

Acute renal failure of medical type in an elderly population

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Abstract. One hundred and nine unselected patients with Acute Renal Failure (ARF) of medical aetiology were hospitalized at the Nephrological Unit of Policlinico University Hospital (Modena) during a 30-month period. ARF was considered as a rapid increase of serum creatinine >2mg/dl over the baseline level or the doubling of pre-existing value in chronic renal failure. Mean age of patients was 67 ± 17 years and median age was 72; 64.2% needing dialytic treatment. Four main causes of ARF were identified: 33 patients had reduced renal perfusion by dehydration, hypotension etc.; 20 multifactorial aetiology; 14 biopsy-investigated renal parenchymal diseases and 39 had drug-related acute renal failure (D-ARF). The clinical outcome was significantly worse in elderly patients as regard mortality ($P < 0.02$), chronic dialytic treatment ($P < 0.04$) and complete recovery ($P < 0.004$). The mean age of D-ARF patients was significantly greater than remaining ARF patients (72.6 ± 12.8 vs 63.2 ± 18.5 ; $P < 0.004$). Nonsteroidal antiinflammatory drugs (NSAIDs) and ACE-inhibitors (Ace-i) caused ARF in 24 and 8 patients respectively. Elderly age, vascular disease and monoclonal gammopathy represented the main risk factors and were significantly more frequent in D-ARF patients ($P < 0.001$, < 0.01 , < 0.04 respectively). Our data confirm the high susceptibility of ageing kidneys to nephrotoxic damage caused by drugs affecting glomerular autoregulation by microvascular mechanisms. Greater attention to renal changes in ageing and an increased dissemination of preventative measures among nephrologists, could reduce the incidence of these serious and potentially lethal diseases.

Introduction

Acute renal failure (ARF) is a heterogeneous disease with a changing spectrum in the last decades. Out of 1347 patients affected by ARF between 1955 and 1980, the median age progressively increased from 35 to 60 years [1] as a result of extending admittance to nephro-

logical units and to dialytic treatment. Post-surgical ARF decreased slowly, probably because of a better knowledge of acid-base and hydro-electrolytic problems, but cardiovascular surgery, now dealing with high-risk patients, is again producing a number of ARFs [1,2]. Obstetric cases have been greatly reduced in Western countries, reflecting the disappearance of septic abortion [1,3]. Presently, the increase in life expectancy produces a new cohort of elderly patients needing nephrological and dialytic assistance. In the nephrological department of Modena University, patient selection was not carried out and the only limitation to nephrological ward admittance consisted of immediate bed availability. The aim of the present investigation is to evaluate the characteristics of ARF of the medical type in the Modena area during the last years.

Patients and methods

Patients

A retrospective analysis of clinical documents concerning patients hospitalized because of ARF of the medical type was performed at the nephrological unit of the Policlinico University Hospital in Modena. The patients hospitalized in different wards of the same hospital and treated by nephrologists on a consultation regimen were not considered, since retrospective studies need homogeneous criteria of evaluation. The 30-month period between January 1995 and June 1997 was examined. The Modena area in 1995 had a population of 613 625, of whom 121 974 (19.7%) were considered elderly being over 65.

ARF was considered arbitrarily as a sudden and recent increase in serum creatinine >2 mg/dl above the normal value, or as the doubling of pre-existing serum creatinine in the case of chronic renal failure (CRF). Each patient was evaluated retrospectively for age, gender, factors most likely to be responsible for the ARF episode, renal function before (when available) and 1 month after ARF, dialytic requirement, outcome and risk factors. Dialysis was started when urea >250 mg/dl and/or resistant hyperkalaemia, acidosis and hyperhydration were present. No patient needed mechanical respiratory support, while cardiovascular instability and congestive heart failure (CHF) represented the main causes of death in 12 patients deceased within the first day of admittance. Out of 21 patients with monoclonal gammopathy, nine presented with multiple myeloma and in three of

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these the ARF episode led us to diagnose the previously unrecognized illness.

Four principal aetiological groups were identified. (i) Reduced renal perfusion inclusive of pre-renal failure and acute tubular necrosis: dehydration and hypotension of whatever origin were the most common causes in this group. (ii) Multifactorial aetiology: when more than one single causative agent such as dehydration, hypovolaemia, cardiac dysfunction, sepsis or drugs were present and inextricably connected. (iii) Renal parenchymal disease such as idiopathic rapidly progressive glomerulonephritis (RPGN), acute interstitial nephritis and RPGN secondary to systemic illness were investigated by renal biopsy and grouped together. (iv) Drug-induced ARF (D-ARF) was identified when an appropriate interval could be found between administration of a known nephrotoxic drug and onset of ARF, without interposition of different noxious events. Recovery or partial recovery after withdrawal of the drug was considered confirmatory. Ischaemic and congestive cardiopathy, transitory ischaemic attack (TCA), peripheral arteriopathy, diabetes and paraproteinaemia were considered risk factors whether on the basis of clinical or instrumental examination or simply anamnestic evidence.

Statistics

Values are means \pm SD. Statistical analysis was performed with the Student's *t*-test for unpaired values or χ^2 when appropriate. A probability of <5% of the null hypothesis was regarded as significant.

Results

At the Policlinico Hospital in Modena, out of 1528 patients (mean age 61.2 years) hospitalized in the 30-month period from January 1st 1995 to June 30th 1997, 119 presented with ARF. Subsequently, 10 patients were found to have obstructive uropathy and were then discarded from the present analysis. The remaining 109 patients presenting with medical ARF had a mean age of 67 ± 17 years and a median age of 72; 58 were males and 51 females, requiring a mean hospitalization period of 17 ± 13 days. Elderly patients represented 64.1% of all ARF cases. Acute dialytic treatment was necessary in 70 (64.2%), thus demonstrating the severity of the renal function impairment in the examined group. Surprisingly, nephrotoxic drugs were the primary cause of ARF (D-ARF) as shown in Table 1. When the age distribution of ARF aetiology was examined, a significant increase in D-ARF was

found in the elderly (Figure 1). The elderly population also presented a worse clinical outcome as regards acute dialytic need, recovery, chronic dialytic treatment and death (Figure 2, Table 2).

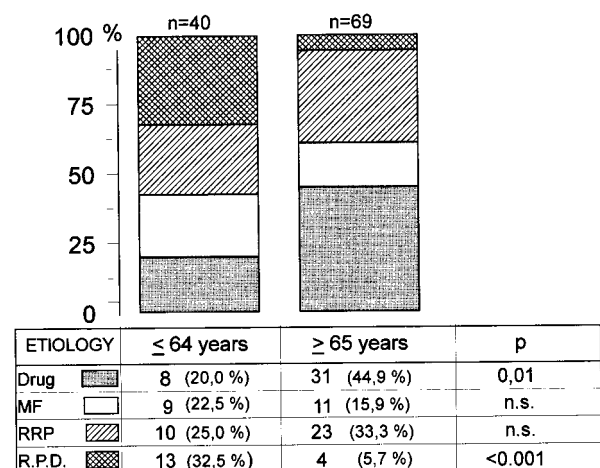


Fig. 1. Acute renal failure—etiology: distribution according to age; MF = multifactorial; RRP = reduced renal perfusion; R.P.D. = renal parenchymal disease.

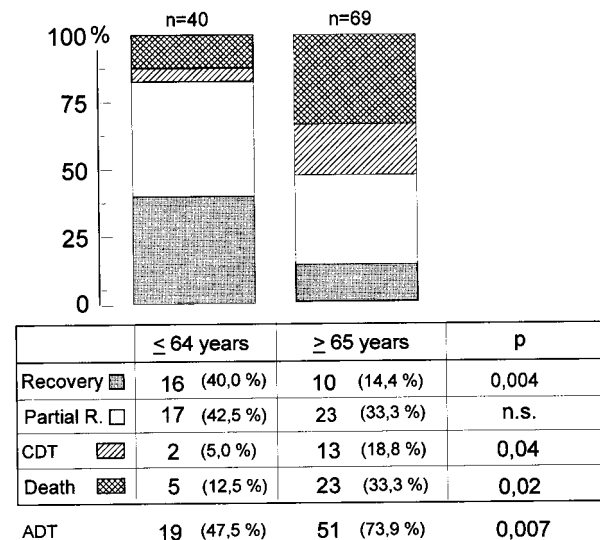


Fig. 2. Acute renal failure—outcome: distribution according to age; Partial R. = partial recovery; CDT = chronic dialysis treatment; ADT = acute dialysis treatment.

Table 1. Aetiology and outcome of medical ARF

Aetiology	Patients n (%)	Death n (%)	CDT n (%)	Partial recovery n (%)	Recovery n (%)
Drugs	39 (35.7)	7 (17.9)	8 (20.5)	17 (43.5)	7 (17.9)
MF	20 (18.3)	7 (35.0)	3 (15.0)	4 (20.0)	6 (30.0)
RRP	33 (30.2)	12 (36.3)	2 (6.00)	11 (33.3)	8 (55.0)
RPD	17 (15.5)	2 (11.7)	2 (11.7)	8 (47.0)	5 (29.4)
	109	28 (25.0)	15 (13.7)	40 (36.6)	26 (23.8)

CDT = chronic dialysis treatment; MF = multifactorial; RRP = reduced renal perfusion; RPD = renal parenchymal disease.

Table 2. Outcome of drugs-related acute renal failure

	<i>n</i>	Mean age (years)	Death (<i>n</i>)	CDT (<i>n</i>)	Partial recovery (<i>n</i>)	Recovery (<i>n</i>)
ACEI	8	72	—	1	5	2
NSAID	24	74	5	7	8	4
Antibiotic	5	76	2	—	2	—
Contrast M	2	53	—	—	2	—
All D-ARF	39	72.6 ± 12.8*	7 (17.9%)	8 (20.5%)	17 (43.5%)	7 (17.8%)
No D-ARF	70	63.2 ± 18.5*	21 (30.0%)	7 (10.0%)	23 (32.8%)	19 (37.1%)

**P* = 0.004; CDT = chronic dialysis treatment.

Non-steroidal anti-inflammatory drugs (NSAID) and angiotensin-converting enzyme inhibitors (ACEIs) were the main causes of D-ARF: the clinical outcome was better if compared with no D-ARF only when considering mortality (Table 2). Recovery was rare, while partial recovery, i.e. stable deterioration of renal function, and chronic dialytic treatment were frequent.

The age-dependent risk factor distribution is shown in Figure 3, while risk factors specific for D-ARF were advanced age, vascular disease and the presence of paraproteinaemia (Table 3).

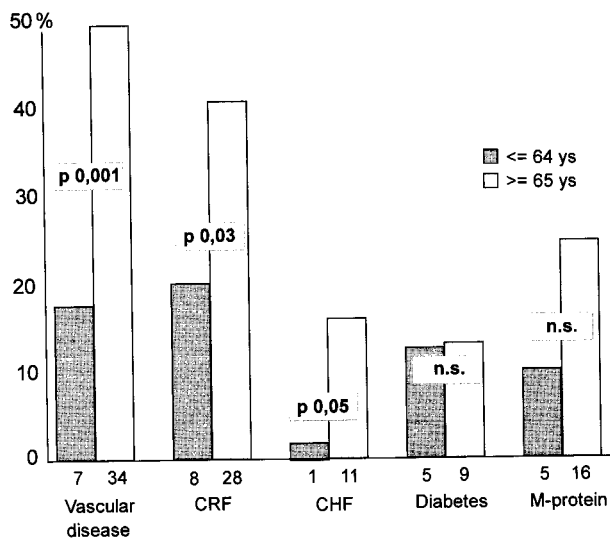


Fig. 3. Age distribution of risk factors in ARF patients; CRF = chronic renal failure; CHF = congestive heart failure; M-protein = monoclonal protein; ys = years.

Discussion

In Italy, the reduced birth rate and the increased life expectancy, now approaching 80 years for females and 73.4 years for males, produces a high percentage of elderly patients. On the basis of epidemiological studies [4], 17.49% of the whole Italian population is over 65, with a peak of 22% in Liguria and 20% in Emilia. The Modena area reflects these conditions and therefore represents a good observation point for diseases of the elderly.

Our patients were affected by ARF of medical aetiology: cardiovascular instability and CHF being poor prognostic indicators. After subtraction of obstructive cases due to prostatic diseases, male and female cases were nearly equivalent, similar to the findings of others [5].

The majority of cases of medical ARF (69 of 109) originated in the elderly population; a 10 times greater incidence as compared with younger patients (Figure 4), as similarly reported by others [2,6]. The overall outcome was significantly worse in ageing patients (Figure 2) as could be expected from the multitude of risk factors (Figure 3). Advanced age can be considered the most important risk factor because of the age-related progression of vascular damage caused by hypertension and atherosclerosis, since as many as 50% of the elderly suffer from hypertension [7]. The ischaemic pathology affecting patients in the last decades involves different target organs: most data presently available regard both the incidence and prevalence of ischaemic and congestive cardiopathy to have at least quadrupled from the 1960s to the 1980s [8,9]. Monoclonal gammopathy and related myelopro-

Table 3. Risk factors for drugs-related acute renal failure

Risk factors	ARF (109 patients) Drug (39 patients)	No drug (70 patients)	<i>P</i>	Odds ratio for D-ARF	Confidence interval
Age ≥ 65 years	31 (79.4%)	38 (54.2%)	0.01	3.2	1.3–8.0
Vascular disease	21 (53.8%)	20 (28.5%)	0.01	2.9	1.2–6.5
M-protein	12 (30.7%)	9 (12.8%)	0.04	3	1.1–7.9
CRF	15 (38.4%)	21 (30.0%)	n.s.	1.4	0.6–3.3
Diabetes	5 (12.8%)	9 (12.8%)	n.s.	0.9	0.3–3.2

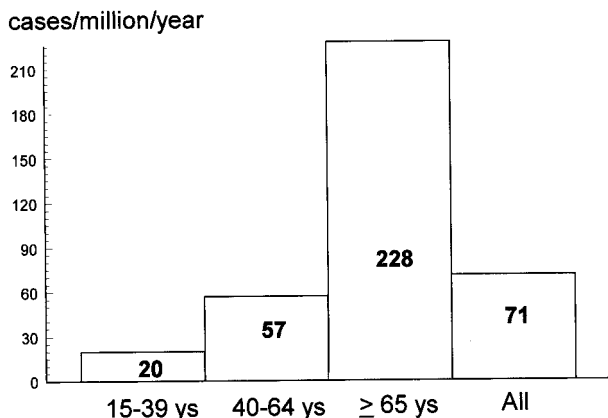


Fig. 4. Incidence of ARF in different age classes.

liferative disorders have increased similarly [10]. The renal modifications linked to morbidity in ageing [6,11] greatly affect both the incidence and outcome of medical ARF.

Not surprisingly, the most frequent aetiological factors in our casuistry were nephrotoxic drugs acting on the microvascular circulation of the kidney i.e. NSAIDs and ACEIs. Reports of ARF of patients in the 1960s have been demonstrated to present slightly smaller percentages of D-ARF [3,12,13]; our patients had a mean age of 67 ± 17 , thus being remarkably older than patients of previously reported studies [3,12,13]. Moreover, our D-ARF patients were significantly older than subjects with ARF of different aetiology (Table 2), thus confirming a strong relationship between ageing and drug-induced renal damage.

Both NSAIDs and ACEIs impair autoregulation of the glomerular filtration rate, especially in athero- or arteriolosclerotic patients with reduced renal perfusion [14]. Community-based studies evidenced high odds ratios for ARF in patients who had recently initiated NSAID treatment, especially among the elderly [15,16]. It could be hypothesized that, in Italy, legal requirements regarding the prescription of opiates could produce a shift towards prescribing NSAIDs.

Impairment of renal function by ACEIs was first described in association with diuretic-induced volume contraction [17] and, subsequently, it was investigated in detail in many exhaustive studies [18–20]. A natriuretic effect of ACEIs themselves was also hypothesized [21], while a role in salt and water resorption for angiotensin II receptors was demonstrated recently in the proximal nephron [22]. The prescription of these drug should be evaluated carefully in elderly patients particularly if they present risk factors or have dehydrating intercurrent illnesses; on the other hand, D-ARF could be considered, at least in part, as a potentially avoidable disease if a few simple precautions, e.g. evaluation of hydration status and calculation of Cockcroft–Gault formula, were more widely implemented.

In summary, our data confirm that ARF of medical

aetiology has a greater incidence and a worse outcome in an unselected elderly population. Age-related co-morbidity, i.e. vascular disease, represents the most important risk factor. Nephrotoxic drugs, especially those acting on the renal microvascular circulation, play an important role in the determination of ARF in the elderly. A wider implementation of simple precautions, well known to nephrologists, could reduce the incidence of this potentially lethal disease.

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