Kidney disease in the elderly

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Abstract

Chronic kidney disease (CKD) and acute kidney injury (AKI) are more common in elderly individuals owing to ageing-related changes in the kidney. Renal disease in the elderly will in future form an increasing proportion of the workload of nephrologists, specialists in internal medicine and general practitioners because of the ageing of the general population. AKI in elderly people can often be anticipated and prevented. Published guidelines concerning the management of CKD in younger adults may not be universally implementable in the elderly, and may ignore complications and challenges specific to this age group. There is a growing demand for renal services to provide renal replacement therapy (RRT) to elderly patients. The decision to start an elderly person on a particular form of RRT should follow careful assessment of their frailty, function and lifestyle, and their health priorities and quality of life must be kept at the centre of decision-making at all times. Patients who are unsuited to or do not wish to commence RRT can do very well with maximal conservative management. End-of-life and palliative care remains somewhat underused in nephrology, and is an area that needs to be developed further.

Keywords Acute kidney injury; aged; chronic kidney disease; MRCP; palliative care; renal replacement therapy

Key points

- Elderly people have a reduced threshold for developing acute kidney injury (AKI) and disorders of fluid and electrolyte balance; this can often be anticipated and prevented
- Serum creatinine is a poor marker of renal function in elderly people, and should not be relied upon to detect AKI or stage chronic kidney disease (CKD) in older patients
- Be aware of potential complications of CKD treatment regimens in elderly patients, and the need to address challenges specific to elderly individuals, such as frailty and the importance of function
- Frailty and the patient's health priorities should be taken into account when assessing an elderly person's suitability for renal replacement therapy or maximal conservative management
- End-of-life planning should be considered at all times, and palliative care implemented when appropriate

Introduction

Glomerular filtration rate (GFR) declines with age, and the prevalence of chronic kidney disease (CKD) rises with increasing age in the populations studied: among women in the Chinese general population, the prevalence of CKD rises from 7.4% in 18–39-year-olds to 24.2% in those aged 70 years or over.[1] The ageing of the general population (primarily consequent to socioeconomic development and greater life expectancy) means that elderly people form an increasing proportion of patients with kidney disease and end-stage renal failure (ESRF).

The ageing kidney

GFR declines by about 8 ml/minute/1.73 m^2 per decade after the fourth decade, although this varies between individuals (Table 1). Loss of function can result from a combination of cumulative exposure to extrinsic risk factors (e.g. hypertension, vascular disease), disease acquisition (often occult) and intrinsic ageing. A history of one or more episodes of acute kidney injury (AKI) has been implicated in the development of CKD.

Kidney mass increases from birth to the fourth decade but is subsequently lost at a rate of 10% per decade, the reduction being greater in the renal cortex than the medulla. The number of functioning glomeruli falls with age (approximately 50% fewer at 70 years than at 30), with the proportion of sclerotic glomeruli increasing.

Renal blood flow exhibits a steady decline with ageing, more so in the cortex than the medulla, with an increase in postglomerular renovascular resistance helping to preserve GFR. However, the renovascular response to vasodilatory agents and the sensitivity of renal arterioles to endogenous and exogenous vasoactive substances is also altered, predisposing to a decline in GFR as a result of haemodynamic changes.

Ageing-related changes in kidney function and fluid and electrolyte homeostasis[2]

Structure	Functional	Complications of functional change
↓ Renal mass	↓ GFR	↓ Renal reserve
↓ Blood flow	↓ Response to sodium loading/depletion	Hyper/hyponatraemia
↓ Functioning glomeruli	↓ Urine concentrating/diluting ability	Nocturia, hyper/hyponatraemia
↓ Functioning tubules	↓ Renin + aldosterone levels	Volume depletion, hyperkalaemia
	↓ Response to vasopressin	Volume depletion, dehydration
	↓ Na^+/K^+ ATPase activity	Hyperkalaemia
	↓ Ammonia + H^+ synthesis	Metabolic acidosis
	↓ 1-Hydroxylase activity	Vitamin D deficiency

Table 1

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Renal tubule number also declines, with a decrease in tubular length and volume, and an increase in tubular atrophy, diverticula (giving rise to cysts) and scarring. Ageing-related changes in tubular anatomy result in altered function. Maintenance of sodium balance in elderly people depends on increased proximal sodium reabsorption coupled with reduced distal fractional reabsorption: this limits the kidney's ability to conserve sodium in response to low salt intake, and predisposes the individual to volume depletion. Reduced activation of the renin–angiotensin–aldosterone system, decreased responsiveness to vasopressin and loss of thirst sensation contribute to this. Elderly people also have a relative inability to excrete sodium excess in response to salt loading, predisposing them to salt and water retention.

Tubular atrophy and scarring lead to reduced Na^+/K^+ ATPase activity. This contributes to an increased risk of hyperkalaemia, alongside declining GFR and reduced activation of the renin–angiotensin–aldosterone system. Elderly people are more likely to develop hyperkalaemia when taking drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), spironolactone and angiotensin-converting enzyme (ACE) inhibitors. Conversely, poor intake and diuretic use can cause hypokalaemia.

The kidneys' ability to dilute and concentrate urine decreases with age: in elderly rats, this has been attributed to reduced expression of urea transporters in the inner medullary collecting ducts, downregulation of vasopressin-2 receptors in the collecting duct and reduced expression of the water channels aquaporin 2 and 3. Reduced concentrating ability commonly gives rise to nocturia, and predisposes to hyponatraemia after a water load. Elderly people are prone to developing acidosis because of an inability to increase ammonia and H^+ synthesis.

Renal 1-hydroxylase activity declines with age, reducing the kidney's capacity to convert 25-hydroxyvitamin-D to 1,25-dihydroxyvitamin-D, and increasing the likelihood of vitamin D deficiency.[2]

Estimating glomerular filtration rate in the elderly

Age-related loss of GFR is accompanied by a reduction in creatinine excretion caused by reduced muscle mass, so the relationship between serum creatinine and GFR changes. When estimating kidney function in older patients, clinicians should use equations that correct for differences in creatinine generation rather than relying solely on serum creatinine levels. The European Renal Best Practice Group (ERBP) does not recommend between equations such as Modification of Diet in Renal Disease (MDRD) or CKD Epidemiology (CKD-EPI), but where cystatin C measurement is available calculations using this to estimate GFR (such as CKD-$EPI_{Cr\text{-}Cy}$s) are more accurate. Where a precise measurement of kidney function is required, true GFR (calculated by Cr-EDTA, inulin clearance or Tc-DTPA) remains the gold standard.[3]

Acute kidney injury

The overwhelming majority of cases of AKI in elderly individuals result from decreased renal perfusion and acute tubular necrosis (Table 2).

Impaired ability to maintain circulating volume in the face of stress increases susceptibility to acute renal hypoperfusion. Older people are more likely to have co-morbid conditions, such as cardiac failure and renovascular disease, that compromise renal perfusion. They are also more likely to be taking medications such as diuretics, which reduce circulating volume, and ACE inhibitors/angiotensin receptor blockers and NSAIDs, which modulate renal haemodynamic autoregulation. They are also more likely to become dehydrated because of decreased sensitivity to thirst and impaired mobility.

Common causes of AKI in elderly individuals

↓ Renal perfusion
Sepsis
Volume loss (e.g. gastrointestinal haemorrhage, diarrhoea + vomiting)
↓ Cardiac output (e.g. myocardial infarction, arrhythmias)
Acute tubular necrosis
Uncorrected renal hypoperfusion
Aminoglycoside antibiotics
Iodinated contrast agents
Myoglobin (rhabdomyolysis)
Parenchymal kidney disease
Glomerulonephritis
Interstitial nephritis (especially drug-induced)
Obstruction
Prostatic enlargement
Renal calculi
Pelvic tumours

Table 2

Acute tubular necrosis most frequently results from ischaemic damage that occurs when reduced renal perfusion is not corrected quickly. Elderly people are also more likely to suffer kidney injury as a result of obstruction of the renal tract.

The increased vulnerability of elderly people to AKI should be recognized and measures taken to prevent it. Volume assessment represents a particular challenge in the elderly. Thirst is often absent despite dehydration. Tachycardia and hypotension can occur as a result of cardiac failure, and postural hypotension because of medication or autonomic dysfunction. Jugular venous pressure can be elevated in cardiac failure and tricuspid regurgitation. Peripheral oedema can occur as a result of hypoalbuminaemia, and collects in the sacrum in bedbound patients.

Regular measurement of kidney function is essential in all elderly inpatients especially those who are acutely unwell or are being given nephrotoxic medications or contrast agents, with attention to appropriately calculated estimated GFR (eGFR) rather than serum creatinine or urea.

Patients with blood and protein on urine dipstick testing, or otherwise suspected to have an intrinsic renal disease such as an acute glomerulonephritis, should be referred to a renal physician. The management of complications of AKI and the indications for RRT are the same in elderly individuals as in the general population (Table 3).

Chronic kidney disease

Controversy exists over what distinguishes pathological CKD from age-related loss of GFR. Current guidelines advise that CKD

Prevention and basic investigation of AKI in elderly individuals

Prevention
Maintain hydration
Monitor vital signs
Withdraw/minimize exposure to nephrotoxic drugs/agents
Monitor eGFR rather than creatinine or urea
Prevent/address sepsis promptly and appropriately
Investigation
Careful fluid balance assessment and judicious fluid challenge with monitoring
Septic screen
Ultrasound of the urinary tract
Medication review
Urine dipstick and protein:creatinine ratio
Creatine kinase

Table 3

be diagnosed at an eGFR of <60 ml/minute/1.73 m^2, in the presence or absence of proteinuria[1]; up to 50% of over-75-year-olds in the general population meet these criteria. Most diagnoses of CKD in elderly people are based on moderate and isolated reductions in eGFR, with approximately 80% not having proteinuria. A GFR >45 ml/minute/1.73 m^2 is generally considered adequate for homeostasis; in the absence of proteinuria, it is not thought to carry significant risk of mortality or progression to ESRF. Thus, there is an argument to suggest that elderly people with an eGFR >45 ml/minute/1.73 m^2 should not be considered to have pathological CKD unless significant proteinuria or another disease process is present.

Other analyses have shown that declining eGFR and proteinuria are independently associated with excess mortality in elderly people (even in the GFR range 45–59 ml/minute/1.73 m^2). When the competitive risk of death (i.e. the greater likelihood of an elderly person with CKD dying before reaching ESRF) is corrected for, they may also have a higher risk of progressing to ESRF. Complications of CKD (e.g. anaemia) do not appear to be age-dependent in their links to progression to ESRF and mortality.

There is also some debate over whether the evidence base for conventional treatments in younger patients with CKD applies to their use in elderly individuals. Elderly patients and those with multiple co-morbidities are generally excluded from trials, and it could be argued that the treatments and targets recommended by these are not applicable to the elderly population. Furthermore, guidelines often fail to acknowledge difficulties associated with complex treatment regimens and polypharmacy in elderly people, and ignore problems such as cognitive decline, falls, functional impairment and frailty; nor do they include outcomes such as independent living and quality of life.

The ERBP, in collaboration with the European Union of Geriatric Medicine Societies (EUGMS), has recently published guidelines for stratifying the risk of CKD progression and the likelihood of morbidity and mortality in older patients with CKD stage 3b or higher. In situations where specific guidance is not available, best practice guidelines for the general adult population should be referred to; however, the altered risk–benefit ratio of recommended treatment strategies should be taken into account, challenges specific to elderly patients addressed, functional outcomes considered and, above all, the patient's and their family's views and wishes given primacy.[3]

Renal replacement therapy in the elderly

Dialysis

The decision to initiate dialysis in an elderly person involves consideration of medical and social factors that might determine the appropriateness of one form of therapy over another, or over maximal conservative management (MCM). The likelihood of death occurring before ESRF is reached should be taken into account.

Non-medical obstacles to dialysis include lack of transportation, lack of social support and poor housing. Elderly people have more cardiovascular and overall co-morbidities than younger patients, and can experience cognitive decline, falls, frailty and loss of function on dialysis. Proper assessment of dialysis adequacy can be confounded by reduced muscle bulk, so elderly people are more likely to be underdialysed.

Shared decision-making should be emphasized, and patients' values and preferences prioritized. Advanced care-planning (including end-of-life care) should be encouraged. Prognostic tools for guiding decision-making are available. In cases where this is uncertain, time-limited trials of RRT can be employed.

Multiple observational studies have compared outcomes of elderly patients undergoing haemodialysis versus peritoneal dialysis: in the North Thames Dialysis Study, there was no difference in 1-year mortality in 125 patients older than 70 years (Table 4).[4]

Transplantation

Transplantation offers improved survival and better quality of life than dialysis, and elderly people who have undergone transplantation show a survival benefit over those still on the waiting list. Careful screening for co-morbidity is essential before the decision to transplant patients or to list them for transplantation. Biological rather than chronological age should determine whether a patient is considered fit for transplantation.

The 5-year survival after transplantation is lower in patients >60 years old (70%) than in younger patients (>90%). The most common cause of graft loss in older patients is death of the host with a functioning graft, with cardiovascular disease being the most common cause of death.

Ageing of the immune system means that elderly recipients are less likely to reject a donated kidney, but are more susceptible to infections. They are also more likely to experience complications of immunosuppressive medication, particularly corticosteroids. The transplantation procedure is made technically more difficult by vascular disease.

Expanded-criteria donor kidneys (from patients >60 years old, or >50 with hypertension, raised creatinine or cause of death from stroke) have a limited lifespan but can be appropriate for an age-matched recipient.

Non-renal replacement therapy management

Patients who do not wish to or are unfit to commence RRT can be managed conservatively, with an emphasis on supportive, symptomatic care. This should involve a multidisciplinary team

Haemodialysis versus peritoneal dialysis in elderly individuals

Haemodialysis	Peritoneal dialysis
Vascular access is potentially difficult	Avoids vascular access
Transportation is time-consuming and costly	Can be done at home
Some patients find haemodialysis sessions burdensome; others enjoy the social interaction	Gentler ultrafiltration
Intradialytic hypotension (↓ cardiac reserve + autonomic dysfunction) → inadequate dialysis/filtration owing to ↓ pump speeds + sessions terminating early	Functional limitations/lack of support can be a barrier (assisted peritoneal dialysis may overcome this if available)
Malnutrition	Inadequate housing prevents appropriate storage and aseptic technique
Infection	Some studies have detected ↑ number of episodes of peritoneal dialysis peritonitis
Gastrointestinal bleeding	

Table 4

including dietitians, social workers and district nurses. One study demonstrated a 2-year survival rate of 76% in dialysis patients compared with 47% for those given conservative management, but no survival benefit was observed for patients with cardiovascular disease or high co-morbidity.[5] Patients managed conservatively spend less time in hospital than dialysis patients, and are more likely to die at home or in a hospice. The decision to opt for MCM should not be predicated entirely on mortality benefit, but should take into account patient goals such as independence.

Palliative care

End-of life-care and planning should be considered at an early stage for all elderly patients with advanced CKD, and high-quality palliative care implemented as soon as it is required. Most deaths are attributable to co-morbid conditions rather than uraemia. Discontinuation of dialysis is more common among older patients. Anuric patients usually die in 8–12 days, whereas patients with some residual renal function can survive several months. Symptoms before death in MCM patients have been found to be similar to those with end-stage cancer. Hospice services remain underused in patients with ESRD, but patients who are referred are more likely to die at home. ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

An 85-year-old woman presented for review. She was well. She had had a right-sided nephrectomy 15 years previously for renal cell carcinoma. She was currently taking amlodipine 10 mg once daily, bisoprolol 5 mg once daily, bendroflumethiazide 2.5 mg once daily and doxazosin 6 mg twice daily. She lived with her husband in a ground floor flat. She was mobile with a stick. She and her husband were both completely independent and enjoyed playing bridge and lawn bowls.

On clinical examination, her heart rate was 58 beats/minute and regular, and blood pressure was 164/80 mmHg. The jugular venous pressure was not raised, the chest was clear and there was only mild ankle oedema.

Investigations

- ECG showed sinus bradycardia
- Estimated glomerular filtration rate 26 ml/minute/1.73 m^2 (>60)
- Urine albumin:creatinine ratio 90 (<2.5)

What is the most appropriate next step in her management?

A Start an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker
B Increase the dose of bisoprolol
C Perform a lying/standing blood pressure measurement
D Increase the dose of doxazosin
E Stop the amlodipine

Question 2

An 78-year-old man was reviewed in the dialysis clinic. He had started on three-times-weekly haemodialysis 18 months previously after emergency repair of an abdominal aortic aneurysm. He had undergone coronary artery and femoral popliteal bypass grafting. He had also had a left middle cerebral artery infarct with residual right-sided weakness. He had a 50 pack–year smoking history. He had been widowed 2 years previously and was living alone in sheltered accommodation. He mobilized with a stick but had become increasingly frail and no longer left the house other than to come to dialysis via transport. His daughter did his shopping and cooking. He had failed to attend dialysis on several occasions, had frequent episodes of intradialytic hypotension (hypotensive episodes during dialysis) and rarely completed a full dialysis session as he asked to be taken off the machine because of leg pain. He was losing weight despite having fluid overload, was anaemic and uraemic, and had had four hospital admissions in the previous few months.

What is the most appropriate next step in his management?

A Increase the number of dialysis sessions to four times a week
B Switch to peritoneal dialysis
C Begin working him up for a transplant
D Discuss whether to stop dialysis
E Continue the current dialysis regimen without any alteration

Question 3

A 90-year-old man presented with acute confusion and agitation. He was usually fit and independent, and other than occasional antihistamines for hay fever was taking no medication.
On clinical examination, confusion was noted. His heart rate was 78 beats/minute, and blood pressure 128/88 mmHg. There was no other gross abnormality. He had remained anuric throughout the day.

Investigations

- Sodium 117 mmol/litre (137–144)
- Potassium 7.0 mmol/litre (3.5–4.9)
- Urea 48 mmol/litre (2.5–7.0)
- Creatinine 650 micromol/litre (60–110)
- Serum bicarbonate 12 mmol/litre (20–28)
- An ECG was unreadable owing to agitation

He was given intravenous calcium gluconate and his hyperkalaemia was temporarily reduced with insulin and dextrose.

What is the most appropriate next step in his management?

A Give 500 ml 1.26% sodium bicarbonate over 4 hours
B Refer the patient to the renal team for emergency haemodialysis
C Perform a bladder scan
D Give a 1 litre fluid challenge with 0.9% sodium chloride
E Request an urgent antiglomerular basement membrane antibody ELISA