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Acute Kidney Injury Post Cardiopulmonary Bypass Surgery

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Abstract: *Despite recent advances in the techniques of Cardiopulmonary bypass (CPB), the incidence of and mortality associated with acute kidney injury (AKI) post CPB surgery remain high. Perioperative risk factors for the AKI include advanced age, diabetes mellitus, underlying kidney disease, and poor cardiac function. Attempts should be made to avoid or modify risk factors such as anemia, pre-operative contrast exposure and excessive hemodilution. The benefits of off-pump coronary artery bypass graft (CABG) surgery on AKI remains equivocal. Well controlled randomized studies are needed to further clarify the role of various pharmacologic agents such as atrial natriuretic peptides and Fenoldopam on the prevention of AKI post CABG. Continuous renal replacement therapy is preferable to intermittent hemodialysis in patients needing dialysis.*

Keywords: *Kidney Injury, Cardiopulmonary Bypass, Coronary Artery Bypass Graft Surgery*

1. INTRODUCTION

Acute kidney injury (AKI) remains a serious complication of cardiac surgery with associated increased morbidity and mortality [1,2]. The incidence of AKI post cardio-pulmonary by pass (CPB) surgery ranges from 1->40%, depending on the definition of AKI. Hospital mortality associated with AKI post CPB could range from 50-67% [2,3].

In a meta-analysis, the global pooled incidence of AKI after cardiac surgery was 23% with an associated short and long term mortality of 10.7% and 30% respectively [4]. The variable and inconsistent definition of AKI by investigators likely contributed to the wide range in the published incidence of AKI. The use of widely accepted definition of AKI has facilitated better analysis and comparison of studies. The Acute Dialysis Quality Initiative Group (ADQI) developed a consensus definition for AKI now termed "Risk-Injury-Failure-Loss-End Stage kidney disease (RIFLE) criteria [5]. A modification of the RIFLE was proposed in 2007 by the Acute Kidney Injury Network now known as AKIN classification [6]. Recently, the Kidney Disease Improving Global Outcomes (KDIGO) has proposed a modification that combines the difference between RIFLE and AKIN [7](Table 1).

Table1. *Classification and Staging for RIFLE, AKIN, and KDIGO Criteria*

Class	RIFLE SCr or GFR	Stage	AKIN SCr	Stage	KDIGO SCr
Risk	Increased Scr x 1.5 or GFR decrease > 25% (within 7 days)	1	Increase in SCr≥ 0.3 mg/dL or ≥ 150% to 200% (1.5- 2-fold) from baseline (within 48 hours)	1	Increase in SCr by ≥ 0.3 mg/dL within 48 hours or increase in SCr 1.5 to l.9 times baseline which is known or presumed to have occurred with the prior 7 days
Injury	Increased Scr x 2.0 or GFR decrease > 50%	2	Increase in SCr to more Than 200% to 300% (>2- to 3-fold) from baseline	2	Increase in SCr to 2.0 to 2.9 times baseline
Failure	Increased Scr x 3.0 or GFR decrease > 75% or SCr≥ 4.0 mg/dL or acute increase ≥ 0.5 mg/dL	3	Increase in SCr to more than 300% (> 3-fold) from baseline or SCr≥ 4.0 mg/dL with an acute increase of at least 0.5 mg/dL or initiation or renal replacement therapy	3	Increase in SCr to 3.0 times baseline or increase in SCr to ≥ 4.0 mg/dL or initiation of renal replacement therapy

Loss	Persistent acute renal failure = complete loss of kidney function > 4 weeks	
End Stage Kidney Disease	End stage of kidney disease (> 3 months)	

Modified from Bellomo et al [5], Mehta et al. [6]and Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group [9]

Biomarkers of renal tubular damage are currently in vogue for the evaluation of AKI. Such markers include: neutrophil gelatinase associated lipocalcin (NGAL), kidney injury marker-1 (KIM-1), urinary Interleukin 18 (IL-18), IGF-binding protein 7 (IGFBP7), tissue inhibitor of metalloproteinase-2 (TIMP-2), liver-type fatty acid-binding protein (L-FABP) and Cystatin C [8]. However, a consensus statement by the ADQI working group has stated that while these markers are useful complement to RIFLE and AKIN definitions of AKI, there is insufficient data to support their use in staging AKI [9].

2. Risk Factors For AKI

Several risk factors for post cardiac surgery AKI have been well documented [10,11]. Most of these are non-modifiable such as: Age, female gender, underlying chronic kidney disease (CKD), reduced ejection fraction, diabetes, and emergency surgery (table 2). However, some modifiable risk factors not included in the table are: pre-operative anemia with blood transfusion and timing of surgery in relation to radio contrast media exposure. Several small studies have reported that cardiac surgery less than one day after cardiac catheterization is associated with increased risk of AKI post coronary artery bypass graft (CABG) surgery [12, 13]. These studies included patients undergoing both elective and emergency CABG. However, data from the Duke Cardiovascular Disease Data bank revealed that in 2441 patients undergoing CABG surgery after Cardiac Catheterization, the risk of post CABG -AKI was inversely related to the time between cardiac catheterization and CABG [14]. The highest incidence was observed in those operated on in less than one day (24%) and lowest in those operated on after 5 days post cardiac catheterization (15.8%).

Table2. *Risk Factors for Acute Kidney Injury*

Preoperative	Age
	Female gender
	Hypertension
	Pulse pressure >40 mmHg
	Chronic kidney disease
	Diabetes
	Peripheral vascular disease
	Chronic obstructive pulmonary disease
	Congestive heart failure
	LV ejection fraction <35%
	Need for emergency surgery
	Cardiogenic shock (IABP)
	Left main coronary disease
	Perioperative myocardial infarction
	Previous cardiac surgery
Procedure-related	Off-pump vs On-pump
	Length of CPB
	Cross-clamp time
	Non-pulsatile flow
	Hemolysis
	Hemodilution
	CABG + Valve surgery
Postoperative	Severe sepsis, septic shock
	Hemorrhagic shock
Nephrotoxic medication	Aminoglycosides, vancomycin, nonsteroidal antiinflammatory drugs

3. Anemia And Transfusion

The renal medulla is in a state of relative hypoxia. Hence the kidneys are vulnerable to hypoxic and oxidative injuries, especially if anemia is present.

Many large studies have reported an association between lower hematocrit and increased incidence of AKI post CABG [15-17]. These studies showed that hematocrit less than 24% during CPB was associated with increased AKI risk [12, 14]. Also, AKI rates increased in direct proportion to the amount of perioperative blood transfusion. [15, 17, 18].

4. Statins, Aspirin and Renin-Angiotensin System Inhibitor (RASI)

Many patients undergoing cardiac surgery are on angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), Statins and or Aspirin therapy. However, it remains unclear if these medication have a protective role in post CABG- AKI. [19-24]. Aspirin is often discontinued 3-10 days before CABG so as to reduce post-operative bleed but continued in emergent CABG patients. An observational study using propensity score and regression analysis suggested that use of aspirin within 5 days of surgery was associated with reduced 30 - day mortality and post-operative renal failure (3.7% vs 7.1%; p <0.001) [17]. However, a randomized controlled study "Aspirin and Tranexamic Acid for Coronary Artery Surgery" (ATACAS), found that in patients undergoing CABG the administration of pre-operative aspirin until the day of surgery resulted in neither a lower risk of death, renal failure nor thromboembolic complications [22].

The beneficial effects of statins in cardiovascular mortality has been well documented but the role of statins in post CABG- AKI remains questionable. In a meta-analysis of over 30,000 cardiac surgery patients it was reported that pre-operative statin use was associated with an absolute risk reduction in mortality, atrial fibrillation and stroke but not myocardial infarction or AKI [23]. However, another study using propensity score, found no difference in the incidence of post CABG- AKI, dialysis or hospital mortality between the statin and the no-statin groups [24]. Thus, the effect of statins and aspirin on AKI post CABG remains unsettled.

5. Hemolysis

Hemolysis is a frequent side effect of CBP and is caused by mechanical shear stress within the extra corporeal system. It may contribute to post CABG- AKI. The AKI is thought to be related to intra tubular hemoglobin precipitation with resultant obstruction versus iron-facilitated oxidant damage to tubulo-epithelial cells [25] and increased intravascular nitric oxide consumption [26].

6. Cardiopulmonary Bypass (CPB)

Cardiopulmonary bypass is the mainstay of most open heart coronary artery or valvular surgery. It involves the use of an extra corporeal circulation to temporarily replace the function of the heart and lungs during surgery in order to maintain perfusion, oxygenation and carbon dioxide removal. Cardiopulmonary bypass therefore predisposes to AKI through multiple mechanism: aortic cross clamping with subsequent ischemia –reperfusion injury; lower perfusion pressures; non-pulsatile blood flow, hemodilution; free oxygen radical generation with systemic inflammatory response; and longer duration of CPB. All of these have been associated with increased risk of AKI in a meta-analysis involving over 12,000 patients [28]. It has therefore been hypothesized that preservation of physiologic renal perfusion by avoidance of CPB would decrease the risk of AKI post CABG [7,10,27]. The process of performing CABG surgery without the use of CPB is known as "off- pump CABG" (OPCABG). It would therefore seem that avoidance of CPB would minimize renal insult and subsequent post CABG-AKI. The effect of OPCABG on post-operative AKI remains contentious. The Randomized on/off bypass (ROOBY) trial in which 2203 patients were randomized to OPCABG vs. on-pump CABG (ONCABG) failed to show any significant difference in 30- day end points of death, stroke or renal failure requiring dialysis [29]. The OPCABG group also had a worse composite outcome at one year follow up. A large international randomized controlled trial "coronary artery bypass grafting surgery off or On-pump revascularization study (CORONARY) randomized 4752 patients to undergo either ONCABG or OPCABG. Of these, 2932 were enrolled into a kidney function sub study. They observed a significant reduction in 30 day risk of post-operative AKI in the OPCABG than the ONCABG (20.8% VS 17.5%, p =0.01) [30] but there was no difference between the 2 groups in the loss of kidney function at 1 year. On the basis of these studies, the KDIGO-AKI workgroup suggests that OPCABG should not be selected solely for the

purpose of reducing perioperative AKI or the need for renal replacement therapy [7]. The lack of renal benefit in OPCABG is thought to be due to the marked hypotension and increased use of inotropes during the surgery [29].

7. Pharmacologic Prophylaxis

Multiple pharmacologic agents have been studied over the years for the prevention of AKI. Two agents worthy of mention in this report are Fenoldopam and Natriuretic peptide. Fenoldopam is a short acting dopamine-I receptor agonist. It increases renal and splanchnic blood flow and induces a natriuretic effect [31]. The randomized study in 80 patients by Ranucci et al [32] showed that infusion of Fenoldopam at 0.1µg/kg/ min from start of CPB until 12 hours after surgery resulted in significantly lower rate of AKI (0% vs 10%). A meta-analysis involving 440 patients from 6 studies showed that Fenoldopam significantly reduced the risk of post CABG- AKI (OR 0.41; p=0.003) but a higher rate of hypotensive episodes and or use of vasopressors but no effect on renal replacement therapy [33]. A large multi-center trial would be needed to confirm these results.

The reno-protective effects of human atrial natriuretic peptide (hANP) have been well publicized. A meta-analysis of 13 randomized trials of natriuretic peptides showed better preservation of renal function in patients randomized to perioperative natriuretic peptide infusion [34]. In Japan, ANP is approved for the prevention of AKI and treatment of congestive heart failure [35]. In a study from Japan involving 303 patients with CKD stage 3 (eGFR<60 ml/min per 1.73 m^2) were randomized to receive carperitide (synthetic hANP) infusion at 0.02 µg/kg/min vs. saline from start of CPB until 12 hours after oral medication recommenced. The dialysis incident rate through 1 year post operatively was 9% in the placebo group vs. 1.4% in the hANP group, p=0.01. It appears that perioperative infusion of hANP may have a sustained reno-protective effect in CDK patients after CABG. However, the KDIGO AKI working group does not recommend the use of hANP for the prevention of post CABG- AKI [7].

New pharmacologic agents currently under investigation include Levosimendan, a novel calcium sensitizer with inotropic and vasodilatory effects that may offer protective effects in endotoxemic and ischemia-reperfusion injury [36]and ABT-719, a novel α- melanocyte-stimulating hormone analog (αMSH) [37]. A recent meta-analysis of 13 randomized trials involving 1345 patients undergoing cardiac surgery noted that perioperative infusion of Levosimendan reduced the incidence of AKI, RRT, length of intensive care unit stay and death [38].

α-Melanocyte-stimulating hormone is an endogenous hormone that inhibits inflammatory, cytotoxic, and apoptotic pathways, hence prevents renal injury caused by ischemia-reperfusion induced AKI . In addition, α-MSH has direct protective effects on the kidney, which may result from stimulation of the melanocortin receptors in the outer renal medulla [39]. However, a recent phase 2b randomized, double-blind, placebo-controlled multicenter study designed to evaluate the safety and efficacy of ABT-719 in preventing AKI associated with high-risk, OPCABG, ABT-719 treatment did not lower AKI incidence using AKIN criteria, influence the elevations of novel biomarkers, or change 90-day outcomes in patients after cardiac surgery [37]. Further randomized controlled studies will be needed to clearly define the role of these newer agents in the prevention of AKI post CABG.

8. Leukodepletion

Induction of systemic inflammatory response is one of the postulated mechanism of CPB induced AKI. [10, 27]. Hence leucocyte depletion (leukodepletion) using mechanical filtration during CPB has been evaluated for its protective effect on AKI. Most of the published studies are small and appear to show some beneficial effects on reno-protection in patients with mild CKD [40]. A retrospective study of 266 cardiac surgery cases with leukodepletion was compared with a similar group of historical controls but failed to show a difference in renal and other outcomes [41].

9. Stem Cells

Mesenchymal stem cells (MSC) are known to possess anti-inflammatory and immune regulatory properties that promote cell survival and tissue repair. Infusion of allogeneic MSC in animal models of AKI has been shown to ameliorate AKI [42]. The primary modes of action are thought to be paracrine and endocrine since engraftment of the MSC into target cells were absent and fusion with renal cells were not observed [43]. In a phase 1 randomized trial of

AKI post CABG, preliminary results show that MSC therapy prevented postoperative deterioration in renal function (by ~20%), reduced length of stay (by ~40%), need for readmission (by ~40%), and prevented late deterioration in renal function . [Clinical Trials.gov # NCT 00733876]

10. Remote Ischemic Pre-Conditioning (RIPC)

Remote ischemic preconditioning (RIPC) is a process whereby non-lethal ischemia is briefly induced in a remote organ (typically a limb) so as to provide protection to vital organs in the body against ischemic insults [44]. Multiple endogenous molecules including: adenosine, bradykinin, cannabinoids, calcitonin gene peptide and nitric oxide may be humoral mediators of RIPC [45]. The beneficial effect of RIPC on the heart has been extensively studied but not on the kidneys. Limited studies on the effect of RIPC on post CABG- AKI produced mixed results. A meta-analysis by Yang et al found no difference in levels of biomarkers of AKI, incidence of RRT and in hospital mortality [46]. Similarly a randomized control trial in 86 patients with isolated CABG using three 5 minute cycles of forearm ischemia also failed to show a significant difference in serum or urinary biomarkers of AKI [47]. A larger study of 240 patients by Zarbock et al [48] observed that fewer patients in the RIPC arm developed post CABG- AKI within 72 hours after surgery (37.5% vs. 52.5% p=0.02). However, a recent meta-analysis of 19 trials with 5100 patients noted RIPC was associated with a significant reduction in AKI post ONCABG but did not impact incidence of RRT, and in –hospital mortality [49]. Therefore, more randomized studies will be needed to fully evaluate the role of RIPC in post CABG AKI.

11. Renal Replacement Therapy

Renal replacement therapy modality utilized in post CABG- AKI needing dialysis should be dictated by the clinical status of the patient. Both conventional intermittent hemodialysis (IHD), various modalities of continuous renal replacement therapy (CRRT) and hybrid modalities (that combine aspects of IHD and CRRT) are equally effective. Multiple studies that have compared IHD to CRRT could not find any survival superiority or advantages on renal recovery between CRRT and IHD [50,51]. Sustained low efficiency dialysis (SLED) is a hybrid modality that has been shown to be equally as effective as CRRT [52]. It involves the use of high flux membranes on a low blood flow rate of 100-300ml/min. and a single- pass dialysate flow rates of 100-300ml/min. for about 8-18 hours per day. Older models of dialysis machines are not equipped for such low dialysate flow rates and would need software upgrades that allows for flexible dialysate flow rates and prolonged treatment time. Most current dialysis machines such as Fresenius 2008K, Fresenius 2008T or Gambro 200S ULTRA in the United States are already equipped to allow for hybrid treatments. Further technical discussions on the methodology and function of the Hybrid System is beyond the scope of this review.

High volume peritoneal dialysis (HVPD) is a viable alternative in resource poor regions of the world but requires careful patient selection and strict monitoring of volume status and metabolic balance [53]. An effective HVPD requires the use of a "Cycler" which can perform continuous 1-2L exchanges with 30 -60 minutes dwell time for about 18-22 exchanges per day. The absence of a cycler would require the services of a 24 hour dedicated nursing staff. Ultimately, the RRT of choice should be based on several factors including material/ equipment availability, expertise of the nephrologist, vascular access, and hemodynamic stability of the patients.

12. Conclusion

Acute kidney injury incidence post CPB surgery remains high especially in patients with underlying CKD and other risk factors. Mortality and increased resource use are also high. Factors to mitigate the AKI should include: correction of anemia; avoidance of excessive transfusion; and maintenance of adequate perfusion pressures and cardiac output during CPB. Although beneficial effects of RIPC, Fenoldopam, hANP, and Levosimendan on AKI post CABG have been reported, the role of pharmaco-prophylactic agents and RIPC remain largely unresolved. Off-pump CABG may be beneficial in patients with underlying CKD with mild to moderate AKI post CABG. In patients needing dialysis, CRRT is the preferred modality however, dialysis modality should be based on the expertise of the nephrologist, resource availability and hemodynamic status of the patient.

REFERENCES

[1] Miceli A, Bruno VD, Capoun R, Romeo F, Angelini GD, Caputo M. (2011). Occult renal dysfunction: a mortality and morbidity risk factor in coronary artery bypass surgery. J. Thorac Cardiovascular Surgery 141 (3): 771-776.

[2] Boyle JM, Moulla S, Arrigain S, Worley S, Bakri MH, Starling RC et al.(2006). Risks and outcomes of acute kidney injury requiring dialysis after cardiac transplantation. Am J Kidn Dis 48:787-796.

[3] Landoni G, Zangrillo A, Franco A, et al: (2006). Long term outcome of patients who require renal replacement therapy after cardiac surgery. Eur J Anaesth 23:17-22

[4] Hu J, Chen R., Liu S, Yu X, Zou J, Ding X. (2016). Global incidence and outcomes of adult patients with acute kidney injury after cardiac surgery: A systematic review and meta-analysis. J Cardio ThoracicVasc Anaesth301(1):82-89.

[5] Bellomo R, Ronco C, Kellum JA, Mehta RH, Palevsky P (2004). Acute Dialysis Quality Initiative working group. Acute renal failure definition, outcome measures, animal models, fluid therapy and information technology needs: The second international consensus conference of the acute dialysis quality initiative (ADQI) group. Crit Care 8(4): R204-212

[6] Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG (2007). Acute kidney injury network: Report of an initiative to improve outcomes in acute kidney injury. Crit Care 11(2): R31

[7] Kidney Disease: Improving Global Outcomes (KDIGO), Acute Kidney Injury Work Group (2012). KIDGO Clinical Practice Guidelines for Acute Kidney Injury. Kidney Int Suppl. 2:1-138

[8] Alge JL, Arthur JM (2015). Biomarkers of AKI: A review of mechanistic relevance and potential therapeutic inplications. Clin J Am SocNephrol 10:147-155

[9] McCullough PA, Shaw AD,, Haase M, Bouchard J, Waiker SS, Siew ED et al: (2013). Diagnosis of acute kidney injury using functional and injury biomarkers; Workgroup statements from the 10th Acute Dialysis Quality Initiative Consensus Conference. ContribNephrol182:13-29.

[10] Rosner MH, Okusa MD (2006). Acute kidney injury associated with cardiac surgery. Clin J. Am SocNephrol1:19-32

[11] Massoudy P, Wagner S, Thielman M, Herold U, Kottenberg-Assenmacher E, Marggraf G et al.(2008). Coronary artery bypass surgery and acute kidney injury- impact of the off-pump technique. Nephrol Dial Transpl23:2853-2860.

[12] Ranucci M, Ballotta A, Kunkl A, De Benedetti D, Kandil H, Conti D et al. 2008). Influence of the timing of cardiac catheterization and the amount of contrast media on acute renal failure after cardiac surgery Am J Cardiol 101:1112-1118

[13] Hennessey A, LaPar DJ, Stukenburg GJ, Stone MW, Mlynarek RA, Kern JA et al. (2010). Cardiac Catheterization within 24 hours of valve surgery is significantly associated with acute renal failures. J Thoracc Cardiov as Surg 104:1011-1017.

[14] Mehta RH, Honeycutt MBI, Uptal D et al. (2011). Relationship of the time Interval between Cardiac Catheterization and elective coronary artery bypass surgery with post procedural acute kidney injury. Circ124 (suppl 1): S149-S155.

[15] Habib RH, Zacharias A, Schwann TA, Riordan CJ, Engoren M, Durham SJ et al. (2005). Role of hemodilutional anemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: implications on operative outcome. Crit Care Med 33:1749-1756.

[16] Mehta RH, Castelvecchio S, Ballota A, Frigiola A, Bossone E, Ranucci M. (2013). Association of gender and lowest hematocrit on cardiopulmonary bypass with acute kidney injury and operative mortality in patients undergoing cardiac surgery. Ann ThoracSurg 96:133-140

[17] Ranucci M, Biagioli B, Scolletta S, Grillone G, Gazzaniga A, Cattabriga I et al. (2006). Lowest hematocriton cardiopulmonary bypass impairs the outcome in coronary surgery: An Italian multicenter study from the national cardio anesthesia database. Tex Heart Inst J 33:300-305

[18] Karkouti K. Transfusion and risk of acute kidney injury in cardiac surgery. (2012). Brit J Anaesth109(51): 729-738.

[19] Coca SG, Garg AX, Swaminathan M, Garwood S, Hong K, Thiessen-Philbrok H et al. (2013). Preoperative angiotensin converting enzyme inhibitors and angiotensin receptor blocker use and acute kidney injury in patients undergoing cardiac surgery. Nephrol Dial Transpl28:2787-2799.

[20] Benedetto U, Scieretta S, Roscitano A, Fiorani B, Refice S, Angeloni E et al. (2008). Preoperative angiotensin converting enzyme inhibitors and acute kidney injury after coronary artery bypass grafting. Ann ThoracSurg86: 1160-1168.

[21] Cao L, Young N, Liu H, Silvestry S, Sun W, Zhao N. et al. (2012). Preoperative aspirin use and outcomes in cardiac surgery patients. Ann Surg255:399-404.

[22] Myles PS, Smith JA, Forbes A, Silbert B, Jayarajah M, et al. (2016). For the ATACAS Investigators of the ANZCA clinical trials network. Stopping vs. continued aspirin before coronary artery surgery. NEngJMed374(8): 728-737.

[23] Liakopoulos OJ, Choi YH, Haldenwang PC, Strauch J, Wittwer T. Dorge H, et al. (2008). Impact of preoperative statin therapy on adverse post-operative outcomes in patients undergoing cardiac surgery: a meta-analysis of over 30,000 patients. Euro Heart J 29:1548-1559.

[24] Argalious M, Xu M, Sun Z, Sonedira N, Koch, CG. (2010). Preoperative statin therapy is not associated with a reduced incidence of post-operative acute kidney injury after cardiac surgery. Anesth Analog 111:324-330.

[25] Vermeulen-Windsant IC, Snoeijs MG, Hanssen SJ, Altintas S, Heijmans JH, Koeppel TA et al. (2010).Hemolysis is associated with acute kidney injury during major aortic surgery. Kidney Int77:913-920.

[26] Vermeulen- Windsant IC, de Wit NCJ, Sertorio JTC, Van Bijnen AA, Ganushahak YM, HeijmansJH et al. (2014). Hemolysis during cardiac surgery in associated with increased intravascular nitric oxide consumption and perioperative kidney interstitial tissue damage. Frontiers Physiol 5(340):1- 9.

[27] Shaw A (2012) Update on acute kidney injury after cardiac surgery. J ThoracCardiovasc Surg143:676-681.

[28] Kumar AB, Suneja M, bayman EO, Weide GD, Tarasi M (2012). Association between post-operative acute kidney injury and duration of cardiopulmonary bypass: a meta-analysis. J CardiothoracVascAnesth26:64-69.

[29] Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, et al. (2009). On-pump versus off-pump coronary artery bypass surgery NEngJMed 361(19): 1827-1837.

[30] Garg AX, Devereaux PJ, Yusuf S, Cuerden MS, Parikh CR, Coca SG, et al. (2014). Kidney function after off-pump or on-pump coronary artery bypass graft surgery. JAMA 311(21): 2191-2198.

[31] Meco M, Cirri S (2010). The effect of various fenoldopam doses on renal perfusion in patients undergoing cardiac surgery. Ann ThoracSurg89: 497-503.

[32] Ranucci M, De Beneddetti D, Bianchini C, Castelvecchio S, Ballotte A, Frigiola A et al. (2010). Effects of fenoldopam infusion in complex cardiac surgical operations: a prospective randomized double-blind placebo-controlled study. Minerva Anestesiol76:249-259.

[33] Zangrillo A, Biondi-Zoccai GG, Frati E, Covell RD, Cabrini L, Guarracino F et al. (2012). Fenoldopam and acute renal failure in cardiac surgery: a meta-analysis of randomized placebo-controlled trials. J CardiothoracVascAnesth 23(3): 407-413.

[34] Nigwekar U, Hix JK (2009). The role of natriuretic peptide administration in cardiovascular surgery associated renal dysfunction: A systematic review and meta-analysis of randomized controlled trials. J CardiothoracVascAnesth23:151-160.

[35] Sezai A, Hata M, Niino T, Yoshitake I, Unosawa S, Wakui S et al. (2011). Results of low dose human atrial natriuretic peptide infusion in non-dialysis patients with chronic kidney disease undergoing coronary artery bypass grafting: The NU-HIT (Nihon University working group study of low-dose hANP infusion therapy during cardiac surgery) trial for CKD. J Am Coll Cardio 58:879-903.

[36] Farmakis D, Alvarez J, Gal TB, Brito D, Fedele F, Fonseca C et al. (2016). Levosimendan beyond inotropy and acute heart failure: Evidence of pleotropic effects on the heart and other organs: An expert panel position paper. Int J Cardiol 222:303-312

[37] McCulloughPA, Bennett-Guerrero E, Chawla LS et al. (2016).ABT-719 for the Prevention of Acute Kidney Injury in Patients Undergoing High-Risk Cardiac Surgery: A Randomized Phase 2b Clinical Trial. J Am Heart Assoc 5(8):e003549

[38] Zhou C, Gong J, Chen D, Wang W, Liu M, Liu B (2016). Levosimendan for prevention of acute kidney injury after cardiac surgery: A meta-analysis of randomized controlled trials. Am J kidney Dis 67(3):408-416

[39] Jo SK, Yun SY, Chang KH, Cha DR, Cho WY, Kim HK, Won NH. (2001). alpha-MSH decreases apoptosis in ischemic acute renal failure in rats: possible mechanism of this beneficial effect. Nephrol Dial Transplant. 16:1583–1591

[40] Rubino AS, Serraino GF, Mariscalco G, Marsico R, Sala A, Renzulli A (2011). Leukocyte depletion during extra corporeal circulation allows better organ protection but does not change hospital outcomes. Ann ThoracSurg91:534-540.

[41] Bechtel JF, Mühlenbein S, Eichler W, Marx M, Sievers HH (2011). Leucocyte depletion during cardio pulmonary bypass in routine adult cardiac surgery. Interact CardiovascThorac Surg12(2): 207-212.

[42] TögelFE, Westenfelder C (2012). Kidney protection and regeneration following acute injury: Progress through stem cell therapy. AJKD 60:1012-1022

[43] Humphreys BD, Bonventre JV (2008). Mesenchymal stem cells in acute kidney injury. Ann Rev Med 59:311-325

[44] Murry CE, Jennings RB, Reimer KA (1986). Preconditioning with ischemia: A delay of lethal cell injury in ischemic myocardium. Circ74:1124-1136.

[45] Kharbanda RK, Nielsen TT, Redington AN (2009). Translation of remote ischemic preconditioning into clinical practice. Lancet 374:1557-1565.

[46] Yang Y, Lang X, Zhang P, Lv R, Wang Y, et al. (2014). Remote ischemic preconditioning for prevention of acute kidney injury: A meta-analysis of randomized controlled trials. Am J Kidney Dis 64(4): 574-583.

[47] Gallagher SM, Jones DA, Kapur A, WraggA, Harwood SM, Mathur R, et al. (2015). Remote ischemic preconditioning has a neutral effect in the incidence of kidney injury after coronary artery bypass graft surgery. Kidney Int87:473-481.

[48] Zarbock A, Schmidt C, Van Aken H, Wempe C, Martens S, Zahn PK et al. (2015). Effect of remote ischemic preconditioning on kidney injury among high risk patients undergoing cardiac surgery. JAMA 313(21): 2133-2141.

[49] Zhang Y, Zhang X, Chi D, et al. (20116).Remote ischemic preconditioning for prevention of acute kidney injury in patients undergoing on-pump cardiac surgery. Med 95(37);e3465

[50] Guerin C, Girard R, Seli JM, Ayzac L. (2002). Intermittent versus continuous renal replacement therapy for acute renal failure in intensive care units: results from a multi-center prospective epidemiological survey. Intensive Care Med 28(10):1411-1418

[51] Schneider AG, Bellomo R, Bagshaw SM, Glassford NJ, Lo S, Jun M et al. (2013). Choice of renal replacement therapy modality and dialysis dependence after acute kidney injury: a systemic review and meta-analysis. Intensive Care Med 39(6): 987-997.

[52] Schwengar V, Weigand MA, Hoffman O, Dikow R, Kihm LP, Seckinger J et al. (2012). Sustained low efficiency dialysis using a simple-pass batch system in acute kidney injury a randomized interventional trial: The REenal Replacement Therapy Study in Intensive Care Unit Patients. Crit Care 16: R140.

[53] Ponce D, Berbel MN, Regina de Goes C, Almeide CT, Belbi AL (2012). High volume peritoneal dialysis in acute kidney injury: Indications and limitations. Clin J Am SocNephrol 7:887-894.

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