoiesis and reducing oxidative stress.^(38,39) In both scenarios, the authors showed that there was a significant difference between

Table 1 - Summary of articles included in the integrative review: antioxidants as nephroprotective agents

Author	Objective	Previous renal dysfunction	Definition of AKI used	Intervention evaluated	Results	Recommendations/ conclusions
Nouri-Majalan et al. ⁽²¹⁾	To evaluate whether vitamin E supplementation combined with allopurinol reduces AKI after CABG	Yes	25% decrease in the glomerular filtration rate	Infusion of vitamin E combined with allopurinol versus placebo	The strategy used did not demonstrate a renoprotective effect but decreased the length of ICU stay.	Use of this strategy in patients with greater Cr levels than are found in the patients in this study.
Song et al. ⁽¹⁹⁾	To evaluate the effectiveness of EPO in the prevention of AKI after CABG	Yes	50% increase from baseline Cr until the 5 th postoperative day	EPO 300U/kg versus saline before surgery	The prophylactic use of EPO reduced the incidence of AKI.	The authors suggest the use of the strategy in other studies involving a larger number of patients.
Oh et al. ⁽²⁰⁾	To evaluate the effectiveness of EPO in the prevention of AKI in patients who undergo CABG	Yes	Increase in Cr \geq 0.3mg/dL from baseline or increase in Cr $>$ 50% 72 hours after surgery	EPO 300U/kg versus saline before surgery	There was a significant difference between the groups, with a higher incidence of AKI in the control group.	EPO reduced the incidence of AKI and mortality due to AKI.
Barkhordari et al. ⁽²²⁾	To evaluate the effect of PTX on the development of AKI in patients who undergo cardiac surgery	No	Increase in Cr \geq 0.3mg/dL or $>$ 50% from baseline value	PTX 5mg/kg 5 minutes before anesthetic induction, followed by 1.5mg/kg/h up to 3 hours after the end of the procedure versus saline	There was no significant difference between the groups regarding the outcomes.	Larger studies are needed to show a beneficial effect of PTX on the renal function of patients who undergo cardiac surgery.
Haase et al. ⁽¹⁷⁾	To evaluate the effect of high doses of NAC in patients who undergo high-risk cardiac surgery	Yes	Greater increase in Cr compared to baseline until the fifth postoperative day	NAC 300mg/kg intravenous versus placebo	There was no difference between the groups regarding the primary outcome.	NAC does not attenuate AKI in high-risk patients undergoing cardiac surgery.
Ristikankare et al. ⁽²⁷⁾	To evaluate the renoprotective role of preoperative intravenous NAC in patients who undergo elective cardiac surgery	Yes	Increase $>$ 1.4mg/L in cystatin-C and increase $>$ 25% in Cr relative to baseline	NAC 300mg/kg for 24 hours starting after anesthetic induction versus saline	There was no difference between the groups regarding baseline values of cystatin-C and Cr.	NAC was not able to attenuate AKI in high-risk patients undergoing cardiac surgery.
Adabag et al. ⁽²⁶⁾	To evaluate the nephroprotective effect of NAC in patients who undergo cardiac surgery	Yes	Increase $>$ 0.5mg/dL in Cr or $>$ 25% from baseline at the 5 th , 6 th and 30 th postoperative day	NAC 600mg orally twice daily, from the preoperative period to the fifth postoperative day versus placebo	There was no significant difference between the NAC and control groups regarding the outcomes.	The use of NAC in the perioperative period of cardiac surgery did not reduce the incidence of AKI, mortality, length of hospital stay, or the need for dialysis.

AKI - acute kidney injury; CABG - coronary artery bypass grafting; ICU - intensive care unit; EPO - erythropoietin; Cr - serum creatinine; PTX - pentoxifylline; NAC - n-acetylcysteine.

the groups and that EPO reduced the incidence of AKI. However, the small number of participants in both studies does not allow the attribution of this difference to the drug. Therefore, the use of EPO in multicenter studies with the same design and a larger number of participants is required.

There are doubts regarding the existence of the renoprotective effect of N-acetylcysteine (NAC) and its intensity and probable mechanism of action, if it indeed exists. In our view, one of the difficulties of comparing the findings of different studies results from the non-standardization of the dose, of the route of

administration, of the time interval between administration of NAC and exposure to the noxious agent, or of the criteria used to define AKI. These difficulties exist even when we consider only well-conducted randomized studies with an adequate number of patients and control group.

Three studies^(17,26,27) included in this review used NAC as a prevention strategy and had as inclusion criteria patients at high risk for developing AKI in the postoperative period. One study administered the drug orally.⁽²⁶⁾ These studies did not show beneficial effects of NAC on renal function, in contrast to the results of a

recently conducted randomized controlled trial,⁽⁴⁰⁾ which used the maximum permitted dose for clinical practice and showed a significant difference between the groups, with the lowest incidence of renal dysfunction in patients treated with NAC compared to untreated patients. In addition, markers of ROS and inflammation were lower in the treated group compared to the control group.

Vasodilators as nephroprotective substances

We know that the most obvious changes in AKI are decreases in GFR and lesions in renal tubular cells. The pathological changes in the renal tubular cells occur primarily as a result of ischemia and hypoxia - common events in the perioperative period of cardiac surgery.

Thus, the use of drugs that can increase renal blood flow, thereby increasing GFR, seems a reasonable strategy. Among the drugs with this effect, we highlight dopamine and fenoldopam. Table 2 shows a summary of studies that used these drugs in the prevention of AKI.

Fenoldopam is a drug capable of promoting renal vasodilation. Cogliati et al.⁽²⁴⁾ tested this effect in 193 patients at high risk for developing AKI after surgery, beginning drug infusion immediately before surgery at a dose of 0.1mcg/kg/min for 24 hours. In this clinical trial, the authors showed that the incidence of AKI was lower in the treated group compared to the control (12.6% versus 27.6%; p=0.02). As in Santana-Santos,⁽⁴⁰⁾ the beneficial effect of the drug tested in both RCTs (NAC or fenoldopam) was able to reduce the incidence of AKI in milder forms that do not require renal replacement therapy. Thus, multicenter clinical trials with larger numbers of patients are needed.

One of the first studies that addressed the effects of dopamine on renal function was performed by Davis et al.,⁽⁴¹⁾ who tested the hemodynamic and renal function responses to low doses of dopamine (100 and 200mcg/min) in 15 patients who underwent cardiac surgery. The infusion of dopamine at these doses caused a significant

Table 2 - Summary of articles included in the integrative review: vasodilators as nephroprotective agents

Author	Objective	Previous renal dysfunction	Definition of AKI used	Intervention evaluated	Results	Recommendations/conclusions
Cogliati et al. ⁽²⁴⁾	To evaluate the renoprotective effect of fenoldopam in patients at high risk for AKI in the postoperative period of cardiac surgery	Yes	Increase ≥ 2 mg/dL in Cr or increase of 0.7 mg/dL relative to postoperative baseline values	Fenoldopam 0.1mcg/kg/min versus placebo	There was a significant difference between the groups regarding the primary outcome; none of the patients required dialysis.	The use of fenoldopam at the dose described reduced the incidence of AKI in patients at high-risk for AKI.
Yavuz, et al. ⁽²⁹⁾	To evaluate the effect of the use of dopamine combined with diltiazem on the renal function of patients undergoing cardiac surgery	No	Greater increase in Cr and Cr clearance up to the 7 th postoperative day	Four groups: a control group; one group only received dopamine (2mcg/kg/min); one group only received diltiazem (2mcg/kg/min); and one group received a combination of diltiazem and dopamine.	There was an improvement in renal function compared to baseline in the group that received the combination of dopamine and diltiazem on the first postoperative day.	The combined use of dopamine and diltiazem is more effective in maintaining renal function post-operatively than the individual use of diltiazem or dopamine. This strategy needs to be tested in higher-risk patients.
Lassnigg et al. ⁽²⁵⁾	To evaluate whether the continuous infusion of dopamine and furosemide exerts a renoprotective effect during the immediate postoperative period of cardiac surgery	No	Increase > 0.5 mg/dL in Cr from baseline value within 48 hours of evaluation	Three groups: a control group; one group received dopamine (2mcg/kg/min); one group received furosemide (0.5mcg/kg/min).	There was no improvement in renal function in any of the groups studied.	The use of any of the drugs is not recommended for the prevention of AKI in the perioperative period in patients who undergo cardiac surgery.
Tang et al. ⁽¹⁶⁾	To investigate whether dopamine offers any type of renal protection in patients who undergo coronary artery bypass grafting	No	Greater increase in Cr in 7 days	Administration of dopamine (4mcg/kg/min) immediately prior to surgery versus control	There was no significant difference between the groups regarding Cr.	The routine use of dopamine is not recommended for the prevention of AKI in patients who undergo cardiac surgery.

AKI - acute kidney injury; Cr - serum creatinine.

improvement in renal function, improving the urinary output with no deleterious effects on hemodynamics.

This review included three studies^(16,25,29) that assessed the effect of dopamine on renal function. In all these studies, the patients included were at low risk for developing AKI. Tang et al.⁽¹⁶⁾ used a dopamine dose of 4mcg/kg/min immediately after induction of anesthesia, maintaining the dose for 48 hours in 20 patients, and the control group had the same number of patients. There was no significant difference between the groups regarding the values of Cr, urea, urine output and fluid balance.

In the other studies, Lassnigg et al.⁽²⁵⁾ and Adabag et al.⁽²⁶⁾ tested dopamine combined with two other drugs - furosemide in the first and diltiazem in the second. In the first study, 132 patients with normal renal function were randomized into three groups: one that received dopamine (2mcg/kg/min), one that received furosemide (0.5mcg/kg/min), and a control group. The results indicated that the continuous infusion of dopamine showed no advantage over placebo for renal function, while the continuous infusion of furosemide, in addition to showing no beneficial effect, induced renal dysfunction. In the second study,⁽²⁶⁾ 60 patients were randomized into four groups: patients who only received dopamine; patients who only received diltiazem; patients who received diltiazem combined with dopamine; and patients who received saline. The dose of dopamine and diltiazem was 2mcg/kg/min and was started 24 hours before surgery, and it was maintained for 48 hours in the postoperative period.

Saline solutions for nephroprotection

Typically, the problems presented by patients in the postoperative period of cardiac surgery are hemodilution and excess extracellular fluid rather than a lack of volume; thus, dehydration is a minor problem. Pharmacological and non-pharmacological interventions have been investigated in several clinical trials for the prevention of AKI. In addition to the strategies previously mentioned, the use of saline solutions for hydration or urinary alkalization was a strategy identified and included in this review. In this section, we present the results (Table 3).

Hydration and urinary alkalization with sodium bicarbonate have been used as a prevention strategy for CIN. In a recent multicenter, randomized, and double-blind clinical trial, Haase et al.⁽¹⁵⁾ randomized 350 patients to receive saline infusion (n=176) or sodium bicarbonate (n=174) during cardiac surgery. In that

study, the authors did not find a significant reduction in the incidence and severity of AKI in the postoperative period nor a reduction of renal tubular damage, evaluated in that study by urinary neutrophil gelatinase-associated lipocalin (NGAL). The authors do not recommend this intervention for the prevention of AKI in high-risk patients who undergo cardiac surgery. The results found by Haase et al.⁽¹⁵⁾ corroborate the results found by McGuinness et al.⁽¹⁸⁾ In that investigation, 427 patients were randomized into two groups, with 215 patients composing the bicarbonate group and 212 patients composing the saline group. There was also no difference regarding the incidence of AKI between the groups. It is worth noting that the intervention was similar in both studies; however, the population studied was different, with patients with renal dysfunction evaluated in the first study and without renal dysfunction in the second.

Marathias et al.⁽²⁸⁾ evaluated the effect of hydration prior to cardiac surgery, initiating the strategy 12 hours before the procedure in patients with renal dysfunction in a randomized controlled trial. The patients were divided into two groups: the hydration group (n=30), in which the participants received intravenous infusion of 0.45% saline solution at 1mL/kg/h 12 hours before surgery; and the control group (n=15), who had liquid restriction before surgery. From the results, the authors observed that intravenous hydration in patients who undergo cardiac surgery prevents postoperative AKI. They also suggested that all patients with renal dysfunction should receive intravenous hydration at least 12 hours before the start of the procedure because it is a low-cost strategy that is well tolerated by patients.

Mannitol, an osmotic diuretic, was one of the first pharmacological agents used for the prevention of AKI in cardiac surgery.⁽⁴²⁾ The osmotic effect, in addition to reducing glomerular and tubular edema, contributes to restoring glomerular blood flow and to removing intraluminal obstructions.⁽⁴³⁾ Smith et al.⁽¹⁴⁾ evaluated 50 patients with preoperative renal dysfunction who underwent cardiac surgery. Patients were prospectively randomized to the mannitol (n=23) or control group (n=24). The results indicated that the addition of mannitol to the CPB prime was not able to preserve renal function after cardiac surgery in patients with renal dysfunction, suggesting that its routine use in the CPB circuit in patients undergoing cardiac surgery is unnecessary.

Table 3 - Summary of articles included in the integrative review: saline solutions for nephroprotection

Author	Objective	Previous renal dysfunction	Definition of AKI used	Intervention evaluated	Results	Recommendations/conclusions
Haase et al. ⁽¹⁵⁾	To evaluate the nephroprotective effect of sodium bicarbonate infusion in patients who undergo cardiac surgery	Yes	RIFLE ⁽⁴⁴⁾ criterion	Sodium bicarbonate (5.1mmol/mL) versus saline solution started immediately before surgery until 24 hours after the end of the procedure	There was no significant difference between the groups regarding the primary outcome (AKI by RIFLE criteria).	The routine use of sodium bicarbonate is not recommended for the prevention of AKI in high-risk patients undergoing cardiac surgery.
McGuinness et al. ⁽¹⁸⁾	To investigate whether perioperative urinary alkalization with sodium bicarbonate infusion reduces the prevalence of acute kidney injury associated with cardiac surgery	No	Increase >25% in Cr relative to baseline for 5 days after surgery	Sodium bicarbonate (5.1mmol/mL) versus saline solution started immediately before surgery until 24 hours after the end of the procedure	There was no significant difference between the groups regarding Cr.	The routine use of sodium bicarbonate is not recommended for the prevention of AKI in low-risk patients undergoing cardiac surgery.
Marathias et al. ⁽²⁸⁾	To evaluate the renoprotective role of preoperative intravenous hydration in patients who undergo elective cardiac surgery	Yes	Significant difference between the groups regarding baseline Cr values	Pre-hydration with 0.45% saline solution 1mL/kg/h versus no previous hydration	There was a significant difference between the groups regarding the values of Cr and GFR relative to baseline values.	Preoperative intravenous hydration in patients with renal dysfunction reduced the incidence of AKI.
Smith et al. ⁽¹⁴⁾	To evaluate the effect of mannitol on the renal function of patients who undergo cardiac surgery with CPB	Yes	Greater increase in Cr and reduced urinary output until the 3 rd postoperative day	Use of mannitol (0.5 g/kg) in CPB prime versus the same quantity of saline solution	There was no difference between the groups treated with mannitol when compared to the control group.	The routine use of mannitol in CPB prime is unnecessary.

AKI - acute kidney injury; Cr - serum creatinine; GFR - glomerular filtration rate; CPB - cardiopulmonary bypass.

Cardiac surgery with pulsatile cardiopulmonary bypass on nephroprotection

Since its development, CPB uses a non-pulsatile flow, which differs from the normal blood flow, which circulates through blood vessels according to the variation in pressure between the systolic and diastolic phases. Recent studies have demonstrated that pulsatile flow has advantages over non-pulsatile flow, particularly with respect to microcirculation and renal and cerebral perfusion.⁽⁴⁴⁾

Despite its wide use, CPB still raises concerns due to the deleterious effects during the postoperative period. Blood, when passing through a non-endothelial surface, releases mediators of inflammation because this circuit is interpreted by the organism as an aggressor. Thus, AKI may develop as a consequence of CPB, caused not only by the activation of the inflammatory cascade but also by changes in coagulation.^(10,45)

In table 4, we show a study conducted by Presta et al.,⁽²³⁾ who studied the impact of pulsatile CPB through the interoperative use of an intra-aortic balloon (IAB), on renal function. The authors divided the patients into two groups, one that underwent surgery without IAB (group A) and one that received IAB (group B). The degree of renal dysfunction was reported based on a 25% reduction

in GFR. Both groups showed a decrease in GFR; however, the decrease of this variable was higher in group A. When comparing groups A and B, there was a significant difference between groups at ICU admission ($p < 0.001$) and at 24 hours ($p < 0.001$) and 48 hours ($p < 0.001$) into the postoperative period. However, there was no significant difference between the groups regarding other outcomes (mortality, length of ICU stay, complications with the use of IAB).

One of the major limitations of any review of AKI is that the definitions used in many publications vary widely. Consequently, the comparison of studies becomes difficult and shows the need to use uniform indicators to indicate the severity of renal dysfunction, such as duration and degree of oliguria, as well as dependence on renal replacement therapy. Fortunately, initiatives with this purpose have been undertaken recently in studies involving patients who undergo cardiac surgery using RIFLE (risk, injury, failure, loss, end-stage kidney disease)⁽⁴⁶⁾ and AKIN (acute kidney injury network)⁽⁴⁷⁾ - systems of classification and definition for acute kidney injury that have proved robust.⁽⁴⁸⁻⁵⁰⁾ Another important limitation of this review was the exclusion of articles with no available full text during searches in databases.

Table 4 - Summary of articles included in the integrative review: pulsatile cardiac surgery with cardiopulmonary bypass on nephroprotection

Author	Objective	Previous renal dysfunction	Definition of AKI used	Intervention evaluated	Results	Recommendations/conclusions
Presta et al. ⁽²³⁾	To study the impact of pulsatile CPB on renal function during the perioperative period	No	Decrease of 25% in the glomerular filtration rate	Surgery with pulsatile CPB versus surgery with non-pulsatile CPB	The renal function in patients who underwent the procedure with non-pulsatile CPB worsened.	The study limitations do not allow extending the findings to other populations.

CPB - cardiopulmonary bypass.

CONCLUSIONS

The occurrence of acute kidney injury after cardiac surgery is a major complication associated with increased mortality and morbidity, which predisposes patients to a longer hospital stay due to the need for additional treatments, increasing the cost of postoperative care. This complication is characterized by progressive deterioration and is caused by the interaction of different pathophysiological mechanisms.

The strategies for prevention of acute kidney injury are limited, and the results of most of the interventions

published are not substantial. Based on the results of the present integrative review, which evaluated the evidence available in the literature on the most effective interventions for preventing acute kidney injury in patients who undergo cardiac surgery, we believe that the best pharmacological renal protection method is hydration with saline. The other strategies reviewed present controversial data. It is important to note that volume expansion is recommended for the prevention of acute kidney injury in cases of hypovolemia, but the use of volume without criteria and without appropriate tools for monitoring the volume status should be avoided.

RESUMO

A lesão renal aguda é uma complicação frequente após cirurgia cardíaca, estando associada ao aumento de morbidade e mortalidade, e ao maior tempo de permanência em unidade de terapia intensiva. Considerando a alta prevalência e a associação da lesão renal aguda com o pior prognóstico, o desenvolvimento de estratégias de proteção renal torna-se indispensável, especialmente em pacientes com alto risco para o desenvolvimento de lesão renal aguda, como aqueles submetidos à cirurgia cardíaca, com o intuito de minimizar a incidência da lesão renal aguda no âmbito hospitalar, reduzindo, dessa forma, a alta morbimortalidade. A presente revisão integrativa teve por objetivo avaliar as evidências

disponíveis na literatura sobre as intervenções mais eficazes na prevenção da lesão renal aguda em pacientes submetidos à cirurgia cardíaca. Para seleção dos artigos, utilizaram-se as bases de dados CINAHL e MedLine. A amostra desta revisão constituiu-se de 16 artigos. Após a análise dos artigos incluídos na revisão, os resultados dos estudos apontaram que apenas a hidratação com solução salina apresenta resultados consideráveis na prevenção de lesão renal aguda. As demais estratégias são controversas e necessitam de mais pesquisas para comprovar eficácia.

Descritores: Lesão renal aguda/prevenção & controle; Cirurgia torácica/complicações

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