

# Usefulness of STS-Renal and ACEF scores as predictive models for acute kidney injury after cardiac surgery in UMAE Cardiology Hospital-CMN IMSS Mexico

Nalleli Adriana Pérez-Rubio<sup>1</sup>, Alberto Ramírez Castañeda<sup>1</sup>, Martín Rosas-Peralta<sup>2</sup>, Gabriela Borrayo-Sánchez<sup>2</sup>, Jaime Salgado Vázquez<sup>1</sup>, Carolina Álvarez Moreno<sup>1</sup>, Lucelli Yañes Gutierrez<sup>3</sup>, Horacio Márquez González<sup>3</sup>, Luis Zúñiga-Alanís<sup>1</sup>, and Carlos Riera-Kinkel<sup>1\*</sup>

<sup>1</sup> Division of Cardiothoracic surgery, Cardiology Hospital XXI century, Instituto Mexicano Del Seguro Social, Mexico, CDMX, Mexico

<sup>2</sup> "A todo corazón-Código Infarto" program, National Medical Center XXI Century, IMSS, CDMX, México

<sup>3</sup> Congenital Heart Disease department, Cardiology Hospital XXI century, Instituto Mexicano Del Seguro Social, Mexico, CDMX, Mexico

Received: November 21, 2018; Accepted: December 03, 2018; Published: December 05, 2018

\*Corresponding author: Carlos Riera Kinkel, Head of Cardiac Surgery Division, Hospital de Cardiología, Centro Medico Nacional Siglo XXI, IMSS, Cuauhtémoc 330, Col Doctors, Deleg Cuauhtémoc, CP 06720, México, D F, México; Phone: (+52) 56276927; E-mail id: rierac7@gmail.com

## Abstract

**Objective:** To Evaluate the STS-renal and ACEF scores which are short-Term Risk Calculators for developing renal failure in patients after cardiac surgery at a unique 3rd level Medical Center in Mexico City.

**Methods:** We conducted a retrospective study, consecutive patients between August 1st 2015 and July 31st 2016 were included. We applied the STS-renal and ACEF scores as predictive methods for acute kidney injury (AKI) after cardiac surgery with cardiopulmonary bypass.

**Results:** They were 525 patients who met the inclusion criteria. Arose kidney injury in 135 (25.5%) of the patients. We found that age, time of aortic clamping, pre-operative creatinine, hypertension and complexity of the procedure level are the principal risk factors for kidney injury, and as a consequence, we observed a correlation among the severity of kidney injury and increases of the hospital stay and mortality. 26(5%) patients died, six of them directly attributable to kidney injury.

**Conclusions:** We assessed two risk scores to predict early kidney injury after cardiac surgery. We found as the most applicable to our population the STS-kidney short term risk calculator. The use of this kind of risk calculators should be applied routinely in México.

**Key words:** Cardiac Surgery; Kidney Injury; ACEF; STS

## Introduction

Postoperative kidney injury after Cardiac surgery is a complication which increases mortality and hospital stay. American Society of thoracic surgery defines acute kidney injury after surgery as the increase of serum creatinine 2 mg/dL or twice the preoperative value, or new requirement of haemodialysis. [1] Several short term risk calculators to predict kidney injury after cardiac surgery have been developed; however, they are focused on the prediction of dialysis requirement and/or severe kidney

injury. Nevertheless, the prediction of mild and moderate kidney injury is also important. Birnie et al., [2] conducted an analysis of about 30,000 patients undergoing cardiac surgery in three hospitals in the United Kingdom, and they developing a model for short risk prediction of all stages of kidney injury, and it was useful for slight and severe types of kidney injury.

Most commonly used risk models include the Score of the American Society of Thoracic Surgeons (STS), published in 2008, and the Age, Creatinine and Ejection Fraction (ACEF) score, published at 2009. For those patients undergoing bypass surgery the STS score has been reported more accurately to predict the risk of post-surgical dialysis requirement, however the validity of the method for predicting slight kidney injury or requirement for dialysis is not weak. [3] It is assumed a greater accuracy of the ACEF score for the prediction of kidney injury with minimum requirements for replacement therapy.

The predictive models in cardiac surgery have been developed from certain population groups, in a defined period of time, and taking into account certain variables selected previously. Therefore, there is doubt of their applicability to different population groups or another point in time. Kidney injury is a complication of cardiac surgery that becomes present in ~30% of patients and as a consequence it increases either mortality or hospital stay, and as a result increased costs for the institution.

Detection of kidney injury in its early stages, yet more identifies patients at high risk, is important to provide correctly early treatment and therefore, decrease mortality and hospital stay. For this reason, it is essential to establish a predictive method applicable to our population.

Considering the above, it was decided to conduct this study to validate predictive methods already established, such as STS-kidney and the ACEF score for the presentation of acute kidney injury in our population of patients undergoing cardiac surgery.

## Primary end point

To Validate the score STS-kidney and ACEF in post-operated patients of valvular heart surgery and coronary artery bypass under cardiopulmonary bypass in Mexico City at a 3rd level Hospital of Cardiology-CMN XXI century, IMSS

## Secondary Aims

- 1) To determine which predictive short term risk calculators is more sensitive for post-surgical kidney injury
- 2) to assess other risk factors already known for kidney injury such as cardiopulmonary bypass time, time of aortic clamping, smoking, sex, weight, hypertension, diabetes mellitus, peripheral vascular disease, dyslipidemia, level of hematocrit in our population
- 3) To determine mortality associated with kidney lesion in the population studied
- 4) To determine length of hospital stay both hospitalization and therapy post-surgical due to kidney injury.

## Patients and Methods

We include consecutive patients undergoing cardiac bypass surgery and valvular surgery under cardiopulmonary bypass from a 3rd level Cardiology Hospital at National Medical Center XXI-Century, IMSS, of Mexico City. All patients had age > 18 years old, both genders and with a full medical record including all variables to evaluate the predictive short term risk calculators (STS and ACEF).

## Statistical analysis

Continuous variables are described as mean and standard deviation or medium and inter quartile range according to their distribution. The qualitative variables are expressed in number, frequency or percentage. The comparison between groups for continuous variables was with student's t or U-Mann Whitney test, as appropriate. Comparison of qualitative variables was performed with the chi square test. Regression and correlation as well as matching models were generated for the predictive models in study. We used the SPSS statistical package version 22.0 software. A value of p less than 0.05 was considered statistically significant.

## Results

548 consecutive patients were selected for this study, we excluded those cases with incomplete record (n=23) and eight with kidney injury prior to the surgery, for a total loss of 31 (5.6%) cases, resulting in 525 patients undergoing surgery cardiovascular that they fulfilled the inclusion criteria. 308 (58.6%) of them were male. The mean age observed was 62 ( $\pm$  11.4 years). The case history is presented in the table 1.

Of the surgeries performed 303 (57.7%) were valve surgery, 162 (30.8%) Coronary Artery Bypass Grafting (CABG) surgery and 60 (11.5%) valve surgery plus bypass surgery. The most frequently performed surgery was the aortic valve surgery at 150 (28.6%) patients, followed by the operation of two or more valves with 91(17.3%), mitral valve with 56 (10.7%) and tricuspid with six (1.1%). Three or more vessels myocardial revascularization

**Table 1:** General characteristics by gender of the total study population

Variable	Gender		Total	%
	Men	Woman		
<b>Body Mass Index</b>				
Under weight = <18.5	2	0	2	0.4
Normal = 18.5–24.9	110	62	172	32.8
Overweight = 25–29.9	146	102	248	47.2
Obesity = 30 or greater	50	53	103	19.6
<b>Type of Surgery</b>				
Elective	133	168	301	57.4
Urgent	134	30	164	31.2
Emergency	41	19	60	11.4
<b>Diabetes mellitus</b>				
Yes	114	59	173	33
No	194	158	352	67
<b>Hypertension</b>				
Yes	184	132	316	60
No	124	85	209	40
<b>Smoking</b>				
Yes	141	77	218	41.5
No	167	140	307	58.5
<b>Dyslipidemia</b>				
Yes	127	60	187	35.6
No	181	157	338	64.4
<b>Prior Myocardial Infarction</b>				
Yes	42	7	49	9.4
No	266	210	476	90.6
<b>Hemodynamic Profile</b>				
Uncompensated	7	9	16	3
Compensated	301	208	509	97
<b>COPD</b>				
Yes	6	14	20	3.8
No	302	203	505	96.2
<b>Cardiac Arrhythmia</b>				
Yes	28	56	84	16
No	280	161	441	84
<b>COPD : chronic obstructive pulmonary disease</b>				

was performed at 154 (29.3%) and two vessels in eight (1.5%). The average time of cardiopulmonary bypass was 98.6 ( $\pm$ 38. 4) minutes and aortic clamping time was 69.3( $\pm$ 28.3) minutes

Distribution of Study Population by the Presence of Kidney Injury

From the analyzed patients (n=525), 390 (74.5%) had no kidney injury and 135 (25.5%) with some degree of kidney injury according to the classification of AKIN, 100 (19%) of them with stage 1, 20 (3.8%) with stage 2, and 15 (2.8%) with stage 3. We developed bivariate crosses between acute kidney injury and other modifying variables such as: history of diabetes mellitus, index of body mass, chronic obstructive pulmonary disease, hypertension, cardiac arrhythmias, dyslipidemia, blood trans-operative transfusion, smoking, preoperative infarction, hemodynamic status, type of surgery procedure performed, cardiopulmonary bypass time and aortic clamping time.

You can observe that age, the presence of high blood pressure and the type of procedure have statistical significance in the

presentation of kidney injury in terms of the background (Table 2). Was also performed Chi2 for the analysis of qualitative variables finding a stochastic significance in preoperative creatinine ( $p < 0.001$ ) and aortic clamp time ( $p < 0.001$ ) for the presence of kidney injury.

The analysis of hospital stay in post-surgical therapy area shown increasing days of stay as more increased the degree of kidney injury ( $p < 0.001$ ), having as average 5.7 days for post-operated total evaluated patients.

In terms of mortality 26 (5%) deaths were recorded as is shown in table 3. From the total number of reported deaths six were due to kidney injury in a direct way, eight to septic shock and 12 due to cardiogenic shock.

**Table 2:** AKIN Kidney injury level by variables of study

Variables	Without Kidney Injury (n=390)	ARI			TOTAL (525)	p Value
		AKIN 1 (n=100)	AKIN 2 (n=20)	AKIN 3 (n=15)		
<b>Age, mean Gender</b>	61.26 ± 10.5	65.55± 4.1	67±13.1	68±12.7		=0.001
Men	225	61	14	10	310	=0.27
Female	165	39	6	5	215	
<b>BMI</b>						
<25 Kg/m2	2	0	0	0	2	=0.61
25-29 kg/m2	131	26	6	9	172	
Overweight	179	51	13	5	248	
Obesity	78	23	1	1	103	
<b>Diabetes mellitus</b>						
Yes	125	38	4	6	173	=0.375
No	265	62	16	9	352	
<b>Hypertension</b>						
Yes	226	71	9	10	316	=0.051
No	164	29	11	5	209	
<b>Smoking</b>						
Yes	157	41	11	9	218	= 0.282
No	233	59	9	6	307	
<b>Dyslipidemia</b>						
Yes	142	36	5	4	187	=0.651
No	248	64	15	11	338	
<b>Prior Myocardial Infarction</b>						
Yes	34	10	3	2	49	=0.742
No	356	90	17	13	476	
<b>Hemodynamic Profile</b>						
Unstable	8	2	0	6	16	= <0.001
Stable	381	98	20	9	508	
<b>COPD</b>						

Yes	14	6	0	0	20	=0.436
No	376	94	20	15	505	
<b>Arrhythmia</b>						
Yes	60	20	2	2	84	=0.596
No	330	80	18	13	441	
<b>Type of Surgery</b>						
Elective	240	49	7	5	301	=0.316
Urgent	133	20	6	5	164	
Emergency	17	31	7	5	60	
<b>Procedure</b>						
Valvular	227	60	15	1	303	= <0.001
Coronary artery bypass grafting (CABG)	130	22	5	5	162	
Valvular + CABG	40	18	0	4	60	
ARI: acute renal injury; * t test, U-Mann Whitney, ANOVA or Chi Square as appropriate						

**Table 3:** Kidney injury and mortality

	Kidney Injury level				Total Number	%
	Without	ARI 1	ARI 2	ARI 3		
<b>Die</b>	12	5	4	5	26	5
<b>Alive</b>	378	95	16	10	499	95
<b>Total</b>	390	100	20	15	525	100

**Table 4:** Staging of acute kidney injury

RIFLE	AKIN	Creatinine	Urinary Output
<b>R-Risk</b>	1	Up 1-2 times from base value	<0.5 mL/Kg/h / 6 h
<b>I-Injury</b>	2	Elevation 2-3 times form basal value	<0.5 mL/Kg/h / 12 h
<b>F-Failure</b>	3	Elevation > 3 times, creatinine > 4 mg/dL, with drastic up > 0.5 mg/dL or, therapy replacement required.	<0.3 mL/Kg/h/24h o anury by 12 hrs
<b>L-Lost</b>		kidney persistent failure < 4 weeks	
<b>E-End kidney</b>		Failure kidney failure > 3 months	
<b>kidney terminal</b>			

## Reliability Test

To assess the internal consistency of the proposed scores, applied a Cronbach alpha test, obtaining a statistician of 0.125 for two items, which is not reliable, which means that, together, STS-kidney and ACEF not present one enough internal consistency to be able to be used in conjunction.

A logistic regression model diagnosis test is applied to each score to evaluate its predictive capacity with kidney injury. Observed that the STS shown a better diagnosis for kidney injury and every one of its degrees in comparison with the ACEF shown no statistically significant differences.

## Discussion

Secondary kidney injury after cardiac surgery ranges between 5-30%, therefore it is considered that it is one of the most frequent complications after cardiac surgery, which increases both the duration of the hospital stay and mortality rate. In our hospital arose in 25% of cases largely in ARI stage 1.

The AKI, has been associated with important risk factors such as male sex in ratio of 2:1 on the female, diabetes mellitus and hypertension, other risk factors dependent on the procedure surgical and anesthetic are very important such as the duration of cardiopulmonary bypass and aortic clamping time, blood transfusion requirements and high doses of vasopressors. In our study the most important risk factors were age, hypertension,

aortic clamping time, creatinine levels pre-surgical and the complexity of the procedure and they acquire statistical significance.

Diagnosis of kidney injury is based on two basic although late criteria such as the elevation of plasmatic creatinine and decrease of the urinary output. In this study the approach most commonly used for diagnosis and classification of kidney injury was the plasmatic creatinine.

It is estimated that approximately 30% of patients undergoing cardiac surgery develop some degree of kidney injury [4] Global mortality cardiac surgery is around 0.9%, and increases up to 20% if the acute kidney injury is developed, and up to 60% when this AKI required a replacement therapy [5] In addition, it is known that increases up to 20% in the plasmatic concentration of creatinine in the postoperative period can result in a significant effect on the clinical evolution [6]

Many of the risk factors associated with kidney injury are not modifiable, such as age, gender, high blood pressure, diabetes mellitus, dyslipidemia and peripheral vascular disease. In the case of age for example, it is estimated that the glomerular filtrate decreases 1 mL/year old, which means that the number of nephrons of an elderly patient has decreased by 30% itself. Kidney failure appears more frequently in males with a 2:1 ratio, probably due to some vascular factor linked to sex, with a major condition of the arterial lights in men which predispose to poor response mechanisms. In the case of the chronic degenerative diseases such as diabetes mellitus and hypertension, kidney injury is related to the micro vessel disease, especially if the patient has more than 10 years with these alterations [7]

Other risk factors are dependent on the surgical and anesthetic procedure, including cardiopulmonary bypass time, aortic clamping time, ejection fraction, blood transfusion and require high doses of vasopressors [8, 9]

These factors modify kidney function, induced by cycles of ischemia and reperfusion, with increased oxidative damage and increasing systemic and kidney inflammation, all these mechanisms are involved in the development of kidney injury [10]

Various strategies have been created to decrease its occurrence such as management of intravenous fluids, extracorporeal circulation and techniques for hemodynamic stability. Pharmacological and non-pharmacological treatments have been developed without having the desired effectiveness. The diagnosis includes the taking of serum creatinine and urine output measurement. However, urine output is not as specific as the increase in serum creatinine, because it takes several days to up, which might slow the onset of treatment to kidney injury.

In addition, mechanisms associated with kidney injury include peri-operatoria ischemia, reperfusion injury, and haemolysis by cardiopulmonary bypass and its nephropathy by pigments, oxidative stress and inflammation [11]

Kidney perfusion is a complex mechanism. Around 20% of the cardiac output is directed to kidneys. Most of the blood is filtered by the glomerular crust; this derivation maintains the

concentration of electrolytes and water in the kidney Medulla that is required for resorption in the tubule and the collector system. The O<sub>2</sub> pressure at the spinal cord level is 10-20 mm Hg, which may be a protective mechanism to oxidative injury but it makes more susceptible to ischemia.

During cardiac surgery, various mechanisms can cause alteration in kidney perfusion. The cardiopulmonary bypass provides a non-pulsatile blood flow leading to an imbalance between cortical and medullary perfusion. Paradoxically, the increase in perfusion may precipitate ischemia, due to the increase in the consumption of oxygen by the increase of transport of solutes [12]

Aortic clamping increases the risk of athero-embolism toward the kidneys, and they exacerbate ischemia and induce inflammation [13] other factors such as the cascade of the Renin-angiotensin-aldosterone system and activation of the sympathetic nervous system may alter kidney oxygenation during surgery [14, 15]

The cardiopulmonary bypass circuit contains a pump, an Oxygenator, suction catheters and filters that damage red blood cells and increases plasma free hemoglobin [16] the free hemoglobin decreases the haptoglobin and injures the kidneys, increasing the production of radical free products, precipitating proteins in the collector system and inducing arteriolar vasoconstriction by elimination of nitric oxide. In addition free iron increases the toxic reaction of oxygen, particularly at kidney level [17, 18]

Various systems have been proposed to classify and staging acute kidney injury. The most recent classification of the AKIN has adapted to the previous criteria from the RIFLE, and it is based on the changes in serum creatinine and urinary output (table 4) [19]

Recently some proteins have been identified that are related with kidney damage. These markers of kidney function and kidney injury (NGL, KIM 1, IL-18, NAG and GST) (Cystatin C) offer many advantages over the taking of serum creatinine, since its increase is earlier and are more specific and sensitive for the detection of kidney injury, however it is still continue in validation due to low reproduction and access to the laboratories that process them [20]

It was further noted that as more severe is the kidney injury as more the risk of both direct and indirect mortality and length of hospital stay is developed, which raises the costs for the care. As for the internal validation of the risk scores, there is controversy about what is best for the timely prediction of kidney injury. This is secondary to the instruments used are applied to a given population, on the time required. In this study we found that the predictive capacity was better determinate by the short term risk calculator STS-kidney. A proper correlation was found in each of the degrees of severity, while the lowest was for AKIN 2.

## Conclusion

**According with our results we can conclude:**

1. Advanced age and the presence of hypertension are common entities that cannot be prevented and are directly related with the risk of AKI.

- Variables inherent in the procedure such as complexity of surgery and aortic clamp time, increases the risk of kidney injury.
- Preoperative creatinine is another variable with stochastic significance associated with the presentation of acute kidney injury.
- Kidney injury increases hospital stay in the post-surgical therapy.
- As greater severity of kidney injury is correlated with increases of mortality risk.
- The STS-kidney showed to be better for acute kidney injury prediction, than the ACEF score, after cardiac surgery.

## References

- Ho A M, Chan SK. Kidney dysfunction and CABG. *Curr Opin Pharmacol*. 2012;12(2):181-188.
- Birnie K, Verheyden V, Pagano D, Bhabra M, Tilling K, Sterne JA, Murphy GJ, et al. Predictive models for kidney disease: improving global outcomes (KDIGO) in acute kidney injury in UK cardiac surgery. *Crit Care*. 2014; 18(6):606. doi: 10.1186/s13054-014-0606-x
- Ranucci M, Castelvechio S, Menicanti L, Frigiola A, Pelissero G. Risk of assessing mortality risk in elective cardiac operations: age, creatinine, ejection fraction, and the law of parsimony. *Circulation*. 2009;119(24):3053-3061. doi: 10.1161/CIRCULATIONAHA.108.842393
- Karkouti K, Wijeyesundera DN, Yau TM, Callum JL, Chheng DC, Crowther M, Dupuis JY, et al. Acute Kidney injury after cardiac surgery: focus on modifiable risk factors. *Circulation*. 2009;119(4):495-502. doi: 10.1161/CIRCULATIONAHA.108.786913
- Weisberg AD, Weisber E, Wilson JM, Collard CD. Preoperative evaluation and preparation of the patient for cardiac surgery. *Anesthesiol Clin*. 2009;27(4):633-648.
- Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11(2):R31.
- Khan IH, Catto GRD, Edward N, MacLeod AM. Acute kidney failure: factors influencing nephrology prekidney and outcome. *QJM*. 1997;90:781-785.
- Wijeyesundera DN, Karkouti K, Beattie WS. Improving the identification of patients at risk of postoperative kidney failure after cardiac surgery. *Anesthesiology* 2006;104(1):65-72.
- Lopez-Delgado JC, Esteve F, Torrado H, Rodríguez-Castro D, Carrio ML, Farrero E y col, Javierre C, et al. Influence of acute kidney injury on short and long term outcomes in patients undergoing cardiac surgery: risk factors and prognostic value of a modified RIFLE classification. *Crit Care*. 2013;17(6):R293. doi: 10.1186/cc13159
- Guerrero AF, Camacho MJ, Sandoval NF, Umana JP, Obandoa CE, Carreño M. Factores asociados a insuficiencia kidney postoperatoria en cirugía de revascularización miocárdica. *Rev Colom Cardiol*. 2016;23(3):230-236.
- Gomez H, Ince C, De Backer D, Pickkers P, Payen D, Hotchkiss J, Kellum JA, et al. A unified theory of sepsis-induced acute kidney injury: inflammation, microcirculatory dysfunction, bioenergetics and the tubular cell adaptation to injury. *Shock*. 2014;41(1): 3-11. doi: 10.1097/SHK.0000000000000052
- O'Neal JB, Shaw AD, Billings FT. Acute kidney injury following cardiac surgery: current understanding and future directions. *Critical Care*. 2016;20:187-195.
- Granata A, Insalaco O. Atheroembolism kidney disease: diagnosis and etiologic factors. *Clin Ther*. 2012;163(4):313-322.
- Fuji T, Kurata H, Takaoaka M, Muraoka T, Fujisawa Y, Shokoji T, Nishiyama A, et al. The role of kidney sympathetic nervous system in the pathogenesis of ischemic acute kidney failure. *Eur J Pharmacol*. 2003;481(2-3):241-248.
- Schrier CW. Pathophysiology of ischemic acute kidney injury: In: *Diseases of the kidney and urinary tract*. 8th ed. Philadelphia: Lippincott Williams and Wilkins. 2007;930-961.
- Billings FT, Yu Ch, Byrne JG, Petrcek MR, Pretorius M. Heme oxygenase-1 and acute kidney injury following cardiac surgery. *Cardiokidney Med*. 2014;4(1):12-21. doi: 10.1159/000357871
- Haase M, Bellomo R, Haase-Fielitz A. Novel biomarkers, oxidative stress, and the role of labile iron toxicity in cardiopulmonary bypass-associated acute kidney injury. *J Am Coll Cardiol*. 2010;55(19):2024-2033. doi: 10.1016/j.jacc.2009.12.046
- Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120(4):179-184. doi: 10.1159/000339789
- Claire R. Lesión kidney aguda: ya no más insuficiencia kidney aguda. *Residente*. 2008;3(3):79-85.
- Haase M, Devarajan P, Haase-Fielitz A, Bellomo R, Cruz DN, Wagener G, Krawczeski CD, et al. The Outcome of neutrophil gelatinase-associated lipocalin-positive subclinical acute kidney injury: a multicenter pooled analysis of prospective studies. *J Am Coll Cardiol*. 2011;57(17):1752-1761. doi: 10.1016/j.jacc.2010.11.051