

Risk factors for mortality in acute kidney injury

EDWA MARIA BUCUVIC¹, DANIELA PONCE², ANDRÉ LUIS BALBI³

¹M.Sc. in Nephrology, Technical Overseer Nurse, Dialysis Unit, Hospital das Clínicas, Medical School of Botucatu — HC-Unesp, Botucatu, SP, Brazil

²Ph.D. in Nephrology, Attending Physician, Discipline of Nephrology, Department of Internal Medicine, HC-Unesp, Botucatu, SP, Brazil

³Ph.D. in Nephrology, Assistant Professor, Discipline of Nephrology, Department of Internal Medicine, HC-Unesp, Botucatu, SP, Brazil

SUMMARY

Objective: This study aims to evaluate the outcome of AKI patients caused by acute tubular necrosis admitted in clinical and surgical units of Botucatu Medical School University Hospital - Unesp. **Methods:** This is a retrospective cohort study with 477 adult patients were observed from January 2001 to December 2008. AKI was defined according to serum creatinine levels as proposed by Acute Kidney Injury Network (AKIN). **Results:** The mean age was 65.5 ± 162 years. The majority of the patients were males (62%) older than 60 years (65.2%). *Diabetes mellitus* was diagnosed in 61.9%, high blood pressure in 44.4% and chronic kidney disease 21.8% of the patients. Death occurred 66% of dialysis requirement, critical care unit admission, age > 60 years and lower attendance time by nephrologists were significant and independently associated with death risk. The renal recovery among survivors was of 96.9%. **Conclusion:** This work shows that the evolution of AKI patients from clinical and surgical wards is similar to literature. However, the high mortality of the group shows the necessity of identifying risk factors for the development of AKI in these patients and training staff assistant for the early diagnosis of this syndrome.

Keywords: Kidney failure acute; mortality; risk factors; early diagnosis.

Study conducted at Universidade Estadual Júlio de Mesquita Filho; Medical School of Botucatu – Department of Internal Medicine/ Hemodialysis Technical Section

Submitted on: 8/21/2010
Approved on: 11/9/2010

Correspondence to:
Edwa Maria Bucuvic
Avenida Universitária, 2263
Jardim Chácara dos Pinheiros
Botucatu – SP
CEP: 18609-353
Phone: + 14 3813 3812/9162 3064
Fax: + 14 3811 6005
embucuvic@fmb.unesp.br

Conflict of interest: None.

INTRODUCTION

Acute kidney injury (AKI) is characterized by a rapid fall in glomerular filtration rate, accompanied or not by nitrogen product retention and water-electrolyte disturbances^{1,2}. It is a complex pathology with multiple and varied etiologies and with no consensus definition³. Currently, classifications based on increased blood creatinine and urine output fall, such as *RIFLE*¹ and *AKIN*⁴, are used.

Several studies show the incidence of this syndrome has increased over the last decades, being associated with a longer life expectancy and multiple comorbidities in the population^{5,6}.

AKI is less frequent in the community (0.4% to 0.9%) than in hospitalized patients (4.9% to 7.2%)^{7,8}. In hospitals, AKI becomes an important complication when associated with the number and severity of comorbidities experienced by the patients, occurring in a rate around 20% to 40% in Intensive Care Units (ICU) and around 1% to 7% in intermediate care units^{2,3}. According to Lameire *et al.*⁶, 5% to 20% of patients in ICUs experience at least one episode of AKI associated with multisystem organ failure.

The identification of risk factors associated with AKI and its poor prognosis is required so that preventive and early diagnosis measures can be taken, aiming to reduce patients' mortality^{9,10}.

Several authors assessed the main AKI risk factors, being hospitalized patients, old age, chronic kidney disease, sepsis and heart surgeries the most usually found, among others¹⁰⁻¹⁴.

Liangos *et al.*¹⁴ found in a study with a great number of in-patients that chronic diseases, such as *diabetes mellitus* (DM), high blood pressure (HBP), coronary artery disease, congestive heart failure, neoplasms and HIV infection were associated with a higher risk to develop AKI and consequently a higher mortality. In contrast, other studies suggest AKI mortality is not associated with preexisting chronic diseases, such as HBP, DM or chronic obstructive pulmonary disease (COPD), but rather with clinical events over the hospitalization, such as dialysis requirement, oliguria and one or more organ failure¹⁰⁻¹².

This work aimed to study patients surviving AKI and proceeding from medical and surgical wards in regard to their clinical and laboratorial characteristics, risk factors associated with death, and recovery of kidney function.

METHODS

This is a retrospective cohort study of patients with AKI from acute tubular necrosis (ATN). They were admitted to internal medicine and surgical gastroenterology wards at the University Hospital of the Medical School of Botucatu – Unesp – attended by the AKI Group of the Discipline of Nephrology from January 2001 to December 2008. Patients with age under 18 years, having chronic kidney failure (CKF) and those undergoing kidney transplantation were excluded.

CKF was defined as the presence of a baseline serum creatinine > 1.4 mg/dL. AKI was defined as proposed by the Acute Kidney Injury Network (AKIN)⁴, while ATN represented a pathological term meaning the kidney tubule cell necrosis triggered by either ischemic and/or nephrotoxic injury¹⁵.

In the initial nephrologist's assessment, ATN-ISS¹⁶, a specific prognosis index for ATN patients, was used.

The patients were followed-up until either the discharge from nephrology service or the death.

This study was submitted to the Research Ethics Committee, Medical School of Botucatu, approved in April 7, 2008

STATISTICAL ANALYSIS

Initially, a patient descriptive analysis was conducted, with central tendency and dispersion measurements being calculated for continuous variables and frequency for categorical variables. The occurrence of death was set as a dependent variable, with the chi-squared test being used for categorical variables, while the T Test (for a parametric distribution) and the Mann-Whitney Test (for nonparametric distribution) were used for continuous variables. The following step was to conduct a multivariate analysis by the logistic regression model with odds ratio (OR) calculation. All variables showing to be associated with the end-point ($p \leq 0.20$) were included in the analysis. Statistical software, SPSS version 15.0, was used for the calculation, with a statistical significance 5% ($p \leq 0.05$).

RESULTS

Four hundred seventy-seven patients diagnosed with AKI were studied. Table 1 shows clinical and laboratorial characteristics in this population. Males were predominant (62%). The mean age was 65.5 ± 16.2 years, with 65.2% older than 60. Regarding comorbidities, 61.9% (out of 426 patients) had DM; 44.4% had HBP and 21.9% (out of 375) had CKF. The median baseline creatinine was 1.1 mg/dL (interquartile range: 0.9-1.5 mg/dL). Among the patients, 78.2% were in an ICU and sepsis was diagnosed in 64.4% of patients. The median first elevated serum creatinine after admission was 2.4 mg/dL (1.7-3.5 mg/dL), while the median serum creatinine at the first nephrologist's evaluation was 3.3 mg/dL (2.4-4.6 mg/dL). The median time between the first elevated serum creatinine after the admission and the nephrologist's evaluation was 3 days (1-7), while the median time of nephrological follow-up was 5 days (2-11). The median ATN-ISS was 0.64 (0.39-0.8). Ischemic AKI had a higher frequency, occurring in 65% of cases. Urine output was present in 58.9% of patients. Dialysis was carried out in 36.5% of cases, with hemodialysis predominating (70.1%). The overall mortality was 66%. Out of 162 surviving patients, 96.9% had a complete or a partial recovery of kidney function, with a median nephrological follow-up time of 7 days (4-14.5), while 3.1% continued on chronic dialysis.

Tables 1 and 2 describe clinical and laboratorial variables associated with death in patients with AKI diagnosed.

In univariate analysis, age over 60 years (survivors = 58.5%; non-survivors = 68.7%; $p = 0.034$), presence of CKF (33.6 and 15.2%; $p < 0.0001$), baseline serum creatinine (median, 1.2 and 1.1 mg/dL; $p < 0.0001$), ICU admission (60.9 and 87.2%; $p < 0.0001$), presence of sepsis (44.5 and 74.8%; $p < 0.0001$) and nephrological follow-up time (median 7 and 3 days; $p < 0.0001$) were significantly different. The non-survivors showed a higher percentage of mixed type AKI (36.7 and 15.8%) and a lower percentage of ischemic (60 and 74.4%) and nephrotoxic (3.3 and 9.8%) AKI ($p < 0.001$), lower presence of urine output (44.7 and 86%; $p < 0.0001$) and higher dialysis requirement (45 and 20.1%; $p < 0.0001$).

In multivariate analysis, dialysis requirement (OR = 3.65; 95% CI = 1.65–8.08; $p = 0.001$), ICU admission (3.10; 1.56–6.08; $p = 0.001$), age over 60 years (1.06;

1.55–5.35; $p = 0.001$) and shorter nephrological follow-up time (1.05; 1.01–1.08; $p = 0.002$) were variables associated with death, while nephrotoxic type AKI (0.40; 0.20–0.77; $p = 0.006$) and presence of urine output (0.16; 0.08–0.31; $p < 0.0001$) were associated with lower mortality.

DISCUSSION

This study investigated a cohort of patients admitted to medical and surgical wards with a diagnosis of AKI from ATN over a period of eight years; clinical and laboratory characteristics were similar to those in other papers^{10,12-14}. There was a predominance of males, elderly and the presence of comorbidities, such as DM, HBP and CKF. Similar outcomes were obtained by Liangos *et al.*¹⁴ and Leblanc *et al.*¹³, whereas Nash *et al.*¹⁷ observed, in a study with 4,622 patients admitted to medical and surgical services, that age over 80 years, male gender and high serum creatinine levels at the hospital admission were associated with a higher AKI risk.

Table 1 – Clinical and laboratorial characteristics of patients diagnosed with AKI

Characteristics	Patients (n = 477)
Males (%)	62
Age (years)*	65.5 ± 16.2
Age > 60 years (%)	65.2
DM (%)	61.9
HBP (%)	44.4
CKF (%)	21.9
Baseline serum creatinine (mg/dL)**	1.1 (0.9-1.5)
Admitted to ICU (%)	78.2
Sepsis present (%)	64.4
1 st elevated serum creatinine after admission (mg/dL) **	2.4 (1.7-3.5)
Serum creatinine at the 1 st nephrologist's evaluation (mg/dL) **	3.3 (2.4-4.6)
Time between the 1 st elevated serum creatinine and the first nephrologist's evaluation (days)**	3 (1-7)
ATN-ISS **	0.64 (0.39-0.8)
Nephrological follow-up time (days)**	5 (2-11)
AKI Type (%)	
Ischemic	65
Nephrotoxic	5.4
Mixed	29.6
Urine output present (%)	58.9
Dialysis requirement (%)	36.5
Dialysis mode (%)	
Hemodialysis	70.1
Peritoneal dialysis	29.9
Mortality (%)	66.0
Kidney recovery among survivors (%)	
Recovery	96.9
Chronic dialysis	3.1

Cr, creatinine; AKI, acute kidney injury; DM, *diabetes mellitus*; HBP, high blood pressure; CKF, chronic kidney failure. Number of patients evaluated according to certain variables: DM = 426; CKF = 375.

* Mean and standard deviation

** Median and interquartile range

Table 2 – Univariate analysis of clinical and laboratory variables related to death in patients with AKI diagnosed

Variables	Survivors (n = 162)	Non-survivors (n = 315)	p value
Males (%)	60.9	62.6	0.80
Age (years) **	68 (51.5-78)	69 (58-76.3)	0.37
Age > 60 years (%)	58.5	68.7	0.034
DM (%)	64.7	60.4	0.42
HBP (%)	50.6	41.2	0.06
CKF (%)	33.6	15.2	< 0.0001
Baseline serum creatinine (mg/dL) **	1.2 (1.0-1.7)	1.1 (0.9-1.3)	< 0.0001
Admitted to ICU (%)	60.9	87.2	< 0.0001
Presence of sepsis (%)	44.5	74.8	< 0.0001
1 st elevated serum Cr after admission (mg/dL)**	2.7 (1.7-3.6)	2.3 (1.7-3.3)	0.055
Serum Cr at the 1 st nephrologist's evaluation (mg/dL)**	3.15 (2.3-4.4)	3.4 (2.5-4.6)	0.224
Time between the 1 st elevated serum creatinine after admission and the 1st nephrologist's evaluation (days)	2.3 (1-5.5)	3 (1-8)	0.17
ATN-ISS * *	0.6 (0.33-0.8)	0.67 (0.43-0.8)	0.062
Nephrological follow-up time (days)**	7 (4-14.5)	3 (1-9)	< 0.0001
AKI type (%)			
Ischemic	74.4	60	
Nephrotoxic	9.8	3.3	< 0.0001
Mixed	15.8	36.7	
Presence of urine output (%)	86	44.7	< 0.0001
Dialysis requirement (%)	20.1	45	< 0.0001
Dialysis mode (%)			
Hemodialysis	60.6	72.4	
Peritoneal dialysis	39.4	27.6	0.265

Cr, creatinine; AKI, acute kidney injury; DM, *diabetes mellitus*; HBP, high blood pressure; CKF, chronic kidney failure ** Median and interquartile range.

Table 3 – Multivariate analysis of clinical and laboratory variables related to death in patients with AKI diagnosed

Variables	Estimate of effect	p value	OR	CI (OR;95%)
Dialysis requirement	1.29	0.001	3.65	1.65 8.08
ICU admission	1.13	0.001	3.10	1.57 6.08
Age > 60 years	1.06	0.001	2.88	1.55 5.35
Nephrological follow-up time (days)	0.04	0.002	1.05	1.01 1.08
Nephrotoxic AKI	- 0.91	0.006	0.40	0.20 0.77
Presence of urine output	-1.79	0.000	0.16	0.08 0.31
Constant	-1.67	0.000	0.18	

$\chi^2 = 57.00$; $g_{\text{model}} = 9$; $p < 0.001$; $n = 294$

ICU admission and the presence of sepsis were predominant characteristics in this study patients. According to the literature, 5% to 20% of patients considered as having a critical illness develop AKI over the course of the illness, accompanied, in many cases, by multisystem organ failure^{11,18,19}. Schrier *et al.*²⁰ showed a relationship between sepsis severity and AKI, with the later present in 19% of patients with moderate sepsis, in 23% with severe sepsis and in 51% with septic shock. In a prospective multicenter study, Uchino *et al.*²¹ found an AKI incidence in 5.7% of patients admitted to an ICU, with sepsis being its main cause.

This study shows patients had a median baseline creatinine of 1.1 mg/dL, while the median first elevated creatinine after admission was 2.4 mg/dL and the first nephrological evaluation occurred only with the median serum creatinine 3.3 mg/dL, suggesting a delay in AKI diagnosis by the team or a difficulty in rating the case severity, not valuating the serum creatinine levels obtained. Chertow *et al.*⁵ demonstrated small increments in serum creatinine are significantly associated with increased mortality in patients with AKI. Lameire *et al.*⁶ reported only 22% of patients developing AKI are referred to a nephrologist.

In this study, the median ATN-ISS was 0.64, very similar to the mortality in the general population (66%), suggesting a good association between this score and the mortality in patients followed. This data is consistent with that reported by Balbi *et al.*²², which upon demonstrating a good calibration, mainly from the third quintile, and an excellent discrimination, with an area under curve of 0.95, concluded this prognosis index shows great reliability to be applied in the nephrologist's daily practice.

The percentage of deaths in the population was generally similar to data found in the current literature, being high because the patients were in critical condition, most of them admitted to an ICU. In studies investigating populations in a less critical condition, Silvester *et al.*²³ found a mortality of 46.8%, Sesso *et al.*²⁴ found 54% and, in Botucatu, Balbi *et al.*²² and Valente *et al.*²⁵ found mortality rates of 44.3% and 40.2%, respectively, in different periods.

Age^{19,26-28}, admission prognosis scores^{18,19,27,28} and sepsis^{28,29} have been classical factors associated with death. In this study, after multivariate analysis, dialysis requirement, ICU admission, age over 60 years and a shorter nephrological follow-up time were associated with death, whereas nephrotoxic type AKI and the presence of urine output were factors associated with a lower mortality. Mortality from AKI varies as a function of the severity of the patient's case and, as result, of the facility where the patient was admitted^{11,30}. Liaño *et al.*³¹ observed patients coming out of an ICU had a mortality of 69.6%, whereas in the wards the variation was 36.3% (medical wards) and 42.8% (surgical wards). The elevated mortality in patients admitted to an ICU is also associated with clearly known poor clinical factors, such as hypotension³², jaundice^{32,33}, coma¹⁶, sedation¹⁶ and oliguria^{16,30,34}.

As shown in this and in other studies, sepsis is a factor clearly associated with increased death risk in patients with AKI^{18,34}. According to Edelstein *et al.*³⁵, a combination of AKI and sepsis is associated with a 70% mortality, compared to a 45% mortality in patients with AKI alone. Neveu *et al.*³⁴, in a prospective study involving 345 patients having AKI with and without sepsis, showed a great difference in mortality (74.5% with sepsis and 45.2% without sepsis; $p < 0.001$).

Concerning clinical AKI characteristics, this study shows reduced urine output and dialysis requirement were associated with a higher mortality. As suggested by evidence, nonoliguric AKI has a better prognosis than oliguric AKI, and this latter is one of the main prognosis factors of mortality, once no urine output is associated with more kidney impairment and, as a result, a poorer clinical course^{18,34,36,37}. Regarding dialysis requirement, Mehta *et al.*³⁸, in a recent study with ICU patients, showed a significantly lower mortality in patients who had nondialytic AKI compared with those undergoing dialysis (24% and 45%, respectively). Balbi *et al.*²² observed that in patients

requiring dialysis, the mortality was 63.8%, much higher than that found in patients undergoing only conservative treatment (23.5%; $p < 0.05$). Other studies apart from this show that requiring dialysis is a death risk factor in patients with AKI^{18,31,34,39}.

CONCLUSION

This study shows, in a cohort with 477 patients diagnosed with AKI and admitted to medical and surgical wards, that the syndrome course is similar to the date obtained from the literature, with high mortality, classical risk factors associated with mortality and elevated kidney function recovery among survivors. The high mortality in the group shows the identification of risk factors for AKI development in these patients and an attending team skilled to diagnose this syndrome early are the key for a good outcome.

REFERENCES

- Bellomo R, Ronco C, Kellum JA, Mehta LR, Palevsky P. 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* 2004;8:204-11.
- Thadhani R, Pascual M, Bonventre JV. Acute renal failure. *N Engl J Med*. 1996;334:1448-60.
- Himmelfarb J, Ikizler TA. Acute kidney injury: changing lexicography, definitions, and epidemiology. *Kidney Int*. 2007; 71: 971-6.
- Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG *et al.* The acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007;11:R31.
- Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol*. 2005;16:3365-70.
- Lameire N, Biesen WV, Vanholder R. The changing epidemiology of acute renal failure. *Nat Clin Pract Nephrol*. 2006;2:364-77.
- Kaufman J, Dhakal M, Hamburger R. Community acquired acute renal failure. *Am J Kidney Dis*. 1991;17:191-8.
- Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT. Hospital-acquired renal insufficiency: a prospective study. *Am J Med*. 1983;74:243-8.
- Barretti P, Soares VA. Acute renal failure: clinical outcome and causes of death. *Ren Fail*. 1997;19:253-7.
- Cosentino F, Chaff C, Piedmonte M. Risk factors influencing survival in UCI acute renal failure. *Nephrol Dial Transplant* 1994;9:179-82.
- Liño F, Junco E, Pascual J, Madero R, Verde E. The spectrum of acute renal failure in the intensive care unit compared with that seen in other settings. *Kidney Int*. 1998;53:16-24.
- Steven D, Weisbord MD. Acute renal failure in the intensive care unit. *Semin Resp Crit Care Med*. 2006;27:262-73.
- Leblanc M, Kellum JA, Gibney RTN, Lieberthal W, Tumlin J, Mehta LR. Risk factors for acute renal failure: inherent and modifiable risks. *Curr Opin Crit Care* 2005;11:533-6.
- Liangos O, Wald R, O' Bell JW, Prince L, Pereira BJ, Jaber BL. Epidemiology and outcomes of acute renal failure in hospitalized patients: A national survey. *Clin J Am Soc Nephrol*. 2006;1:43-51
- Brady HR, Clarkson MR, Lieberthal W. Acute renal failure. In: Brenner MB, Rector HR, editors. *The Kidney*. 7th ed. Boston: Saunders; 2004. v. 1, p.1215-92.
- Liano F, Gallego A, Pascual J, Martín FG, Teruel JL, Marcén R *et al.* Prognosis of acute tubular necrosis: an extended prospectively contrasted study. *Nephron*. 1993;63:21-3.
- Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. *Am J Kidney Dis*. 2002;39:930-6.

18. Brivet FG, Kleinknecht DJ, Loirat P, Landais PJM. Acute renal failure in intensive care units- causes, outcome and prognostic factors of hospital mortality: A prospective, multicenter study. The French Acute Renal Failure Study Group. *Crit Care Med.* 1996;24:192-8.
19. De Mendonca A, Vincent JL, Suter PM, Moreno R, Dearden NM, Antonelli M *et al.* Acute renal failure in the ICU: risk factors and outcome evaluated by the SOFA score. *Intensive Care Med.* 2000;26:915-21.
20. Schrier RW, Wang W. Acute renal failure and sepsis. *N Engl J Med.* 2004;351:159-69.
21. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S *et al.* Beginning and ending supportive therapy for the kidney (BEST Kidney) investigators. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA* 2005;294:813-8.
22. Balbi AL, Gabriel DP, Barsante RC, Caramori JT, Martin LC, Barretti P. Mortalidade e prognóstico específico em pacientes com insuficiência renal aguda. *Rev Assoc Med Bras.* 2005;51:318-22.
23. Silvester W, Bellomo R, Cole L. Epidemiology, management, and outcome of severe acute renal failure of critical illness in Australia. *Crit Care Med.* 2001;29:1910-5.
24. Sesso R, Roque A, Vicioso B, Stella S. Prognosis of ARF in hospitalized elderly patients. *Am J Kidney Dis.* 2004;44:410-9.
25. Valente SF, Balbi AL. Insuficiência renal aguda no Hospital das Clínicas da Faculdade de Medicina de Botucatu - UNESP: descrição da população e análise dos fatores de risco associados à mortalidade [dissertação]. Botucatu: Faculdade de Medicina, Universidade Estadual Paulista; 2007.
26. Urney JH, Marshall DH, Brownjohn AM, Ellis CM, Parsons FM. The evolution of acute renal failure. *Q J Med.* 1990;74:83-104.
27. Levy EM, Viscoli CM, Horwitz RI. The effect of acute renal failure on mortality: A cohort analysis. *JAMA* 1996;275:1489-94.
28. Schwilk B, Wiedeck H, Stein, Reinelt H, Treiber H, Bothner U. Epidemiology of acute renal failure and outcome of haemodiafiltration in intensive care. *Intensive Care Med.* 1997;23:1204-11.
29. Weisberg LS, Allgren RL, Kurnik BR. Acute tubular necrosis in patients with diabetes mellitus. *Am J Kidney Dis.* 1999;34:1010-15.
30. Chew SL, Lins RL, Daelemans R, Broe ME. Outcome in acute renal failure. *Nephrol Dial Transplant.* 1993;8:101-17.
31. Santos WJQ, Zanetta DMT, Pires AC, Lobo SMA, Lima EQ, Burdmann EA. Patients with ischaemic, mixed and nephrotoxic acute tubular necrosis in the intensive care unit- a homogeneous population? *Crit Care* 2006;10:R68.
32. Barton IK, Hilton PJ, Taub NA, Warburton FC, Swan AV, Dwight J *et al.* Acute renal failure treated by haemofiltration: factors affecting outcome. *Q J Med.* 1993;86:81-90.
33. Paganini E, Tapolyai M, Goormastic M, Halstenberg W, Kozlowski L, Leblanc M *et al.* Establishing a dialysis therapy/patient outcome link in intensive care unit acute dialysis. *Am J Kidney Dis.* 1996;28:81-9.
34. Neveu H, Kleinknecht D, Brivet F, Loirat PH, Landais P. Prognostic factors in acute renal failure due to sepsis: results of a prospective multicenter study. *Nephrol Dial Transplant* 1996;11:293-9.
35. Edelstein CL, Schrier RW. Pathophysiology of ischemic acute renal failure. In: Schrier RW, editor. *Diseases of the kidney and urinary tract.* 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2001. v. 2, p.1041-69.
36. Weisberg LS, Allgren RL, Genter FC, Kurnik BR. Cause of acute tubular necrosis affects its prognosis. The Auriculin Anaritide Acute Renal Failure Study Group. *Arch Intern Med.* 1997;157:1833-8.
37. Uehlinger DE, Jakob SM, Ferrari P, Eichelberger M, Huynh-Do U, Marti HP *et al.* Comparison of continuous and intermittent renal replacement therapy for acute renal failure. *Nephrol Dial Transplant.* 2005;20:1630-7.
38. Mehta RL, Pascual MT, Soroko S, Savage BR, Himmelfarb J, Ikizler TA *et al.* Spectrum of acute renal failure in the intensive care unit: the PICARD experience. *Kidney Int.* 2004;66:1613-21.
39. Mehta RL, Pascual MT, Gruta CG, Zhuang S, Chertow GM. Refining predictive models in critically ill patients with acute renal failure. *J Am Soc Nephrol.* 2002;13:1350-7.