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Acute renal failure in patients over 80 years old: 25-years' experience

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Abstract *Objective*: To determine the epidemiological trends, spectrum of etiologies, morbidity and mortality of acute renal failure (ARF) in patients over 80 years old.
Design: Historical cohort analysis.
Setting: Intensive care unit (ICU) of nephrology, Tenon Hospital, Paris.
Patients and participants: The criteria of inclusion was ARF, defined on the basis of a creatinine value over 120 μmol/l, in patients over 80 years of age admitted between October 1971 and September 1996. When moderate chronic nephropathy was pre-existing, ARF was defined by the increase of at least 50 % over the basal creatininemia.
Measurements and results: Three hundred and eighty-one patients over 80 years of age were included. The etiology and mechanism of ARF are detailed. 29 % of the patients received dialysis. Global mortality at the hospital was 40 %. Factors significantly associated with a poor prognosis are identified. Mean survival after hospitalization was 19 months.
Conclusion: The frequency of admission to ICUs for ARF in patients older than 80 years seems to be on the increase. Mortality is less severe than expected. These patients could benefit from the renal replacement therapy of modern intensive care medicine.

Key words Acute renal failure · 80 years old · Etiology · Prognosis

Introduction

Acute renal failure (ARF) in the elderly has been studied predominantly in patients over 65 years of age [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12]. However, life expectancy has dramatically increased in developed countries during recent decades (in France, for example, it is 73.39 years for men, 81.55 years for women), making the definition of aged people more difficult. Recently, a controversial debate has taken place in the United States on the question of rationing health care for the elderly [13, 14]. The care of elderly people always raises philosophical, emotional and ethical debate, but age-based stereotypes by which aged patients are denied aggressive therapies has declined, since numerous studies have shown that age itself is a poor marker of medical outcome [1, 3, 4, 5, 6, 7, 8], in contrast with others [12, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. The question is thus still unresolved concerning whether there is an age cutoff for intensive care. As budget constraints increasingly weigh on clinical decision making, guidelines for hospitalization of elderly people in intensive care units (ICUs) will more than ever include economic considerations [13], and a larger question is who, at this extreme age, benefits from admission to an ICU. Large studies are needed to evaluate the controversial decision whether or not to initiate aggressive treatments in older people and to identify patients who have such a poor

prognosis that they would not benefit from such care, because physicians will continue to refer these patients.

We conducted a historical cohort analysis, which included 381 patients over 80 years of age, referred to our renal ICU between 1971 and 1996 and followed up for survival until June 30 1997. Our main objective was to specify the epidemiological trends, the spectrum of etiologies, the morbidity and the mortality (during hospitalization and after discharge) of ARF in this population.

Patients and methods

Acute renal failure cohort

The criteria for inclusion in our study was ARF in patients over 80 years of age. ARF was defined on the basis of a serum creatinine value over 120 μmol/l. When moderate chronic nephropathy was pre-existing (creatinine value from 120 to 250 μmol/l), acute renal failure was defined by an increase of at least 50 % of the basal creatininemia. The severity of the clinical state was evaluated by the SAPS II scoring during the 24 h following admission [26]. Before 1993, SAPS II scoring was not done systematically, so that a bias in retrospectively evaluating this scoring may have occurred, especially for the determination of the Glasgow coma scale. This scale was, in this period, based on the neurological data reported in the patients' files.

Clinical and biological variables were used for statistical analyses: sex, age, weight, life style (patient coming from home, retirement house, medical service, surgical service), initial serum creatinine, blood urea nitrogen, oliguria, dialysis, complications (including death). ARF etiology was recorded as obstructive, pre-renal, or organic.

Medical history was also reviewed for the following: pre-existing renal failure, diabetes mellitus, hypertension and the existence of another chronic disease. The following comorbidity factors were evaluated, such as recent myocardial infarction or cerebral stroke, malignant disease and metastasis, single kidney, recent use of a potentially nephrotoxic drug, and the existence of a urinary infection or any other septic episode on the admission day. In some cases, a renal biopsy was performed after controlling hemostasis parameters.

Outcome assessment

We assessed patient mortality in two ways: first, mortality during hospitalization in the ICU; second, after hospital discharge, details of patients, including date of birth and national health number, were reported to the central register of the town hall in the patient's place of birth. The register issued copies of death certificates for patients who died between the date of their discharge and June 30 1997.

Statistical analyses

Univariate analyses were performed by using a non-parametric Mann-Whitney test for comparing continuous variables between patients who died during hospitalization and patients who survived. Multivariate stepwise logistic regression analysis was performed with forward selection for evaluation of risk factors for hospital death. The following variables were studied: age, year of hospital admission, sex, comorbidity factors including hypertension, diabetes mellitus, lithiasis, cerebral stroke, myocardial stroke, cancer, single kidney, urinary infection. Continuous variables were dichotomized using the median as the cutoff point (age, duration of hospitalization). Statistically significant variables at $\alpha = 0.05$ (two-tailed formulation) were retained in the final step and are given in the result tables. The odds ratio with the 95 % confidence interval estimated by the model are presented. Mortality after hospital discharge was analyzed by using Kaplan-Meier analyses with the log-rank test to compare survival according to gender. Analyses were processed on BMDP statistical software. We also compared the mortality after discharge in elderly patients admitted to our ICU for ARF with the mortality of the age-matched population in France (INED: Institut National des études Démographiques) by using the standardized mortality ratio (SMR) [27, 28].

Results

Characteristics of the patients population

Between October 1971 and October 1996, 403 patients over 80 years of age were hospitalized in our ICU for ARF. Twenty-two of the patients' files were not found, or with too much missing data, so that 381 files remained for analysis. The mean characteristics of the patients are shown in Table 1.

The median age was 85 years. When compared to the global population admitted for ARF in our center (Fig. 1), the proportion of elderly people is distinctly growing. Before 1978, the percentage of patients over 80 years of age admitted for ARF out of the total number of patients with ARF was always lower than 4 %. This number has grown from 1979 to today, with the current proportion equaling about 40 %. There were 189 male and 192 female patients. The median age was 84 for the males and 84.8 for the females. Among the comorbid factors (Table 1), 51.4 % of the patients were treated for hypertension, 27 % had a past history of myocardial infarction, 24.7 % of cancer, 16.5 % of diabetes mellitus, 13.6 % of cerebral stroke, and 3.9 % of urinary lithiasis.

Two-thirds of the patients had no history of chronic nephropathy. Their mean serum creatinine value at the admission was 509 ± 17 μmol/l (range from 124 to 1980 μmol/l). The other third had a basal creatinine value from 120 to 250 μmol/l and the mean creatinine value at admission for this group was 637 ± 24 μmol/l (range from 316 to 1670 μmol/l).

Among our patients, 49.3 % came from home to the ICU, referred by an emergency unit; 37.2 % came from a medical unit, 12.2 % from surgery and 1.3 % from a retirement home.

The mean severity SAPS II score was 54.4 ± 1 (range from 21 to 121). This markedly elevated score of severity of disease is explained by age and a high blood urea nitrogen level. Patients who died in the hospital had a mean SAPS II score of 65 ± 2, whereas patients who survived had 47 ± 1 points ($P < 0.0001$).

Table 1 Mean characteristics of the elderly patients admitted in our ICU for acute renal failure

	Males $n = 189$	Females $n = 192$	
Age: years (Mean ± SD)	84.9 ± 4.0	84.8 ± 3.0	NS
Life Style			
Home	98	90	NS
Retirement home	1	4	NA
Hospital	91	97	NS
Basis serum creatinine (120–250 μmol/l)	$n = 65$	$n = 56$	NS
Creatinine value at the admission (μmoles/l ± SD)	533 ± 25	488 ± 22	$p = 0.05$
Comorbidity			
Single kidney	11	10	NS
Hypertension	91	105	NS
Diabetes mellitus	39	24	NS
Cancer	52	42	NS
Myocardial infarction	59	44	NS
Cerebral stroke	25	27	NS
Lithiasis	7	8	NS

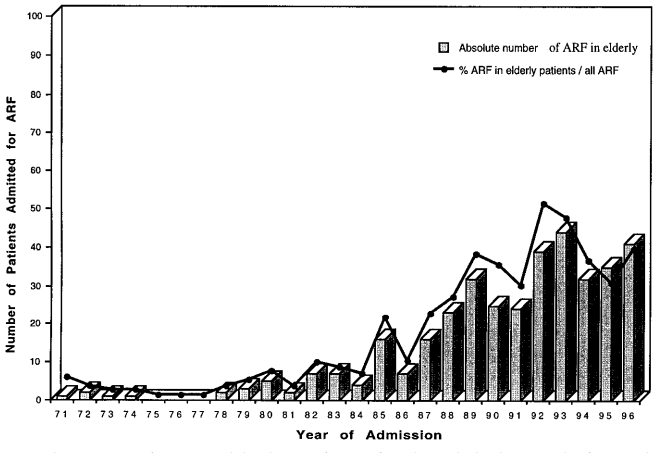

Fig. 1 Proportion of elderly patients in the global population admitted to our ICU for ARF by each year of admission

Table 2 shows the pattern of causes of ARF in our population. ARF of obstructive origin (85/381: 22.3 %) was predominantly due to prostatic tumor and other malignant pelvic tumors. Pre-renal ARF (92/381: 24.1 %) was essentially due to extracellular dehydration (59.7 %), and was mostly observed in the summer months. Organic renal failure (204/381: 53.5 %) was due to shock in 49.1 %, nephrotoxic drug in 6 %, rhabdomyolysis in 9.8 %, and multiple myeloma in 6.8 %. Whatever the origin of ARF, a nephrotoxic drug was implicated in 18 % of the cases.

A percutaneous renal biopsy was performed in 23 patients who had an organic renal failure of unclear origin. Only one biopsy was complicated (peri-renal hematoma, spontaneously reabsorbed). The results (Table 3) show a large distribution of the lesions.

Hemodialysis was necessary in 111 patients (29.1 %). As expected, most patients (3/4) who required dialysis suffered from organic ARF. Conventional hemodialysis was the most frequent method, but in some cases, hemofiltration or peritoneal dialysis was used.

Evolution at hospital

In our study the median duration of hospital stay was 10 days. Hospital mortality was 40 % (152/381) and 93 of these 152 patients died within the first 10 days following the admission; odds ratio (OR) for long hospitalization: 0.33, 95 % Confidence Interval (CI), 0.2 to 0.5. In addition, 12 patients (3.1 %) who would have required chronic hemodialysis because of terminal, irreversible renal lesions, were discharged from the hospital with familial agreement. Of the patients who died at the hospital, 69 % had an organic renal failure. The prognosis seemed to be better when a drug was implicated in the occurrence of ARF (OR for drugs logistic regression: 0.23, 95 % CI, 0.11 to 0.46). Cause of death was multiorgan failure in 29 % of the patients, disseminated sepsis from pulmonary or urinary infection in 41 %, gastro-intestinal bleeding in 16.5 %, acute myocardial infarction in 5 %, and cerebral stroke in 1.9 %. Miscellaneous causes were involved in 6.6 % of the patients.

Concerning the type of ARF, multivariate analyses of the evolution of the patients during the hospitalization showed that the following variables were independently associated with survival. Among the obstructive ARF, the risk factors identified were a previous history of nephrolithiasis (OR = 5.78; 95 % CI, 2.9 to 18.9), and a female gender (OR = 2.82, 95 % CI, 0.9 to 8.17). Among the pre-renal ARF, mortality seemed to be higher in patients who had a history of cerebral stroke (OR 4.29; 95 % CI, 1.11 to 16.5). Among the organic ARF, a previous history of cancer (OR: 2.8, 95 % CI, 1.1 to 7.07), requirement of dialysis (OR 3.17, 95 % CI, 1.51 to 6.64), and the level of serum creatinine at entry (OR 2.01; 95 % CI, 0.98 to 4.12) were poor prognosis factors.

Table 2 Spectrum of etiologies of acute renal failure in the elderly population admitted in our ICU between 1971 and 1996

ARF etiology	*n*	%
Obstructive renal failure	85/381	22,3
Prostatic adenoma	22	5,8
Prostatic cancer	19	5,0
Bladder/ureteral cancer	15	3,9
Uterus/ovaria cancer	9	2,4
Colo-rectal cancer	5	1,3
Nephrolithiasis	5	1,3
Retroperitoneal fibrosis	8	2,1
Ureteral stenosis	1	0,3
Fecaloma	1	0,3
Pre renal failure	92/381	24,1
Dehydratation	55	14,4
Heart failure	14	3,7
Dysregulation of GFR	21	5,5
Hepato-renal syndrome	2	0,5
Organic renal failure	204/381	53,5
Tubulopathy		
Shock	99	26,0
cardiogenic shock	21	5,5
septic shock	54	14,2
hypovolemic shock	34	8,9
Rhadomyoloysis	20	5,2
Multiple myeloma	14	3,7
Drugs (Aminoglycosides; NSAID; ACEI; iodinated contrast media)	23	6,0
Interstitial		
Pyelonephritis	8	2,1
Immunoallergic nephropathy	8	2,1
Glomerulopathies	8	2,1
– Goodpasture		
– Wegener		
– Post-infectious glomerulonephritis		
Vascular thrombosis	6	1,6
Cholesterol embols	3	0,8
Blood incompatibility	1	0,3

Table 3 Distribution of the lesions observed in 23 patients in whom a renal biopsy was performed because of acute renal failure of undetermined origin

Histologic findings: 23	
Tubular Cast Nephropathy	6
Post-infectious glomerulonephritis	3
Cholesterol embolization	1
Wegener granulomatosis	1
Goodpasture syndrome	1
Glomerular Thrombotic Microangiopathy	1
Acute tubular necrosis	3
Acute pyelonephritis	2
Drug associated acute interstitial nephritis	3
Tubular cell vacuaolization	2

Patients who had no previous history of renal failure, and who were discharged from the ICU, had a mean creatinine serum level of 144.5 μmol/l ± 109 μmol/l (mean creatinine decrease of 352 μmol/l or 53.2 %). The patients who had a chronic renal failure left the ICU with a mean serum creatinine level of 222.2 ± 91.2 μmol/l (mean creatinine decrease of 232.8 μmol/l or 38 %).

Evolution after discharge

By June 30 1997, we had received 107 responses from the town hall of the birth-place of the 229 patients who survived after hospitalization. Thus, depending on the date of admission, patients were followed up from 6 days to 142 months after discharge. The mean survival time after hospitalization was 572 days (19 months), ranging from 6 to 4153 days (more than 11 years). As depicted by the survival curve (Fig. 2), 20 % of the patients died during the first year following their discharge and, within 6 years, only 20 % of males were still alive when compared to 40 % of females. The patients discharged from the hospital had a slight but significant increase in mortality (SMR = 2.24, $P < 0.001$, Fig. 3). These results must be interpreted with circumspection as we received information for only 46 % of the patients.

Discussion

Our ICU policy of admitting all proposed patients in need of intensive care regardless of age has not changed since the first study year, and survival to the age of 80 and beyond has increased in many developed countries. To our knowledge, there is no published study about ARF in such an elderly population. "ARF in the elderly" is a term usually employed to designate people over 60 [5, 10], 65 [3, 4, 6, 7] or 70 [1, 8] years old.

Our study is retrospective and so the assessment of some of the patients' data was difficult, but it clearly shows an increase in frequency of elderly people admitted for ARF, and we are very confident that the results presented here provide important information about the epidemiology and prognosis of ARF in aged patients during the last 25 years. Actually, the epidemiology of ARF has changed a lot in recent decades, e. g., the disappearance of post-abortum ARF has contributed to a reduced proportion of young women [29] with this condition. The proportion of elderly people among patients admitted to ICUs for acute renal failure is increasing, being between 20 to 45 % in the 1990 s, whereas it barely represented 5 % in the 1970 s.

Noteworthy is the large proportion of ARF from obstructive and pre-renal causes. The frequency of neoplasias at this age explains the obstructive type of ARF, since neoplasms are the origin of over 50 % of obstructive ARF.

Principle causes involved in pre-renal failure were dehydration and drugs interfering with the renal

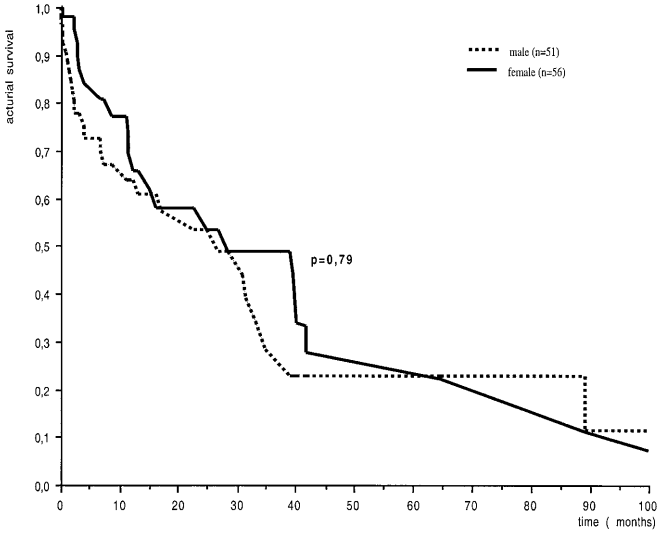

Fig. 2 Actuarial survival of the patients who were discharged of the hospital

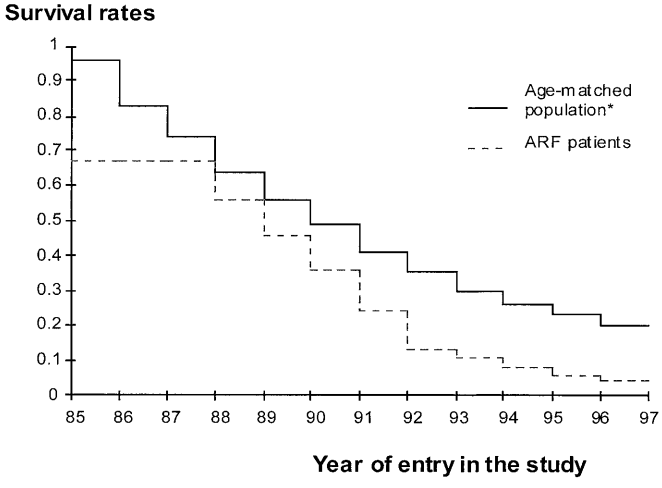

Fig. 3 Mortality of patients discharged from ICU compared to the age-matched global population in France (standardized mortality ratio: 2.24 p < .001). * = survival rates estimated according to the French age-sex-matched population

autoregulatory mechanisms (ACEI, diuretics, and NSAID). The proportion of pre-renal failure has continued to increase, as has the mean age of the patients (83.35 ± 0.4 between 1971 and 1980 versus 85.58 ± 0.27 between 1991 and 1996), partly because this population is very sensitive to dehydration and drug side effects [30, 31]. Indeed, the elderly have a higher tendency to develop pre-renal failure for several reasons: a reduction in renal mass of up to 30% by the eighth decade [32]; a reduction in renal blood flow [33]; and diminished water ingestion, probably because of a reduction in thirst and more difficult access to water.

Organic renal failure represents 50% of the causes of ARF in our series and was essentially due to septic or cardiogenic shock. Most ARF occurring during hospitalization in other departments was from iatrogenic causes. More specifically, 7.6% (29/381) of the patients had received either aminoglycosides or iodinated contrast media. These patients belong to the category of the 18% of ARF for which a nephrotoxic drug was implicated, and which could potentially have been avoided if these drugs had been carefully monitored in the elderly [30].

Age per se is not a contraindication to renal biopsy [34]. It was performed in 6% of our patients, who had an acute renal failure of undetermined origin, or because of findings compatible with systemic illnesses (vasculitis, rapidly progressive glomerulonephritis, acute interstitial nephritis).

Mortality has not decreased in such patients and has even increased in recent decades despite the advances in modern intensive care/renal replacement therapy [35]. This lack of impact on survival in ARF patients is thought to result from the increasing age of the patients treated and a rise in the severity of the underlying disease with a growing proportion of subjects acquiring multiple organ system disease [21, 36, 37]. Thus, the rising number of older and more severely ill patients would offset the favorable effect of modern medicine. But whether age per se contributes to the persisting high mortality of ARF patients has never been convincingly demonstrated. Our patients most certainly had a slight but significant increase in mortality when compared to an age-matched population in France at each year of the study as attested by an SMR of 2.24 ($P < 0.001$), which indicates that ARF and ICU stay are morbid events at this age [38]. But, unexpectedly, mortality in the elderly in our study was no worse than the overall mortality of ARF in the literature, in spite of "physiological" impairment due to the aging kidney. A tempting explanation is the relative ease of recovery of renal function when the mechanism of renal failure is either obstructive, or pre-renal (46.4% of the patients). On the other hand, this population is weakened by age and associated comorbidities and is more prone to cardio-vascular complications. As suggested by Finn [39], the cause of the observed paradox may rely on the fact that in younger patients the severity of the underlying disease and number of complications necessary to induce ARF are higher, and the insult leading to ARF more severe than in the elderly. Druml [3] found an overall survival of 39% (similar to the mortality in the younger population) in 242 elderly patients over 65 years old. He further divided the series into age steps of 3 years, finding that mortality in patients over 80 years was no higher than in those aged 65–68 years. In numerous studies [12, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25], however, age is regarded as a bad prognostic factor, with a mortality ranging from 60 to 100%.

In occidental countries, physicians will have to take up a very delicate challenge. Extremely aged people are an expanding population, due to the increase in life expectancy, especially in occidental countries and particularly in the United States [40]. The improvement in geriatric medicine will have to be seen in the context of the quality of family support and the mental functioning and physical ability of the patients. Decision-making should be based on potential benefit to the individual, for age alone is often a poor marker of disability. Our study did not address whether patients were able to return to a normal pre-hospitalization lifestyle, or the effect of hospitalization in the ICU on eventual quality of life.

In conclusion, our society will face, more than ever, intensive care problems in the elderly. Our results show an increase in the number of patients over 80 years of age who are admitted to the ICU for ARF. Mortality at the hospital and after discharge seems to be less catastrophic than expected, so that age per se does not have a major impact on the evolution. We think that these patients could benefit from the renal replacement therapy of modern intensive care medicine, whenever they have some chance of benefit or whenever the outcome is uncertain. Determining that a certain form of care is futile or inappropriate is no more rational in the case of the elderly than in any other group. These data should now be balanced by the estimation of the cost-effectiveness index of admission of elderly people to the ICU. A special difficulty is in deciding whether the relevant criterion is to compare the cost with further life expectancy, or with survival.

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