

**PREVALENCE AND RISK FACTORS OF ACUTE RENAL FAILURE AFTER CARDIAC SURGERY**

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**ABSTRACT**

Postoperative renal dysfunction is a serious complication of cardiac Surgery under cardiopulmonary bypass. Even a minor change in serum creatinine are related to an increase morbidity and mortality. A prospective observational study was conducted over a period of eight months from September 2011 to April 2012 including 66 patients. The analysis of the results according to the Software Epi Info 6 allowed to define the main risk factors and outcome of kidney failure. Studies have shown that postoperative renal function deterioration in cardiovascular surgery patients increases in-hospital mortality and adversely affects long-term survival. However, our results do not support the other studies resuming the risk factors of acute renal failure in cardiac surgery because of limited sample based on.

**KEYWORDS:** Kidney failure, cardiac surgery, risk factors.

**INTRODUCTION**

The development of acute kidney injury after cardiovascular surgery has been well recognized in the past,<sup>[1]</sup> and is implicated as a contributing factor in the elevated mortality and poor outcomes of these patients.<sup>[2,3]</sup>

The definition of acute kidney failure after cardiovascular surgery differs in published studies; some describe it as a percent of increment from baseline creatinine, while others call it a doubling of the preoperative creatinine.

However, this syndrome is characterized by a deterioration of kidney function over a period of hours or days following surgery, with symptoms including, paralleling elevations of serum blood urea nitrogen and creatinine, and the development of serious electrolyte and acid-base disorders.

Recently, the Kidney Disease Improving Global Outcomes (KDIGO) developed a staging classification of acute kidney injury that includes three stages based on elevation of serum creatinine from baseline and urinary output.

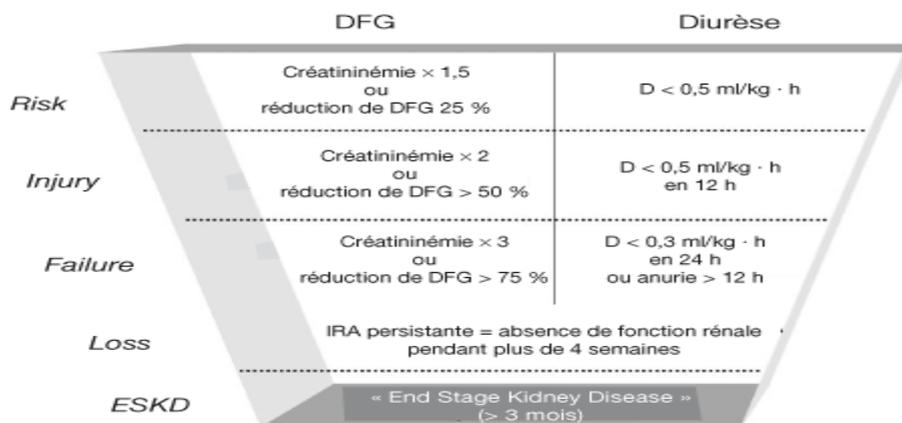


Figure 1: The KDIGO staging classification of acute kidney injury.

Postoperative renal dysfunction is a frequent and serious complication of cardiac surgery under extra corporal circulation associated to significant morbidity despite advances in anesthetic and surgical techniques.

Many studies have been carried out to assess incidence, risk factors, pathophysiological mechanisms as well as repercussions on the medium- and long-term prognosis.

Our challenges in this work is to study risk factors of renal failure and its short- and medium-term outcome.

## MATERIAL AND METHODS

This exploratory and descriptive study was conducted in the operating room of cardiac surgery and intensive care unit of Ibn Rochd hospital center in Casablanca over a period of eight months (September 2011 to April 2012).

For each patient, we have analyzed:

- Demographic data (age, gender, weight, size and body mass index);
- Medical and surgical history of patients;
- Current treatments;
- Per operative data:
  - Surgery data: reason and duration of surgery
  - Management of extra-corporeal circulation (ECC) and myocardial protection: we have noted the duration of ECC, aortic clamping and assistance.
- Per operative complications:
  - Hemodynamic instability, type and dose of catecholamines used.
  - Significant bleeding and intraoperative transfusion.
  - Arrhythmias, conduction and repolarization disorders.
- Post-operative data:
  - Length of stay in intensive care;
  - Complications: cardiac, respiratory, renal, hemorrhagic, infection, surgical resumption and mortality.
  - Biological results: The blood creatinine analysis was performed on admission, after the intervention and every day for the 5 post-operative days.

We have noted the peak of postoperative creatinine, the percentage of variation in creatinemia compared to the preoperative value, diuresis, the onset of oliguria and / or anuria and the need to use diuretics or dialysis.

Postoperative renal dysfunction was defined as an increase in serum creatinemia of more than 25% compared to preoperative result and the RIFLE criteria were used to classify this complication (Figure 1).

## Statistical methods

Statistical analysis was performed using EPI INFO 6 software. The results are expressed as mean standard deviation from the mean. Univariate analysis was performed to analyze risk factors of kidney failure.

Chi-2 test was used to compare categorical variables. For quantitative variables we have chosen the Student test. A *p* value less than 0.05 were considered significant.

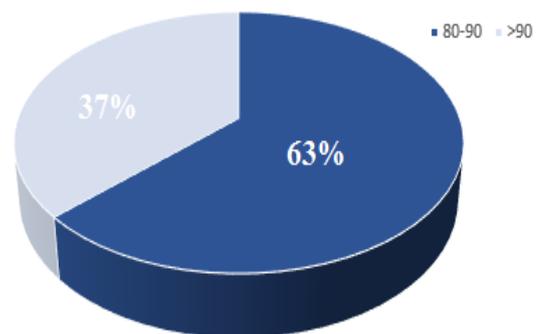
## RESULTS

Over a period of eight months, 448 patients were hospitalized in the cardiovascular surgery department of Ibn Rochd University Hospital in Casablanca.

Eighty-four patients aged 18 or over were operated on for scheduled cardiac surgery (18.75% of hospitalizations).

Eighteen patients were excluded from the study: 12 with a preoperative renal failure and 6 died within the first 24 hours.

The mean pre-operative creatinine level was  $67.18 \mu\text{mol} / \text{l} \pm 19.8$  with an average creatinine clearance of  $99.6 \text{ ml} / \text{min} \pm 19.2$ .



**Figure 2: preoperative creatinine clearance.**

**Twenty-five patients have developed a renal failure after cardiac surgery with an incidence of 37.87%.**

**Table 1: Renal failure according to the type of surgery.**

	General population (N=66)	Coronary surgery (n=8)	Valve Surgery (n=58)	P
<b>Renal failure</b>	25 (37,87%)	3 (37,50%)	22 (37,93%)	0,98
<b>Classe I R</b>	8 (12,11%)	2 (25%)	6 (10,34%)	0,24
<b>Classe II I</b>	11 (16,67%)	1(12,5%)	10 (17,25%)	0,76
<b>Classe III F</b>	6 (9,09%)	0	6 (10,34%)	0,36
<b>Hemodialysis</b>	2 (3,03%)	0	2 (3,44%)	0,59

Age, gender and mean body index were not associated with the occurrence of kidney dysfunction. In contrast,

the Euro score was significantly higher in patients with acute postoperative renal failure.

**Table 2: Characteristics of the population and their associations with the renal failure.**

	Without kidney dysfunction (n = 41)	With kidney dysfunction (n = 25)	P
<b>Age</b>	46,6 ± 13,73	45,04 ± 9,14	0,45
<b>Sex M/F</b>	21/20	15/10	0,5
<b>BMI</b>	21,68 ± 2,81	22,17 ± 3,37	0,34
<b>25 &lt; BMI &lt; 30</b>	5 (12,19%)	5 (20%)	0,39
<b>Euro score</b>	4,13 ± 6,32	8,12± 4,52	<b>0,01</b>

Co-morbidities were not significantly associated with the occurrence of post-operative renal failure.

**Table 3: Co-morbidities and their associations with the post-operative renal failure.**

	Without renal dysfunction (n = 41)	With renal dysfunction (n = 25)	P
<b>High blood pressure</b>	3 (7,31%)	4 (16%)	0,26
<b>Diabetes</b>	3 (7,31%)	2 (8%)	0,91
<b>Left ventricle ejection fraction &lt; 50%</b>	4 (9,75 %)	6 (24%)	0,11
<b>Recent myocardial infarction</b>	2 (4, 87%)	3 (12%)	0,28

The type of cardiac surgery in our series as well as the mean durations of surgery, extra corporal circulation and

aortic clamping had no impact on the incidence of kidney injury.

**Table 4: Incidence of renal failure depending on the type and conditions of surgery.**

	Without renal dysfunction (n = 41)	With renal dysfunction (n = 25)	P
Coronary artery bypass surgery	5 (12,9%)	3 (12%)	0,98
Mitral valve replacement	18 (43,9%)	14 (56%)	0,34
Aortic valve replacement	6 (14,63%)	5 (20%)	0,57
Double mitro-aortic valve replacement	12 (29,26%)	3 (12%)	0,1
Mean surgery time	149,39 ± 68,52	166,6 ± 108,58	0,12
Mean extra-corporal circulation duration	107,02 ± 60,29	115,48 ± 93,32	0,18
Mean aortic clamping time	80,14 ± 53,12	81,92 ± 52,30	0,32
Assistance duration	1,80 ± 4,27	1,96 ± 3,07	0,65
Use of vasoactive drugs	21 (51,21)	17 (68%)	0,18

Postoperative bleeding, infection, revision surgery, and heart rhythm disorders were not significantly associated with the occurrence of acute kidney failure.

**Table 5: Renal failure and postoperative parameters.**

	Without renal dysfunction (n = 41)	With renal dysfunction (n = 25)	P
Post operative bleeding	13 (31,7%)	13 (52%)	0,1
Postoperative infection	5 (12%)	4 (16%)	0,66
Surgical recovery	0	2 (8%)	0,06
Postoperative atrial fibrillation	5 (12 %)	4 (16%)	0,66

The mean length of stay in the intensive care unit in patients with acute kidney failure was  $2.72 \pm 0.84$  vs

$2.51 \pm 0.98$  in patients without renal dysfunction with an increased risk of short-term mortality.

**Table 6: impact of renal failure after heart surgery.**

	Without renal dysfunction (n = 41)	With renal Dysfunction (n = 25)	P
Ventilation time	14,24 ± 21,23	18,44 ± 21,73	0,44
Duration of stay	2,51 ± 0,98	2,72 ± 0,84	0,32
Severe ventricle dysfunction	1 (2,44%)	2 (8%)	0,29
Mortality	1 (2,44%)	5 (20%)	<b>0,01</b>

## DISCUSSION

More than 30 different definitions for acute renal failure have been used in the past. The new diagnostic scales use variations in serum creatinine values and urinary output to define the presence and severity of kidney failure and have been validated by numerous studies.<sup>[4]</sup>

In 2004, the risk-injury-failure-loss-end-stage kidney disease (RIFLE) definition by the Acute Dialysis Quality Initiative Group was introduced.<sup>[5]</sup> The dysfunction criteria were based on a relative rise in creatinine serum, the absolute level of urine output, or both.

In 2007, the Acute Kidney Injury Network (AKIN) proposed a modification of the RIFLE classification.<sup>[6-7]</sup> It occurred when the impact of small elevations of creatinine on mortality ( $>0.3$  mg/dL [ $>26$  mmol/L]) was reported.

This scale defines acute kidney injury as an abrupt reduction (within 48 hours) of renal function with an absolute increase in creatinine value ( $\geq 0.3$  mg/dL [ $\geq 26.4$  mmol/L] or  $\geq 50\%$  [1.5 times compared to baseline]), or a reduction in urine output  $<0.5$  mL/kg/hour for  $>6$  consecutive hours. The application of AKIN and RIFLE criteria following cardiac surgery without correcting for creatinine changes owing to fluid balance leads to acute kidney injury under-diagnosis.<sup>[7]</sup>

The Kidney Disease: Improving Global Outcomes (KDIGO) definition of acute kidney injury was associated with a higher sensitivity to diagnose acute kidney injury and to predict in-hospital mortality (8), compared to RIFLE or AKIN.<sup>[9]</sup>

The KDIGO definition, which is a combination of the RIFLE and AKIN classification, is the most commonly used definition. However, the main limitation of these definitions is that they rely on creatinine, which is known to be affected by factors not related to glomerular filtration, including age, sex, race, body surface area, diet, diabetes, liver disease, different drugs and laboratory analytical methods.<sup>[10]</sup>

In our study, we have adopted the RIFLE classification based on clinical and biological criteria.

Acute renal failure, depending on the specific definition, occurs in up to 30% of all patients who undergo cardiac surgery. It requires dialysis in approximately 1%.<sup>[11,12]</sup>

Conlon *et al.*<sup>[11]</sup> described a cohort of 2843 patients who underwent cardiopulmonary bypass over a period of 2 years. Acute renal failure (defined as a rise in serum creatinine  $>1$  mg/dl above baseline) occurred in 7.9% of patients.

Other studies that used a definition of acute renal failure as a 50% or greater rise in serum creatinine from baseline demonstrated a rate as high as 30%.<sup>[12,13]</sup>

Chertow *et al.*<sup>[12]</sup> analyzed 42,773 patients who underwent cardiopulmonary bypass and found an incidence of acute renal failure of 1.1%. The incidence is dependent on the particular type of cardiopulmonary bypass surgery. Typical coronary artery bypass grafting has the lowest incidence of acute renal failure (approximately 2.5%), followed by valvular surgery with an incidence of 2.8%.<sup>[14,15]</sup> The highest risk group includes combined coronary artery bypass grafting/valvular surgery,<sup>[14,15]</sup>

In our study, kidney failure after cardiac surgery occurs in 25 patients corresponding to an incidence of 37, 87% following the RIFLE classification.

In general, it is agreed that pre-existing chronic kidney disease, advanced age, diabetes mellitus, congestive heart failure, generalized atherosclerosis, cardiovascular collapse, and dye exposure immediately followed by surgery are all risk factors for acute kidney injury after cardiovascular surgery and warrant the need for preoperative nephrology consultation<sup>[16,17]</sup>

Female gender appears to have an increased incidence of AKI after open-heart surgery.<sup>[18]</sup> Lower serum ferritin levels ( $<130$  mg/dL) appear to be associated with acute kidney injury due to the inability to bind free iron (a potent oxidative stress inducer) generated during cardiopulmonary bypass-induced hemolysis.<sup>[19]</sup> These factors had no impact on the frequency of renal failure after surgery in our series

Acute kidney injury carries a poor prognosis. Despite advances in bypass techniques, intensive care, and delivery of hemodialysis, mortality and morbidity associated with renal failure have not markedly changed in the last decade.

Studies have shown that postoperative renal function deterioration in cardiovascular surgery patients increases in-hospital mortality and adversely affects long-term survival.

Chertow *et al.*<sup>[12]</sup> in a multivariate analysis that adjusted for comorbid factors identified the occurrence of acute renal failure as an independent determinant of the risk for death with an odds ratio of 7.9. It is interesting that even small rises in serum creatinine are associated with significant mortality.

Lassnigg *et al.* demonstrated that the mortality of patients who developed a 0 to 0.5 mg/dl and  $>0.5$ -mg/dl rise in serum creatinine was 2.77 and 18.64 fold higher, respectively, than patients without a change in serum creatinine.

These results are qualitatively similar to studies by Thakar *et al.*<sup>[20]</sup> in which 31,677 patients who underwent cardiac surgery were analyzed. Mortality was 5.9% ( $P < 0.0001$ ) when glomerular filtration rate declined 30% or

more but did not require dialysis and 0.4% ( $P < 0.001$ ) in patient with  $<30\%$  decline in glomerular filtration rate.

In our study, renal failure after cardiac surgery leads to a marked increase in short-term mortality. (2.44% vs 20% with kidney failure corresponding to a  $p$  value of 0,01).

The link between the development of acute renal failure and mortality likely involves numerous factors, including those directly related to hemodialysis; immune dysregulation associated with renal failure; platelet dysfunction; and other, less defined associations.

Registry data from Liano *et al.*<sup>[22]</sup> demonstrated that in patients with acute renal failure, infections were the cause of death in 40%. In patients who underwent cardiopulmonary bypass, Thakar *et al.*<sup>[23]</sup> also demonstrated a high risk for infections.

## CONCLUSION

Acute kidney failure continues to be a common and important complication of cardiac surgery and it is associated with increased mortality, complications, and length of hospital stay.

The pathogenesis of kidney injury after cardiac surgery is complex and involves hemodynamic, inflammatory, and other mechanisms that interact at a cellular level. At present, no pharmacologic interventions have demonstrated conclusively efficacy in the prevention of renal dysfunction after cardiac surgery.

Prolonged aortic cross-clamping, intravascular hemolysis or contrast dye exposure should be avoided.

The results of our study could not follow those of the literature concerning the risk factors for occurrence of post-operative renal dysfunction in cardiac surgery since the number of our patients was reduced.

But it has been demonstrated that the incidence of this dysfunction is significant after cardiac surgery under extra corporal circulation and that it is a predictor of mortality.

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