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Original Article

Treatment-related acute renal failure in the elderly: a hospital-based prospective study

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Abstract

Background. Elderly individuals need a host of diagnostic procedures and therapeutic interventions to take care of ailments. This prospective study was carried out to determine the magnitude of treatment-related acute renal failure (ARF) in the elderly in a hospital setting, to know about pathogenetic factors and to study the factors that could predict an adverse outcome.

Methods. All elderly patients (>60 years) admitted over a 12-month period were screened prospectively throughout their hospital stay for the development of ARF.

Results. Of 31 860 patients admitted, 4176 (13%) were elderly. Of these 59 (1.4%) developed ARF in the hospital. Nephrotoxic drugs contributed towards development of ARF in 39 (66%), sepsis and hypoperfusion in 27 (45.7%) each, contrast medium in 10 (16.9%) and postoperative ARF occurred in 15 (25.4%) patients. These pathogenetic factors were responsible for ARF in different combinations. Amongst these combination of pathogenetic factors, radiocontrast administration (partial χ^2 28.1, $P<0.0001$), surgery (partial χ^2 14.89, $P=0.001$), and drugs (partial χ^2 6.22, $P=0.0126$) predicted ARF on their own. Nine patients (15.23%) needed dialytic support. Of 59 patients, 15 (25.4%) died, of those who survived, 38 (86.3%) recovered renal function completely and six (13.6%) partially. Mortality in the elderly with ARF was significantly higher than in those without ARF (25.4 *vs* 12.5%; χ^2 8.3, $P=0.03$). Sepsis (odds ratio 43), oliguria (odds ratio 64), and hypotension (odds ratio 15) were independent predictors of poor patient outcome on logistic regression analysis.

Conclusion. Incidence of treatment-related ARF in the elderly was 1.4%, with more than one pathogenetic factor playing a role in the development of ARF in the majority. Sepsis, hypotension, and oliguria were the independent predictors of poor patient outcome.

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Key words: geriatric; hospital acquired; nephrotoxic drugs; radiocontrast; sepsis

Introduction

Low mortality rate due to better medical care has resulted in an increased geriatric population in both the developed and developing countries [1,2]. Elderly individuals need a host of diagnostic and therapeutic interventions to take care of a variety of ailments. Hospitalization itself exposes them to problems that are less often seen among elderly outpatient or young inpatients. Iatrogenic problems are also of major concern in the elderly. One such problem is the development of ARF [2].

ARF in the elderly *per se* is not an uncommon illness in the developed world because of sizeable geriatric population. In fact, ARF has been considered a typical geriatric disease. Good studies on the epidemiology of ARF in community are available [3,4]. However, the important point is to distinguish the elderly who present with well-established ARF from those who develop ARF when they are being treated for a non-nephrological illness. Not only are the causes different in these two situations but the incidence of the latter can also be minimized if not prevented altogether. Studies on the elderly with ARF have included patients with established ARF at presentation as well as those where some form of therapy resulted in ARF [5–8]. Some have looked only at one aspect of treatment-related ARF such as postoperative [9], radiocontrast nephropathy [10] and NSAIDs-induced renal failure [11]. In some studies, elderly patients admitted to the medical unit alone [12] or to the intensive care unit [13] have been studied. Those studies that have looked at hospital-acquired ARF in general have not studied the elderly as a separate group [14–16].

This prospective study was therefore carried out to determine the magnitude of treatment-related ARF in the elderly in a hospital setting, to examine various

pathogenetic factors, and to study factors that could predict an adverse outcome.

Subjects and methods

This prospective study was carried out at the Postgraduate Institute of Medical Education and Research, Chandigarh, which is a 1000-bed teaching hospital in North India with all the specialities and superspecialities. All elderly patients (>60 years old) admitted over a 12-month period between December 1996 and November 1997 were screened prospectively throughout their hospital stay for the development of acute renal insufficiency. A daily record of elderly patients admitted in different wards was obtained from the central hospital registration department. All elderly patients were then followed up during the hospital stay for the development of ARF. Serum creatinine was recorded at the time of admission in all cases. Only those patients where serum creatinine was stable (<25% variation) at admission and after 48 h were included in the study. Those who had established ARF with rising creatinine at the time of entry were excluded.

The first serum creatinine obtained after admission to the hospital was taken as the baseline value. ARF for the purpose of this study was defined as elevation of serum creatinine to over 176.8 μmol/l in the patients with normal baseline serum creatinine, and increase of more than 132.6 μmol/l when baseline serum creatinine was over 176.8 μmol/l despite correction of any clinically obvious haemodynamic or mechanical factors. After identification, a detailed record of the patient's history, physical examination, and laboratory investigations was made to document the demographic characteristics and the pathogenetic factors causing ARF. The underlying original disease for which patients were admitted were broadly categorized as surgical (those who needed surgery), cardiac (admitted for evaluating cardiac disease), infectious (presented with infection involving different organ systems), and a miscellaneous group comprising all other illnesses. These patients were then followed daily until their discharge, death, or the return of their renal functions to baseline. A serial record of urine output and serum creatinine was maintained. Various complications of renal failure that were specifically looked for and recorded were hyperkalaemia, neurological abnormalities, metabolic acidosis, gastrointestinal bleeding, pericarditis and congestive cardiac failure. Dialytic support was instituted according to standard clinical indications. Patients were classified as oliguric or non-oliguric based on the lowest daily urinary output during the azotaemic phase. Oliguria was defined as urine volume of less than 400 ml/day.

In order to assign a possible cause for ARF, a number of clinical criteria were applied. Nephrotoxic drugs were considered the cause of renal failure if a patient had received a drug with known nephrotoxic potential for a minimum of 3 days prior to the defined increase in serum creatinine concentration [14]. Sepsis was considered to be present when two or more of the following were present as a result of systemic infection: (i) temperature >38°C or <36°C; (ii) heart rate >90/min; (iii) respiratory rate >20/min or pCO_2 <32 mm, and (iv) white blood count >12 000/mm^3, <4000/mm^3 or >10% band forms [17]. Surgery was assumed to be responsible for ARF where serum creatinine concentration showed a significant increase within 72 h of surgery. Radiographic contrast agents were considered to be the cause of renal failure when serum creatinine rose within 72 h following a radiological procedure employing such agents [14]. Decreased renal perfusion or hypoperfusion was identified as a causative factor if there was overt/orthostatic hypotension, loss of skin turgor with decrease of more than 5% of body weight or clinically apparent congestive cardiac failure [16]. Hypotension was defined as systolic BP less than 80 mmHg. Those patients in whom the renal function improved with correction of haemodynamic factors were not included.

Statistical analysis

The pathogenetic factors causing ARF in different combinations were analysed. To study whether these pathogenetic factors were able to predict the cause of ARF, a hierarchical log linear model for the analysis of categorical data to explain the potentially complex relationships amongst various pathogenetic factors in a multiway cross tabulation was employed [18]. A number of variables including age, hypotension, sepsis, presence and duration of oliguria, need for dialysis, and surgery were compared in survivors and non-survivors. The predictive ability of these variables was examined using a logistic regression model by multivariate analysis using the SPSS version 6 computer software. All the values were expressed as mean $\pm$2 SD and P values of less than 0.05 were considered significant.

Results

During the study period of 12 months, a total of 31 860 patients were admitted, of whom 4176 (13.1%) were elderly, 59 (1.4%) of these elderly developed ARF during hospitalization. Mean age was 67.9 $\pm$7.6 years. Forty-seven (79.6%) of 59 elderly patients had normal basal creatinine, while 12 (20.4%) had an elevated serum creatinine at admission. Demographic characteristics are shown in Table 1. Various pathogenetic factors that could have caused ARF during hospitalization were nephrotoxic drugs, sepsis, hypoperfusion, surgery, and contrast media either alone or in different combinations.

Amongst the causes of ARF, drugs constituted the largest group, being responsible in 39 patients (66%). Aminoglycosides were the offending agents in 24 (40.7%) followed by NSAIDs in 11 (18.6%) and ACE inhibitors in seven patients (11.8%). Four patients received both aminoglycosides and NSAIDs, while two received ACE inhibitors and aminoglycosides. Two of the seven patients on ACE inhibitors were receiving diuretics in addition. Drugs alone contributed to ARF in only six patients.

Sepsis was responsible in 27 patients (45.7%). Cultures yielded positive growth of bacteria in 15 and fungal organisms in two patients. *Escherichia coli*, *Pseudomonas aeruginosa,* and *Staphylococcus aureus* were the common bacterial organisms and Candida and Aspergillus were the fungi most often isolated. Foci of infection were intravenous line in 13, lungs in seven, urinary tract in six, and bedsores in three patients. Sepsis alone contributed to ARF in three patients.

Hypoperfusion was the cause of ARF in 27 (45.7%)

Table 1. Demographic characteristics of patients

Total number of admissions in 1 year, 31860			
<60 years	27 684 (86.9)		
		Males	19 379 (70)
		Females	8305 (30)
>60 years	4176 (13.1)		
		Males	2762 (66)
		Females	1414 (34)
Treatment related ARF (>60 years) 59 (1.4)			
		Males	40 (67.7)
		Females	19 (32.2)
Mean age (years)	67.9 ± 7.6		
Range (years)	60–90		
Total number of deaths in 1 year, 3466 (10.8)			
<60 years	2934 (10.6)		
		Males	1914 (65.2)
		Females	1020 (34.8)
>60 years	532 (12.7)		
		Males	328 (61.7)
		Females	204 (38.3)
Deaths in elderly without ARF	517 (12.5)*		
Deaths in elderly with ARF	15 (25.4)*		
		Males	8 (53.3)
		Females	7 (46.7)

Numbers in parentheses indicate percentage.
ARF, acute renal failure.
*$\chi^2 = 8.3$, $P = 0.03$.

patients. Hypoperfusion resulted from hypotension due to volume contraction in 16 (27%) and cardiac dysfunction including cardiac arrhythmias and congestive cardiac failure in six (10.2%). Septic shock in five patients (8.5%) was the cause of hypoperfusion. Volume contraction was due to diuretics in two patients. Hypoperfusion alone contributed to ARF in five patients.

Surgery could be implicated as cause of ARF in 15 (25.4%). In the majority of these, ARF occurred following abdominal surgery (10), followed by cardiac surgery (three), neurosurgery (one) and vascular surgery (one). Post-operative ARF occurred only in presence of other pathogenetic factors such as nephrotoxic drugs (13), sepsis (nine) and hypoperfusion (five).

Contrast agents accounted for renal failure in 10 patients (16.9%). These agents were administered during contrast enhanced computerized tomographic scans in five, cardiac catheterization in three and during endoscopic retrograde cholecystopancreatography (ERCP) in two patients. Contrast alone contributed to ARF in two patients.

The above pathogenetic factors were responsible for ARF in different combinations. A total of 31 such combinations were seen. Frequently seen combinations are shown in Table 2. On applying the hierarchical log linear model, radiocontrast administration (partial χ^2 28.1, $P < 0.0001$), surgery (partial χ^2 14.89, $P = 0.001$), nephrotoxic drugs (partial χ^2 6.22, $P = 0.0126$) on their own and the combination of radiocontrast, surgery, and sepsis (partial $\chi^2$4.08, $P = 0.0434$) achieved statistical significance in predicting ARF.

Mean basal creatinine was 126.4 ± 51.3 μmol/l (79.6 − 265.2 μmol/l) and the peak creatinine was 371.3 ± 194.5 μmol/l (176.8 − 937 μmol/l). Of 59 patients, 20 (33.8%) had oliguric renal failure. Duration of renal failure until recovery or death was 9.6 ± 2.2 days (range 2–60 days). Nine patients (15.2%) needed dialytic support: four received haemodialysis, four peritoneal dialysis, while one required continuous venovenous haemofiltration. Polysulphone membrane was used for haemodialysis. Various complications related to ARF were encephalopathy in nine (15.2%), metabolic acidosis in four (6.7%), hyperkalaemia in four (6.7%), congestive cardiac failure in four (6.7%), and gastrointestinal bleeding in two (3.4%). Only one patient was on ventilatory support. A total of 470 patients were admitted in adult intensive care unit (ICU) of these only 30 (6.4%) were elderly and two (6.6%) of these developed ARF, One of them died (50%)

Table 2. Combinations of pathogenic factors causing ARF

Pathogenetic factors	No of patients (%)
Drugs, sepsis	17 (28.8)
Drugs, hypoperfusion	15 (25.4)
Drugs, surgery	12 (20.3)
Sepsis, hypoperfusion	11 (18.6)
Sepsis, surgery	8 (13.5)
Drugs, contrast	7 (11.8)
Drugs, hypoperfusion, sepsis	6 (10.1)
Drugs, sepsis, surgery	6 (10.1)
Surgery, hypoperfusion	5 (8.5)
Drugs, hypoperfusion, surgery	4 (6.8)
Sepsis, contrast	4 (6.8)
Contrast, hypoperfusion	3 (5.1)
Contrast, drug, sepsis	3 (5.1)

Overall mortality in all elderly hospitalized patients was 12.7%, while in the elderly with ARF it was 25.4% (Table 1). Comparison of survivors and non-survivors is shown in Table 3. Sepsis, oliguria and hypotension were independent predictors of poor patient outcome on multivariate analysis by logistic regression analysis (Table 3). There was no significant difference in the effect of underlying original disease on the mortality. In the surgical group, four of 16 died, and in those with cardiac illness three of 12 died. In the infectious and miscellaneous four of the eight patients died in each group (χ^2 1.33, $P=0.249$). Of 44 patients who survived, 38 (86.3%) recovered renal functions completely, while 6 (13.6%) had deranged renal functions at the time of discharge.

Discussion

Many studies classify the elderly as those who are 65 years old or more, while some accept a cut-off age of 60 years [19]. The life expectancy in India is 61 years as compared to 72–82 years in the developed countries. Thus, this cut-off age of 65 years may not be appropriate in the Indian context and therefore a lower cut-off age of 60 years was taken in the present study. The median age of the patients with hospital-acquired ARF was found to be significantly higher than those with community-acquired ARF, and also carried a poor outcome [20]. Hospitalization exposes elderly individuals to a number of iatrogenic problems, with the development of acute renal insufficiency being an important one [2]. Incidence of treatment-related ARF in the elderly in present study was 1.4%, which is twice the incidence in a previous study carried out in this centre where predominantly younger patients were included (mean age 47 years) [14]. Both the studies included patients admitted to all the specialities and the definition of ARF used was similar.

In a hospitalized patient, despite a wide variation in spectrum of disease in which ARF can occur, only a limited number of pathophysiological factors such as reduced renal perfusion, sepsis, surgery, nephrotoxic drugs, and radiocontrast agents are operative in the majority of the patients [14–16]. The above pathogenetic factors generally seldom operate in isolation in this setting. Combinations of different factors are present in individual patients. In the studies carried out so far, a single factor has been incriminated arbitrarily as the cause of ARF despite the presence of other factors. This, we feel is not correct as it is extremely difficult to blame a single factor as a sole cause of ARF. In this study, in addition to individual factors, we also studied the combination of different causative pathogenetic factors and their predictive values. Drugs along with sepsis, hypoperfusion, or surgery were the common pathogenetic combinations observed. Amongst different combinations, radiocontrast administration (partial χ^2 28.1), surgery (partial χ^2 14.89), and nephrotoxic drugs (partial χ^2 6.22) on their own were statistically significant in predicting the ARF.

Radio contrast administration contributed to ARF in 17% of patients in the elderly in the present study as compared to 4% in the young [14]. In a prospective study in which elderly patients were subjected to cardiac catheterization, 10.5% developed ARF [10]. Though contrast-induced renal insufficiency is moderate and reversible, it increases the morbidity significantly. Drugs contributed to renal failure in 66% of patients in this study as compared to 39% in younger individuals [14]. Aminoglycoside antibiotics were the most frequent offending agents. This is quite expected as the erroneous estimation of glomerular filtration rate in the elderly based on serum creatinine concentration leads to inappropriate dosing with resultant renal toxicity. [20,21]. Haemodynamically mediated ARF is common in the elderly due to NSAIDs and ACE inhibitors [22,23]. In a prospective study, a significant rise of blood urea nitrogen and serum creatinine was seen in 13% of elderly patients receiving NSAIDs [11]. The syndrome of haemodynamic ARF caused by ACE inhibitors occurs in around 2.3% of all causes of drug induced ARF in elderly [23]. Bridoux *et al.* [24] found a high incidence of ARF caused by ACE inhibitors in older patients without renal artery stenosis.

Surgery was another independent predictor of ARF. Hypotension during and after surgery, postoperative fluid loss, cardiac arrhythmias, postoperative infections and the drugs used to treat these can be detrimental to renal function, with resultant higher incidence of ARF [21]. The incidence of postoperative ARF in the present study was similar to that in a previous study

Table 3. Predictive value of various parameters for survival

	Died (15)	Survived (44)	Odds ratio	*P* value[1]
Age (years)	63 ± 7.8	69.0 ± 7.8	0.905	0.177
Hypotension	9 (60)	18 (41)	15.2	0.046[2]
Sepsis	13 (86.6)	14 (31.8)	43.2	0.011[2]
Surgery	4 (26.6)	16 (36.4)	11.5	0.621
Oliguria	11 (73.3)	9 (20.4)	64.1	0.048[2]
Duration of oliguria (days)	5.9 ± 3.7	1.8 ± 3.7	0.883	0.667
Dialysis	5 (33.3)	4 (9.1)	0.305	0.441

Figures in parentheses indicate percentages.
[1]Logistic regression analysis; [2]*P* = significant.

from this centre where predominantly younger patients were included (25.4 *vs* 24%). Acute tubular necrosis after elective or emergency surgery for abdominal aortic aneurysm is particularly frequent in aged people and is a common cause of ARF. At this centre, the number of vascular surgeries carried out is very small, this could account for the relatively lower incidence of postoperative ARF in this study.

Sepsis and hypoperfusion are two other important causative factors for ARF in the elderly. Infections particularly Gram-negative septicaemia accounted for 30% of ARF in the elderly in one study [7]. Hypovolaemia has been reported to cause ARF in 50–60% of patients admitted in a geriatric unit [12]. In the present study sepsis and hypovolaemia contributed to renal failure in 45.7% of elderly patients each, as compared to 27% in young patients in a previous study [14]. However, if we look at different pathogenetic combinations, these two factors were not predictive of ARF on their own. Reduced renal water conserving capacity and thirst leads to dehydration and renal failure. Diminished renal perfusion has been thought to be a major cause of ARF in elderly [25]. However, in a hospitalized elderly patient where a number of pathogenetic factors are operating, our study suggests that factors other than hypoperfusion are more important.

Mortality in the elderly with ARF varies considerably in different series. It also depends on how aggressively they are subjected to interventions and high-risk surgeries [26]. It is as high as 63% where patients admitted to intensive care unit (ICU) alone have been studied [13]. Renal failure as a part of multiorgan failure has a grave prognosis. In the present study, the mortality in the elderly with ARF was twice the mortality of the elderly in-patients without ARF (25.4 *vs* 12.5%, $P=0.03$). Thus renal failure not only adds to the morbidity but also significantly increases mortality. In the elderly with ARF of various aetiologies admitted to ICUs, failure of more than two organs, high blood lactate, high catabolic rate associated with sepsis [13], coma, and the need for assisted ventilation [19] have been found to be markers of a poor prognosis. In developing countries with meagre resources, younger patients requiring ICU admissions are preferred over the elderly with similar comorbid conditions. Pascual *et al.* from Spain in their study of very old (>80 years) patients reported a low rate of ICU admissions in this age group. They have postulated that younger age could be criteria for preselection of patients for admissions to the ICU [27]. Hence, to evaluate accurately the prognosis and the prognostic factors it is necessary to include broader areas than ICU setting alone. Poor prognostic factors in a non-ICU setting include need for dialysis, oliguria, sepsis, shock [28], and hypoalbuminaemia [12]. In the present study, patients admitted all over the hospital have been studied, and on logistic regression analysis the independent predictors of poor patient outcome were sepsis, hypotension, and oliguria. The problem of sepsis and renal failure is a great challenge to the nephrologist. Endotoxins directly sensitize the renal tubular tissue to the effect of ischaemia even in the absence of detectable haemodynamic changes. Moreover, endotoxaemia also impairs tubular regeneration. [29] This phenomenon is much more marked in the elderly due to age-related changes in the kidneys. Ongoing sepsis results in multiorgan failure, which carries a grave prognosis.

To conclude, incidence of treatment-related ARF in the elderly is 14%, with more than one pathogenetic factor playing a role in the development of ARF in the majority. Sepsis, hypotension, and oliguria are the independent predictors of poor patient outcome. ARF in hospitalized elderly patients increases the mortality significantly. Precautions should be taken to minimize the development of ARF in this group of patients.

References

1. *Statistical Outline of India.* TATA Services Limited, 1993, 203
2. Robbins LJ, Oholer SK. The hospitalised elderly patient. In: Schrier RW, ed. *Geriatric Medicine.* Saunders, Philadelphia, 1990; 54–67
3. Liano F, Pascual J and The Madrid Acute Renal Study Group. Epidemiology of acute renal failure: A prospective,multicenter, community-based study. *Kidney Int* 1996; 50: 811–818
4. Feest TG, Round A, Hamad S. Incidence of severe acute renal failure in adults: results of a community based study. *Br Med J* 1993; 306: 481–483
5. Druml W. Lax F, Grimm G, Schneeweiss B, Lenz K, Laggner AN. Acute renal failure in the elderly 1975–1990. *Clin Nephrol* 1994; 41: 342–349
6. Lameire N, Matthys E,Vanholder R *et al.* Causes and prognosis of acute renal failure in the elderly. *Nephrol Dial Transplant* 1987; 2: 316–322
7. Kumar R, Hill CM, McGeown MG. Acute renal failure in the elderly. *Lancet* 1973; 1: 90–91
8. Arora P, Kher V, Kohli HS, Sharma RK, Gupta A, Jha R. Acute renal failure in the elderly: experience in a single centre in India. *Nephrol Dial Transplant* 1993; 8: 827–830
9. Johnson JC. The medical evaluation and management of the elderly surgical patient. *J Am Geriatr Soc* 1983; 31: 621
10. Rich MW, Crecelius CA. Incidence, risk factors and clinical course of acute renal insufficiency after cardiac catheterization in patients 70 years of age or older. A prospective study. *Arch Intern Med* 1990; 150: 1237–1242
11. Gurwitz JH**,** Avorn J, Ross-Dengan D, Lipsitz LA. Nonsteroidal antiinflammatory drug-associated azotemia in the very old. *J Am Med Assoc* 1990; 264: 471–475
12. Gentric A, Duquesne F, Cledes J. Incidence, causes, prognosis of renal failure in old patients admitted in an internal medicine unit. *Geriatr Nephrol Urol* 1993; 3: 151–154
13. Klounche K, Cristol JP, Kaaki M, Ture-Baron C, Canaud B, Beraud JJ. Prognosis of acute renal failure in the elderly. *Nephrol Dial Transplant* 1995; 10; 2240–2243
14. Jha V. Malhotra HS, Sakhuja V, Chugh KS. Spectrum of hospital acquired acute renal failure in the developing countries—Chandigarh study. *Q J Med* 1992; 84: 497–505
15. Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT. Hospital acquired renal insufficiency: a prospective study. *Am J Med* 1983, 74: 243–248
16. Shusterman N, Strom DL, Murray TG, Morrison G, West SL, Maislin G. Risk factors and outcome of hospital-acquired acute renal failure. Clinical epidemiologic study. *Am J Med* 1987; 83: 65–71
17. Bone RC. Balk RA, Cerra FB *et al.* The ACCP/SCCM Consensus Conference Committee. Definitions for sepsis and organ failure and guidelines for the use of Innovative therapies in sepsis. *Chest* 1992; 101: 1644–1655

18. Benedetti JK, Brown MB. Strategies for the selection of log linear models. *Biometrics* 1978; 34: 680–686
19. Macias-Nunez JF, Lopez-Novoa JM, Martinez-Maldonado M. Acute renal failure in the aged. *Semin Nephrol* 1996: 16: 830–838
20. Abraham G, Gupta RK, Senthilselvan A, Vander Meulen J, Johny KV. Causes and prognosis of acute renal failure in Kuwait: a 2-year prospective study. *J Trop Med Hyg* 1989; 92: 325–329
21. Pascual J, Liano F, Ortuno J. The elderly patient with acute renal failure. *J Am Soc Nephrol* 1995; 6: 144–153
22. Lamy PP. Renal effects of nonsteroidal antiinflammatory drugs. Heightened risk to the elderly? *J Am Geriatr Soc* 1986; 34: 361–367
23. Kleinknecht D, Landais P, Goldfarb B. Pathophysiology and clinical aspects of drug-induced tubular necrosis in man. *Contrib Nephrol* 1987; 55: 145–158
24. Bridoux F, Hazzar M, Palloj JL. Acute renal failure after the use of angiotensin converting enzyme inhibitors in patients without renal artery stenosis. *Nephrol Dial Transplant* 1992; 7: 100–104
25. Lameire N. The elderly acute renal failure in a special setting. In: Davison AM, Cameron JS, Grunfeld JP, Kerr DNS, Ritz E, Winearls CG, eds. *Oxford Textbook of Clinical Nephrology*. Oxford University Press, Oxford, 1998; vol. 2: 1734–1748
26. Pascual J, Orofino L, Liano F *et al.* Incidence and prognosis of acute renal failure in older patients. *J Am Geriatr Soc* 1990; 38: 25–30
27. Pascual J, Liano F and the Madrid Acute Renal Failure Study Group. Causes and prognosis of acute renal failure in the very old. *J Am Geriatr Soc.* 1998: 46; 721–725
28. Bustillo EM, Mignel E, Berns C, Barril G, Traver JA. Outcome of acute renal failure in the elderly: a different approach. *Nephrol Dial Transplant* 1996; 11: 1672–1673
29. Fan J, Char D, Kolasa AJ *et al.* Alterations in hepatic production and peripheral clearance of IGF-1 after endotoxin. *Am J Physiol* 1995; 269: E 33–42

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