Prevalence and socio-economic aspects of chronic kidney disease

Jürgen Bommer

Department of Internal Medicine, University of Heidelberg, Heidelberg, Germany

Abstract
The incidence and prevalence of end-stage renal disease (ESRD) are rising in Europe, the USA, and Japan. Prevalence is rising more steeply than incidence, due mostly to improved efficiency of treatment – patients are surviving longer. Hypertension and diabetes, the main causes of progression from chronic kidney disease (CKD) to ESRD, are becoming more frequent in the general population and make a large contribution to the rising incidence of ESRD. More effective therapies for other conditions have introduced new complications for patients with CKD, thereby also increasing the incidence of ESRD. Increased survival in the general population is reflected in the greater number of elderly people requiring care for ESRD. ESRD is a great economic burden and one that will increase as the incidence and prevalence of the disease increase. This needs to be considered when planning treatment. Prevention and early treatment of hypertension and diabetes will have the greatest impact on the future prevalence of ESRD and the costs associated with its treatment.

Keywords: chronic kidney disease; diabetes; ESRD; haemodialysis; hypertension; socio-economic

Introduction
The number of patients with end-stage renal disease (ESRD) is increasing at an alarming rate. In the USA, about 200,000 patients are on haemodialysis (HD) and another 90,000 are living with a transplanted kidney. ESRD patients represent about 0.12% of the total US population of 270 million (about 1200 per million population (p.m.p.)). Caring for these patients costs more than US$18 billion per year, around 6% of the total annual Medicare budget [1]. The prevalence of ESRD is even higher in Japan at 1565 p.m.p., but the incidence is comparable with the USA (about 256 p.m.p.) [2]. In Germany and other middle-European countries such as Italy, Austria, Spain, and France, the prevalence is much lower, ranging from 670 to 764 p.m.p. in 1998. The incidence in these European countries is also lower than in Japan and the USA. Whether these lower rates are influenced by factors such as less complete data collection, race, age, patient education, and the attitudes of general practitioners and other physicians is not clear. However, these factors seem likely to play a part since widely differing rates can be seen even in the same country. In Germany as a whole, the incidence rate in 2001 was reported as 145 p.m.p. [3], much lower than that seen in the USA. However, in Heidelberg, the incidence recorded was 183 p.m.p., which is much closer to the rates reported in white patients in the USA [1,3].

Prevalence of chronic kidney disease (CKD)
Before 1995, German data for the prevalence of CKD were incomplete. Data collection methods were improved in 1995 and, as a result, the reported number of patients with ESRD doubled between 1994 and 1995 [4]. During the following 5 years, the incidence increased from 11.731 p.m.p. in 1995 to 14.370 in 2000, with an annual increase of 4.5%. Prevalence has also increased by a similar margin (5.4%) [2]. The steeper increase in prevalence compared with incidence probably results from greater efficacy of treatment for HD.

A more interesting question asks why incidence should be rising. Tables 1 and 2 show that the origin of renal disease in new patients on HD (incident HD patients) differs markedly between countries. For example, glomerulonephritis accounts for about 15% of ESRD in Germany [2], but only 8.7% in the United States Renal Data System (USRDS) report [1]. One reason for the differences might be that diagnosing glomerulonephritis depends on kidney biopsies, which are performed at different rates in different centres. Countrywide studies of patients with glomerulonephritis, such as the UK Medical Research Council’s
Glomerulonephritis Registry, might help to optimize treatment and reduce progression of renal failure.

Different diagnostic procedures and techniques cannot fully explain the difference in frequency of cystic kidney disease between Germany and the USA. It can be assumed that ultrasonography is performed on all patients with CKD, so polycystic kidney disease will rarely be missed. However, cystic kidney disease was observed in 2.1% of patients on dialysis in the USRDS report compared with 5.5–6.4% in Germany. More intense education and genetic counselling of young people may have resulted in a reduced incidence of polycystic kidney disease in Germany from 1997 to 2000. Similarly, recent legal changes in the use of analgesia may have reduced the incidence of reported analgesic nephropathy in Germany. The incidence of interstitial nephritis may have decreased because the risk of its occurrence is better understood and therefore prevented in clinical practice, although the evidence for this is not clear.

### Diabetes mellitus: an increasing problem in CKD

Table 2 shows that the incidence of ESRD in the USA has increased steadily from 6.3 to 7.3% per year in the last decade. The increase was only 3–4% in patients with glomerulonephritis and cystic kidney disease. In contrast, the number of patients on HD with hypertension-induced ESRD increased by nearly 8%. Over the last 5 years, hypertension has been reported in about a quarter of patients on dialysis in the USA.

Table 3 shows a marked influence of race on hypertensive ESRD. For example, between 1995 and 1999, a third of black patients but only 12% of Native Americans on dialysis had ESRD with underlying hypertensive kidney disease. However, diabetes is found in more than two-thirds of Native American patients on dialysis. Since hypertension is frequently found in patients with diabetic nephropathy, the influence of hypertension in this population may be an underestimate. Interestingly, only 24% of white
patients have hypertension, significantly less than black patients, although the incidence of diabetes is similar between black and white patients. This indicates that black patients may need more careful and intensive antihypertensive therapy. Without doubt, modern antihypertensive therapy can effectively reduce the progression of renal failure. Genetic influences need to be taken into consideration and optimal therapy prescribed, but explaining to patients about their condition and the compliance of treatment is equally vital. Pharmacological studies have found an inverse correlation between patients’ compliance and number of prescribed drugs. This finding is equally applicable to renal patients as to the general population.

In the USA, more than 40% of patients with ESRD have diabetes. Furthermore, the percentage of patients on HD with diabetic nephropathy has increased more than for any other cause of CKD. The number of patients on HD with diabetes has increased by 9–10% per year in the last decade. The German register, QuaSi-Niere, indicated that the percentage of such patients increased from 31 to 36% between 1996 and 2000. According to this analysis, 14% of patients with renal disease and diabetes suffer from type 1 diabetes. In our hospital as a whole, diabetes has been diagnosed in more than half of our patients with ESRD, and the incidence of type 1 diabetes in them is only 7% [1]. The incidence of diabetes in our area is 98 p.m.p. [3], which is comparable with the incidence in white patients in the USA (100 p.m.p.) [1].

Diabetic nephropathy may be underestimated as an underlying cause of ESRD as type 2 diabetes can remain undetected for many years and yet can still induce hypertension, proteinuria, and finally ESRD. The Dialysis Outcomes and Practice Patterns Study (DOPPS) found different incidences of diabetic nephropathy in patients on dialysis in five European countries (unpublished data from DOPPS 2001). Diabetes was a cause of ESRD in 28.8% of German patients who survived more than 90 days on HD. The percentage was considerably lower in Italy, Spain, and the UK (between 20.1 and 21.7%), and only 15.3% in France.

It is as important to know why the incidence of diabetic nephropathy varies between European countries, as it is to know why the incidence is increasing in all of them. The rising incidence of diabetic nephropathy is due partly to more liberal and frequent HD therapy, and partly to the increasing incidence of diabetes in the general population. At the end of the 1980s, the national diabetes register of the former East Germany [5] and registers of West German insurance companies, such as AOK Dortmund [6], recorded a prevalence of diabetes of between 4 and 5% in the German population. A survey by the German Bundesgesundheitsamt in 1997–1998 reported diabetes in 4.7% of all males in the general population and 5.6% of males aged between 18 and 79 years. Recent epidemiological studies show that 7–8% of adults suffer from diabetes mellitus [7]. Diabetes mellitus has been diagnosed from haemoglobin A1c measurement in 8.2% of a representative sample of Germans [7]. Data from Palitzsch et al. [8] indicate that the number of patients with diabetes in Germany increased from 5.0 to 6.7 million from 1996 to 2001. The German Diabetes Society expects it to increase to 9 million by the year 2010.

Recent surveys using a 75 g oral glucose tolerance test observed a comparable prevalence of diabetes throughout Europe, i.e. between 8.4 and 10.9% of patients over 40 had diabetes [9,10]. Similar results were reported by the Monitoring Trends and Determinants in Cardiovascular Diseases (MONICA) surveys in Finland and Germany [11,12]. In light of this similarity in prevalence in Europe, previous estimates for Germany may need to be revised.

These more recent studies also show a continuing increase in the incidence of diabetes over time, adding support to analyses in performed in 1991 [5]. Michaelis et al. [5] found that in the former East Germany that the incidence of type 1 and type 2 diabetes in the general population increased from 0.19 and 0.44% in 1960, respectively, to 0.66 and 3.48% in 1989, respectively. These changes represent 3.5- and 7.9-fold increases for type 1 and type 2 diabetes, respectively. Equivalent longitudinal data are not available for

### Table 3. Primary disease (%) in incident dialysis patients 1995–1999 ($n = 392,847$)

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>White</th>
<th>Black</th>
<th>Native American</th>
<th>Asian</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>42.8</td>
<td>41.6</td>
<td>68.2</td>
<td>46.0</td>
<td>59.6</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>10.3</td>
<td>8.2</td>
<td>8.4</td>
<td>15.6</td>
<td>9.1</td>
</tr>
<tr>
<td>Secondary glomerulonephritis/vasculitis</td>
<td>2.3</td>
<td>2.6</td>
<td>2.1</td>
<td>2.3</td>
<td>2.5</td>
</tr>
<tr>
<td>Interstitial nephritis</td>
<td>5.0</td>
<td>2.1</td>
<td>1.9</td>
<td>3.2</td>
<td>2.4</td>
</tr>
<tr>
<td>Hypertension of large vessels</td>
<td>24.1</td>
<td>32.8</td>
<td>12.0</td>
<td>23.3</td>
<td>16.6</td>
</tr>
<tr>
<td>Cystic/congenital kidney disease</td>
<td>4.0</td>
<td>1.5</td>
<td>1.3</td>
<td>2.2</td>
<td>2.6</td>
</tr>
<tr>
<td>Tumours</td>
<td>2.3</td>
<td>1.2</td>
<td>0.9</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>3.5</td>
<td>4.8</td>
<td>1.8</td>
<td>1.4</td>
<td>2.1</td>
</tr>
<tr>
<td>Uncertain</td>
<td>4.3</td>
<td>3.0</td>
<td>2.6</td>
<td>4.1</td>
<td>3.6</td>
</tr>
<tr>
<td>Missing</td>
<td>1.4</td>
<td>2.2</td>
<td>0.8</td>
<td>1.1</td>
<td>0.6</td>
</tr>
</tbody>
</table>
the former West Germany. Currently, in Germany as a whole, about 5–7% of people with diabetes are reported to suffer from type 1 diabetes. However, recent studies in adults with so-called delayed type 1 diabetes suggest that insulin deficiency diabetes from auto-immune disease in adulthood is much more common than previously thought, and may be responsible for 10–15% of all diabetes in the middle and older age groups [13].

The data will be important for nephrologists in the future, since about 20–30% of all patients with type 1 and type 2 diabetes will develop diabetic nephropathy [14]. The prevalence of proteinuria has been reported as 21% in patients with type 1 diabetes and 35% in those with type 2 [15]. This predicts that diabetic nephropathy will become an increasing problem for nephrologists. About 6–7% of the German population has diabetes and 20% of these have diabetic nephropathy. Therefore, nearly 2% of all Germans will have impaired renal function due to diabetic nephropathy. If diabetic nephropathy progresses to ESRD in only 5–10% of these patients, there will be twice the current number of patients with ESRD. Thus, diabetes and diabetic nephropathy present a tremendous challenge for nephrologists and everything possible should be done to prevent or delay progression of renal failure in these patients. Angiotensin-converting enzyme inhibitors and angiotensin II type 1 blockers can reduce the progression to renal failure by about 25% [16–18]. This is a huge benefit but further research into prevention or delay of disease progression is urgently needed.

New renal complications

More effective treatments can offer a better quality of life and longer survival to many patients, but new treatments can also cause new complications. For example, heart transplantation has been welcomed as a medical breakthrough but the required continuous immunosuppression can cause progressive renal failure. In 151 patients with transplanted hearts followed for 1–9 years (a mean follow-up time of 4.9 years), 6% became dialysis dependent. A further 20% experienced a severe reduction in renal function and were consequently at high risk of requiring dialysis [19]. Van Gelder et al. [20] also reported ESRD in about 8% of long-term survival patients with transplanted hearts.

Longer survival of patients with chronic diseases may also lead to an increase in renal problems resulting from conditions such as amyloidosis and oxalosis. A recent case study reported the development of secondary renal amyloidosis in long-term survivors of cystic fibrosis, possibly as a result of recurrent pulmonary infections. The authors speculated that severe renal insufficiency due to secondary amyloidosis might complicate cystic fibrosis and become an important adverse prognostic factor in adults [21].

Economic aspects in CKD

Every effort must be made to prevent ESRD. The cost to the public health system increased by 5–6% between 1994 and 1998, and it is still rising [22]. In contrast, the national productivity of Germany increased only by 1–2% each year. The benefits of improved therapy for ESRD must be carefully analysed against the costs incurred. For example, in Germany, 65% of dialysis patients are taken to dialysis centres by taxi. Ambulances are used for only 6.9% of patients compared with 26% of patients in the four other European countries covered by DOPPS. In many centres, transport accounts for 10% of dialysis costs. Home HD and continuous ambulatory peritoneal dialysis do not incur transport expenses, making these treatments even cheaper in comparison with HD conducted at a dialysis centre.

An analysis of the costs of dialysis must include all direct and indirect expenses and consider the possibility of cost savings. The USRDS [1] shows that the number of dialysis patients increased between 1995 and 1999 by about 5% per year. But the cost per patient only increased by 1.2%, and the costs of physicians and suppliers even decreased by 1%. The proportion of elderly people in the general population is rising and so is the number of elderly people requiring dialysis. This will have serious repercussions on hospice costs and other costs of caring for elderly dialysis patients. In the USRDS report, the annual increase in hospice costs was about 12% between 1995 and 1999 [1]. This indicates that the increasing cost of ESRD results from greater numbers of patients rather than from an increase in dialysis cost per patient. No increase in transplantation rate has been seen, and increasing survival rates further increase the cost burden of treatment for ESRD.

The costs of medication and patient care are also rising. Between 1994 and 1999 spending on recombinant human erythropoietin increased by 100% in the USA, the cost of intravenous (i.v.) iron supplementation increased by 50% and the cost for i.v. calcitriol or other vitamin supplements increased by 200%. This is worth noting as, during the same period, spending on cancer screening and other preventative measures increased by less than 4% [1].

Conclusion

Longer survival of patients with CKD results in more comorbid hypertension and diabetes. These diseases are the major causes of ESRD in patients already on dialysis. They will be the determining factor for the number of patients developing ESRD in the future and of the cost of their care. Prophylaxis and treatment of these two diseases will influence the future incidence of CKD and ESRD.
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