Int Urol Nephrol (2006) 38:787–793
DOI 10.1007/s11255-006-0084-4

REVIEW ARTICLE

Acute renal failure in the elderly: particular characteristics

Carlos G. Musso · Vassilis Liakopoulos · Iraklis Ioannidis · Theodoros Eleftheriadis · Ioannis Stefanidis

Accepted: 9 December 2006 / Published online: 11 December 2006

Abstract Elderly individuals comprise the fastest growing patient population group and acute renal failure (ARF) is quite common among them, although exact numbers are not known. We reviewed the literature with regards to the characteristics of ARF in elderly patients and describe some useful guidelines. The ageing kidney is characterized by many structural and functional changes, which are mainly due to various chronic disorders, such as hypertension, diabetes and atherosclerosis, which are highly prevalent in these patients. A number of structural and functional changes characteristic of the ageing kidney make elderly people especially prone to renal damage. ARF in the elderly is frequently of multifactorial origin and often with an atypical presentation, like the ''intermediate syndrome'', which combines characteristics of pre-renal azotemia and acute tubular necrosis. Physical examination and laboratory blood and urine indices may sometimes be misleading occasionally leading to misdiagnosis. Prophylaxis remains the preferred approach to therapy: one should avoid nephrotoxic drugs and poly-pharmacy, adjust drug doses and achieve adequate hydration of the patient as cautiously as possible. Dialysis therapies can be used for treatment of ARF irrespective of age and carry a good prognosis.

Keywords Acute renal failure · Elderly · Ageing kidney

C. G. Musso
Nephrology Department, Medical School, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

V. Liakopoulos (✉) · I. Ioannidis · T. Eleftheriadis · I. Stefanidis
Nephrology Department, Medical School, University of Thessaly, 22 Papakyriazi street, 41222 Larissa, Greece
e-mail: liakopul@otenet.gr

Introduction

Older individuals comprise nowadays about 12% of the total US population, a percentage expected to rise to 21% by the year 2040. Life expectancy is also rising, making the group of people over 65 years of age the fastest rising age group in Europe and other developed countries. As a result older patients represent the bulk of any adult practitioner's practice now and to a greater degree in the near future. This tendency is reflected in the gradual rise in the number of rehabilitation beds in contrast to emergency and acute care beds, seen mainly in the developed nations [1].

Acute renal failure (ARF) is the term used for an abrupt, sustained and in most cases reversible decrease in renal function resulting in retention of nitrogenous waste products. Despite the absence of a universally accepted definition, ARF can be

defined as an acute and sustained increase in plasma creatinine of 0.5 mg/dl, if the baseline is less than 2.5 mg/dl, or an increase in plasma creatinine by more than 20%, if the baseline is in excess of 2.5 mg/dl [2].

In the old population the incidence of ARF is increased, favored by certain pre-disposing factors; such as histological and functional changes of the aged kidney, reduced capability of metabolizing drugs and the high prevalence of systemic diseases like diabetes mellitus, hypertension and heart failure [3]. Moreover, many elderly patients suffer from various chronic disorders, are likely to undergo various surgical procedures and are exposed to poly-pharmacy. True incidence of ARF in seniors is hard to define, but it's estimated to be around 950 cases per million population in those aged 80–89 [4]. ARF is more common in the hospital setting than in the community, especially in the ICU, where it carries a worse prognosis [5, 6].

The ageing kidney

One should always bear in mind that many of structural and functional changes occur as age progresses (Table 1). For example, the glomeruli undergo a lot of anatomic modifications, mostly in the cortical area [7]. The renal parenchyma gradually diminishes, with a resultant reduction in total renal mass, which can reach 90 gr at the age of 80, compared to the 160 gr in young adults. There is diffuse reduction of active cortical parenchyma, which can range up to 30–40% of the glomeruli. Glomerulosclerosis is found in 12–14% of glomeruli, while there's also wide focal or diffuse thickening of the glomerular basement membrane [8]. Mesangial expansion is also evident and mesangial cells can comprise up to 15% of the total renal mass at the age of 70. All the above-mentioned structural changes do not appear to have a great functional consequence in the, otherwise, healthy elderly individual [9].

Table 1 The ageing kidney

Reduction in total renal mass (90 gr compared to 160 of young adults)
Glomerulosclerosis (12–14% of glomeruli)
Reduction in active cortical parenchyma (30–40% of glomeruli inactive)
Thickening of the GBM
Mesangial expansion
Reduction in the amount and length of tubules
Thickening of large vessels' walls
Reduction of the total renal blood flow (10% per decade above 40)
Reduction in GFR (8 ml/min/1.73m^2 per decade above 45)
Decreased maximum osmolality (900 mOsm/kg compared to 1,200 in young adults)

With regard to tubules there's a reduction not only in their number, but also in their length, especially that of the proximal tubules [9]. There appears to be loss of tubular basement membrane and widespread presence of vacuoles, but the glomerulo-tubular functional balance is well preserved [10, 11].

The walls of the large vessels become thicker, due to the ageing process, but the small vessels become involved only in the presence of concurrent hypertension. Hyalinosis of the cortical vessels results in the reduction of the total blood supply and the arterioles become aglomerular. The total renal blood flow is diminished by about 10% for each decade above 40 years, which means that at the age of 80 the expected values should range between 280 and 320 ml/min. Although the reduction is widely distributed, it's more prominent in the cortex [12, 13].

In the healthy adult glomerular filtration rate (GFR) remains stable until the age of 45; thereafter there's a stepwise reduction of nearly 8 ml/min/1.73 m^2/decade. The Cockroft–Gault formula has been found to overestimate the true values of creatinine clearance by about 12–15 ml/min, so the most precise method of creatinine clearance determination is the 24-h urine collection [14, 15].

The ageing process influences renal water excretion and absorption capability, as well as formation of dilute or concentrated urine. Maximum osmolality achieved in those aged more than 65 is about 900 mOsm/kg; a value well below the normal value for younger individuals (1200 mOsm/kg). Several studies have come to conflicting results concerning basal antidiuretic hormone (ADH) secretion, but it is universally accepted that tubular ADH-receptors fall short of responsiveness [16].

Conclusively, the most important of senile renal changes that make old people prone to ARF are

- A reduction in the number of glomeruli and glomerular capillaries [13, 15].
- A disturbance in the autoregulatory vascular defense [13].
- Renal tubular frailty [10] and salt and water wasting secondary to a reduced tubular reabsorption capability [9, 11].

Based on the current evidence the following particular characteristics of ARF in the elderly can be described:

Multifactorial nature of ARF

In fact, multifactorial physiopathology is an anticipated finding of renal failure in any age group. However, different etiologies frequently co-exist in the elderly patient:

Pre-renal causes

(i) True hypovolemia: due to dehydration, bleeding, vomiting, or diarrhea, appears to be the most frequent cause of ARF in this population and can easily lead to acute tubular necrosis [17].
(ii) Functional hypovolemia; occurring in cardiac failure, and sepsis. It's estimated that over a quarter of patients will manifest a mild hypovolemia at presentation, due mainly to febrile illnesses, laxative or diuretic abuse and sedentary life style [18]. Hypernatremia, a frequent finding in the elderly, if left untreated manifests a great mortality risk (> 50%) [19].
(iii) Hemodynamically mediated pharmacological damage: non-steroidal anti-inflammatory drugs, angiotensin converting enzyme inhibitors and angiotensin II receptor blockers are frequently prescribed to elderly patients and can potentially worsen the already altered autoregulatory mechanism of the aged kidney [20].
(iv) Acute renal vascular obstruction: This is more common than previously believed and can often be iatrogenic (surgery, radiologic manipulations). Acute bilateral vascular obstruction (or unilateral in a single functioning kidney) can present with nausea, vomiting, abdominal pain and fever. About a third of patients will present with micro or macroscopic hematuria and very high levels of LDH, with no change at AST/ALT levels. Fractional excretion of sodium (FE_{Na}) is usually around 100% [21].

Renal causes

(i) Drug-induced acute interstitial nephritis e.g.: nephritis induced by diuretics, analgesics or allopurinol [22].
(ii) Acute glomerulonephritis: crescentic disease (39%) [23].
(iii) Acute tubular necrosis: mediated by ischemia and/or nephrotoxicity (radio-contrast media, aminoglycosides, rhabdomyolysis or cardiac surgery) [17].
(iv) Cholesterol emboli.

Post-renal causes

Acute urinary obstruction: intrarenal, urolithiasis, urethral obstruction, prostatism in men or retroperitoneal fibrosis. These entities comprise about 9% of all cases of ARF in those aged >70 [21].

''Atypical'' presentation of the disease

In the elderly, diseases usually have patterns of presentation different to that observed in the young population, signs and symptoms are frequently less clearly defined and can be overlooked by the physician. Moreover, any disease could present merely as one of the entities known as the *geriatrics giants:* confusional syndrome (dementia), falls, immobility syndrome and acute urinary or fecal incontinence. These presentation patterns are called ''atypical'', but they could actually be regarded as ''typical'' in this population [24–26].

Unreliable physical examination

In old patients physical signs may be misleading. For instance, dry mucosae and skin, orthostatic

hypotension and loss of skin turgor are all signs frequently present in the healthy elderly, not necessarily implying a clinically significant dehydration state. Moreover, the finding of edema in immobilized patients does not always mean volume overload as the lack of thirst does not signify absence of dehydration [27].

Tubular frailty

This condition of the senile kidney pre-disposes to acute tubular necrosis easily, even after a mild renal insult. Aging tubular cells may be more vulnerable to ischemia because cellular antioxidant defenses decline with age and oxidant injury may be a critical determinant of ischemic ARF [12, 28]**.** Besides, the increased propensity to vasoconstriction (e.g. to angiotensin II, endothelins and PAF) may enhance susceptibility of the aged kidney to toxic substances and ischemic injury [29]. Moreover tubular recovery from the established tubular necrosis is very slow. It may take more than the usual 2 weeks, compared to younger patients, and elderly patients may necessitate dialysis well before their tubular recovery [3].

Non-reliable urinary indices

In the elderly, many urinary indices such as urinary sodium, FE_{Na}, fractional excretion of urea (FE_U) and urinary osmolality should be interpreted with caution, due to changes in renal physiology because of the ageing process. Thus sodium and urea reabsorption, as well as urinary concentration capability are reduced in the elderly. Therefore, FE_{Na} and FE_U are higher and urinary osmolality lower than the ones achieved by young people in renal hypoperfusion states. These altered index patterns can lead to an incorrect interpretation, making pre-renal azotemia resemble parenchymal renal failure [27].

The ''intermediate syndrome'' pattern

Due to tubular frailty and dysfunction, the so-called ''intermediate syndrome'' is frequently observed in the elderly. In this case elderly patients with high plasma urea and creatinine, due to pre-renal causes, may also have urinary indices compatible with acute tubular necrosis. However, renal failure can resolve with volume expansion, as is the case with pre-renal azotemia. The intermediate syndrome resolves in about a week, in contrast to the classical recovery time of 24–48 h after rehydration in the case of pre-renal azotemia [29, 30].

Prophylaxis

Avoiding situations that could damage the kidney is the best strategy against the consequences of ARF in the elderly. The following principles summarize these concepts:

– Avoid nephrotoxic substances
– Avoid poly-pharmacy
– Prescribe low doses of drugs (the lowest desired dose of drugs)
– Adjust drug doses to the expected functional reduction of the senile kidney
– Assess renal function before and after the introduction of any drug that could be potentionally nephrotoxic [31].

The concept of these maneuvers is to provide a stable cardiac supply, a satisfactory renal blood supply and adequate oxygenation.

Clinical research has yielded conflicting results concerning many drugs used to prevent or even cure ARF, but certain guidelines can be described:

- If there's no contraindication to their use, mannitol and loop diuretics can be safely used, since they can convert oliguric situations to non-oliguric.
- Low dose dopamine, on the other hand, has no proven benefit, although widely used [32, 33].
- Calcium channel blockers have been proven useful in preventing ARF, at least in cases after cardiac surgery [34].

Rehydration—almost always but cautiously

Practically in any case of ARF (irrespective of age) rehydration is crucial as the first therapeutic maneuver. This fact becomes more important in aged people, since they are more prone to volume contraction due to primary hypodipsia and salt

and water wasting. It is crucial to highlight the importance of rehydration as the first therapeutic approach, since it is not always easy to distinguish, based on laboratory tests, between pre-renal and parenchymal ARF, as already mentioned. However, since old people usually have rigid cardiac walls (diastolic cardiac failure), secondary to original myocytes replacement by fibroblastic (presbicardia) and reduced GFR, secondary to the ageing process, they should be rehydrated cautiously, in order to avoid pulmonary edema during aggressive volume infusion [27].

Renal biopsy and dialysis

Principles and means for etiological diagnosis and treatment of ARF are the same both in young and aged population. Renal biopsy does not carry a greater risk in the older patient compared to the younger and adequate renal tissue can be obtained in almost 90% [35], with a complication rate of 2.2–9%, compared to 7% in younger patients [7, 36]. However, because of complex changes in the aged kidney or concomitant diseases such as arteriosclerosis or global sclerosis, the interpretation of the histological finding may be more difficult [23].

Dialysis therapies can be used in the treatment of ARF irrespective of age. Most elderly patients respond well to dialysis, either peritoneal dialysis or hemodialysis [37]. Although large prospective studies have not compared the different dialysis strategies with respect to outcome in patients with ARF, continuous extracorporeal therapies are increasingly recommended as an alternative to hemodialysis in the management of the critically ill ARF patient in intensive care units [38]. The slow extended daily dialysis (SLEDD) modalities may be particularly indicated in elderly, critically ill ARF patients because these techniques combine the advantages of continuous therapies and hemodialysis, i.e. fluid removal with mild solute transport, high biocompatibility, isotonic hyperfiltration, lack of solute rebound, stable fluid balance and good clinical outcomes [39].

However, there are some particular points, specific to elderly patients, which need to be answered prior to commencing dialysis, such as concurrent illnesses (especially neoplastic diseases), nutrition, inflammation, and infection. Apart from these considerations indications for dialysis remain the same, regardless of age [40].

Survival rates differ from center to center and between studies, due mainly to different study methods and patient selection and are estimated to be around 40% [41]. Current evidence suggests that elderly patients with non-oliguric ARF, normal blood lactate levels, low catabolic state and less than three organs involvement manifest a fair chance of recovery and should therefore receive aggressive treatment [40].

Mortality is higher in parenchymal ARF (64%) compared to prerenal (35%) and postrenal (40%) ARF and is higher in patients suffering from sepsis (62%) [42]. Relative risk of death in patients over the age of 80 is 1.09 compared to patients aged less than 65 [43]. In the setting of hospital-acquired ARF factors that are associated with higher mortality include neurological failure (Odds ratio—OR = 3), hematological disorders (OR = 4.3) and oliguria (OR = 12), while neoplasia, cardiac/hepatic disease, oliguria and sepsis are more decisive in the community-acquired ARF [44].

Conclusion

ARF in old people has some particular characteristics and their identification is crucial for an optimal handling of this renal syndrome. Apart from those special characteristics, ARF in the elderly is not a different entity than that encountered in other age groups and age alone should never be a drawback to appropriate therapy.

References

1. Canada Health Organisation (2000) A guide to end of life care for seniors
2. Lameire N (2005) Recent advances in clinical acute renal failure. Rev Port Nefrol Hypert 19(1):15–30
3. Lameire N, Nelde A, Hoeben H, Vanholder R (2000) Acute renal failure in the elderly. In: Oreopoulos D, Hazzard W, Luke R (eds) Nephrology and geriatrics integrated. Kluwer Academic Publishers, Dordrecht, pp93–111
4. Obialo CI, Crowell AK, Okonofua EC (2002) Acute renal failure mortality in hospitalised African Americans: age and gender considerations. J Am Med Assoc 94(3):127–134

5. Lou LM, Boned B, Gomez Sanchez R (2002) Characteristics of acute renal failure in elderly patients admitted to a small town hospital. Nefrologia 22(6):547–554
6. Groeneveld ABJ, Tran DO, Van der Meulen J (1991) Acute renal failure in the intensive care unit: predisposing, complicating factors affecting outcome. Nephron 59:602–610
7. Silva FG (2005) The aging kidney: a review-part 1. Int Urol Nephrol 37(1):185–205
8. Abrahamson DR (2003) Unveiling mesangial mysteries. Kidney Int 64:363–364
9. Baylis C, Corman B (1998) The aging kidney: insights from experimental studies. J Am Soc Nephrol 9:699–709
10. Musso CG (2002) Geriatric nephrology and the ''nephrogeriatric giants''. Int Urol Nephrol 34:255–256
11. Macías Núñez JF, García Iglesias C, Bondía Román A, Rodríguez Commes JL, et al (1978) Renal handling of sodium in old people: a functional study. Age and ageing 7:178–181
12. Percy C, Pat B, Poronnik P, Cobe G (2005) Role of oxidative stress in age-associated chronic kidney pathologies. Adv Chronic Kidney Dis 12(1):78–83
13. Beck LH (1998) Changes in renal function with aging. Clin Geriatr Medicine 11:199–209
14. Verhave JC, Balje-Volkers C, Hillege HL, de Zeeuw D, et al (2003) The reliability of different formulae to predict creatinine clearance. J Intern Med 253(5):563–573
15. Hoang K, Tan JC, Derby G, et al (2003) Determinants of glomerular hypofiltration in aging humans. Kidney Int 64:1417–1424
16. Johnson TM, Miller M, Pillion DJ, Ouslander JG (2003) Arginine vasopressin and nocturnal polyuria in older adults with frequent nighttime voiding. J Urol 170(2):480–484
17. Kohli HS, Nuthukumar T, Sakhuja V (2000) Treatment-related acute renal failure in the elderly: a hospital-based prospective study. Nephrol Dial Transplant 15(2):212–217
18. Spangler PF, Risley TR, Bilyew DD (1984) The management of dehydration and incontinence in non-ambulatory geriatric patients. J Appl Behaviour Anal 17:397–401
19. Weinberg AD, Pals JK, Levesque PG (1994) Dehydration and death during febrile episodes in the nursing house. J Am Geriatr Soc 42:968–971
20. Huerta C, Castellsague J, Varas- Lorenzo C, Garcia Rodriguez LA (2005) Non-steroidal antiinflamatory drugs and risk of acute renal failure in the general population. Am J Kidney Dis 45(3):531–539
21. Zarich S, Fang LST, Diamond JR (1985) Fractional excretion of sodium: exceptions to its use. Arch Int Med 1451:108–112
22. Pascual J, Ortofino L, Liano F, et al (1990) Incidence and prognosis of acute renal failure in older patients. J Am Geriatr Soc 38:25–30
23. Nair R, Bell JM, Wakler PD (2004) Renal biopsy in patients over 80 years and older. Am J Kidney Dis 44(4):618–626
24. Perez Almeida E, Blanco Pascual E (2000) The patient with immobility syndrome. In: Macías Núñez JF, Guillén Llera FG, Ribera Casado JM (eds) Geriatrics from the beginning, Editorial Glosa, Barcelona, pp 135–152
25. Baum N, Suarez G, Appell RA (1991) Urinary incontinence. Not a normal part of aging. Postgrad Med 90:99–102
26. Wielinski CL, Erickson-Davis C, Wichmann R, Walde-Douglas M, Parashos SA (2005) Falls and injuries resulting from falls among patients with Parkinson's disease and other parkinsonian syndromes. Mov Disord 20:410–415
27. Musso CG, Macías Núñez JF (2000) The aged kidney: structure and function. Main nephropathies. In: Salgado A, Guillén Llera FG, Ruipérez I (eds) Geriatrics from the beginning. Masson, Barcelona, pp 399–412
28. Linas SL, Whittenburg D, Parsons PE, Repine JE (1992) Mild renal ischemia activates primed neutrophils to cause acute renal failure. Kidney Int 42:610–616
29. Jerkic M, Vojvodic S, Lopez-Novoa JM (2001) The mechanism of increased renal susceptibility to toxic substances in the elderly. Part I. The role of increased vasoconstriction. Int Urol Nephrol 32(4):539–47
30. Musso CG, Luque K, Reynaldi J, Pidoux R, et al (2004) Intermediate syndrome: a typical pattern of acute renal failure in the elderly. biomed.uninet.edu 3
31. Adhiyaman V, Asghar M, Oke A, White AD, Shah IU (2001) Nephrotoxicity in the elderly due to co-prescription of angiotensin converting enzyme inhibitors and nonsteroidal anti-inflammatory drugs. J R Soc Med 94:512–514
32. Pereira CN, Machado FR, Guimavalo HP, Senna AP, do Amaral J (2004) Hemodynamics and renal function during administration of low-dose dopamine in severely ill patients. Sao Paolo Med J 122(4):141–146
33. Ischai C, Passeron C, Carles M, Bouregba M, Grimand D (2000) Prolonged low-dose dopamine infusion induces a transient improvement in renal function in hemodynamicaly stable, critically ill patients: a single-blind, prospective, controlled study. Crit Care Med 28(5):1329–1335
34. Piper SN, Kumle B, Boldt J (2003) Diltiazem may preserve renal tubular integrity after cardiac surgery. Can J Anaesth 50(3):285–292
35. Parrish AE (1992) Complications of percutaneous renal biopsy. A review of 37 years experience. Clin Nephrol 38(3):135–141
36. Gonzalez-Michaca L, Chew-Wong A, Soltero L (2000) Percutaneous renal biopsy: analysis of 26 years—complications' rate and risk factors. Rev Invest Clin 52(1):125–131
37. Baraldi A, Ballestri M, Rapana R, Lucchi L, et al (1998) Acute renal failure of medical type in an elderly population. Nephrol Dial Transplant 13(Suppl 7):25–29
38. Stefanidis I, Hagel J, Kierdorf H, Maurin N (1995) Influencing hemostasis during continuous venovenous hemofiltration after acute renal failure: comparison with intermittent hemodialysis. Contrib Nephrol 116:140–144

39. Van de Noortgate N, Verbeke F, Dhondt A, Colardijn F, et al (2002) The dialytic management of acute renal failure in the elderly. Semin Dial 15(2):127–132
40. Mandal AK, Baig M, Koutoubi Z (1996) Management of acute renal failure in the elderly. Treatment options. Drugs Aging 4:226–250
41. Klouche K, Cristol JP, Kaaki M, Turc-Baron C, et al (1995) Prognosis of acute renal failure in the elderly. Nephrol Dial Transplant 10(12):2240–2243
42. Santacruz F, Barreto S, Mayor MM, Cabrera W, et al (1996) Mortality in elderly patients with acute renal failure. Ren Fail 18(4):601–605
43. Pascual J, Liano F (1998) Causes and prognosis of acute renal failure in the very old. J Am Geriatr Soc 46(6):721–725
44. Sesso R, Roque A, Viciosos B, Stella S (2004) Prognosis of ARF in hospitalized elderly patients. Am J Kidney Dis 44(3):410–419