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*Original Article*

## Outcome and Epidemiology of Hospital-Acquired Acute Renal Failure (ARF) - a Multicenter Study

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### Abstract

**Background.** ARF is a common hospital clinical entity with varying mortality rates in different reports (25-40%). Aim of this study was to determine the epidemiology of ARF in Greece; to characterize etiology, management and outcome of ARF in hospitalized patients (except intensive care unit [ICU] patients).

**Methods.** Prospective multi-center study of patients with ARF from September 2005 to 15 December 2005 (except ICU patients). ARF was defined as serum creatinine  $>1.44$  mg/dl  $\pm$  daily urine output  $<800$ ml in patients with normal renal function or sudden rise in creatinine  $>0.72$  mg/dl in patients with known renal failure.

**Results.** 30 hospitals participated in the study. 504 patients (age:  $69.26 \pm 14.26$ ) presented with ARF. The majority of these patients were male (60%) and 46% had normal renal function prior to admission. 71% and 37.5 % had a history of hypertension and diabetes respectively. Medical causes of ARF were almost 77.3%; volume depletion was the commonest of these (47.4%). Sepsis accounted for 6% of ARF causes. Post operative ARF accounted for 34% of the surgical causes. The length of hospital stay was 9 days (range 1-90 days). 21.75% of the patients finally died.

Renal replacement therapy (RRT) was required in 34% of the cohort. Intermittent hemodialysis was the most commonly performed modality (83%). Peritoneal dialysis was performed in only 3 cases.

Independent risk factors for mortality were age (hazard ratio per year increase 1.02,  $p=0.003$ ) and daily urine output (hazard ratio per liter/day increase 0.58,  $p=0.003$ ). In Cox regression analysis RRT, diabetes, hypertension and pre-existing renal failure were not found statistically significant risk factors for mortality.

**Conclusion.** Mortality rate for patients with ARF in hospitalized patients in Greece is comparable to rates referred in other reports. In our study, only age and urine output were statistically significant mortality risk factors.

**Keywords:** Acute renal failure, hospital, mortality rate, dialysis

### Introduction

Acute renal failure (ARF) is a syndrome characterized by a sudden deterioration in renal function of several hours to several weeks duration resulting in the failure of the kidney to excrete nitrogenous waste products and to maintain fluid

and electrolyte homeostasis [1]. ARF may complicate a host of diseases that for purposes of diagnosis and management are conveniently divided into three categories: (a) diseases characterized by renal hypoperfusion in which the integrity of renal parenchymal tissue is preserved (prerenal azotemia, prerenal ARF), (b) diseases involving renal parenchymal tissue (intrarenal azotemia, intrinsic renal ARF) and (c) diseases associated with acute obstruction of the urinary tract (postrenal azotemia, postrenal ARF). Most acute intrinsic renal azotemia is caused by ischemia or nephrotoxins and is classically associated with acute tubule necrosis (ATN) [2].

ARF is a common hospital clinical entity, an independent risk factor for mortality and is associated with a significant prolongation in length of hospital stay [3,4]. The incidence and mortality rate of ARF vary extremely in the numerous studies in the literature because of different definitions of ARF, different populations studied (ICU patients, community-acquired ARF, hospital acquired ARF), different countries and so on [5,6]. Despite this difficulty, it has been possible to detect notable variations in the epidemiology of ARF during the past few decades. The absolute incidence of ARF has increased, while associated mortality rate has remained relatively static [5,7]. This lack of improvement in outcome despite significant advances in supportive care may reflect a reduction in the percentage of isolated ARF combined with an increase in ARF complicating sepsis.

We prospectively studied the etiology and outcome of adult patients with ARF in our country. We also aimed to establish the demographic characteristics of such patients and the different treatments used.

### Patients and methods

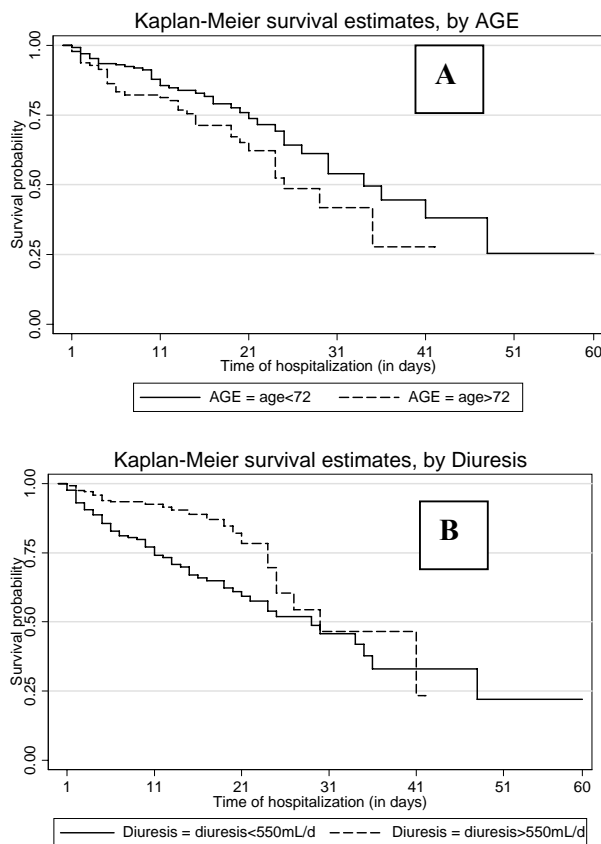
During a three month period (from September 2005 to 15 December 2005) we prospectively studied all patients with ARF occurring in tertiary hospitals in Greece (except ICU patients).

ARF was defined as serum creatinine  $>1.44$  mg/dl  $\pm$  daily urine output  $<800$ ml in patients with normal renal function or sudden rise in creatinine  $>0.72$  mg/dl in patients with known renal failure. We used a questionnaire including a number of variables and information; demographic questions, date of admission and discharge, original disease, initial admission to hospital, etiology of ARF, use of drugs, prior to admission medical history, clinical situation at the first visit, dialysis needs and techniques etc. All the cases were recorded by one or two nephrologists in each hospital.

All the questionnaires were sent to our office in our clinic and entered in a database and then analyzed with a statistical program (Stata, version 8). Survival analysis was performed using Kaplan Meier survival curves. Cox regression analysis was performed to estimate hazard ratios for continuous variables, under the assumption of proportionality. Variables statistically significant in univariate Cox analysis were included in multivariate Cox models and stepwise procedure was used to identify independent mortality risk factors.

## Results

30 tertiary hospitals participated in the study. 504 patients (mean age:  $69.26 \pm 14.26$ ) presented with ARF. The majority of these patients were male (60%). Mean age of women was  $71.6 \pm 12.95$ , while the analogue of the men was  $67.7 \pm 14.95$ . 46% of the patients had normal renal function prior to admission, while 71% and 37.5 % had a history of hypertension and diabetes respectively. Medical causes of ARF were almost 77.3%; volume depletion was the commonest of these (47.4%) whilst ATN accounted for 25%. Sepsis comprised 6% of ARF causes while glomerulonephritis was responsible for ARF only in 10 cases (0.02%). Post operative ARF accounted for 34% of the surgical causes (55% of these were due to prostatic obstruction). The length of hospital stay was 9 days (range 1-90 days). 21.75% of the patients finally died. Patients above 72 years old had 64% higher mortality risk compared to those below 72 (hazard ratio 1.64,  $p=0.0014$ ).



**Fig. 1.** Kaplan-Meier survival survival estimates by; A) age (hazard ratio per year increase 1.02,  $p=0.003$ ); B) daily urine output (hazard ratio per liter/day increase 0.58,  $p=0.003$ )

Renal replacement therapy (RRT) was required in 34% of the cohort. Intermittent hemodialysis was the most commonly performed modality (83%). Peritoneal dialysis was performed in only 3 cases. Nephrologists and dialysis unit personnel were responsible for the RRT treatments in almost all cases.

Independent risk factors for mortality were age (hazard ratio per year increase 1.02,  $p=0.003$ ) and daily urine output (hazard ratio per liter/day increase 0.58,  $p=0.003$ ) (Figure 1). In Cox regression analysis RRT, diabetes, hypertension and pre-existing renal failure were not found statistically significant risk factors for mortality.

## Discussion

This is the first multicenter prospective study of ARF epidemiology in our country. Designing this study, we had to confront with all the already known problems of epidemiological studies. First of all, which definition of ARF we should use? We decided to use the definition by Bellomo and Ronco[8] because of its simplicity and accuracy (RIFLE criteria were not widely used by the time our study was designed) [9].

There are many problems with the design of most of the clinical studies that examine the efficacy of several therapeutic interventions on the outcome of ARF. Measurement of the effect of treatment interventions in ARF is complicated by our inability to accurately define the onset and resolution of ARF beyond the heterogeneous nature of the patient population, variations in technical resources and expertise among treatment centers, and the timing of renal referral. In our country severe ARF is usually treated in dialysis units and only patients requiring ventilation are admitted to ICU. Moreover nephrology consultation is a common policy for other hospital departments. For all these reasons we decided to exclude the ICU patients realizing the quite different severity, co-morbidity conditions and treatment decisions in these patients.

The male predominance in ARF patients is something well documented in most studies [10,11] but it has not been commented on. Probably the high incidence of prostatic obstruction (55% of the surgical causes of ARF) could be a possible explanation.

Prerenal ARF was the most frequent cause of ARF in our hospitals. In Western countries etiology of ARF has changed dramatically the last decades: ATN and prerenal causes outnumber surgical and obstetrical causes outside ICU [4,12-14]. In ICU patients septic shock is the commonest cause of ARF (40-50%) and this answers for the high ICU mortality noticed in recent epidemiological studies [15-17]. We should emphasize the small percentage of glomerulonephritis-induced ARF (only 10 cases). Liano *et al.* had also referred similar percentages in their study [4].

Despite the disappointing ARF mortality rates (>50%) most meta-analysis reveal [7], most agree that ICU high mortality is responsible for the unchanged ARF mortality during the last decades [15]. Nevertheless mortality rate for patients with ARF in hospitalized patients outside ICU in Greece (almost 22%) is comparable –even better– to rates referred in other reports-20-40% [4,6] The mean duration of ARF hospital stay was 9 days, a bit longer than other studies [18, 19].

In our study, only age and urine output were statistically significant mortality risk factors. Age seems to be a risk factor in almost all studies. It is a fact that elderly patients with ARF have greater risk for death than younger [13,20-22]. Moreover anuria or oliguria are associated with poor outcome, a finding conforming with other studies [11-13,23-26]. Quite the opposite, risk factors such as need for dialysis proved not to be significant in our statistical analysis. Finally the percentage of patients needed dialysis (one in three) is comparable to that referred in Liano et al. [4]. On the contrary conventional hemodialysis (vs continuous techniques) was the commonest choice in our patients (80%), while in other studies continuous RRT is preferred [4,27,28]. This prospective multicenter hospital-based study has limitations; it is nephrology unit-based and lacks unique ARF severity scores. However it highlights the basic epidemiological characteristics of ARF in a tertiary hospital in a developed country. Moreover it indicates the improvement achieved treating patients with ARF as the mortality rate seems better than that referred in older epidemiological studies.

*Conflict of interest statement.* None declared.

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