

# End-stage renal disease in the very elderly

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**ABSTRACT** The prevalence of end-stage renal disease in the UK looks set to increase for several more years. Since CKD is essentially a disease of older age, and because age is no longer seen as a contraindication for treatment, it follows that older people are now the fastest growing group of patients starting dialysis. Sadly this has not always been matched by an increase in services necessary to support them on dialysis. Expansion of dialysis facilities does not necessarily mean that all 80-year-old patients with end-stage renal disease should be offered treatment, which will often be inappropriate because of functional impairment, or will become inappropriate in the setting of severe dementia, advanced cancer or other serious co-morbid illness. Many questions about the management of older people with end-stage renal disease remain unanswered. Well designed prospective studies are required.

**KEYWORDS** Chronic kidney disease, dialysis, octogenarians, palliative care, very elderly

**LIST OF ABBREVIATIONS** Albumin:creatinine ratio (ACR), angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARBs), automated peritoneal dialysis (APD), chronic kidney disease (CKD), chronic renal failure (CRF), continuous ambulatory peritoneal dialysis (CAPD), end stage renal disease (ESRD), estimated GFR (eGFR), glomerular filtration rate (GFR), Modified Diet in Renal Disease (MDRD), myocardial infarction (MI), protein:creatinine ratio (PCR), renal replacement therapy (RRT), urea and electrolytes (U&E)

**DECLARATION OF INTERESTS** No conflict of interests declared.

## INTRODUCTION

Chronic kidney disease is essentially a disease of the elderly. It is rare in childhood, then increases progressively in incidence with age, such that half of all new dialysis patients in Scotland are currently over 65 years of age.<sup>1</sup> To write about CKD is therefore to write about the elderly. There is no shortage of reviews on this important topic. Our comments are therefore limited to the assessment and management of patients who are very elderly, i.e. over 80 years of age. The reasons for doing this are threefold: firstly, the number of the very elderly with end-stage renal failure is increasing; secondly, it is likely that many of these patients will be managed by general physicians and not referred to nephrologists; and thirdly, much less has been written on the subject of CKD in patients who are over 80 years of age.

## A SCOTTISH PERSPECTIVE

One of the authors recently conducted a survey on behalf of the Scottish Renal Registry of all adult CKD patients who started dialysis in Scotland in the years 1994–2001.<sup>2</sup> Of 3,944 patients, 213 (5.4%) were aged 80 years or over, including 47/513 (9.2%) of all new starts in 2001. Ninety per cent of these older patients had hospital haemodialysis

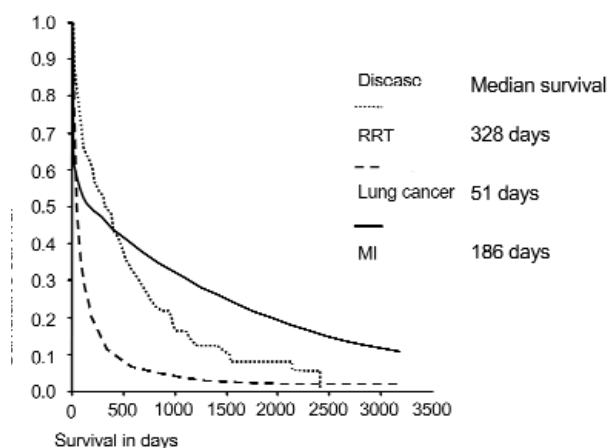
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**FIGURE 1** Survival of patients aged 80 or more at the start of RRT, cancer diagnosis, or hospital admission for MI.

as their first mode of RRT. Only 10% of the older patients started peritoneal dialysis, compared with 18% of those aged 65–79 years and 32% of those aged 64 years or less. None of the older group had a pre-emptive transplant. The most common diagnosis in older patients was CKD of unknown cause (41%). We went on to compare the survival of our 213 very elderly Scottish CKD patients with that of age- and sex-matched MI and lung cancer controls using data provided by the Information and

Stage	Description	GFR (ml/min/ 1.73m <sup>2</sup> )	Prevalence (%)	Focus of care*
1	Kidney damage with normal or increased GFR	> 90	3.3	Diagnosis and disease specific therapy
2	Kidney damage with mildly impaired GFR	60–89	3.0	Slowing of progression and reduction of cardiovascular risk
3	Moderately impaired GFR	30–59	4.3	Addressing complications of CKD
4	Severely impaired GFR	15–29	0.2	Preparation for dialysis
5	End-stage renal failure	< 15	0.2	Dialysis, transplantation, or conservative care

**TABLE 1** The US National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (K/DOQI) Classification of CKD. (\* Each stage also incorporates the areas of care of the previous stage.)

Statistics Division of NHS Scotland. Median survival of the CKD patients was 328 days, i.e. less than one year from the start of treatment. This was similar to that of MI patients and considerably greater than the survival of octogenarians with lung cancer (see Figure 1). Myocardial infarction patients who survived the first 90 days went on to do better than their renal counterparts. Further comparison with the general population aged 80 years and over showed that all three groups had much poorer life expectancy than their peers. In 2000, the average Scottish man and woman aged 80–85 years could expect a further 6.7 and 8.4 years of life, respectively.<sup>3</sup> Median survival of Scottish octogenarians on dialysis is less than that of their counterparts in Berlin (26 months)<sup>4</sup> and Paris (29 months)<sup>5</sup>, but similar to that of octogenarians undergoing dialysis in the North Thames Study (just over one year).<sup>6</sup>

## SEVERITY OF CHRONIC KIDNEY DISEASE

The assessment of patients with all stages of CKD has been simplified greatly by the move to prediction equations for GFR and albumin or protein creatinine ratios for proteinuria.<sup>7</sup> The 24-hour collection has been all but abandoned as the means by which both creatinine clearance and proteinuria are measured. Few tears will be shed: 24-hour urine collections are cumbersome and frequently inaccurate. Some patients try to help by filling the 24-hour urine container to the brim, even if it takes more than 24 hours to do so, while others simply do not understand that the 24-hour collection begins by discarding the first specimen of urine, even when provided

with written instructions to do so. We now estimate GFR using the MDRD equation, while for quantitative proteinuria a spot urine for ACR or PCR is preferred. The move to estimated GFR (or eGFR) has facilitated a more practical approach to the management of CKD (see Table 1), while adoption of ACR and PCR allows us to identify people with proteinuric nephropathy (see Table 2). This in turn has implications for diagnosis and treatment, particularly with drugs that block the renin–angiotensin system. Neither of these newer tests is perfect, but their convenience and simplicity seems likely to guarantee their widespread use for the foreseeable future.

## CAUSE OF CHRONIC KIDNEY DISEASE

Previously, patients of all ages with CKD were classified by the cause of their renal failure. The most common cause in the very elderly is unknown, a category used to describe patients in whom glomerulonephritis, diabetes, hypertension, interstitial nephropathy, and other multi-system diseases have either been excluded or are considered unlikely. Hypertension and diabetes are also common causes, whereas glomerulonephritis, an important cause of CRF in young adults, becomes much less frequent with age. Obstructive uropathy, particularly that due to prostatic hypertrophy or prostatic carcinoma is an important cause of CRF in the very elderly, but does not commonly lead to dialysis once the obstruction has been relieved by catheterisation, nephrostomy, or stent. Myeloma should always be excluded by serum and urine electrophoresis in any older person presenting with CKD.

Patients with tight bilateral renal artery stenosis or unilateral renal artery occlusion and contralateral stenosis may be suitable for revascularisation but are encountered far less frequently than those with hypertensive nephrosclerosis, which is perhaps best thought of as a form of bilateral intrarenal artery stenosis. Both are likely to show greater than 30% increase in serum creatinine with renin–angiotensin system blockade, which unfortunately does not distinguish those who will and will not be suitable for revascularisation (see Table 3). Rapidly progressive renal failure due to Goodpasture's syndrome, Wegener's granulomatosis, or microscopic polyarteritis is another important cause of CKD in the elderly. The presence of a pulmonary renal syndrome is a clue to diagnosis which must then be confirmed by serology and urgent renal biopsy. The prize that awaits an early diagnosis is the prospect that renal function may recover with prednisolone, cyclophosphamide, and plasma exchange, though the reality is that this does not happen as often as is suggested in the literature.

## PREDICTING PROGRESSION OF CHRONIC KIDNEY DISEASE

The rate of progression from early CKD, here defined as eGFR 30–60 ml/min/1.73 m<sup>2</sup>, to end stage renal

	Albumin:creatinine ratio (mg/mmol)	Albumin excretion rate (mg/24 h)	Protein:creatinine ratio (mg/mmol)	Protein excretion rate (mg/24 h)
Normoalbuminuria	<3	<30	<15	<150
Microalbuminuria	3–30	30–300	15–45 (better assessed by ACR)	150–450
Proteinuria	>30 (better assessed by PCR)	>300	>45	>450

**TABLE 2** Albumin:creatinine ratio and protein:creatinine ratio with cutpoints for normoalbuminuria, microalbuminuria, and proteinuria. Adapted from Rohrich *et al.*<sup>4</sup>

#### Indications for use in renal disease

Angiotensin-converting enzyme inhibitors and ARBs have antihypertensive and antiproteinuric properties that make them drugs of first choice in non-diabetics with urine PCR >100 mg/mmol (estimated protein output >1 g/24 h) and in diabetics with microalbuminuria (urine ACR 3–30 mg/mmol).

#### Which drug?

We believe that the benefits of ACEI and ARBs are likely to be class effects so that the choice of agent may be reasonably decided by convenience and cost. Angiotensin receptor blockers appear to share most of the benefits of ACEI on the kidneys and are particularly indicated with ACEI-related cough.

#### Renal risks of renin–angiotensin system blockade

A small rise in serum creatinine is a normal haemodynamic response to renin–angiotensin system blockade and is not a reason to stop these drugs. We advise checking U&E at five days and one month, and thereafter as clinically appropriate. As a general rule we will accept a rise in creatinine of up to 30% from baseline provided the final value is less than 300 µmol/l. Patients whose serum creatinine is going to increase by more than 30% will usually declare themselves within a month of introducing the drug or increasing the dose. Important causes of an exaggerated rise in creatinine are:

- excessive hypotension;
- volume depletion, e.g. vomiting or diarrhoea;
- co-prescription of a non-steroidal anti-inflammatory drug;
- bilateral renovascular disease or hypertensive nephrosclerosis.

#### Renin–angiotensin system blockade and renovascular disease

Bilateral renovascular disease should be considered in middle-aged or elderly patients with vascular disease at other sites who develop ARF following an ACEI or ARB. These patients are likely to have inequality of renal size on renal ultrasound. Surgically correctable renovascular disease is uncommon.

#### Intercurrent vomiting and diarrhoea

All patients with renal impairment on RAS blockade should be advised to contact their GP if they develop vomiting or diarrhoea for any reason, as ARF may occur. It is usually sufficient to stop the ACEI or ARB temporarily and restart when symptoms have resolved.

#### Hyperkalaemia

Hyperkalaemia may also occur with renin–angiotensin system blockade. We normally accept values of up to 5.5 mmol/l. Values >5.5 mmol/l should prompt a review of diet and drugs, particularly non-steroidal anti-inflammatory drugs. Serum potassium >6 mmol/l should lead to discontinuation of ACEI or ARB, at least temporarily. Refer immediately if serum potassium >7 mmol/l.

**TABLE 3** Renin–angiotensin system blockade.

disease is low. Three-thousand and sixty-nine participants in a Norwegian population survey with eGFR <60 ml/min were followed for eight years during which time there were only 38 cases of incident ESRD. For patients with eGFR 45–59 ml/min the rate of developing ESRD was 0.4 per thousand patient years of follow up. For those with eGFR 30–44 ml/min, the rate was 2.0 per thousand patient years.<sup>8</sup> These observations are quite consistent with the population prevalence of CKD 3, 4 and 5 which is 5.0, 0.2 and 0.2% respectively. Most patients with CKD 3 do not have progressive renal failure therefore.

This was debated at some length during the Consensus Conference on Early Chronic Kidney Disease, held in Edinburgh in February 2007.<sup>9</sup> Evidence was presented to show that proteinuria may be just as important as eGFR 30–60 ml/min in predicting progressive renal failure.<sup>10</sup> Taking the data on proteinuria with that showing greater rate of renal progression in patients with lower eGFR within the CKD 3 subgroup, the Consensus Panel made two recommendations. First, that detection and quantification of proteinuria by urine PCR should be included in the next iteration of the GP contract, and second that patients with CKD 3 should be subdivided by

	eGFR ml/min	Urine PCR mg/mmol	Notation
Low Risk	45-59	<100	3A
Intermediate Risk	45-59	>100	3AP
	30-44	<100	3B
High Risk	30-44	>100	3BP

**FIGURE 2** Risk stratification within CKD 3.

GFR and proteinuria status to give lower, intermediate and higher risk subgroups (see Figure 2). Thus a patient with eGFR 38 ml/min and urine PCR 132 mg/mmol will have CKD stage 3BP. It remains to be seen whether the terminology will catch on, although the attempt to define higher risk subgroups within CKD 3 clearly has merit.

## NEPHROLOGY REFERRAL

The introduction of eGFR has led to a large increase in the number of GP referrals, as anticipated. The Renal Association's list of circumstances in which a GP might wish to seek a nephrology opinion is bewilderingly long,<sup>11</sup> but for patients whose main clinical problem is CKD, this can be simplified as follows:

- Routine referral of patients with deteriorating CKD stage 3 (eGFR 30–60 ml/min);
- Urgent referral of patients with CKD stage 4 (eGFR 15–29 ml/min) unless known to be stable; and
- Immediate referral of patients with CKD stage 5 (eGFR less than 15 ml/min) for consideration of dialysis unless dialysis would be inappropriate.

The problem for general physicians and nephrologists is that up to 5% of the population may have CKD stages 3, 4, or 5. The largest groups are patients with CKD 3, for whom cardiovascular disease usually poses a greater threat than progressive renal failure. A difficulty for many octogenarians is that the MDRD equation estimates GFR to lie between 30 and 60 ml/min when the serum creatinine is only modestly elevated, particularly in women.

To illustrate this point, an 85-year-old man with a serum creatinine of 160  $\mu\text{mol/l}$  (a level which previously might not have triggered a nephrology referral) has an eGFR of 38 ml/min. An 85-year-old woman with the same level of creatinine has an eGFR of 28 ml/min. It is our view that most of these patients need not be seen by a nephrologist unless one or more of the following conditions is met.

- Their renal failure is progressive and/or they have heavy proteinuria;

### Measures to reduce risk of cardiovascular disease and progression of renal failure in CKD 3–5 (added value of nephrology referral likely to be low)

- Target BP ideally <130/80 mmHg (<140/85 mmHg for GP contract).
- Angiotensin-converting enzyme inhibition or ARB in non-diabetics with urine PCR >100 mg/mmol and in diabetics with microalbuminuria (urine ACR 3–30 mg/mmol).
- Aspirin and statin.
- Lifestyle advice, especially smoking cessation.

### Treatment of complications of renal failure in CKD 3–5 (added value of nephrologist likely to be high)

- Anaemia – consider erythropoietin if Hb <110 and other causes excluded.
- Bone disease – monitor calcium, phosphate, parathyroid hormone, and consider phosphate binders, alfacalcidol as clinically indicated.
- Correction of acidosis by sodium bicarbonate if clinically indicated.
- Nutritional assessment by renal dietitian – renal patients are often under-nourished.
- Advice on hyperkalaemia when serum K >6 mmol/l – stop relevant drugs, review diet.

**TABLE 4** Think before you refer.

- They have a specific renal diagnosis, for example polycystic kidney disease or lupus nephritis; or
- They have a specific renal complication for which a nephrology opinion might reasonably be expected to add value (see Table 4).

## CHOICE OF THERAPY FOR END-STAGE RENAL FAILURE

Treatment options for younger patients with end-stage renal disease include:

- Haemodialysis, which can be undertaken in a centre or at home;
- Peritoneal dialysis, which can be CAPD or APD, both of which are done at home; or
- A transplant which may be pre-emptive (i.e. before the patient starts dialysis), and either cadaveric or live donor.

The position for the very elderly is slightly different. Options here are palliative care or dialysis, with most patients who start RRT opting for hospital haemodialysis.

We will return to the question of palliative care shortly, but need to dismiss transplantation as a realistic option for the very elderly. Although there is evidence that older patients may require less immunosuppressive therapy than younger recipients of a graft, there are no data to suggest a survival advantage over the age of 75.<sup>12</sup> Many very elderly patients have co-morbidities that would prejudice complex surgery of this sort. A further reason

for not considering octogenarians for transplantation is that we already have over 5,000 patients in the UK on the transplant waiting list. Shortage of donors means that the waiting time for a transplant is now commonly 3–4 years.

## PALLIATIVE CARE

As little as 30 years ago, patients who had end-stage renal failure with significant co-morbidities and were over 55 years of age were likely to be nursed in a side room until they died. The pendulum has since swung to the other extreme, which means that patients in their late 80s and even 90s are now regularly brought into renal units from nursing homes for hospital haemodialysis. The unrealistically high expectations of patients and their families are at least partly responsible for this seismic change in clinical practice. Dialysis is a demanding form of treatment for younger and middle-aged adults who have nothing else wrong with them except kidney failure and it must be very demanding indeed for the octogenarian who lives alone, has cognitive impairment, poor mobility, and heart failure. Although respectable survival rates and quality of life have been reported by some centres, it does not always work out this way, as a visit to any UK haemodialysis unit would confirm.

Against this background there has been a surge of interest in renal palliative care in recent years. 'Googling' on 'renal palliative care' gave no fewer than 1.34 million hits at the beginning of May 2007. Renal palliative care allows patients either not to start dialysis in the first place or to withdraw from dialysis, secure in the knowledge that such a decision does not mean that they will receive no treatment. Circumstantial evidence suggests that octogenarians with end-stage renal disease have a median survival of around one year on dialysis<sup>2</sup> and of around six months without dialysis.<sup>13</sup> This is not to deny otherwise healthy octogenarians a life-saving form of treatment, but simply makes it acceptable not to initiate or to withdraw dialysis when the burden of symptoms from co-morbidity, the presence of other life-threatening illness, or the demands of dialysis itself, come to outweigh the benefits.<sup>14</sup>

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Key components of a palliative care programme for renal patients include:

- A designated nurse specialist;
- Written protocols;
- Blood transfusion, intravenous iron, and erythropoietin to treat renal anaemia;
- The use of advance directives;
- Good communication between healthcare professionals, patient, and family; and
- Support for carers.

Suggestions for developing renal palliative care services are given in the National Service Framework for Renal Services.<sup>15</sup> A national survey of palliative care provision in end-stage renal disease in the UK was published in 2005.<sup>16</sup>

## KEYPOINTS

- The introduction of eGFR has led to an increase in the number of referrals of very elderly patients. The eGFR is lower than anticipated for a given level of serum creatinine, particularly in women.
- The most common causes of CKD in the very elderly are unknown causes, hypertensive nephrosclerosis, and diabetes.
- Referral to a nephrologist is likely to add value when renal failure is progressive, there is a specific renal diagnosis, or a complication of renal failure such as anaemia or bone disease is present.
- Treatment options for those who reach end-stage renal failure are palliative care or dialysis, with most patients who start RRT opting for hospital haemodialysis.
- Renal palliative care may be more appropriate than dialysis when the burden of symptoms from co-morbidity, the presence of other life-threatening illnesses, or the demands of dialysis itself, come to outweigh the benefits.

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## Physician Assisted Suicide – a good death?

Wednesday, 3 October 2007

Venue: Royal College of Physicians of Edinburgh, 9 Queen Street, Edinburgh

- Some of the most poignant stories in the media are from people with terminal illness who do not want to continue living and appeal for help to those whose vocation is to save life. How do health professionals cope with this dilemma? In some countries, it is legal for doctors to assist a person to commit suicide and there are calls for the law to be changed in the UK. How do we hold together the difficult knowledge we have about life-threatening disease, the better understanding we have about palliative care, our hesitancy in speaking about death and a 'rights culture' where people want to be in control of their lives? What is a 'good death' today?

The College invites you to consider this important and solemn question in the company of physicians, lawyers, ethicists and people for whom this is a very personal issue. The conference will be of interest to healthcare professionals, lawyers, students in related disciplines and concerned members of the public.

### Session 1: Context

Chair: The Rt Hon The Lord MacKay of Clashfern KC PC

- Setting the Scene  
*Rev Professor Kenneth Boyd*
- Legal Context  
*Professor Kenyon Mason*
- Culture and Spiritual  
*Rev Dr Ewan Kelly*
- Discussion

### Session 2: What might change mean?

Chair: Rev Professor Peter W Brunt CVO OBE

- Argument for Change  
*Professor Sheila McLean*
- What might this change mean for clinicians?  
*Dr George Fernie*
- What might this change mean for patients?  
*Dr Patricia Wilkie*
- Discussion

### Session 3: Clinicians' experiences

Chair: Dr John Duncan

- The Dutch Experience, truth or double Dutch?  
*Dr Rob Jonquière*
- Palliative Care  
*Dr David Jeffrey*
- How the doctor and patient come to a decision  
*Professor Roger Higgs MBE*
- Discussion

### Session 4: Legislation

Chair: Dr Alison Elliot OBE

- For a change in legislation  
*Mr Jeremy Purvis MSP*
- Against a change in legislation  
*Lord Phillips of Sudbury*
- Discussion
- Closing remarks  
*Dr Alison Elliot OBE*

- As you will see from the above, we have been extremely fortunate in securing the participation of excellent speakers and session chairs. Full details on them along with a copy of the finalised programme and registration form can be obtained from the RCPE website: [www.rcpe.ac.uk/education/events/index.php](http://www.rcpe.ac.uk/education/events/index.php)

- Further details available from: Margaret Farquhar, Symposium Co-ordinator, Royal College of Physicians of Edinburgh, 9 Queen Street, Edinburgh, EH2 1JQ.

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