Acute renal failure in the medical ICU still predictive of high mortality

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Background. We aimed to determine the outcome and certain predictors of outcome for acute renal failure (ARF) in the medical intensive care unit (ICU) at Tygerberg Hospital.

Method. We conducted a retrospective, single-centre cohort study over 12 months comprising all patients admitted to the medical ICU with all causes of renal failure or who developed renal failure following admission to the ICU.

Results. Of 198 medical patients admitted to the ICU, ARF occurred in 46 (23.2%). The leading cause of ARF was acute tubular necrosis. The ICU mortality for ARF patients was 47.8%, compared with 17.5% in ICU patients without ARF. Acute haemodialysis was performed in only 17.3% of the 46 ARF patients. Using Cox proportional hazard regression, we found that mean duration of stay ($p<0.001$), acute physiology and chronic health evaluation II (Apache II) score ($p<0.001$), mechanical ventilation ($p<0.01$), dialysis ($p<0.04$) and multi-organ failure ($p<0.05$) affected survival time.

Conclusions. We found that ARF is still associated with a high mortality rate and longer duration of stay, higher Apache II score, and need for mechanical ventilation; dialysis and presence of multi-organ failure were indicators of a higher mortality rate.

S Afr Med J 2009; 99: 873-875.

Acute renal failure (ARF) in the intensive care unit (ICU) is associated with mortality rates of 50 - 90%,[1] frequently occurring as part of multiple organ dysfunction syndrome in critically ill patients.[2] The high mortality is mostly due to severity of the underlying disease or co-existing condition, rather than the renal failure itself.[3-6] Risk factors for mortality include infection, oliguria, advanced age, sepsis, need for mechanical ventilation, number of failing organs and presence of circulatory shock.[4,7] Greater severity of illness and increasing co-morbidities in an ageing population may explain why technological advances in renal replacement therapy have had a disappointing effect on survival since they were first introduced in the 1960s.[6]

The optimal treatment of ARF in the ICU remains undetermined. Investigations suggest that increased haemodialysis or haemofiltration results in a survival benefit.[5] The choice of dialysis in critically ill patients is controversial. Meta-analyses comparing continuous renal replacement therapy (CRRT) with conventional intermittent haemodialysis in unselected ICU patients found no significant difference in mortality.[1] However, compared with intermittent haemodialysis, CRRT had a lower mortality rate when patients of similar baseline severity of illness were compared.[1] Although a recent study[8] suggests that almost all patients with ARF as part of multiple-organ dysfunction syndrome requiring dialysis can be treated with intermittent haemodialysis as opposed to continuous veno-venous haemodialysis (CVVHD), both techniques produced similar outcomes.

Despite limited evidence, some authorities advocate initiating renal replacement therapy before the development of clinical azotaemia in critically ill patients with ARF. A retrospective study of 100 trauma patients with ARF (aged >8 years) indicated an increased survival rate when CRRT was initiated at urea levels <22 mmol/l. Similarly, a retrospective analysis of early and aggressive CRRT in patients with ARF after cardiac surgery was associated with better than predicted survival. No large prospectively randomised controlled trial has addressed this issue. Traditional indications for dialysis are refractory pulmonary oedema, severe metabolic acidosis, uncontrollable hyperkalaemia, or uraemic complications. Suggested criteria for earlier introduction of renal replacement therapy include oliguria (<200 ml/12 h), anuria (<50 ml/12 h) and urea levels >30 mmol/l. Renal units and nephrologists use many factors in deciding when to initiate dialysis, since there are no fixed guidelines on when to do so.

Methods

Ours was a retrospective, single-centre cohort study over 12 months commencing 1 December 2003. All patients admitted to the medical ICU with all causes of renal failure or who developed renal failure following admission to the ICU were

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included. ARF was defined as a serum creatinine level ≥177 µmol/l, or a twofold increase in baseline serum creatinine after pre- and post-renal causes were corrected or excluded.

Data collected included age, sex, human immunodeficiency virus (HIV) status and pre-existing chronic diseases. HIV status was obtained because of the potential need for dialysis and the logistics of which dialysis machines to use. The acute physiology and chronic health evaluation II (APACHE II) score was calculated at 24 hours after admission to the ICU. Oliguria was defined as <400 ml of urine in 24 hours. The premorbid urea and creatinine figures were recorded if available. The number of days on mechanical ventilation, and urea and creatinine levels on ICU entry and study entry, peak levels, and levels on discharge from the ICU were noted.

The causes of ARF were identified. The aetiological group of acute tubular necrosis (ATN) (more than one category possible) was subdivided into nephrotoxic, septic or renal hypoperfusion ATN.[4]

Multi-organ failure was defined as two or more organ system failures not including renal failure. The failure of the cardiovascular, respiratory, haematological, hepatic, gastro-intestinal, and neurological systems was based on the definitions by Tran *et al*.[11]

The American College of Chest Physicians consensus criteria were used to determine the presence of sepsis.

Statistical analysis

Stepwise logistic regression was used to explore the effect of several variables on death in the ICU. The dependent (response) variable was defined as death in the ICU or survival to discharge. Independent variables were either categorical (age, gender, oliguria, sepsis, dialysis and multi-organ failure) or continuous (APACHE II, study entry creatinine and peak ICU creatinine). The step selections were based on the maximum likelihood ratio. Odds ratios were given with a 95% confidence interval. The analysis was performed using SAS statistical software.

A Cox proportional hazard regression was performed on the following variables: age, gender, mean duration of stay in the ICU, HIV status, APACHE II, study entry creatinine, peak ICU creatinine, dialysis, oliguria, sepsis, mechanical ventilation and multi-organ failure. The dependent (response) variable was survival time. The survival time was defined as the time of entry to the study, to either discharge or death in the ICU.

Results

A total of 198 medical patients were admitted to the ICU, of whom 46 (23.2%) had or developed ARF. Their characteristics are shown in Table I.

The aetiology of ARF in the study was as follows: ATN 38 (82%), acute glomerulonephritis 4 (8.6%), malignant hypertension 3 (6.5%) and vasculitis 1 (2.2%). Some patients had multiple causes of ATN. The ATN mechanisms were sepsis in 24 cases, hypoperfusion in 15 and nephrotoxin in 6. The nephrotoxins were aminoglycosides, vancomycin and non-steroidal anti-inflammatory drugs.

Dialysis was performed on 8 (17.3%) patients; intermittent haemodialysis was used on 6, and CVVHD on 2. Patients receiving dialysis had a mean ICU stay of 13.9 days, mean Apache II score of 18.56, and mean age of 32.4 years. Patients with ARF who were not dialysed had a mean ICU stay of 10.2 days, mean Apache II score of 25.2, and mean age of 47.2 years.

Table I. Characteristics of patients with acute renal failure (*N*=46)

Variable	Study	Control
Age (years) (mean ± SE)	44.4±19	41.5±14.5
Gender (male:female)	1.5:1	1:1.2
ICU stay (days) (mean ± SE)	10.8±12.2	7.24±9.3
APACHE II score (mean ± SE)	23.4±8.5	13.22±4.5
HIV (+/-/not tested)	3/24/19	
Oliguria	23 (50%)	
Study entry serum urea (mmol/l)/serum creatinine (µmol/l) (mean ± SE)	24.6±17.2/451±388.6	
Peak ICU serum urea (mmol/l)/serum creatinine (µmol/l) (mean ± SE)	35.7±25.1/629.2±416.5	
Mechanical ventilation (days) (mean ± SE)	9.1±11.8	
Multi-organ failure	36 (78%)	
Sepsis	23 (50%)	
Dialysis	8 (17.3%)	
Pre-existing chronic illness		
Diabetes mellitus	9	
Hypertension	10	
Congestive cardiac failure	2	
Chronic renal failure	4	
Respiratory failure	4	
Immunocompromised (SLE, AIDS, malignancy, immunotherapy)	4	

Outcome

The ICU mortality of patients with ARF was 47.8% (22) compared with 17.5% for the control group. The in-hospital mortality rate of patients with ARF was 58.7%. We did not analyse the in-hospital mortality rate for patients who were not entered in the study. The ICU mortality for patients who received dialysis was 37.5% (3), and the in-hospital mortality was 50% (4).

Multivariate analysis

Using stepwise logistic regression, we found that the following variables influenced ICU mortality: Apache II ($p<0.05$), dialysis ($p<0.007$), multi-organ failure ($p<0.01$), and oliguria ($p<0.02$). Using Cox proportional hazard regression, the following variables affected survival time: mean duration of stay ($p<0.001$), Apache II ($p<0.001$), mechanical ventilation ($p<0.01$), dialysis ($p<0.04$) and multi-organ failure ($p<0.05$), while sepsis ($p=0.7$), oliguria ($p=0.8$) and HIV status ($p=0.9$) were not statistically significant.

Discussion

Despite advances in renal replacement since the 1960s, there has been little improvement in mortality, which has been attributed to increasing severity of illness and increasing co-morbidities because of an ageing population.[3,6,9,10] Our overall ICU mortality rate for patients with ARF was 47.8%, which is comparable to studies from developed nations.[1] The overall in-hospital mortality of 58.7% was significantly higher than that of patients who had never developed ARF in the ICU (mortality rate of 17.5%); this highlights the importance of renal failure in the excess mortality rate in ICU patients. The risk factors associated with increased mortality vary between studies, with infection, oliguria, need for mechanical ventilation, multi-organ failure, Apache II score, mean duration of ICU stay, advanced age and dialysis having been identified.[4,7,9,10]

In several studies, sepsis was considered to be predictive of a poor outcome, whereas other studies failed to demonstrate a link by multivariate analyses. We were unable to confirm sepsis as a predictor of mortality in ICU patients, but a need for mechanical ventilation, presence of multi-organ failure, and higher APACHE II score were predictors of a worse prognosis, as in other multivariate analysis studies.[4,9] Oliguria has been demonstrated to be a predictor of worse prognosis in various studies, whereas in others,[12] including ours, it was not. HIV status did not contribute statistically to the outcome.

The ICU mortality rate for patients who received intermittent haemodialysis was 15%, compared with the 2 patients who received CVVHD, who both died. The study group that received dialysis was too small to draw significant statistical comparisons between the two modalities. Two meta-analyses comparing CRRT and intermittent haemodialysis in unselected ICU patients found no significant difference in mortality.[1] However, compared with intermittent haemodialysis, CRRT had a lower mortality rate when patients of similar baseline severity of illness were compared.[1] A study of 360 patients in which the patients were randomised and treated with intermittent haemodialysis or CVVHD showed that almost all patients could be treated with intermittent haemodialysis.

Conclusion

The ARF mortality rate of 47.5% in our medical ICU is comparable to data from developed nations, and the main predictors of survival time in ICU were shorter duration of stay, lower Apache II score, and avoidance of the requirement for mechanical ventilation.

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Accepted 29 April 2009.