Clinical aspects of the relation between diabetes mellitus and kidney disease: From hyperfiltration to dialysis

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CHAPTER 4

Survival in dialysis patients is different between patients with diabetes as primary renal disease and patients with diabetes as a co-morbid condition

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Abstract

Aims/hypothesis

A previous study in Dutch dialysis patients showed no survival difference between patients with diabetes as primary renal disease and those with diabetes as a co-morbid condition. As this was not in line with our hypothesis, we aimed to verify these results in a larger international cohort of dialysis patients.

Methods

For the present prospective study, we used data from the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Registry. Incident dialysis patients with data on co-morbidities (*n*=15,419) were monitored until kidney transplantation, death or end of the study period (5 years). Cox regression was performed to compare survival for patients with diabetes as primary renal disease, patients with diabetes as a co-morbid condition and non-diabetic patients.

Results

Of the study population, 3,624 patients (24%) had diabetes as primary renal disease and 1,193 (11%) had diabetes as a co-morbid condition whereas the majority had no diabetes (*n*=10,602). During follow-up, 7,584 (49%) patients died. In both groups of diabetic patients mortality was higher compared with the non-diabetic patients. Mortality was higher in patients with diabetes as primary renal disease than in patients with diabetes as a co-morbid condition, adjusted for age, sex, country and malignancy (HR 1.20, 95% CI 1.10, 1.30). An analysis stratified by dialysis modality yielded similar results.

Conclusions/interpretation

Overall mortality was significantly higher in patients with diabetes as primary renal disease as compared with those with diabetes as a co-morbid condition. This suggests that survival in diabetic patients undergoing dialysis is affected by the extent to which diabetes has induced organ damage.

Abbreviations

ERA-EDTA	European Renal Association-European Dialysis and Transplant Association
ESRD	End-stage renal disease
HD	Haemodialysis
NECOSAD	Netherlands Cooperative Study on the Adequacy of Dialysis
PD	Peritoneal dialysis
RRT	Renal replacement therapy

Introduction

Diabetes mellitus has become the leading cause of end-stage renal disease (ESRD) worldwide[1–4]. In Europe 23% of the patients starting renal replacement therapy (RRT) had diabetes as the primary cause of renal disease[5]. Survival among dialysis patients with diabetes mellitus is inferior to survival of non-diabetic dialysis patients[6–8]. Due to the complications of diabetes mellitus, patients with diabetic nephropathy have the largest number of co-morbid conditions within the ESRD population when compared with non-diabetic dialysis patients[2].

We hypothesised that in patients with diabetic nephropathy, organ damage is not limited to the kidney but also might involve other organs resulting in retinopathy, neuropathy and cardiovascular complications. Since patients on dialysis with diabetes as a co-morbid condition may have less pronounced multisystem involvement, we assumed that patients with diabetes mellitus as primary renal disease might have worse survival than patients with diabetes as co-morbid condition on top of another primary renal disease. However, despite these theoretical considerations, in a previous study using data from the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD), we could not show that survival in dialysis patients was different between patients with diabetes as primary renal disease and patients with diabetes as a co-morbid condition[9]. However, that study was performed in a single country and, additionally, the sample size may have been too small to detect a survival difference. To gain power, we conducted this new study using a larger, international cohort of dialysis patients.

The primary aim of our present study was to compare the survival of dialysis patients in whom diabetes mellitus was the primary renal disease with that of dialysis patients in whom diabetes was a co-morbid condition on top of another primary renal disease. Mortality rates in these two groups were compared with mortality rates in dialysis patients who did not have diabetes mellitus. Furthermore, female patients on peritoneal dialysis (PD) with diabetes as primary renal disease have been shown to have impaired survival compared with their male counterparts[9–12]. Therefore, our second aim was to compare patient survival, stratified by sex, age and dialysis modality.

Methods

Data collection

The European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Registry contains individual data on patients receiving RRT for ESRD. Data collection occurs annually via national and/or regional renal registries in Europe and includes data on date of birth, sex, primary renal disease, date of first RRT, history of RRT (including dates and changes of modality) and date of death. The present analysis included only data from registries that were able to provide additional data on co-morbid conditions at the start of RRT (Austria, Belgium [French-speaking part], Spain [Catalonia], Greece, Norway, Sweden and the UK)[13,14]. Approval for this study has been obtained from those individual registries. All patients of 20 years and older who started dialysis between 1998 and 2006 and who survived the first 3 months on dialysis were included. For the present analysis we chose day 91 as the start of the study because at that time most patients needed RRT as a chronic therapy and the choice of treatment modality (haemodialysis [HD] or peritoneal dialysis) can be considered to be more definitive. The following co-morbid conditions were collected and were coded as being present or absent in the medical history at initiation of dialysis: diabetes mellitus, ischaemic heart disease, peripheral vascular disease, cerebrovascular disease and malignancies. If data for all of these five types of co-morbid conditions were missing, patients were excluded from analyses. No information on medication was contained in the database.

Diabetes mellitus

For the present analysis we categorised the patients as follows: (1) non-diabetic patients, (2) patients with diabetic nephropathy as primary renal disease and (3) patients with non-diabetic origin as primary renal disease but diabetes as co-morbid condition. This distinction relied on the information provided in the database, which was based on the physician's judgment and/or a histological diagnosis.

Statistical analysis

We used descriptive statistics and performed Student's t tests and χ^2 test for direct comparisons of continuous and dichotomous outcomes. To estimate patient survival (from day 91) we performed Cox regression analyses. We restricted our survival analysis to 5 year survival because otherwise the number of patients at risk during follow-up became too small (i.e. below 10–20% of the total study population)[15]. We calculated crude all-cause mortality rates expressed as number of deaths/1,000 patient-years. Crude and adjusted HRs with 95% CIs were calculated using Cox proportional hazards models. Follow-up time was censored at recovery of renal function, kidney transplantation, loss of follow-up and at the end of the observation period (31 December 2008), whichever came first. The multivariable models used to calculate adjusted HRs included the variables age, sex, country and the presence of malignancy. Cerebrovascular and cardiovascular diseases were not included as possible confounders in our models as we considered them as potential intermediate variables between diabetes and death. However, to facilitate comparison with previous studies, we repeated our regression models with adjustment for cerebrovascular and cardiovascular disease (i.e. cerebrovascular, peripheral vascular and ischaemic heart disease). In addition, because some studies showed higher mortality for patients with type 1 diabetes compared with patients with type 2 diabetes [4, 8] we performed an additional analysis in which we differentiated the primary renal disease patients by type 1 and type 2 diabetes. The data stratified by type 1 or type 2 diabetes were not available for patients with diabetes as a co-morbid condition and therefore we performed this additional analysis only in patients with diabetes as primary renal disease. We performed a survival analysis stratified by sex and age and another analysis stratified by dialysis modality[16]. Furthermore we tested for interaction between sex, age and the presence of diabetes and tested whether or not sex or age had an additive effect on the presence of diabetes. For all analyses exposure and treatment status were used as time-independent variables. Analyses were performed using SAS 9.2 (1999–2001; SAS Institute, Cary, NC, USA).

Results

Patient characteristics A total of 15,419 patients, starting dialysis between 1998 and 2006, were included. Of these, 3,624 (24%) patients had diabetes as primary renal disease and 1,193 (11%) patients had diabetes as a co-morbid condition; the majority of patients did not have diabetes (*n*=10,602). Thirty-eight per cent of patients were women. Detailed characteristics of included patients are shown in Table 1**.** Patients with diabetes as a co-morbid condition were older at baseline (mean age 67.7 ± SD 12.6 years) compared with patients with diabetes as primary renal disease (63.0±12.8 years) and patients without diabetes (62.8±15.7 years). PD was the dialysis modality in 20% of the non-diabetic patients, in 20% of patients with diabetes as primary renal disease and in 16% of patients with diabetes as a co-morbid condition. At baseline the prevalence of cerebrovascular and cardiovascular disease did not differ between patients with diabetes as primary renal disease and patients with diabetes as a co-morbid condition.

Table 1. Baseline characteristics of the study population (*n*=15,419)

Characteristic	**No DM (n=10,602)**	**DM PRD (n=3,624)**	**DM Co-M (n=1,193)**	**p value[a] (DM PRD vs DM Co-M)**
Age, continuous, mean±SD	62.8±15.7	63.0±12.8	67.7±12.6	<0.001
Age category, *n* (%)				
<70 years	6,340 (60)	2,400 (66)	580 (49)	<0.001
≥70 years	4,262 (40)	1,224 (34)	613 (51)	
Men, *n* (%)	6,615 (62)	2,156 (59)	744 (62)	0.08
HD at day 91, *n* (%)	8,521 (80)	2,909 (80)	1,007 (84)	<0.001
PRD, *n* (%)				
Diabetes		3,624 (100)		<0.001
Renal vascular disease	2,269 (21)		329 (28)	
Glomerulonephritis	2,052 (19)		189 (16)	
Other	6,278 (59)		675 (57)	
Cerebrovascular disease, *n* (%)				
No	9,335 (88)	2,860 (79)	938 (77)	0.42
Yes	1,253 (12)	760 (21)	254 (20)	

Characteristic	No DM (n=10,602)	DM PRD (n=3,624)	DM Co-M (n=1,193)	p value[a] (DM PRD vs DM Co-M)
Peripheral vascular disease, *n* (%)				
No	8,670 (82)	2,211 (61)	781 (65)	0.56
Yes	1,900 (18)	1,406 (39)	410 (34)	
Ischaemic heart disease, *n* (%)				
No	8,094 (76)	2,219 (61)	684 (57)	0.53
Yes	2,464 (23)	1,395 (38)	506 (42)	
Malignancy, *n* (%)				
No	9,329 (88)	3,372 (93)	1,036 (87)	<0.001
Yes	1,251 (12)	249 (7)	154 (13)	
Country, *n* (%)[b]				
Austria	1,962 (60)	1,098 (33)	226 (7)	<0.001
Belgium (French-speaking)	258 (68)	91 (24)	29 (8)	
Spain (Catalonia)	2,269 (72)	655 (21)	214 (7)	
Greece	1,300 (66)	494 (25)	187 (9)	
Norway	748 (78)	125 (13)	88 (9)	
Sweden	1,124 (66)	422 (25)	165 (10)	
UK	2,941 (74)	739 (19)	284 (7)	

[a]*p* values for DM as PRD vs DM as co-morbidity
[b]Percentages are row percentages
Co-M, co-morbid condition; DM, diabetes mellitus; PRD, primary renal disease

Mortality

During 5 year follow-up, 7,584 (49%) patients of the total group died. Mortality rates per patient group are shown in Table 2**.** Twenty-six per cent of patients (*n*=2,704) without diabetes received a renal transplant compared with 13% (*n*=479) of patients with diabetes as primary renal disease and 13% (*n*=152) of patients with diabetes as a co-morbid condition. Other reasons for censoring during follow-up were end of the study period (27%) and loss to follow-up (2.4%). Evaluating the loss to follow-up in more detail showed that this loss was 2.7% in patients without diabetes, 1.7% in patients with diabetes as primary renal disease and 2% in patients with diabetes as co-morbid condition.

Table 2. Overall mortality rates

Patient group	Overall mortality rate (deaths/1,000 patient-years)		
	No DM	DM PRD	DM Co-M
All	151.4	226.9	233.5
<70 years	89.9	187.3	158.0
≥70 years	250.6	316.9	317.0
Women	148.2	243.8	225.3
Men	153.5	215.9	238.6
HD	160.0	231.0	233.2
PD	118.9	210.7	235.2

Co-M, co-morbid condition; DM, diabetes mellitus; PRD, primary renal disease

Results from the survival analysis are presented in Table 3 and Fig. 1. Mortality in patients with diabetes as primary renal disease (HR 1.61, 95% CI 1.53, 1.69) or as a co-morbid condition (HR 1.34, 95% CI 1.24, 1.45) was increased compared with that in non-diabetic patients. Mortality was higher in patients with diabetes as primary renal disease than in patients with diabetes as a co-morbid condition (HR 1.20, 95% CI 1.10, 1.30). Additional adjustments for cerebrovascular and cardiovascular events did not materially change these results. An additional analysis in which we differentiated the patients with diabetes as primary renal disease by type 1 and type 2 diabetes showed a higher mortality in patients with type 1 diabetes (HR 1.45, 95% CI 1.30, 1.61). In patients with diabetes as primary renal disease, for both type 1 diabetes (HR 2.17, 95% CI 1.97, 2.39) and type 2 diabetes (HR 1.50, 95% CI 1.42, 1.59) mortality was higher compared with non-diabetic patients. Furthermore, mortality in patients with type 1 or type 2 diabetes as primary renal disease was higher compared with patients with type 1 or type 2 diabetes as a co-morbid condition, with HRs of 1.62 (95% CI 1.44, 1.82) and 1.12 (95% CI 1.03, 1.22), respectively.

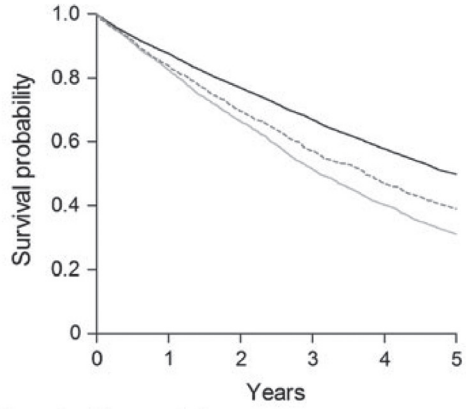
Table 3. HRs comparing mortality in dialysis patients in whom diabetes was the primary renal disease with patients in whom diabetes was a co-morbid condition

Patient group	N	Crude HR (95% CI)	Adjusted HR (95% CI)a	Adjusted HR (95% CI)b
Overall				
No DM	4,608	1 (reference)	1 (reference)	1 (reference)
DM PRD	2,236	1.51 (1.43, 1.59)	1.61 (1.53, 1.69)	1.51 (1.43, 1.59)
DM Co-M	740	1.55 (1.44, 1.68)	1.34 (1.24, 1.45)	1.26 (1.16, 1.36)
DM PRD vs DM Co-M		0.97 (0.89, 1.05)	1.20 (1.10, 1.30)	1.20 (1.11, 1.31)
Women				
No DM	1,722	1 (reference)	1 (reference)	1 (reference)
DM PRD	948	1.66 (1.53, 1.79)	1.66 (1.53, 1.80)	1.52 (1.40, 1.65)
DM Co-M	274	1.53 (1.35, 1.74)	1.32 (1.16, 1.50)	1.18 (1.04, 1.35)
DM PRD vs DM Co-M		1.09 (0.95, 1.24)	1.25 (1.09, 1.43)	1.29 (1.12, 1.48)
Men				
No DM	2,886	1 (reference)	1 (reference)	1 (reference)
DM PRD	1,288	1.42 (1.33, 1.51)	1.58 (1.48, 1.69)	1.50 (1.40, 1.61)
DM Co-M	466	1.57 (1.43, 1.73)	1.35 (1.23, 1.49)	1.30 (1.18, 1.43)
DM PRD vs DM Co-M		0.90 (0.81, 1.00)	1.17 (1.05, 1.30)	1.16 (1.04, 1.29)
Age <70 years				
No DM	1,687	1 (reference)	1 (reference)	1 (reference)
DM PRD	1,282	2.10 (1.95, 2.26)	1.96 (1.82, 2.11)	1.78 (1.64, 1.92)
DM Co-M	263	1.77 (1.55, 2.01)	1.51 (1.32, 1.72)	1.39 (1.22, 1.58)
DM PRD vs DM Co-M		1.19 (1.04, 1.36)	1.30 (1.13, 1.48)	1.28 (1.12, 1.47)
Age ≥70				
No DM	2,921	1 (reference)	1 (reference)	1 (reference)
DM PRD	954	1.28 (1.19, 1.37)	1.35 (1.25, 1.46)	1.30 (1.21, 1.41)
DM Co-M	477	1.28 (1.16, 1.41)	1.25 (1.14, 1.38)	1.19 (1.08, 1.35)
DM PRD vs DM Co-M		1.00 (0.89, 1.12)	1.08 (0.96, 1.21)	1.09 (0.98, 1.22)

[a]Model adjusted for age, sex, country and malignancy

[b]Model additionally adjusted for cerebrovascular and cardiovascular disease

Co-M, co-morbid condition; DM, diabetes mellitus; PRD, primary renal disease



Number of patients at risk						
No DM	10,580	9,371	8,048	6,884	5,484	4,918
DM PRD	3,621	3,094	2,461	1,892	1,451	1,102
DM Co-M	1,190	1,005	811	646	528	418

Figure 1. Cox regression 5 year survival stratified by the three different patient groups based on diabetic status: .no diabetes (black line); diabetes as co-morbidity (dashed line); diabetes as primary renal disease (grey line). Model adjusted for age, sex, country and malignancy. Co-M, co-morbid condition; PRD, primary renal disease

Survival analysis stratified by sex and age

In both women and men mortality was higher in patients with diabetes as primary renal disease compared with patients with diabetes as a co-morbid condition (HR 1.25, 95% CI 1.09, 1.43 and HR 1.17, 95% CI 1.05, 1.30, respectively) (Table 3). No formal interaction between sex and diabetes status was found (p=0.18).

In patients aged <70 years, mortality was higher in patients with diabetes as primary renal disease than in patients with diabetes as a co-morbid condition (HR 1.30, 95% CI 1.13, 1.48), whereas this effect was smaller in patients aged ≥70 years (HR 1.08, 95% CI 0.96, 1.21). The interaction between age and diabetes status was statistically significant (p<0.001), meaning that higher age attenuated the effect of diabetes on survival.

Survival analysis stratified by dialysis modality

Twenty per cent of patients started RRT on PD (***n***=3,097). Compared with the reference group of PD patients without diabetes, the HR for mortality was 1.95 (95% CI 1.73, 2.20) in patients with diabetes as primary renal disease on PD and 1.73 (95% CI 1.58, 1.89) in patients with diabetes as primary renal disease on HD. We stratified our analysis by sex and age and showed that mortality in women and men, younger (age <70 years) and older (age ≥70 years) patients was the highest in patients with diabetes as primary renal disease on PD (Figure. 2). When examining the specific group of older female patients (age ≥70 years) with diabetes as primary renal disease in more detail, we found an adjusted HR of 1.41 (95% CI 1.08, 1.84) for patients receiving PD vs HD. Similar results were found in older female patients (age ≥70 years) with diabetes as a co-morbid condition: HR of 1.40 (95% CI 0.87, 2.24) for patients receiving PD vs HD. However, for this group the difference did not reach statistical significance. Additional adjustment for cerebrovascular and cardiovascular disease did not materially influence the study results (data not shown).

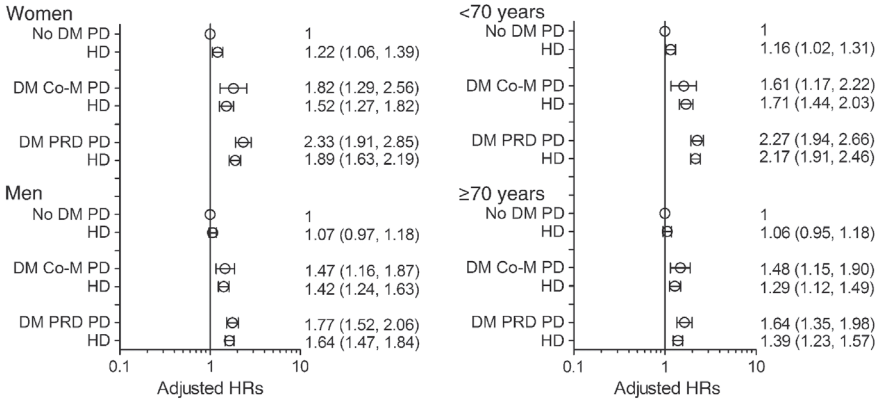


Figure 2. HRs (95% CIs) in HD and PD patients comparing mortality in dialysis patients with diabetes as primary renal disease with patients with diabetes as co-morbid condition, stratified for sex and age. Data were adjusted for age, sex, country and malignancy. Co-M, co-morbid condition; DM, diabetes mellitus; PRD, primary renal disease

Discussion

In this large European cohort study in dialysis patients we compared survival between patients with diabetes as the primary cause of renal failure to patients with diabetes as a co-morbid condition. Mortality in patients with diabetes either as primary renal disease or as a co-morbid condition was clearly higher than in non-diabetic patients. We showed that overall mortality was higher in patients with diabetes as primary renal disease as compared with those with diabetes as a co-morbid condition.

There is no doubt that diabetes contributes to mortality in dialysis patients. However, most earlier studies did not take into account the difference between patients with diabetes as primary renal disease and diabetes as a co-morbid condition[17–22]. In the NECOSAD study, a smaller study of Dutch incident dialysis patients (*n*=1,853) we did not find a difference in mortality between patients with diabetes as primary renal disease and patients with diabetes as a co-morbid condition. In this NECOSAD study, 15% (*n*=281) of patients had diabetes as primary renal disease, 6% had diabetes as a co-morbid condition (*n*=107) and the remaining 79% did not have diabetes (*n*=1,465). Mortality was not higher in patients with diabetes as primary renal disease compared with patients with diabetes as a co-morbid condition (HR 1.06, 95% CI 0.79, 1.43). Although the analysis in NECOSAD did not show a clear effect on mortality, the results from the present study fit in the margins of uncertainty from the NECOSAD study (i.e. CIs overlap). This means that the apparent difference in study results might reflect the low power of the NECOSAD study[9].

In the present larger cohort study we showed that mortality rates were highest in patients with diabetes as primary renal disease. Our results were in line with our initial hypothesis. In diabetic ESRD patients organ damage is not limited to the kidney but involves multisystem micro- and macrovascular complications, and these complications may be more pronounced in patients with diabetes as primary renal disease than in patients with diabetes as a co-morbid condition. This increased vascular damage may be due to longer diabetes duration in patients with diabetes as primary renal disease compared with patients with diabetes as a co-morbid condition. Unfortunately in our data set we had no information on duration of diabetes. Although no clear differences in the prevalence of vascular co-morbidities between diabetes as primary renal disease and diabetes as a co-morbid condition were shown, it should be kept in mind that patients with diabetes as primary renal

disease were almost 5 years younger. Several sensitivity analyses were performed to assess the robustness of our findings. First, a sensitivity analysis excluding patients with diabetes as a co-morbid condition and a primary diagnosis of renal vascular disease yielded similar results. Second, a sensitivity analysis excluding patients with a primary diagnosis of glomerulonephritis yielded similar results. Finally, a sensitivity analysis excluding patients with malignancy showed similar results. The difference in survival between diabetes as primary renal disease and diabetes as a co-morbid condition was a consistent finding across sex and age categories and initial treatment modality. Since this is a comparison according to disease status, this comparison cannot be randomised. Such comparisons are prone to confounding, which we tried to deal with by adjustments in a statistical model. We cannot, however, rule out that residual confounding is present. Late referral of patients with chronic kidney disease to a nephrologist is associated with increased morbidity and mortality[23–25]. It has been shown that pre-ESRD nephrologist care for more than 12 months is more frequent in patients with diabetes as a co-morbid condition than in patients with diabetes as primary renal disease (53.5% and 46.4%, respectively)[26]. It might be that differences in pre-dialysis care contributed to a worse survival for patients with diabetes as primary renal disease in our study, which emphasises the need for optimal pre-dialysis care in patients with diabetes as primary renal disease.

Previous studies showed impaired survival for older diabetic women on PD[6, 10, 11, 27, 28]. In line with these studies we also showed higher mortality in women aged ≥70 years with diabetes as primary renal disease who were treated with PD compared with their counterparts on HD. A similar, but not statistically significant, trend was found in patients with diabetes as a co-morbid condition. It could be speculated that in older diabetic female patients with vascular complications (e.g. heart failure) the preferred treatment modality is PD, with the aim of avoiding haemodynamic instability during dialysis. However, in our study, cardiovascular complications, cerebrovascular and peripheral vascular disease, but not ischaemic heart disease, at baseline were significantly more prevalent in older female diabetic HD patients compared with PD patients. Although adjustment for differences in cardiovascular disease did not change the observed difference in mortality between older female HD and PD patients, we cannot rule out the possibility that residual confounding is present.

The major strength of this study is that it is based on a large cohort of incident dialysis patients with a differentiation of the subtype of diabetes either as diabetes as primary

renal disease or as diabetes as a co-morbid condition. Furthermore, this cohort is based on well-established national and regional registries. Additionally, because it is based on patients from various countries, the probability of systematic biases due to selection or healthcare systems is reduced.

This study has potential limitations. First, the ERA-EDTA Registry does not include data such as residual renal function, ethnicity and difference between type 1 and type 2 diabetes in patients with diabetes as a co-morbid condition. We performed a sensitivity analysis in which we differentiated the patients with primary renal disease by type 1 and type 2 diabetes, showing that mortality was higher in patients with both type 1 and type 2 diabetes in whom diabetes was the primary renal disease compared with those in whom diabetes was a co-morbid condition. This suggests that differences in the underlying pattern of diabetes (type 1 or type 2) cannot fully account for the difference in mortality found between patients with diabetes as primary renal disease and patients with diabetes as a co-morbid condition. Moreover, the availability of type of diabetes for the whole cohort would not qualitatively have changed our results and conclusion. When comparing the patients with type 1 and type 2 diabetes as primary renal disease the highest mortality was found for patients with type 1 diabetes, in line with other studies[4, 8]. Importantly, information on glycaemic control was unavailable. The (international) guidelines for treating diabetes do not differ for patients with diabetes as primary renal disease and patients with diabetes as a co-morbid condition, so it is unlikely that glycaemic targets differed between these groups. Although glycaemic targets do not differ between these two diabetic patient groups, we cannot exclude the possibility that a difference in HbA_{1c} level might exist between patients with diabetes as primary renal disease and patients with diabetes as a co-morbid condition, and this might translate into differences in mortality[29–34]. Increased vascular damage in patients with diabetes as primary renal disease might be therefore due to poorer glycaemic control compared with patients with diabetes as a co-morbid condition.

Second, routine renal biopsies were probably not performed in all patients with a clinical diagnosis of diabetes and ESRD. Although a histological diagnosis would add to the robustness of the study results, a renal biopsy is an invasive procedure with the risk of serious complications[35]. Biopsies are not routinely performed in clinical practice and the distinction between diabetes as primary renal disease and diabetes as a co-morbid condition will often be based on the opinion of the physician as is

common in clinical practice. In a study comparing the clinical vs histological diagnosis of diabetic nephropathy in 84 Austrian patients with type 2 diabetes, a high sensitivity and specificity for the clinical diagnosis of diabetic nephropathy was shown[36].

In conclusion, we showed that mortality in dialysis patients with diabetes either as primary renal disease or as a co-morbid condition is higher compared with non-diabetic dialysis patients, with the highest mortality in patients with diabetes as primary renal disease. Therefore, in studies comparing diabetic patients (as a total group) with non-diabetic patients, survival of the patients with diabetes as primary renal disease may be overestimated. The difference in survival between patients with diabetes as primary renal disease and diabetes as a co-morbid condition was a consistent finding across sex and age categories and initial treatment modality. This suggests that survival in diabetes patients with ESRD is affected by the extent to which the diabetes has induced organ damage. Future studies should elucidate the causal mechanisms underlying this difference in survival as this will have relevance to intervention and management of this increasing patient population.

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