ORIGINAL ARTICLE

Port J Nephrol Hypert 2010; 24(4): 273-278
Advance Access publication 17 September 2010

Outcome of acute renal failure at a tertiary hospital

Luís Oliveira, Rui Castro, Mónica Fructuoso, Catarina Prata, Teresa Morgado

Nephrology Department, Centro Hospitalar de Trás-os-Montes e Alto Douro.
Vila Real, Portugal.

Received for publication: 14/10/2009
Accepted in revised form: 18/08/2010

ABSTRACT

Data on overall epidemiology of acute renal failure are scarce. It is crucial to know the aetiology and clinical features of acute renal failure to promote prevention strategies and implement adequate resources for management of this entity.

A retrospective protocol was developed to assess acute renal failure in our hospital during a three-year period. Acute renal failure was defined as a sudden rise in serum creatinine concentration to values higher than 1.2 mg/dl or a sudden rise of at least 30% over its previous value in patients with mild-to-moderate chronic renal disease.

Of the 647 cases of acute renal failure studied, 295 episodes were superimposed on chronic renal failure and the remaining 352 were isolated acute renal failure episodes. The most frequent causes of acute renal failure were acute tubular necrosis, obstruction and prerenal.

Interestingly, maximum serum creatinine was higher in acute renal failure alone than in the acute on chronic renal failure group. Also, the mortality was higher in acute renal failure (29.3% *vs.* 21.4%; p<0.02). Patients with acute tubular necrosis had lower mortality from nephrotoxic insults (7.9%) than those with ischaemic (26.6%; p<0.01).

In noncritical patients, dialysis was required in 38 (12.2%) acute renal failure patients and 37 (12.7%) acute on chronic renal failure patients (p=NS). Renal recovery and mortality (42.1 *vs.* 40.0%; p=NS) were similar between the two noncritical groups who underwent dialysis (52.6 *vs.* 56.8%; p=NS).

In the intensive care unit, the majority of critical patients with acute renal failure had sepsis (96.4%). Dialysis was required in 24 (58.5 %) acute renal failure and 10 (71.4 %) acute on chronic renal failure patients (p=NS). Patients who had undergone dialysis had less renal function recovery (14.7 *vs.* 71.4%; p<0.001) and higher mortality (70.6 *vs.* 28.6%; p>0.001).

Dialysis support and sepsis were associated with higher overall mortality (40.0 *vs.* 20.5 %; p<0.001 and 38.2 *vs.* 24.2 %; p=0.01, respectively).

Acute renal failure is iatrogenically induced at a high rate. There are many frequent iatrogenic combinations such as radiological contrast agents, aminoglycosides, angiotensin-converting enzyme inhibitors, diuretics, and/or cardiovascular surgery. Despite significant advances in our knowledge of the pathophysiology of acute renal failure, much needs to be done before we can apply effective therapies in patients with acute kidney injury.

Key-Words:
Acute on chronic kidney failure; acute renal failure; dialysis; mortality; outcome.

INTRODUCTION

The modern history of acute renal failure (ARF) began during the air raids over London sixty years ago. Since then, despite thousands of published reports addressing many different aspects of the problem, epidemiology has been almost forgotten[1]. The rapid breakdown of renal function that occurs in ARF leads to the accumulation of high levels of uraemic toxins in the blood. It has many aetiologies which have changed over the years as society has developed.

ARF affects 5% of hospital admissions and 25% of critical patients[2]. It is associated with high mortality rates varying between 27% in general wards and 50-80% in Intensive Care Units (ICU)[3]. This high mortality rate may be explained by the progressive aging of the population and high comorbidity[4].

We intended to evaluate the aetiology, clinical features and evolution of patients with ARF admitted to our hospital. Clinical factors that could have impacted on outcomes were also evaluated.

PATIENTS AND METHODS

All internal requests for nephrological consultation for ARF and acute on chronic renal failure (ACKF) between January 2002 and December 2005 were evaluated.

Several parameters were assessed: demographic data, time to request nephrological consultation, requesting department, ARF aetiology, dialysis support and techniques, evolution, mortality and patient orientation after discharge. In our ICU, nephrologists are only involved in severe cases of ARF.

We considered the following criteria:

- Oliguria when urine excretion was lower than 400 millilitres per day.
- Acute renal failure for a serum creatinine higher than 1.2 mg/dl.
- Acute on chronic renal failure as an increase of serum creatinine by at least 30% when previous values were obtained.
- Prerenal ARF when renal function recovered after volume repletion and fractional excretion of sodium was less than 1%.
- Acute tubular necrosis (ATN) when correction of possible prerenal causes did not improve renal function after exclusion of glomerulonephritis, interstitial nephritis, vascular, obstructive aetiologies and a fractional excretion of sodium greater than 2%.
- Acute glomerulopathies when clinical condition was highly suggestive (haematuria and/or dysmorphism of urinary red blood cells) or after histological confirmation.
- Acute tubulointerstitial nephritis (ATIN) in the presence of at least three of the following clinical criteria (drug ingestion, fever, cutaneous rash and eosinophilia) or histological confirmation.
- Vasculitis after histological confirmation.
- Renal thromboembolism evidenced by absence of isotope uptake and high clinical suspicion.
- Obstructive ARF confirmed by ultrasound without renal cortical atrophy.
- Renal recovery was defined as a decrease of serum creatinine to less than 1.2 mg/dl and partial recovery as a decrease of 50% of the maximum creatinine attained. Nonrecovery of renal function was also considered in patients with acute kidney injury (AKI) who have died.

We also evaluated clinical factors that could have impact on outcomes, such as age, gender, dialysis support, sepsis, multiple organ dysfunction syndrome, heart failure, chronic obstructive pulmonary disease, Diabetes mellitus, cerebrovascular disease, neoplasia and time to nephrology referral. All patients were followed until their hospital discharge.

The majority of results are presented as mean and standard deviation except for time to request nephrology consultation, which is presented as median [minimum, maximum]. Continuous variables were compared using the t-test. The chi square tests was used for categorical variables comparison.

RESULTS

A total of 647 patients (71±14 years old; 357 male) were evaluated: 352 had ARF and 295 ACKF. There was a male predominance in both groups (193 and 164, respectively) and ACKF patients were older (73±13 *vs.* 70±11 years old; $p=0.001$).

There was no annual variation in ARF and ACKF over the 3 years but we noticed a higher frequency (21%) of ARF in the first trimester ($p<0.05$).

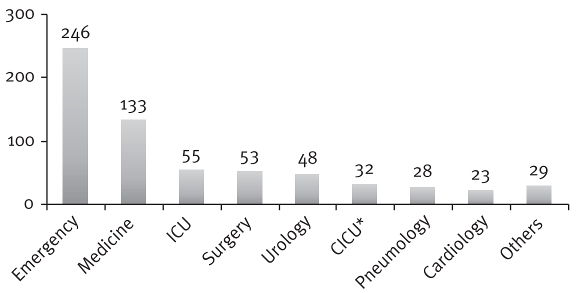

Figure 1

Department distribution of requests for nephrology consultation

***CICU** – coronary intensive care unit.

The departments with a higher number of requests for nephrology consultations were emergency room (38%), internal medicine (21%) and ICU (9%), as listed in Figure 1.

The median time to request nephrology consultation was 5.3 days [1-70] after hospital admission and the main causes of ARF and ACKF were ATN and obstruction. Prerenal factors occurred in 6.0 and 4.1% of ARF and ACKF, respectively (n=NS). The aetiology of ARF and ACKF is presented in Table I.

Ischaemic insult (59.4%) was more frequent as a cause of ATN, followed by nephrotoxic injury (14.8%). Similar values were obtained for ischaemic ATN in ACKF (79.2%) and nephrotoxicity (3.1%). Prostatic disease was the main cause of obstructive ARF and ACKF (35 *vs.* 46%).

Dialysis support was similar in the two groups: 17.6% (n=62/352) of ARF and 15.9% (n=47/295) of ACKF (p=NS).

Table I

Causes of acute renal failure (ARF) and acute on chronic renal failure (ACRF)

	ARF (n=352)	*ACRF* (n=295)	P
ATN*	74.2 %	82.3 %	‹0.001
Obstructive	13.1 %	9.5 %	NS
Prerenal	6.0 %	4.1 %	NS
ATIN#	3.0 %	0.3 %	0.02
UTI§	1.7 %	1.4 %	NS
Others	1.8 %	2.0 %	NS

***ATN** – acute tubular necrosis; **#ATIN** – acute tubulointerstitial nephritis; **§UTI** – urinary tract infection.

ARF patients had higher serum creatinine values than ACKF patients (4.8±2.6 *vs.* 4.4±2.2 mg/dl; p=0.02) and more than 60% in both groups recovered renal function (p=NS). Sepsis and multiple organ dysfunction syndrome (MODS) were more frequent in ARF (10.2 *vs.* 5.1%; p=0.02 and 7.4 *vs.* 0.3%; p‹0.01, respectively). Morbidity was similar except for diabetes mellitus which was more prevalent in ACKF (24.7 *vs.* 7.7%; p‹0.01), as shown in Table II.

Mortality in non-ICU ARF patients treated with conventional haemodialysis was higher than those treated with conservative treatment (42.1 *vs.* 24.5%; p=0.02). ARF patients who had undergone dialysis had less renal recovery (52.6 *vs.* 75.4%; p=0.04) as shown in table III.

We have obtained similar results for non-ICU ACKD group. Nondialysis patients had higher renal recovery rate (84.4 vs. 56.8%; p‹0.001) and lower mortality (16.0 *vs.* 37.8%; p‹0.001).

Twenty-two of the 55 critical patients evaluated in the ICU underwent continuous replacement renal therapies and 12 were treated with intermittent haemodialysis. In our critical ARF patients, continuous renal replacement therapy (CRRT) was associated with the highest mortality rate (75.0%; p‹0.001) followed by conventional dialysis (62.5%; p‹0.001)

Table II

Morbidity and laboratory evolution for renal failure and acute on chronic renal failure patients

	ARF (n=352)	*ACRF* (n=295)	P	Total (n=647)
Creatinine (maximum; mg/dl)	4.8 ± 2.6 [1.3-17.7]	4.4 ± 2.2 [1.3-18.1]	0.02	4.6 ± 2.4
Creatinine (at discharge; mg/dl)	2.8 ± 2.1 [0.6-15.7]	3.2 ± 2.0 [0.5-18.1]	‹0.01	3.0 ± 2.1
Kidney function recovery (n; %)	244 (69.3%)	228 (77.2%)	NS	435 (67.2%)
Sepsis (n; %)	36 (10.2%)	15 (5.1%)	0.02	51 (7.9%)
MODS* (n; %)	26 (7.4%)	1 (0.3%)	‹0.01	27 (4.2%)
Heart failure (n; %)	23 (6.5%)	20 (6.8%)	NS	43 (6.7%)
COPD# (n; %)	2 (0.6%)	1 (0.3%)	NS	3 (0.5%)
Diabetes mellitus (n; %)	27 (7.7%)	73 (24.7%)	‹0.01	100 (15.5)
Cerebrovascular disease (n; %)	5 (1.4%)	2 (0.7%)	NS	7 (1.1%)
Neoplasia (n; %)	10 (2.8%)	9 (3.1%)	NS	19 (2.9%)

***MODS** – multiple organ dysfunction syndrome; **#COPD** – chronic obstructive pulmonary disease.

Table III

Acute renal failure patients: comparison between dialysis support and conservative treatment

ARF		Renal recovery	Without renal recovery	Non survivors
ICU				
CRRT	16	2*	2	12*
Conventional dialysis	8	2*	1	5*
Conservative	17	14	0	3
Non-ICU				
Conventional dialysis	38	20*	2	16*
Conservative	273	206	0	67
TOTAL	352	244	5	103

*p<0.05 (compared to conservative treatment)

Table V

Acute renal failure patients: comparison between survivors and non survivors

	Non survivors (n=103)	Survivors (n=249)	P
Age (years-old)	77 ± 6	64 ± 19	NS
Male (n)	35.9%	55.0%	<0.001
Sepsis (n;%)	26 (25.2%)	10 (4.0%)	<0.001
MODS* (n;%)	21 (20.4%)	5 (2.0%)	<0.001
Heart failure (n;%)	7 (6.8%)	16 (6.4%)	NS
COPD# (n;%)	1 (1.0%)	1 (0.4%)	NS
Diabetes mellitus (n;%)	9 (8.7%)	18 (7.2%)	NS
Cerebrovascular disease (n;%)	2 (1.9%)	3 (1.2%)	NS
Neoplasia (n;%)	6 (5.8%)	4 (1.6%)	0.04

***MODS** – multiple organ dysfunction syndrome; **#COPD** – chronic obstructive pulmonary disease.

when compared to patients submitted to conservative treatment (17.6%). Renal recovery in critical patients was less frequent in CRRT (12.5 *vs.* 82.3%; p<0.001) and classic dialysis (25.0 *vs.* 82.3%; p=0.005) when compared to conservative treatment (Table III). In ICU ACKD group, there was no difference in terms of mortality and renal recovery between CRRT, conventional dialysis and conservative treatment, as listed in Table IV.

Overall mortality was higher in ARF than ACKF (29.3% *vs.* 21.4%; p<0.02). There were fewer deaths among male patients with ARF (35.9 *vs.* 55.0%; p<0.001). We found no age differences for mortality between ARF and ACKF (Tables V and VI). Mortality was lower (7.9%) in nephrotoxic ATN than ischaemic ATN (26.6%; p<0.01).

Dialysis was required in 17% of all patients (17.6% in ARF and 15.9% in ACKF, p=NS) and was associated with a higher mortality (49.5 *vs.* 20.5 %; p<0.001). Furthermore, the 68 sepsis-related AKI episodes had higher mortality (38.2 *vs.* 24.2 %; p=0.01).

Neoplasia (Table V) was more prevalent in non-survivor ARF group (5.8 *vs.* 1.6%; p=0.04). Heart failure (20.6 *vs.* 3.0 %; p<0.001) and neoplasia (9.5 *vs.* 1.3%; p<0.001) were also more prevalent in non-survivor ACKF group (Table VI).

There was a trend to later referrals in patients who ultimately died (5.8±8.9 *vs.* 4.4±8.3 days; p=0.08).

Table IV

Acute on chronic renal failure patients: comparison between dialysis support and conservative treatment

ACRD		Renal recovery	Without renal recovery	Non survivors
ICU				
CRRT	6	1	1	4
Conventional dialysis	4	0	1	3
Conservative	4	1	0	3
Non-ICU				
Dialysis support	37	21*	2	14*
Conservative	244	205*	0	39*
TOTAL	295	228	4	63

* p<0.05 (compared to conservative treatment).

Table VI

Acute on chronic renal failure patients: comparison between survivors and nonsurvivors

	Non survivors (n=63)	Survivors (n=232)	P
Age (years-old)	82 ± 211	67 ± 17	NS
Male	52.4%	56.5%	NS
Sepsis (n;%)	12 (19.0%)	3 (1.3%)	<0.001
MODS* (n;%)	1 (1.6%)	0 (0.0%)	NS
Heart failure (n;%)	13 (20.6%)	7 (3.0%)	<0.001
COPD# (n;%)	1 (1.6%)	0 (0.0%)	NS
Diabetes mellitus (n;%)	13 (20.6%)	60 (25.9%)	NS
Cerebrovascular disease (n;%)	1 (1.6%)	1 (0.4%)	NS
Neoplasia (n;%)	6 (9.5%)	3 (1.3%)	<0.001

***MODS** – multiple organ dysfunction syndrome; **#COPD** – chronic obstructive pulmonary disease.

Mortality in critical patients (n=55) admitted to ICU with AKI was much higher than that of the other patients (54.5 *vs*. 23.0 %; p<0.001). The majority of them had severe sepsis (96.4%) and MODS (83.6%).

The majority of patients (n=248) were referred to Nephrology consultation after discharge followed by referral to first care physician (n=141), other consultation (n=49), transfer to other hospital (n=31) and discharge against medical opinion (n=3). Global mortality was 25.7% (n=166).

DISCUSSION

The purpose of this study was to evaluate the aetiology, clinical features and evolution of patients with ARF admitted to our hospital. The aetiological spectrum of ARF has changed in developed countries. We tried to evaluate if similar changes have occurred in our population. ATN, sepsis and obstruction were the most frequent causes of ARF and ACKF. Prerenal factors were responsible for acute kidney injury in less than 6% in both groups. This aetiological distribution was similar to the Liano[5] study that showed a 50% decrease of prerenal ARF along the years and found that ischaemia was the most frequent cause of ATN either on ACKF and ARF.

The ARF group comprised patients who were 69.8±10.6 years old and ACKF patients were older (73.3±14.7 years old; p=0.001).

Global mortality was 25.5%, similar to the 19% rate reported by a large prospective cohort study that was conducted at a US urban academic centre[6]. ARF patients had higher mortality (29.3%; n=103/352) than ACKF patients (21.4%; 63/295). In fact, despite similar morbidity there were more patients with sepsis (10.2 *vs*. 5.1; p=0.02) and MODS (7.4 *vs*. 0.3; p<0.01) in the ARF group than the ACKF.

In studies of ARF in hospitalised patients, the prevalence of preexisting chronic kidney disease has been as high as 75%[7]. Not surprisingly, our CKD patients had a higher rate of ATN, when compared to ARF group (82.3 *vs*. 74.2 %; p<0.001).

Acute renal failure is universally reported to carry a bleak prognosis. Incidence and mortality rates vary according to the definition of ARF and location. Mortality rates in ARF range from approximately 7% among patients with prerenal azotaemia to more than 80% among patients with severe ARF and this has changed little over time despite technical advances in renal replacement therapy and supportive care, possibly due to aging and increased morbidity[4]. In addition to sepsis and MODS, other morbidity factors may have deleterious effects in both groups: neoplasia (Table V) may be related to poor prognosis in ARF, just like heart failure and neoplasia in ACKF (Table VI).

Mortality was higher in our critical patients with acute renal failure. This may be justified by two facts. Firstly, ARF patients treated in the ICU are obviously different from other hospital departments. In fact, the majority of them had severe sepsis, conferring a worse prognosis. Conflicting results have been published to estimate the prognostic value of sepsis *per se* in ARF patients. Several authors have found that sepsis-related ARF had a significantly worse prognosis than ARF in the absence of sepsis[8,9]. It is generally impossible in those studies to assess the respective role of sepsis and of the associated organ failures without stepwise logistic regression analysis. Using multivariate analysis only a few authors have found that sepsis did not increase the risk of mortality[10]. In a number of other studies sepsis was an independent predictor of death[11]. The second cause of higher ARF mortality in the ICU is related to complications that developed over the course of the ARF, mainly shock and respective therapeutic measures. In the same way, dialysis support mainly CRRT was associated with higher mortality.

When patients with ARF develop dialysis-requiring ATN, our data in critically ill patients also suggest that renal recovery is less likely than in patients without dialysis need. In ICU, mortality was higher in CRRT followed by conventional dialysis. Patients who underwent conservative therapy survived best. We did not find any difference in terms of survival or renal recovery between CRRT, conventional dialysis and conservative treatment in critical ACKD patients. This lack of difference must be explained by the reduced number of ACKD patients, as nephrology consultation was limited to severe cases of ARF.

In addition to dialysis support, we also evaluated other clinical factors that could have impacted on outcomes. Romão *et al.*[13] prospectively analysed 361 elderly ARF patients and noted that oliguria and need for RRT were associated with poor outcomes. More recently, Sesso *et al.*[13] followed up 325 elderly ARF patients and found that underlying malignancy, surgery, oliguria, dialysis support, sepsis and MODS were associated with poor outcomes.

Mortality was lower in nephrotoxic ATN (7.9%) than ischaemic ATN (26.6%; $p<0.01$). This may be explained by the high morbidity, older age and cardiovascular disease of these two latter groups of patients.

In acute renal failure, nonsurvivor group seems to have delayed nephrology consultation (5.8±8.9 *vs*. 4.4±8.3 days; $p=0.08$). Using observational data, we could not determine whether these findings reflect the benefits of nephrology consultation or residual confounding, selection bias and adverse effects of delayed recognition of acute renal failure. Nevertheless, an earlier diagnosis of ARF seems important as functional recovery may be markedly delayed in patients with persistent septic physiology and circulatory shock, or who have repeated episodes of renal ischaemia and/or nephrotoxin administration. In those settings, tubular cell apoptosis and/or necrosis have occurred and the regeneration of tubular cells that is required for the restoration of renal function may be delayed or abolished.

Although many different urinary and serum proteins have been intensively investigated as possible biomarkers for the early diagnosis of ATN, the following steps are necessary before they are used clinically, such as validation in different settings of AKI (cardiac surgery, sepsis), development and testing of rapid assays. It is likely that a panel of biomarkers will be necessary to recognise acute renal injury before functional abnormalities are manifest and define better prevention and therapeutic strategies in order to minimise its long-term consequences.

The prognosis of patients with acute kidney injury is directly related to the cause of renal failure and to the duration of renal failure prior to therapeutic intervention. Patients with acute renal failure due to sepsis had a worse prognosis. Oliguria, need for dialysis and the above-defined morbidity factors should be considered in ARF prognosis.

In conclusion our knowledge about ARF is still partial. Although significant progress has been made in defining the major components of ARF, current treatment consists of supportive and preventive strategies, which do not alter mortality.

Conflict of interest statement. None declared.

References

1. Liaño F, Pascual J. Epidemiology of acute renal failure: A prospective, multicenter, community-based study. Kidney Int 1996;50:811-818
2. Abernethy V, Lieberthal W. Acute renal failure in the critically ill patient. Crit Care Clin 2002;18:203-222
3. Oppert M, Engel C, Brunkhorst F, *et al.* Acute renal failure in patients with severe sepsis and septic shock–a significant independent risk factor for mortality: results from the German Prevalence Study. Nephrol Dial Transplant 2008;23:904-909
4. Ronco C. Blood Purification in Intensive Care. 1st edition. Switzerland: S. Karger AG, 2003:1-6
5. Liaño F. Fracaso renal agudo: Revision de 202 casos. Aspectos pronósticos. Nefrologia 1984;4:181-190
6. Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis 2002;39:930-936
7. Hsu C, Ordonez J, Fan D. The risk of acute renal failure in patients with chronic kidney disease. Kidney Int 2008;74:101-7
8. Neveu H, Kleinknecht D, Brivet F, Loirat P, Landais P. Prognostic factors in acute renal failure due to sepsis: Results of a prospective multicentre study. The French Study Group on Acute Renal Failure. Nephrol Dial Transplant 1996;11:293-299
9. Schor N: Acute renal failure and the sepsis syndrome. Kidney Int 2002;61:764-776
10. Liano F, Gallego A, Pascual J, *et al.* Prognosis of acute tubular necrosis: an extended prospectively contrasted study. Nephron 1993;63:21-31
11. Neveu H, Kleink D, *et al.* Prognostic factors in acute renal failure due to sepsis. Results of a prospective multicentre study. Nephrol Dial Transplant 1996;11:293-299
12. Romão J, Haiashi A, Vidonho A, Abensur H, *et al.* Causes and prognosis of acute renal failure in elderly patients. Rev Assoc Med Bras 2000;46:212-217
13. Sesso R, Roque A, Viciso B, *et al.* Prognosis of ARF in hospitalised elderly patients. Am J Kidney Dis 2004;44:410-419

Correspondence to:
Dr Luís Oliveira
Avenida da Noruega
5000-508 Vila Real
PORTUGAL
luissoliveira06@yahoo.com