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ACUTE RENAL FAILURE REQUIRING RENAL REPLACEMENT THERAPY IN THE INTENSIVE CARE UNIT SETTINGS

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PËRMBLEDHJE

Insuficenca renale akute (IRA) e trajtuar me terapi zëvendësuese renale në njësine e terapisë intensive është në rritje. U studiuan 4517 pacientë të shtruar në reanimacionet e Qendrës Spitalore Universitare në Tiranë nga Janari 2005 në Dhjetor 2007. **Rezultatet:** Nga 76 pacientë që plotësonin kriteret për IRA, 22 (16 M, 6 F) pacientë u trajtuan me 96 seanca hemodialize. Mosha mesatare ishte 51±18.9 years, APACHE II score 27.8±6.4. Ditëqëndrimi në reanimacion 13.6±6.8. Mortaliteti deri në dalje nga spitali 45%. Rekuperimi i funksionit renal në 54.5% të pacientëve. Test *t* Studentit tregoi diferencë të rëndësishëme midis të mbijetuarëve dhe jo për moshën mesatare (42.9±19.3 vs. 60.7±15; p=0.028), APACHE II score (24.4±4.3 vs. 31.9±6.7; p<0.05). **Konkluzionet:** Mortaliteti midis pacientëve kritik që kanë nevojë për terapi zëvendësuese renale mbetet i lartë. Mosha e avancuar, APACHE II score, ishin faktorë që lidhen me një mortalitet më të lartë.

ABSTRACT

Acute renal failure (ARF) requiring renal replacement therapy (RRT) in the intensive care unit (ICU) is growing. 4517 patients admitted to the ICUs of the University Hospital in Tirana from January 2005 to December 2007 were reviewed retrospectively. Patients who met criteria for ARF were identified. **Results:** Twenty-two (16 M, 6 F) of the 76 patients who met criteria for ARF underwent 96 IHD sessions. The mean patient age 51±18.9 years, APACHE II score 27.8±6.4. Length of ICU stay 13.6±6.8. The overall in-hospital mortality 45%. Recovery of renal function as possibility to interrupt RRT in 54.5% of patients. Student's *t* test showed significant difference between survivors and non survivors for mean age (42.9±19.3 vs. 60.7±15; p=0.028), APACHE II score (24.4±4.3 vs. 31.9±6.7; p<0.05). **Conclusions:** The mortality rate among critically ill patients needing RRT remains high. Advanced age, APACHE II score were associated with a worse outcome.

Key words: Acute renal failure, intensive care unit, dialysis, complications, mortality.

INTRODUCTION

The clinical condition of acute renal failure (ARF) occurs from 1% to 25% of critically ill patients, depending on the population being studied and the criteria used to define its presence [1]. Critically ill patients with severe ARF requiring renal replacement therapy (RRT) have a mortality of 50% to 80% which varies with clinical severity [3, 14]. Moreover, by increasing the hospital length of stay [4, 5, 6] and by inducing the need for renal replacement therapy, acute renal failure has substantial economic consequences [4, 5].

The presence of the following factors has been related to a worse outcome in ARF patients: age, comorbid condition, mechanical ventilation, low perfusion status (identified as persistent arterial hypotension, need for inotropic drugs or cardiovascular failure), sepsis, jaundice or hepatic failure, coma or disturbance of consciousness, need for RRT [15]. Oliguric ARF is an independent risk factor for ICU mortality [6]. A wide agreement has been established; the higher the number of organs in failure, the higher the mortality.

There has been a decline in the use of peritoneal dialysis in critically ill patients with ARF, however especially in children this might be still an option at least to be considered.

Continuous renal replacement therapies (CRRTs) have been in use since 1977 [13]. The complexity of the patient with ARF with associated multiple organ failure suggests that CRRT should probably be utilized as a first choice treatment in intensive care unit settings, but a survival advantage is yet to be clearly demonstrated.

Intermittent Hemodialysis (IHD) has been the mainstay of RRT in ARF over the past 30 years. Intradialytic hypotension is a common complication.

Slow extended daily dialysis (SLEDD) is an intermittent dialysis with a treatment time 6-12 h, reduced blood flow rate 100-200 ml/min and reduced dialysate flow rate 300 ml/min. The cost of this new technique is lower than CRRT and also intradialytic complications.

The aim of this study was to evaluate (1) clinical outcomes: in-hospital mortality, recovery of renal function, length of stay, clinical complications, and (2) to determine the relative influence of comorbid conditions and severity of illness on outcomes of critically ill patients with ARF treated by daily IHD.

METHODS

We considered all adult ICU patients with ARF in whom a nephrology service consultation was obtained at the University Hospital in Tirana between January 2005 and December 2007. Patients were reviewed retrospectively through computer data base and medical notes.

ARF was defined using standard laboratory parameters. For patients with no prior history of kidney disease or available laboratory values, ARF was defined by a serum creatinine of $\geq$1.7 mg/dL. In patients with known pre-existing mild to moderate renal disease, ARF was defined by a rise in serum creatinine $>$50% of the baseline values. Exclusion criteria included patients with mean arterial blood pressure $<$70 mmHg and cardiogenic shock, previous dialysis for CRF, kidney transplantation. The study was approved by the institutional review boards of hospital.

Hemodialysis was performed daily with INTEGRA-HOSPAL machines. Bicarbonate dialysate, adjusted according to individual sodium requirements were used.

Vascular access was obtained with a dual-lumen hemodialysis catheter (femoral, jugular intern, subclav). Patients who required anticoagulant therapy received systemic unfractionated heparin. Only first-use, high-flux, synthetic dialyzer membranes (polysulfone F60, Fresenius) were used. The duration of hemodialysis was 3-4 hours, with a blood-flow rate which varies from 150 to 250 ml/min depending on hemodynamic status, and dialysate flow rate was 500ml/min.

Causes of ARF were classified into medical, surgical and obstetrical. Medical causes were categorized as cardiovascular, neurological, gastrointestinal, hematological, metabolic and renal. Type of surgery was not included, but the onset of surgery as scheduled or nonscheduled was included.

Clinical parameters were reviewed in the first 24 hours of admission to the ICU.

The overall severity of illness was based on the Acute Physiology and Chronic Health Evaluation (APACHE II) score [12] and SOFA score [16].

Definitions of clinical parameters

Acute Renal Failure: serum creatinine>1.7 mg/dl.

Oliguria: urine output<400 ml/24 h.

Complete recovery of renal function: return of serum creatinine to <2 mg/dl, or return to baseline creatinine concentration for patients with acute on chronic renal disease.

Partial recovery: hospital discharge with a serum creatinine >2 mg/dl, but the patient was no longer dialysis dependent.

End Stage Renal disease: need for dialysis therapy for longer than 3 months.

Hypotension: systolic blood pressure below 90mmHg, one or more episodes.

Need for inotropic drugs: any dosage and any inotropic drug-except dopamine used at a dose$\leq$2μg/kg/min.

Comorbid condition: presence of DM, Hypertension.

Statistical analysis

Statistical analysis and calculations were performed using SPSS statistical package, version 14.0. Data are reported as mean ± standard deviation (m ± SD) or percentages. Comparison between groups was analyzed by using analysis of variance (ANOVA) test for numerical values and chi-square test for categorical data. Logistic regression analysis was used for independent risk factors. *P* less than 0.05 is considered significant.

RESULTS

A total of 4517 patients were admitted initially or after some time to the five ICUs of the University Hospital Center "Nënë Tereza" in Tirana from January 2005 to December 2007. A total of 76 patients (1.68% of ICU admissions) were identified for ARF. Twenty-two of these ARF patients (28.9%) were treated by daily intermittent hemodialysis with a total of 96 IHD

sessions. These patients received an average of 4.36±4.45 (range 2-20) dialysis treatments per patients.

This twenty-two patients 16 male and 6 female with a mean age 51±18.9 years (range 16-76), had an APACHE II score 27.8±6.4 (range 19-39) on the first day of the ICU admission.

We found that medical causes of ARF constituted 72.3%, obstetrical 9%, and surgical causes 18.8%, which were divided into scheduled and unscheduled surgery (13.6% and 5.2% respectively). Medical causes were divided into: cardiovascular 18.8%, neurological 5.2%, gastrointestinal 13.6%, hematological 9.0%, metabolic and renal 27.7%. Respiratory support occurred in 82%, coma in 64%, vasopressor support in 63.6%. Sepsis was present in 55.0% of patients, oliguric ARF in 91.0%, comorbid condition in 45.0%.

For renal function, sCr values are presented as baseline sCr before ICU admission, peak sCr in the first 24 hours of ICU admission and sCr values at hospital discharge or death (Table 1).

Parameter	Mean ± SD (range)
*Baseline sCr (mg/dl)	1.1 ± 0.38 (0.8-2.1)
Peak sCr (mg/dl)	11.9 ± 3.7 (6.1-13.5)
sCr at discharge or death (mg/dl)	4.3 ± 3.7 (0.9-9.2)
*BUN at admission (mg/dl)	100.9 ± 41.1 (55-110)
BUN at IHD start (mg/dl)	117.6 ± 32.4 (60-155)
Mean Ultrafiltration (ml)	2000 ± 1087 (1000-4000)

*Baseline sCr; serum creatinine before admission,
*BUN; Blood urea nitrogen

Table1. Renal Function of hemodialysed patients

During the IHD treatments hypotensive episodes or need for therapeutic interventions happened in 72% of patients. Difficulties in obtaining venous access were encountered in 9% of cases. 4.5% of patients developed bleeding complications. Recovery of renal function as possibility to interrupt RRT was in 54.5% of patients (91.6% for survivors, 10% for non survivors). Complete recovery was in 45% of patients, partial recovery in 9.5% of patients. Of the surviving patients, 4.5% remained on chronic dialysis (ESRD) at hospital discharge. Duration of admission days in ICU for the hemodialysed patients was 13.6±6.8 and for the 76 ARF patients was 10.1±6.3 with a significant difference p=0.027. The overall in-hospital mortality for the hemodialysed in ICU patients was 45%.

Student's *t* test showed significant difference between survivors and non survivors in mean age (42.9±19.3 vs. 60.7±15; p=0.028), APACHE II score (24.4±4.3 vs. 31.9±6.7; p<0.05) and SOFA score (9.3± 2.4 vs. 14.0± 2.5; p< 0.001) (Table2).

Parameters at admission ICU	Survivors (55.0%)	Non Survivors (45.0%)	*P* value
Age	42.9±19.3	60.7±15	0.028
Mean arterial pressure	76.4±28.2	72.3±16.1	0.677
Serum Creatinine	7.3±2.4	7.6±3.3	0.733
APACHE II score	24.4±4.3	31.9±6.7	0.05
SOFA score	9.3± 2.4	14.0± 2.5	0.001
BUN at IHD start	110.4±36.5	126.3±27.8	0.273

Table 2. Statistical Analysis (Student's *t* test) for Predictive Factors of Hemodyalised Patients

Chi-square test for clinical parameters of hemodialyzed patients didn't show significant difference between the two groups (Figure1).

Logistic Regression analysis applied for 76 ARF in ICU patients showed as independent risk factors for death: respiratory support, coma, vasopressor support, sepsis and comorbid condition (Table3).

Clinical Parameters	OR (95% CI)	*P* value
Respiratory support	0.028 (0.002- 0.33)	0.005
Coma	0.147 (0.028- 0.774)	0.024
Vasopressor support	0.101 (0.019- 0.544)	0.008
Sepsis	0.048 (0.008- 0.283)	0.001
Oliguria	1.095 (0.151- 7.924)	0.928
Comorbid condition	0.215 (0.051- 0.916)	0.038

Table 3. Logistic Regression analysis for independent risk factors for death (n.76 ARF patients in ICU)

DISCUSSION

Acute renal failure often occurs as part of a more complex syndrome in critically ill patients. The patient is different from those followed in renal wards. ARF is often complicated by other pathologic conditions. When severe ARF occurs in patients with severe systemic illness, septic shock and multi-organ dysfunction [8, 11], it considerably complicates patient management. The patient is "unstable" and under

pharmacologic support, is mechanically ventilated and unconscious. The patient presents sepsis symptoms and MOF syndrome.

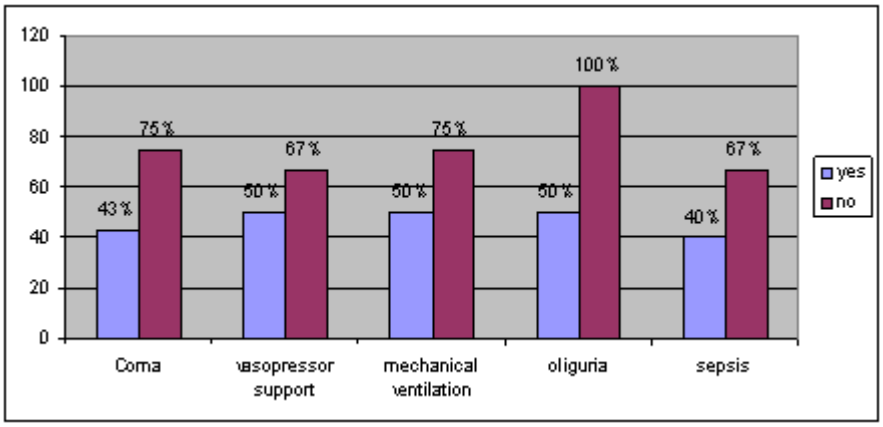

Figure 1. IHD in patients with ARF and MODS (n=22). Predictive factors and survival rate (chi-square test).

This study was designed to evaluate how ARF needing RRT affects mortality, recovery of renal function and length of stay.

Starting from the definition of ARF itself, many controversies surround its management [2, 10].

CRRT has theoretical advantages over IHD for critical patients, but a survival advantage with CRRT is yet to be clearly demonstrated [14].

The overall in-hospital mortality of our patients treated by daily IHD was 45%, considerably lower than 60 to 80% rates reported in most published studies. This finding may be due to an improved level of care or may reflect the exclusion of patients to ill (hypotensive).

Mortality in the critically ill patient is likely to be influenced by several factors related or unrelated to dialysis. Dialysis-related factors include: the timing of initiation, frequency, intensity, membrane choice, and dose of dialysis [7]. The Acute Dialysis Quality Initiative (ADQI) conference [1] recommended that initiation of RRT begin before complications are present (BUN>80 mg/dl). In our study initiation of RRT was more frequently guided by oliguria than by increases in creatinine and BUN (BUN at IHD start 117.6 ± 32.4 mg/dl). There was no significant difference between survivors and no survivors for the time of IHD start (Table2). The other dialysis-related factors are not analysed in this study.

It is well recognized that severity of illness affects outcomes in critically ill patients. In this study, each of tow indices of severity of illness APACHE II score and SOFA score were significantly associated with mortality. Other factor significantly associated with mortality was advanced age. Chi-square test and logistic regression analysis didn't show any significant factor associated with mortality when applied for the 22 hemodialysed patients.

When applied for the whole group of ARF patients logistic regression analysis showed as independent risk factors for death: respiratory support, coma, vasopressor support, sepsis and comorbid condition. There was no significance for oliguria as independent risk factor. If oliguria is an independent risk faktor for death or a marker of disease severity this is going to be objective in future studies.

Recovery of renal function and the need for short and long-term dialysis is a more specific outcome for patients with ARF. Renal recovery was rare in patients who died, also in patients with higher APACHE II score; however, survivors had varying levels of recovery of renal function. Even though peak sCr of hemodialysed patients was significantly higher than that of all ARF patients (11.9±3.7 vs. 9.52±4.91, P=0.035) survivors in the first group significantly improved renal function at discharge.

Although serum creatinine has been the biomarker of choice for evaluation of kidney function for many years, future biomarkers may be used to measure it in earlier phases of acute kidney injury [17, 18].

The daily cost for IHD is much lower than other techniques [14], but the significant difference for the

duration of admission days in ICU between patients who need dialysis and the whole group of ARF patients shows once again that severe ARF increases the cost of care.

In summary, this study demonstrated that mortality between patients with ARF and high severity of illness, needing RRT, remains high and increases the hospital length of stay and the economic costs.

REFERENCES

1. Bellomo R, Ronco C, Kellum A, Mehta RL, Palevsky P and the ADQI workgroup. Acute renal failure-Definition, outcome measures, animal models, fluid therapy and information technology needs: The second Cons. Conf. of the ADQI Group. Crit.Care 2004,**8**:R204-R212.

2. Bellomo R, Ronco C. Acute renal failure in the intensive care unit: adequacy of dialysis and the case for continuous therapies. Nephrol Dial Transplant 1996; 11: 424–428

3. 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. *Crit Care Med* 1996; 24:192–198.

4. Chertow GM, Burdick E, Honour M. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol (2005) 16:3365–3370.

5. Dasta JF, Kane-Gill SL, Durtschi AJ. Costs and outcomes of acute kidney injury (AKI) following cardiac surgery. Nephrol Dial Transplant (2008) 23:1970–1974.

6. De Mendonca A, Vincent JL, Suter PM. Acute renal failure in the ICU: risk factors and outcome evaluated by the SOFA score. Intensive Care Med (2000) 26:915–921.

7. DuBose TD JR, Warnock DG, Mehta RL, et al: Acute renal failure in the 21st century: recommendations for management and outcomes assessment. *Am j Kidney Dis* 29:793-799, 1997

8. Gaudino M, Luciani N, Giungi S et al. Different profiles of patients who require dialysis after cardiac surgery. Ann Thorac Surg 2005; 79: 825–830

9. Hoste EA, Clermont G, Kersten A. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Crit Care (2006) 10:R73.

10. Joshua J Augustine, Diane Sandy, Tracy H Seifert, Emil P Paganini. A randomized controlled trial comparing intermittent with continuous dialysis in patients with ARF. Am J Kidney Dis 2004; 44: 1000–1007

11. Kleinknecht D. Risk factors for acute renal failure in critically ill patients. In: Ronco C, Bellomo R, eds. Critical Care Nephrology. Dordrecht: The Netherlands, Kluwer Academic Publishers, 1998: 143–152

12. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACH II score: A severity of disease classification system. *Crit Care Med* 1985; 13(10): 818-829.

13. Kramer P, Wigger W, Riege Y. Arteriovenous hemofiltration: a new and simple method for treatment of overhydrated patients resistant to diuretics. Klin. Wochenschr., 55, 1121, 1977.

14. Mehta RL, McDonald B, Gabbai FB.: A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. *Kidney int* 60:1154-1163, 2001

15. Paganini EP, Halstenberg WK. Risk modeling in acute renal failure requiring dialysis; the introduction of a new model. Clin Nephrol 1996; 46:206-211.

16. Vincent JL, de Mendonça A, Cantraine F. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. *Crit Care Med* 1998; 26:1793-1800.

17. Herget-Rosenthal S, Marggraf G, Husing J, et al: Early detection of acute renal failure by serum cystatin C. *Kidney Int* 2004; 66:1115-1122.

18. Murray PT, Devarajan P, Levey AS, et al: A framework and key research questions in AKI diagnosis and staging in different environments. *Clin J Am Soc Nephrol* 2008; 3:864-868.