INTRODUCTION

Acute kidney injury (AKI) after surgery is an important cause of morbidity and mortality. The most well studied among all post-surgical AKI is post-cardiac surgery . AKI after cardiac surgery is seen in 5–30% of patients .The AKI requiring dialysis is observed in 1–5% of patients after surgery ***(Hoste et al., 2008).***

The mortality in patients with AKI is high as compared to those who do not develop AKI. The mortality is very high and seen in about 40–80% of patients requiring dialysis. Minor changes in serum creatinine of 0.2–0.3 mg/dL predict a significant increase in short-term mortality ***(Jyrala et al., 2010).***

Patients who are undergoing cardiac surgery are already at risk for development of AKI because of various predisposing conditions like low EF, valvular dysfunction, which reduces the renal perfusion ***(Karkouti et al., 2009)*** .In addition these patients usually receive diuretics, which reduce intravascular volume and renal blood flow, predisposing them to AKI. Many of these patients are also on angiotensin-converting enzyme inhibitor (ACEI/ angiotensin receptor blocker (ARBs), NSAID, which impair the renal autoregulation ***(Arora et al., 2008).***

In a clinical situation, about 10% of cardiac surgical patients with cardiopulmonary bypass (CPB), especially high-risk patients, experience hepatic injury, which directly influences their cure rate and mortality ***(Chaney, 2002)***.

The pathogenesis of AKI after cardiac surgery involves an interaction between the susceptible host and preoperative, intraoperative, and postoperative factors. Ischemia-reperfusion injury, oxidative stress, and systemic inflammation are factors considered to play a significant role in the development of AKI after cardiac surgery ***(Rosner and Okusa, 2006).***

Several recent studies have documented the high morbidity and mortality associated with performing cardiac surgery in patients with cirrhosis ***(Hayashida et al., 2004)***.

Intraoperative period is a critical time as patients are exposed to anesthesia and cardiopulmonary bypass. During CPB the heart lung machine is used to provide blood to various tissues and organs during surgery. The goal is to maintain tissue perfusion at an optimal level to prevent ischemic injury to various organs and post-operative complications ***(Murphy et al., 2009)***.

Efforts to decrease complications associated with the use of the heart-lung machine have included the investigation of the

impact of on-pump vs off-pump cardiac surgical procedures on the primary composite end point of death or complications (reoperation, new mechanical support, cardiac arrest, coma, stroke, or renal failure) before discharge or within 30 days after surgery ***(Shroyer et al., 2009)***.

A variety of different agents have been studied for prevention and treatment of post-cardiac surgery AKI; however, results of most of them are disappointing ***(Stafford, 2005)*** There are several reasons for that; adult cardiac surgery is a very heterogeneous population and ischemic ATN is not always the cause of AKI (***Bansal, 2012).***

AIM OF THE ESSAY

To focus on the renal and hepatic injury as a post operative complications of patients undergoing open heart surgery including early detection and role of intensive care unit in decreasing mortality and co-morbidity during post operative period.

Epidemiology and Pathophysiology

The incidence of AKI following cardiac surgery has historically been difficult to determine. Mild renal injury (creatinine rise <25%) may occur in as many as 50% of patients undergoing cardiac surgery. Moderate kidney injury has been reported in 8-15% of patients, while up to 5% of patients develop renal failure requiring dialysis following cardiac surgery **(*Shaw et al., 2008*).**

Individual reports differ significantly as a result of inconsistent definitions, varied surgeries, and a heterogeneous patient population ***(Bellomo et al., 2004).***

In many series, renal failure is defined as a 50% rise in serum creatinine, while others define it arbitrarily as a doubling of the creatinine, and yet others include only dialysis dependent patients in their analyses ***(Bellomo et al., 2004).***

The RIFLE and AKIN criteria were developed by panels of experts to provide a uniform definition of AKI and facilitate recommendations for patients suffering from renal failure ***(Mehta et al., 2007)***.this is described in fig (1).

These definitions rely upon serum creatinine levels and urine output to define and categorize the severity of kidney injury. Regardless of the definition, once renal failure progresses and a patient becomes dialysis dependant ***(Chertow et al., 1998)***.

Even with the progress of modern medicine and implementation of newer dialysis technology, the mortality associated with post operative renal failure has not noticeably improved ***(Ympa et al., 2005)***.

Renal failure in itself is often not the primary problem, but only a sign of significant low cardiac output and multi-organ failure, however, this is likely not the case. Other authors have proposed that the high mortality associated with renal failure is not related to renal replacement therapy (RRT) itself, rather it predisposes patients to other morbidities. A large study reviewing 16,000 patients with contrast induced nephropathy suggested that patient'swhose hospitalizations were complicated by sepsis, coagulopathies, respiratory, or neurologic failure, were more likely to die during their hospitalization, while it was rare for patients with uncomplicated renal failure not to survive ***(Levy et al., 1996).***

Chertow et al, reporting on over 43,000 patients with AKI following cardiac surgery, found that these patients were more likely to suffer myocardial infarction, require reoperation for bleeding, and develop endocarditis or mediastinitis ***(Chertow et al., 1997)***.

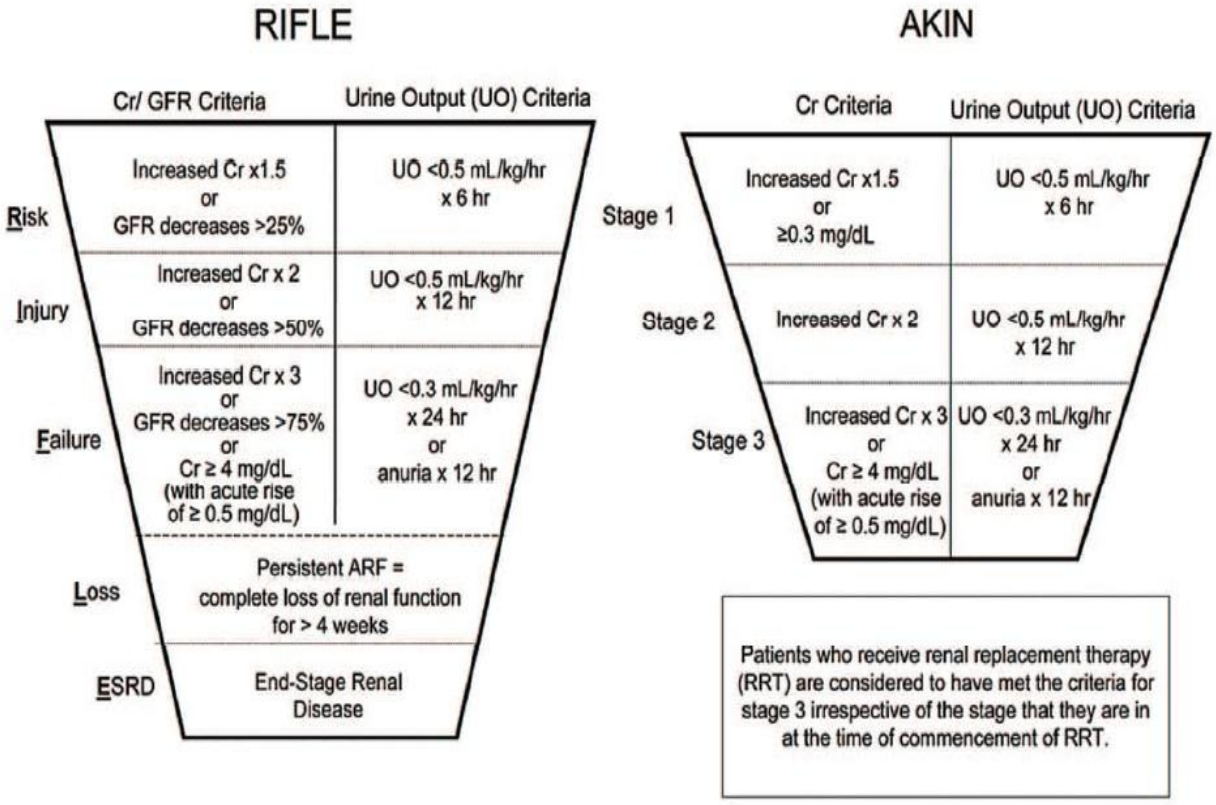

Fig. 1. RIFLE and AKIN criteria ***(Cruz et al. 2009).***

While patients with AKI requiring renal replacement therapy demonstrate substantially elevated mortality rates, even patients with milder renal dysfunction not requiring RRT show

decreased survival and worse outcomes compared to those without postoperative AKI ***(Conlon et al., 1999)***.

Although it may be intuitive that morbidity will increase with severe renal dysfunction, it is less obvious that a modest rise in creatinine can negatively affect quality of life and life expectancy ***(Lassnigg et al., 2008).***

The incidence of post-cardiac surgery AKI differs according to type of procedure. Typical CABG has lowest incidence of AKI (approximately 2.5%) and AKI-D (approximately 1%), followed by valvular surgery with incidence of 2.8% and 1.7%, respectively. The highest risk is observed in patients who undergo combined CABG + valvular surgery with incidence of AKI of 4.6% and AKI-D of 3.3% respectively (***Grayson et al., 2003).***

Post-surgical AKI not only lead to increase in short-term mortality, but it also lead to increase in long-term mortality ***Lafrance et al., 2010).***Loef et al found that patients who had post-surgical AKI (25% or greater rise in serum creatinine), the hazard ratio for death was 1.63, 100 months after discharge ***(Loef et al., 2005)*** this increase in mortality was unrelated to the recovery of renal function after surgery.

In another study, ***Lok et al*** showed that patients who sustained AKI post-surgery had relative risk of death of 4.6 at 1 year compared to patients without AKI ***(Lok et al., 2004).***

Lafrance et al found that patients with AKI had 41% increased risk of mortality as compared to patients without AKI after a mean follow-up of 2.3 years. This cohort had various other patients in addition to post-cardiac surgery AKI. The increase in mortality after recovery of renal function has been explained by phenomenon of loss of renal reserve. According to this hypothesis, that although serum creatinine returns to normal after AKI, but the renal reserve in these patients is impaired, and combined with ongoing progressive damage caused by rarefaction of peritubular capillaries results in adverse outcomes associated with AKI ***(Lafrance et al., 2010).***

In addition to increasing mortality, AKI prolongs ICU stay and increases the proportion of patients discharged to a nursing care facility. This data suggests that the illeffects of AKI are not simply a sign of sicker patients with other comorbid conditions, rather AKI is an independent predictor of morbidity and mortality following cardiacsurgery. As a result, all efforts must be made to identify patients at risk for AKI, focusing on prevention of renal dysfunction rather than simply treating it once the injury has occurred ***(Moss et al., 2012).***

Pathophysiology

There is very little data about mechanism of kidney injury in patients associated with cardiac surgery. The mechanism is considered same as in other causes of ischemic ATN, i.e. initially there is afferent arteriolar constriction and reduction in blood flow leading to decrease in filtration and GFR and later on cellular ATP depletion and oxidative injury ***(Conger, 2001).***

Studies in post-ischemic acute renal failure (ARF) after cardiac surgery has revealed that some 40–50% of the filtrate is lost by tubular feedback, indicating that intratubular obstruction as an important event in the course of AKI. Clinically the pathogenesis of AKI associated with CPB can be divided into pre-operative, post-operative and intraoperative events ***(Bansal et al., 2012).***

Pre-operative events

Patients who are undergoing cardiac surgery are already at risk for development of AKI because of various predisposing conditions like low EF, valvular dysfunction, which reduces the renal perfusion ***(Karkouti et al., 2009)***

In addition, these patients usually receive diuretics, which reduce intravascular volume and renal blood flow, predisposing them to AKI. Many of these patients are also on ACEI/ARBs, NSAID, which impairs the renal autoregulation ***(Arora et al., 2008).***

Some patients might be in cardiogenic shock and on intra-aortic balloon pump, which is a strong risk factor for development of AKI ***(Tuttle et al., 2003).***

Episodes of pre-operative hypotension may lead to sublethal endothelial injury, which impairs the ability of endothelium to secrete vasodilatory substances like nitric oxide and increases the secretion of vasoconstrictors like endothelin, catecholamine and angiotensin II, leading to further ischemia and tubular injury ***(Sutton et al., 2002).*** Inflammatory mediators are found to be elevated in many of these patients. Intravenous contrast in pre-operative period also predisposes for AKI.

Intraoperative events

Intraoperative period is a critical time as patients are exposed to anesthesia and CPB. During CPB the heart lung machine is used to provide blood to various tissues and organs during surgery. The goal is to maintain tissue perfusion at an optimal level to prevent ischemic injury to various organs and post-operative complications ***(Murphy et al., 2009).***

Three things are important to maintain adequate perfusion during bypass. These are mean arterial blood pressure (MAP), blood flow rates and hemodilution. Imbalance of these can lead to serious consequences.

A) Mean arterial blood pressure

The optimal blood pressure during CPB is not defined. The rationale behind keeping low pressure (MAP 50–60 mmHg) is to keep injury to blood elements to minimum and reduction in non-coronary blood flow to heart. MAP of 50 mmHg is required to maintain cerebral blood flow ***(Murphy et al., 2009).***

However, other data suggest that higher MAP > 70 mmHg is better, as sometimes there is impaired autoregulation and low pressure is not sufficient to maintain perfusion in vital organs. There is insufficient data to make any specific recommendation regarding low or high perfusion pressure for prevention of complications including AKI. However, in certain situations, high perfusion pressure is required to maintain cerebral perfusion, e.g. hypertensive, old patients, patients with severe atherosclerotic disease or history of previous cerebrovascular disease ***(Gold et al., 1995).***

B) Systemic bypass flow rates

The adequate pump flow rates are required to maintain adequate tissue perfusion during CPB. There is no consensus on any fixed flow rates, however mostly flow rates of 2.2–2.5 L/min/m² are kept as it approximates the normal cardiac index of normothermic anesthetized patients.

However, many centers advocates lower flow rates up to 1.2 L/min/m² as lower blood blow is associated with less chances of hypertension and reduced warming of myocardium via non-coronary collaterals (***Ranucci et al., 2005).***

C) Hemodilution

Hemodilution is an inevitable consequence of bypass because of priming. There are conflicting reports about what level of hemodilution is safe during CPB. Some hemodilution is required to keep blood viscosity lower as to improve microcirculation, reduced risk of hypertension during higher bypass flow sand reduction in requirement of transfusion ***(Murphy et al., 2009).***

However, some studies have shown that reducing hematocrit below 23%–24% results in more adverse events including increased incidence of AKI ***(Karkouti et al., 2005).***

The oxygen delivery (DO2) to tissues is reduced if hematocrit is very low. On the other hand, blood transfusion during surgery increase the chances of perioperative inflammation and increased morbidity and mortality ***(Kuduvalli et al., 2005).***

Pulsatile perfusion

With the availability of pulsatile perfusion, it is used in most patients with CPB. There is some evidence of its benefit in reducing renal and neurological damage in patients on CPB ***(Ji, 2006).***

Inflammation

CPB is thought to specifically activate the inflammatory response via activation of the immune system following exposure of blood to the foreign surfaces of the CPB circuit, ischemic perfusion injury to the end organs, and endotoxemia ***(Laffey et al., 2002).***

The inflammatory response after cardiac surgery can also be activated non-specifically by surgical trauma, blood loss or transfusion, and hypothermia. The off pump coronary artery bypass (OPCAB) techniques by avoidance of aortic cross clamping and CPB, may decrease the inflammatory response and improve post-operative organ function and patient

outcome, particularly in high-risk patients. Available evidence from a large number of prospective randomized controlled trials (RCTs) suggests that OPCAB reduces the elaboration of key mediators of the systemic inflammatory response ***(Raja et al., 2004).***

Minimally invasive cardiac surgical technique is another approach to reduce complications ***(Gu et al., 1998).***

The surgical incision may affect the inflammatory response generated, with reduced complement activation following a limited anterolateral thoracotomy compared to a median sternotomy, although this is disputed ***(Hamano et al., 2001).***

Leukocytes play a central role in the inflammatory response to cardiac surgery. Leukocyte depletion during cardiac surgery, by means of leukocyte-specific filters, decreases circulating leukocyte and platelet concentrations, and attenuates indices of inflammation and oxidative stress ***(Gu et al., 1999).***

So, inflammation during or after cardiac surgery plays an important role in injury to various organs. Although there is little data about renal involvement but kidney can also be affected as other organs. Therefore reducing inflammation might be protective to development of AKI as well.