Chapter 1

Changing patterns of renal replacement therapy

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1.1 Introduction

End-stage renal disease (ESRD) is inevitably fatal unless treated by renal replacement therapy (RRT). Although George Hass undertook the first haemodialysis (HD) in a human in 1926, his patient died, and it was not until 1945 that the first successful HD was performed by Kolff for acute renal failure (ARF). It was only through the development of the arteriovenous shunt in the early 1960s that the outlook then also changed for patients with chronic renal failure (CRF).

Following the first partially successful renal transplant in 1950[1] and the first long-term survivor in 1954, the uptake of transplantation increased throughout the 1960s. Renal transplantation only became more successful once graft rejection could be effectively countered with the introduction of the effective immunosuppressant ciclosporin in 1983.

Although the first peritoneal dialysis (PD) was also performed in the human around 1926 by Georg Ganter through improvements in technology, it only became established as an important mode of therapy for chronic renal failure in the 1980s. The use of PD varies between countries and in developed countries the cost is lower than that of HD and there is no requirement for major infrastructure. In many developing countries with lower staffing costs and high ‘disposables’ costs, PD remains expensive. There has been a revolution in the care of patients with renal failure in these 50 years in all developed countries, with a continuing growth in the provision of RRT. This has come at considerable cost to healthcare systems as these treatments are expensive and have to be administered lifelong. In 2006 the US spent $33 billion on end-stage renal disease (ESRD) expenditure, while the UK estimate is about £1 billion.

In the decades up to 1990s there was considerable debate about the equity of provision of this high-cost technology which, at population level, only benefits a relatively small number of patients. Treatment in some countries, particularly tax-based systems such as the UK’s National Health Services (NHS), was rationed, with care being restricted to younger, fitter patients. However, as technology and clinical expertise have advanced, it is now possible to treat older, sicker patients successfully. This success in treatment has led UK patients to dislike the use of the term ‘End-Stage’ Renal Failure/Disease and in the UK, the term Established Renal Failure (ERF) is now synonymous with ESRF/ESRD, which remains in common use around the world.

The debate about provision of RRT has widened to include not only concern about who is not being treated, but also consideration of formally not providing RRT to those likely to have a poor outcome on RRT. In parallel with this has been the development of alternative palliative models of care to dialysis. The great success of RRT has generated the new problem of caring for a very large and growing pool of patients on RRT and emphasized the public health importance of ESRD. Moreover, the significant and rising cost of RRT programmes make it a crucial issue for all healthcare systems.
This chapter outlines the scale of this growth in RRT and considers the implications for renal service provision.

1.2 Chronic kidney disease

Until recently, it was widely held that kidney disease affected only a very small proportion of the population. It is not feasible to accurately measure renal function outside of the research setting using inulin or iothalamate clearances, and additionally 24-h urine collections are often inaccurate due to incomplete collection. The identification of impaired renal function in epidemiological studies and clinical practice was therefore based on serum creatinine measurements, which took no account of differences in rates of creatinine generation specific to gender or age. As a result, marked renal impairment was often overlooked in poorly nourished, elderly females.

1.2.1 Estimating renal function

Although equations have been used in clinical practice for over 30 years to estimate kidney function from serum creatinine, these were not in widespread use[2] as they required additional factors such as patient weight. With the development of new equations to estimate kidney function – estimated glomerular filtration rate (eGFR) – from demographic and serum variables without requiring weight[3] it was possible to consider more widespread application. The National Kidney Federation then set up a working group to define and classify what they now called chronic kidney disease.[4] This led to the development of a global consensus on a simple definition of CKD – kidney damage or a GFR < 60 ml/min/1.73 m^2 for 3 months or more, irrespective of cause.[5] Kidney damage in many kidney diseases could be ascertained by the presence of proteinuria, defined as a urinary protein-to-creatinine ratio > 50 mg/mol in two of three spot urine specimens. The GFR could be estimated from calibrated serum creatinine using equations such as the Modification of Diet in Renal Disease (MDRD) Study equation[6] or the Cockcroft–Gault formula.

Severity of CKD was initially categorized according to the level of eGFR into one of five stages, with later revisions further dividing some stages and recognizing the prognostic importance of proteinuria (Table 1.1).

All the equations used to estimate kidney function are unreliable with an eGFR >60 and a decreasing GFR may also be a normal part of the ageing process. Possibly for these reasons, a cut-off

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR (ml/min/1.73m^2)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥ 90</td>
<td>Normal or increased GFR, with other evidence of kidney damage</td>
</tr>
<tr>
<td>2</td>
<td>60–89</td>
<td>Slight decrease in GFR, with other evidence of kidney damage</td>
</tr>
<tr>
<td>3A</td>
<td>45–59</td>
<td>Moderate decrease in GFR, with or without other evidence of kidney damage</td>
</tr>
<tr>
<td>3B</td>
<td>30–44</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15–29</td>
<td>Severe decrease in GFR, with or without other evidence of kidney damage</td>
</tr>
<tr>
<td>5</td>
<td>&lt; 15</td>
<td>Established renal failure</td>
</tr>
</tbody>
</table>

* Use the suffix (p) to denote the presence of proteinuria when staging CKD (recommendation 1.2.1).

of 60ml/min/1.73m² was applied for the diagnosis of CKD in the absence of evidence of kidney damage. Using this definition, it was estimated that 13% of the general population in the United States of America had CKD in the period 1999–2004, although less than 0.5% would have had stage 4 or 5 CKD.[7] Similar rates (16%) have been observed in the AusDiab study in Australia.

In the UK, data are only available from blood samples taken as part of routine clinical practice and identified either in laboratory or general practice databases. Such results must therefore be interpreted with some caution as they overlook individuals who avoid contact with the healthcare system unless it is essential. In addition, individuals with proteinuria but with an eGFR >60 are largely excluded from such studies. Despite this, UK rates of CKD of 10.6% for females and 5.6% for males do not seem dissimilar to those reported elsewhere.[8]

One of the major criticisms of using eGFR to diagnose CKD has been that it labels many elderly individuals – whose kidney function is decreasing as part of the normal ageing process – as having a ‘disease’. This has been exemplified in a Dutch general-population cohort of ‘healthy’ individuals (i.e. no history of hypertension, diabetes, vascular disease, or kidney disease), in which the median GFR estimated using the MDRD equation decreased from 90–100 ml/min/1.73m² in the age range of 18–24 years to 60–65 ml/min/1.73m² in the age group of 85+ years.[9] As a result of this decrease, 42% and 44% of ‘healthy’ males and females over the age of 85 had a GFR of less than 60 ml/min/1.73m² and would be labelled as having CKD stages 3–5 (Fig. 1.1).[9]

Much of the current literature talks about an epidemic of CKD.[10] The definition of an epidemic (from Greek *epi-* upon + *demos* people) is when new cases occur in a given human population, during a given period, at a rate that substantially exceeds what is ‘expected’, based on recent experience (the disease does not have to be communicable). Does CKD meet these criteria? It remains difficult to measure changes in historical prevalence rates of CKD in general populations and changes in incidence rates with time have not been measured, so a caution in the use of such phraseology is advised.

So what are the benefits of identifying individuals with reduced eGFR? Historically the answer to this question was simply to diagnose the cause of kidney disease, delay or halt progression to

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**Fig. 1.1** Prevalence of CKD stages 3–5 (GFR: 60 ml/min/1.73m²) according to age in the non-diseased Caucasian Nijmegen Biomedical Study population. Black bars represent men and open bars women. Source: Wetzels JFM et al. (2007). Age- and gender-specific reference values of estimated GFR in Caucasians: The Nijmegen Biomedical Study. *Kidney Int*, **72**(5), 632–7, with Permission.
kidney failure, and, when necessary, to prepare for RRT. However, the cardiovascular risk associated with CKD – independent of traditional risk factors – has increasingly been recognized.[11] Indeed, data from a large Health Maintenance Organization in the USA has shown that individuals with an eGFR of 30–60 ml/min have a 5-year mortality risk of 24% compared with a 1% risk of receiving RRT in the same time interval.[12] As expected, the risk of requiring RRT was 20% higher amongst those with an eGFR of 15–30 ml/min, but so was the risk of death (46%).[12] A diagnosis of CKD should therefore act as a flag for a high cardiovascular risk and lead to such patients’ cardiovascular risk factors being appropriately managed.

1.3 Renal replacement therapy

1.3.1 Background

Most data on RRT have come from Renal Registries, which were established in many of the developed countries to monitor the patterns of this emerging technology. There are two widely used measures of RRT rates: incidence and prevalence. The incidence (or take-on) rates of RRT are ‘new’ cases started on RRT and reported per year per million population. These are influenced not only by the underlying incidence of ERF in the population, but also by levels of detection, referral, and acceptance onto RRT.

There are variations in the definition of a new case. For example, in many countries a new case is not included until after 90 days of treatment; this clearly excludes patients with established renal failure who die in the first 90 days and it underestimates incidence and workload for healthcare providers. However, ascertaining patients at day 0 is difficult. Some patients requiring HD may have acute renal failure; if those that die early are included, this may inflate estimates as some of these cases may have recovered renal function and not needed chronic HD. Some countries also include patients restarting dialysis after a failed renal transplant as ‘new’ patients. Such differences in definition need to be borne in mind when comparing rates.

Although RRT rates are not true epidemiological measures of the underlying rate of ERF in the population, they are widely available and are frequently used as proxy measures. To be diagnosed with ERF, a patient should have insufficient renal function to remain alive and well without RRT. The somewhat subjective nature of this definition is reflected by the considerable central and international variation in mean eGFR observed in patients commencing RRT. A more reproducible measure of RRT need is the number of patients with a GFR below 15 ml/min/1.73m² – stage 5 CKD – but as this represents only 0.2% of the general population,[13] large numbers of subjects would need to be screened to reliably determine an incidence rate. Alternative approaches to measuring the burden of renal disease in a population include use of mortality data, but these are unreliable because of significant under-ascertainment of renal disease on death certificates.[14] Moreover, the International Classification of Disease (ICD) coding does not reliably distinguish between acute and chronic forms of renal failure. Nor is it possible to use hospital-utilization data as these only relate to known treated cases; they overlook a large portion of RRT activity which is delivered to outpatients or to patients at home and they are limited by the shortcomings of the ICD coding discussed above.

This chapter utilizes Renal Registry data, based on the authors’ experience in the UK and contrasted where appropriate with data from other developed countries.

1.3.2 Trends in incidence rates

In the UK the number and rate of patients accepted onto RRT has steadily increased over the last 25 years from 20 per million population in 1982 to 109 per million population. in 2007 (Fig. 1.2) with similar changes in other European countries. The characteristics of the patients being treated have
changed dramatically in this time. In the early 1980s, RRT was restricted almost exclusively to those under 65, but 20 years later nearly half of all cases receiving RRT in the UK were over 65 (Fig. 1.3). Similar changes in the age of patients starting RRT have been reported in other European countries (Fig. 1.4). The UK age- and gender-specific patterns of RRT incidence in 2007 demonstrate higher rates in older ages and amongst males (Fig. 1.5). The interaction of factors that influence RRT rates is depicted in Fig. 1.6.

It is important to recognize the use of chronological age as a bar to treatment (Mignon 1993 OTN 504) is unethical, and in the UK the Department of Health has stated this to all Health Commissioners. Although older patients are likely to have a greater burden of co-morbidity and social problems, their relative quality-of-life gain is better than that of younger HD patients. One study found that the mental health-component score of the Short Form-36 (SF-36) was almost the same in elderly dialysis patients as in the age-specific general population.[15]

1.3.3 Cause of ERF

Establishing the cause of ERF can be difficult and coding systems vary between registries. Most European countries use the coding system of about 90 diagnostic categories established by the European Renal Association which has now been in place for over 30 years and is currently under major revision. Nevertheless, it is possible to discern a change in the pattern of causes of ERF over the last 25 years from Registry data. While rates of some primary renal diseases, such as glomerulonephritis, polycystic kidney disease, and pyelonephritis, have remained fairly constant, big increases have been seen in diabetic, hypertensive, and renovascular disease (Fig. 1.7).[16] In particular, diabetes mellitus has changed from being a rare cause of ERF (2%) to being the single commonest cause of ERF amongst those accepted (21% in the UK, 34% in Germany, France, and Canada, and 44% in the USA)[17] (Table 1.2). While the changing population demographics may have partly contributed to this shift, it is widely recognized that 25 years ago diabetes mellitus was often seen as a relative contraindication to being accepted onto RRT. The improved survival
**Fig. 1.3** Incidence rates for RRT in the UK from 1980 to 2007 by age and diabetes. Source: UK Renal Registry unpublished data.

**Fig. 1.4** Median age of patients starting RRT 1980–2006 from ERA-EDTA Registry. Source: UK Renal Registry Report 2008.
of patients with diabetes (and therefore reduced competing risk of death prior to reaching ERF) is also thought to have contributed to these changes.[18]

The current international differences in rates of ERF caused by diabetes, however, are likely to be due to differences in patterns of diabetes, especially Type 2, and the effectiveness of preventive health measures and variation in ascription (i.e. the proportion of patients with diabetic ERF that

![Incident rates by age and gender in 2007](image)

**Fig. 1.5** Incidence rates for RRT by age and gender in the UK in 2007. Source: UK Renal Registry Report 2008.

![Factors influencing RRT incidence](image)

**Fig. 1.6** Factors influencing RRT incidence. Source: Caskey FJ et al. (2006). Exploring the differences in epidemiology of treated ESRD between Germany and England and Wales. *Am J Kidney Dis, 47*(3), 445–54.
Fig. 1.7 Trends in incident rates of new acceptances by cause of established renal failure from European Renal Association Registry 1980–99.

Table 1.2 International rates of RRT incidence, prevalence, diabetic nephropathy and RRT modality

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence (pmp)</th>
<th>Prevalence (pmp)</th>
<th>Diabetes %</th>
<th>In-centre HD* %</th>
<th>Home HD* %</th>
<th>PD* %</th>
<th>New transplants (pmp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>115</td>
<td>778</td>
<td>32.4</td>
<td>68.4</td>
<td>9.5</td>
<td>22</td>
<td>31.1</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>9</td>
<td>92</td>
<td>99.6</td>
<td>0</td>
<td>0.4</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Jalisco, Mexico</td>
<td>346</td>
<td>929</td>
<td>49.9</td>
<td>29.5</td>
<td>0</td>
<td>70.5</td>
<td>52.2</td>
</tr>
<tr>
<td>Malaysia</td>
<td>119</td>
<td>615</td>
<td>57.5</td>
<td>90</td>
<td>1.1</td>
<td>8.9</td>
<td>4.5</td>
</tr>
<tr>
<td>Norway</td>
<td>100</td>
<td>753</td>
<td>16.4</td>
<td>80.4</td>
<td>0.4</td>
<td>19.2</td>
<td>45.3</td>
</tr>
<tr>
<td>Romania</td>
<td>75</td>
<td>304</td>
<td>12.4</td>
<td>80.7</td>
<td>0</td>
<td>19.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Russia</td>
<td>28</td>
<td>130</td>
<td>13.9</td>
<td>91</td>
<td>0</td>
<td>9</td>
<td>2.9</td>
</tr>
<tr>
<td>Spain</td>
<td>132</td>
<td>991</td>
<td>23.1</td>
<td>88.6</td>
<td>0.1</td>
<td>11.3</td>
<td>60.2</td>
</tr>
<tr>
<td>Taiwan</td>
<td>418</td>
<td>2226</td>
<td>42.4</td>
<td>92.4</td>
<td>0</td>
<td>7.6</td>
<td></td>
</tr>
<tr>
<td>United Kingdom</td>
<td>110</td>
<td>759</td>
<td>21</td>
<td>78.8</td>
<td>2</td>
<td>19.1</td>
<td>36</td>
</tr>
<tr>
<td>United States</td>
<td>363</td>
<td>1641</td>
<td>44.3</td>
<td>91.1</td>
<td>0.7</td>
<td>9.4</td>
<td>60.3</td>
</tr>
</tbody>
</table>

*In-centre HD, Home HD and PD percentage are all for prevalent patients.
has been proven on biopsy). In the UK, e.g. 19% of patients accepted onto RRT have diabetes listed as the primary cause of ERF, but data on co-morbidity indicate that a further 7% of patients have diabetes that is not considered to have caused their ERF. Interestingly, rates of survival of these two patient groups are identical. Many countries do not specify whether or not ‘diabetes’ is limited to those who have diabetes as the cause of ERF.

Within the UK there is also variation in the incidence of RRT with higher rates in Wales, mostly due to the higher incidence of diabetic ERF and glomerulonephritis (GN) (Table 1.3).

### 1.3.4 Current international differences in incidence of RRT

There is substantial variation in the incidence rates with Taiwan having the highest rate, closely followed by the USA (Table 1.2). In Europe, the highest rate is seen in Germany (213 p.m.p. in 2006). In Eastern Europe, RRT programmes have developed rapidly since they became independent of the Soviet Union, with the Czech Republic and Hungary having RRT incidence rates of 173 p.m.p. and 159 p.m.p., respectively, in 2006.[17] How can these differences be explained?

An increasing number of nationally representative screening studies have been undertaken to establish the prevalence of CKD in countries around the world and the evidence suggests that, despite the variation in RRT incidence, there is little variation in the prevalence of CKD. One study has looked at the transition from CKD to ERF in an attempt to better understand this discrepancy and demonstrated that although the prevalence of CKD in Norway and the USA is comparable, the incidence of ERF in Norway is lower, suggesting greater progression to ERF in the USA.[19]

A true variation in the incidence of ERF therefore remains a possibility, but factors such as variation in competing risk (i.e. death from cardiovascular disease prior to reaching ERF), referral to a nephrologist, and acceptance onto RRT may also be important. One study comparing RRT incidence rates in the UK and Germany found that the higher rates in Germany could be largely explained by the higher rates of hypertensive and diabetic ERF,[20] but it also highlighted marked differences in organization and supply of renal services that may have been cause or effect.

### Table 1.3 Primary Renal diagnosis: incidence rates p.m.p. by UK country

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>England pmp</th>
<th>Northern Ireland pmp</th>
<th>Scotland</th>
<th>Wales</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncertain aetiology</td>
<td>25.2</td>
<td>17.1</td>
<td>14.8</td>
<td>40.3</td>
<td>24.8</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>10.2</td>
<td>8.5</td>
<td>10.3</td>
<td>17.1</td>
<td>10.5</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>6.7</td>
<td>10.8</td>
<td>8.6</td>
<td>7.4</td>
<td>7.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>21.3</td>
<td>23.9</td>
<td>18.1</td>
<td>34.2</td>
<td>21.7</td>
</tr>
<tr>
<td>Polycystic kidney</td>
<td>6.5</td>
<td>10.8</td>
<td>10.3</td>
<td>7.4</td>
<td>7.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5.9</td>
<td>7.4</td>
<td>2.7</td>
<td>7.0</td>
<td>5.7</td>
</tr>
<tr>
<td>Renovascular disease</td>
<td>6.6</td>
<td>10.8</td>
<td>11.5</td>
<td>10.7</td>
<td>7.3</td>
</tr>
<tr>
<td>Other</td>
<td>15.0</td>
<td>15.9</td>
<td>13.6</td>
<td>14.4</td>
<td>14.9</td>
</tr>
<tr>
<td>Data not available</td>
<td>10.8</td>
<td>0.0</td>
<td>18.3</td>
<td>1.0</td>
<td>10.6</td>
</tr>
<tr>
<td><strong>All</strong></td>
<td><strong>108</strong></td>
<td><strong>105</strong></td>
<td><strong>108</strong></td>
<td><strong>140</strong></td>
<td><strong>110</strong></td>
</tr>
</tbody>
</table>

Perhaps linked to the availability of resources, earlier studies demonstrated differences in the attitudes of physicians and nephrologists towards patient suitability for dialysis over the last two decades.[21–23] This is no longer considered to be a major reason for inter-country variation in RRT incidence rates.

Ethnicity is another key factor, and one that is likely to become increasingly important over the next decade. In the USA, black patients with hypertension or diabetes are 2–3 times more likely to develop ERF than their white counterparts;[24] rates 3–4 times higher than in the white population have been observed in blacks and Indo-Asians in the UK.[25] In the UK, the ethnic minority populations are younger than the white majority population, and this is reflected by a lower median age of incident ethnic minority RRT patients (57 years compared with 64 years for white incident patients). The maturation of these minority populations over the next two decades is likely to lead to a significant increase in demand for RRT.

1.4 Prevalence of renal replacement therapy

Prevalence rates, also called stock rates sometimes, are measures of the total number of patients on RRT at any time (usually at the year end) in a defined population per million. They indicate the healthcare burden and costs of an RRT programme.

As has already been described for RRT incidence, wide variation exists in RRT prevalence and RRT modality mix amongst countries (Table 1.2) with cultural acceptance of organ donation, the organization of cadaveric and live donation programmes, financial incentives for HD in certain healthcare systems and conversely for PD in others, clinician preferences, and historical precedent all contributing to each country’s modality mix.

In the UK, the prevalence rate increased from only 27 p.m.p. in 1981 to 746 p.m.p. in 2007, with the annual increase in prevalence currently around 6%. This rise is due to a combination of the increase in incidence rates onto RRT, as outlined above, and improvements in patient survival on RRT as outlined below. In 2007 there were over 45 000 patients receiving dialysis treatment or living with a kidney transplant in the UK – 45% with a functioning renal transplant, 43% on in-centre HD and 11% on PD. In the last two decades the major absolute growth has been in the numbers of HD patients. The percentage of patients on PD is decreasing after the initial rapid rise at its introduction in the early 1980s from 16% up to 22% in 1990; it has now fallen to 10% of RRT patients (Fig. 1.8). Although the total numbers of patients on dialysis continues to rise, the total numbers on PD are in decline. The percentage on home HD has steadily fallen over the years from 24% of RRT patients in 1982 to 1% in 2007 accounting for 480 patients. The fall in these patients appears to have now plateaued.

Kidney transplantation is associated with better survival and quality of life for patients with ERF. Two countries that have been particularly successful at achieving high rates of kidney transplantation have done so by very different means – Spain instituted a systematic approach to cadaveric organ donation with an opt-out donation programme and Norway has the most active live donation programme. Despite a decrease in heart-beating deceased-donor kidney transplants, the organ donor rate in the UK has increased slightly in recent years as a result of expansion of the living kidney donor and non-heart-beating donor programmes. The percentage of RRT patients in the UK with a functioning renal transplant continues to decrease, but this reflects partly the disproportionate growth of the >75-age group on the dialysis programme.

Not everyone is suitable for a kidney transplant, The UK Renal Registry has shown that approximately 50% of the 35–44-year-old dialysis population are on the active transplant waiting list and this falls to 25% in the 55–64-year-old dialysis population.[26] A subsequent analysis looking at time-to-listing showed that only 45% of patients in the age group
<65 years were activated on the transplant list within 1 year of starting RRT and 66% within 5 years.[27] Amongst patients who do receive a kidney transplant in the UK, the average waiting time is currently around 28 months.

1.5 Survival on renal replacement therapy

Much of the analysis of patient outcomes on RRT has come from Registry data rather than controlled trials comparing one treatment to another (e.g. poor phosphate control versus better phosphate control). This is very important as Registry data showing that a high serum phosphate is associated with poor survival does not demonstrate causality; i.e. lowering phosphate will improve survival even though this may be clinically plausible.

The key factors that are related to patient survival on RRT are listed below.

- **Sociodemographic**
  - Age – poorer survival with increasing age
  - Ethnic minority (blacks and South Asians have better survival than whites)
  - No difference in survival by gender, or socioeconomic status

- **Co-morbidity**
  - Cardiovascular disease, diabetes, malignancy, major organ system (e.g. respiratory). These factors have been incorporated into various developed scoring systems (Khan, Charlson, Lister, etc.).
  - The degree of independence as measures by the Karnofsky Performance Score is also predictive.

- **Primary renal disease**
  - Certain primary renal diseases have better survival, e.g. glomerulonephritis, polycystic kidney disease compared to systemic causes, e.g. diabetic nephropathy, renovascular disease.
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- **Status at the start of RRT**
  - Nutritional status
  - Symptomatic with complications of ERF e.g. fluid overload
  - Vascular access using a non-tunnelled line catheter
  - Patients who present late are more likely to have several of these factors.

- **Care on RRT**
  - Dialysis adequacy
  - Control of anaemia
  - Control of serum phosphate
  - Management of cardiovascular disease

Compared with the general population, patients with ERF have a considerably higher risk of death (Fig. 5.2, Chapter 5), although the relative risk declines with age. There is also significant inter-country variation in mortality in patients with ERF. A wide-ranging and influential study in the 1980s demonstrated that mortality in such patients was lower in Japan than in Europe, and that mortality in Europe was lower than in the USA.[28] A case-mix adjusted follow-up study restricted to Europe and the USA confirmed these disparities in survival although an attenuation in the effect was observed.[29]

Registry data on survival are also available and are used for both central and international comparisons. Adjustment for case-mix requires survival to be stratified by modality, age, and cause of ERF (i.e. diabetic or non-diabetic). Table 1.4 shows the differences in case-mix of incident RRT patients from different national registries.

**Table 1.4** Summary of co-morbidity of incident RRT patients in selected national renal registries

<table>
<thead>
<tr>
<th>National registries</th>
<th>ANZDATA</th>
<th>USRDS</th>
<th>UK RR</th>
<th>Nerosad 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1953</td>
<td>696 043</td>
<td>15 197*</td>
<td>1041</td>
</tr>
<tr>
<td>Ischaemic heart disease incl. MI</td>
<td>30.5%</td>
<td>23.8%</td>
<td>24.7%</td>
<td>11.1%</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>11.0%</td>
<td>9.0%</td>
<td>11.7%</td>
<td>7.2%</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>19.0%</td>
<td>14.3%</td>
<td>14.2%</td>
<td>13.0%</td>
</tr>
<tr>
<td>COPD</td>
<td>12.0%</td>
<td>7.1%</td>
<td>7.7%</td>
<td>7.2%</td>
</tr>
<tr>
<td>Diabetes**</td>
<td>35.0%</td>
<td>41.2%</td>
<td>18.8%</td>
<td>19.5%</td>
</tr>
<tr>
<td>Malignancy</td>
<td>not collected</td>
<td>5.3%</td>
<td>11.5%</td>
<td>10.1%</td>
</tr>
<tr>
<td>Smoking</td>
<td>11.0%</td>
<td>5.2%</td>
<td>18.4%</td>
<td>not collected</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>not collected</td>
<td>32.0%</td>
<td>not collected</td>
<td>12.3%</td>
</tr>
<tr>
<td>Patients with no co-morbidity at start of RRT***</td>
<td>39.0%</td>
<td>9.4%</td>
<td>38.7%</td>
<td>not collected</td>
</tr>
</tbody>
</table>

Notes: *Comprehensive co-morbidity information was only available in 5916 patients.
**Countries may sometimes include those patients who were diabetic not as a primary cause of renal failure in this total.
***US data includes hypertension (74%) and also congestive cardiac failure as a co-morbidity. COPD: chronic obstructive pulmonary disease.
Data from countries that collect data from all RRT patients from day zero has consistently shown that half of all deaths in the first year occur between day 0 and day 90. This is potentially important in making decisions about commencing RRT. There is apparent variation in early mortality amongst centres and countries. Differences in the timing of reporting of patients with acute or acute-on-chronic renal failure to registries may account for much of this quoted variation in 1-year survival. To overcome this, most registries quote first-year survival starting from day 90 to 1 year +90.

The UK has shown improvement in the survival of dialysis patients over the past 10 years,[30] and the survival of renal transplant recipients has also improved significantly.[31] In the UK, e.g. 1-year age-adjusted survival of all patients commencing RRT has improved from 85.8% in 1999 to 89.1% in 2006. The 1-year prevalent dialysis-survival has also improved from 82.8% in 1997 to 88.6% in 2007. Similarly, the USA – which began with higher mortality rates in the 1980s – saw a marked reduction in first-year mortality on dialysis during the early 1990s, which paralleled national-level improvements in dialysis adequacy.

The prognosis for some patients on RRT remains poor. For example, a patient over 75 would have a 63% chance of surviving for 1 year after commencing RRT and a 34% chance of remaining alive 3 years after commencing RRT (Fig. 5.1, Chapter 5). In addition, there are important differences in relative risk for ERF patients compared with their general-population counterparts. Older patients with diabetes have considerably lower survival rates than younger patients, but the impact of diabetes on their relative risk of death, compared to younger patients, is much less (Fig. 1.9). Such data, which are published annually by the UK Renal Registry, may be helpful for patients and their families when making difficult decisions about the propriety of commencing RRT.

### 1.6 Causes of death

Cardiovascular events dominate as the cause of death for patients with ERF in all countries[31] reflecting a complex interrelationship between CKD and cardiovascular disease, although it should be noted that cardiovascular disease is also a major cause of death within the general population. Renal impairment leads to secondary hypertension, abnormal lipid profiles, arterial wall damage, and adversely alters other cardiovascular disease risk factors (e.g. homocysteine and fibrinogen levels). Some factors, such as smoking, and diseases, such as diabetes, are important risk factors for both conditions. The UK Renal Registry data show that smoking remains as common in the RRT population as the general population.

A significant proportion of patients choose to withdraw from dialysis, although for cultural reasons these rates vary considerably between countries. Data on withdrawal from dialysis, however, are often not reliably collected by registries. The UK Renal Registry has found that 12% of deaths on dialysis are ascribed to withdrawal and this was significantly higher in the first year of RRT at 16%.[30] There was also a difference by age – withdrawal accounted for 19% of deaths in those in the age group >65 on dialysis compared with 8% in those <65 (Table 1.5). In the ERA, withdrawal was coded less frequently at under 5%; it is not clear whether this represents a true difference or under-recording.[31]

With the increasing acceptance of older, more co-morbid patients onto RRT programmes, the number of such patients is likely to increase further. In Australia, 33% of deaths in dialysis-dependent patients in 2006 were ascribed to withdrawal, mostly in older age groups. This contrasts with the 14% of deaths due to withdrawal from RRT for the period 1983–92.[32]

It is impossible to predict the survival of individual patients and also how they will adapt to treatment, so some nephrologists have suggested a ‘trial of dialysis’ except in cases with severe dementia or advanced malignancy.[33] Others think that a trial is poor clinical practice.
Fig. 1.9 Age-stratified survival of diabetic and non-diabetic nephropathy patients on RRT after 90 days.
Consequently, withdrawal from RRT will remain an important and increasing cause of death which has considerable implications for supportive terminal care of such patients and their families. However, some patients who are referred for RRT may be considered unsuitable for RRT due to poor prognosis and/or associated problems, and this number is likely to increase over time. There is a challenge to develop alternative models of supportive care to sustain such patients and their families.

### 1.7 Late presentation (referral) for renal replacement therapy

A major and enduring problem is that 25% of all patients commencing RRT are presented to the renal unit within 3 months of their first treatment.[34] This late presentation may be a consequence of the patient’s disease (unavoidable) or of late referral from another clinician. Late referral for RRT impacts on pre-ESRD care, affects selection of dialysis modality, vascular access, and also has economic implications. Patients presenting late generally fare less well, as they are more likely to be in a sub-optimal clinical state at the start (e.g. lower haemoglobin and albumin) and tend to have more temporary access, longer initial hospitalization, and a higher early mortality.[30] One study showed that whilst a proportion are unavoidable (e.g. late presenters with no prior symptoms or signs of CRF, or irreversible acute renal failure), around 50% are potentially avoidable due most frequently to having had documented rising creatinine levels for several years.[35] In the UK, the CKD Quality Outcomes Framework for primary-care physicians may improve these late-referral rates.

### 1.8 Future demand for renal replacement therapy

As a result of the ageing population – the effects of which are going to be most marked in ethnic minority and indigenous populations – the increasing rates of type 2 diabetes, and the improvements in RRT survival, the number of patients on RRT looks set to continue to rise in most countries. Indeed, modelling exercises in the UK suggests that there will be substantial

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**Table 1.5** Cause of death by age in 1 year after 90 days for UK incident patients, 2000–06

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>All age groups</th>
<th>&lt;65 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of deaths</td>
<td>%</td>
<td>Number of deaths</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>534</td>
<td>25</td>
<td>165</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>137</td>
<td>6</td>
<td>36</td>
</tr>
<tr>
<td>Infection</td>
<td>400</td>
<td>19</td>
<td>114</td>
</tr>
<tr>
<td>Malignancy</td>
<td>213</td>
<td>10</td>
<td>79</td>
</tr>
<tr>
<td>Treatment withdrawal</td>
<td>344</td>
<td>16</td>
<td>51</td>
</tr>
<tr>
<td>Other</td>
<td>373</td>
<td>17</td>
<td>109</td>
</tr>
<tr>
<td>Uncertain</td>
<td>153</td>
<td>7</td>
<td>56</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2154</strong></td>
<td><strong>610</strong></td>
<td><strong>1544</strong></td>
</tr>
<tr>
<td>No cause-of-death data</td>
<td>2578</td>
<td></td>
<td>730</td>
</tr>
</tbody>
</table>

growth in the RRT numbers in the medium term, with a steady state not being reached for at least 25 years. The UK Registry data have shown a year-on-year 6% rise in prevalence over the last 10 years. The rate of this rise varies between RRT modalities, with HD rates increasing by 8% annually. All renal units remain in a perpetual state of expansion requiring annual funding increases beyond just inflation. Similar projections have been made for populations in Europe, Asia-Pacific, and North America.

1.9 Conclusion

There has been a continuing and substantial growth in the incidence and prevalence of RRT in all developed countries, although there are substantial inter-country variations. Increasing numbers of patients with ERF are elderly and have a greater co-morbid burden, yet patients are now living longer on RRT. Early referral of patients with CKD allows patients to be fully informed about RRT so they can make an informed decision about whether to embark on treatment or not.

The predominant mode of RRT for elderly, frail patients is likely to continue to be HD, irrespective of the success of efforts to enhance live and cadaveric kidney transplant programmes. As conservative care becomes an increasingly accepted treatment option, our new challenge as healthcare professionals is to support our patients and their carers and provide them with high-quality care, tailored to their individual wishes, as they live with renal failure.

References

31 van Dijk PCW et al. (2001). Renal replacement therapy in Europe: the results of a collaborative effort by the ERA-EDTA registry and six national or regional registries. *Nephrol. Dial. Transplant*, 16(6), 1120–9.
Chapter 2

The concept of supportive care for the renal patient

E Joanna Chambers and Edwina A Brown

The utility of living consists not in the length of days, but in the use of time: a man may have lived long, and yet lived but little.  
*Montaigne, 1533–92*

2.1 Introduction

End-stage renal disease (ESRD) presents many challenges to the patients – who experience and suffer from it – and the healthcare professionals who care for them. Its chronicity and the morbidity associated with it – which often includes difficult and intractable symptoms – make palliative and supportive care natural accompaniments to its management. The team-based approach to the care of patients with ESRD makes it ideally suited to incorporate palliative and supportive care. Programmes for the management of ESRD should include a supportive care plan as well as routine prevention, diagnosis, renal replacement therapy (RRT), and transplantation.

2.2 The development of palliative care

In 1990 the World Health Organization (WHO) defined palliative care (see also Appendix 1) as:

> The active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological, social and spiritual problems is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families. Many aspects of palliative care are also applicable earlier in the course of the illness in conjunction with anticancer treatment.[1]

World Health Organization (1990)

Although this definition applied primarily to patients with cancer it is equally appropriate for people with other chronic diseases, in particular ESRD. It significantly highlights that palliative care has applications early in the course of an illness and looks at the needs of the whole person in the context of his or her social situation. Many subsequent definitions have built on this concept of addressing patient symptoms as well as psychosocial and spiritual needs in addition to disease-directed therapy in chronic and life-limiting illnesses. This distinction with regard to the broad clinical applicability and appropriateness of palliative care is important, because supportive and palliative care can then be seen as care that goes alongside ‘active’ or aggressive therapies such as dialysis. Ahmedzai and Walsh[2] have further developed this model in relation to cancer (Fig. 2.1) where patient- and family-directed care are integrated with disease-directed care, e.g. chemotherapy.