Ethnic differences in survival on dialysis in Europe

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2013

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Increased survival of immigrant compared to native dialysis patients in an urban setting in the Netherlands

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Nephrol Dial Transplant 23:3571-3577, 2008

ABSTRACT

Background Data from the United States and Canada suggest that survival rates of Caucasian dialysis patients are lower compared to those of black patients and patients from Asian regions. Information regarding the survival rate of immigrant dialysis patients in Europe is scarce.

Methods We retrospectively analysed incident haemodialysis (HD) and peritoneal dialysis (PD) patients who entered an Amsterdam renal service between January 1996 and December 2005. To explore the origin of differences in survival between natives and immigrants, we ran a series of Cox-models with adjustment for demographic, clinical and laboratory variables at baseline and initial adequacy variables.

Results Of 303 incident dialysis patients, 58% were natives and 42% were immigrants. Fifty-nine percent of natives and 54% of immigrants had HD as initial treatment modality. At initiation of dialysis, native patients were older and had higher rates of vascular and coronary artery diseases and malignancies and a lower prevalence of hypertension. Glomerulonephritis was more common among immigrants as primary kidney disease. Mean haematocrit and calcium levels for natives were higher compared to immigrants. Cox proportional hazards analysis revealed an increased relative mortality risk (RR) of 2.7 (95% confidence interval [CI] 1.9 - 3.9) for natives compared to immigrants. Adjustment for age at the start of dialysis attenuated the RR to 1.9 (CI 1.3 - 2.7). Adjustment for the other variables did not materially influence this RR.

Conclusion We demonstrate increased survival for immigrant compared to native dialysis patients in an urban setting in the Netherlands. This survival advantage is only partly explained by younger age of immigrants at the start of dialysis compared to native patients.

INTRODUCTION

Racial differences in survival on dialysis are well known in the United States and Canada. In these countries survival rates of black and Asian end-stage renal disease (ESRD) patients appear to be higher compared to survival rates of Caucasian ESRD patients.[1-11] For example, in US Renal Data System (USRDS), mortality rates of black and Asian dialysis patients from 2002 were 33% and 37% lower, respectively, compared to mortality rates of white dialysis patients.[12] In most studies the survival advantage persists after careful adjustment for demographic, clinical and laboratory characteristics.[6;7;9;11] However, in one recent study the relationship between race and survival lost significance after case-mix adjustment.[8]

In contrast to well-documented differences in survival of ESRD patients in the United States and Canada, data concerning the outcome of ethnic minorities on dialysis in Europe are scarce. An English study concluded that Indo-Asian and Afro-Caribbean dialysis patients in London have survival comparable to Caucasian patients.[13] To our knowledge, other data are lacking. These data, however, could be important, as there are important differences between these countries.

First, the racial composition of both continents is different.[14] Second, survival rates of dialysis patients have been considerably lower in the United States than in Europe.[14] This could be partly attributable to general differences in mortality among the general population in the various countries.[15] Third, dialysis- and dialysis population-related factors could also cause differences in survival. Some of these factors include variation in comorbidity (e.g., decreased prevalence of diabetes mellitus, coronary artery disease, congestive heart failure, hypertension, peripheral vascular disease and cerebrovascular disease in Europe)[16] and patient age (lower percentage of 75+ aged patients in Europe).[14] Given these considerations, it is unclear whether differences in survival between Caucasians and non-Caucasians also exist in countries in Europe.

Our department furnishes dialysis service in an urban setting in the Netherlands, with immigrants representing ~40% of all patients. This patient group provides a good opportunity to get more insight in the survival rates of dialysis patients of ethnic minorities in Europe. The aim of this study is to determine possible differences in patient survival between native Dutch dialysis patients and immigrant dialysis patients, and to explore whether differences could be explained by demographic, clinical and laboratory characteristics at baseline and initial adequacy characteristics.

SUBJECTS AND METHODS

Patients

In this retrospective study, we analysed survival data for all ESRD patients who started chronic dialysis treatment in the Sint Lucas Andreas Hospital in Amsterdam, the Netherlands, between 1 January 1996 and 31 December 2005. Also, we analysed survival data for all chronic ESRD patients who started dialysis treatment in another hospital for at most 1 month between 1 January 1996 and 31 December 2005, and were transferred to the Sint Lucas Andreas dialysis centre to continue their dialysis treatment for at least 30 days. We excluded those who survived for <30 days or ended dialysis within 30 days. Only patients undergoing renal replacement therapy for the first time and patients who were 18 years or older were included.

Data collection procedures

Data were obtained from medical records. Country of birth was used to determine ethnicity. Natives in this study are those born in the Netherlands, immigrants are those born outside the Netherlands and Caucasians are those born in European countries or in North America. Patients were followed up until 1 June 2006. The following demographic and clinical characteristics at the start of dialysis were collected: age, gender, body mass index (BMI), presence or absence of predialysis treatment, glomerular filtration rate (GFR), primary cause of renal failure and comorbidity. The initial dialysis technique was also determined, defined as the type of dialysis being used 6 months after the start of dialysis or the most recent treatment if the patient dropped out within 6 months. Predialysis treatment was reported when the patient was under the care of a nephrologist 6 months before the initiation of dialysis. GFR was estimated using two different formulas. The first is the Cockcroft-Gault (CG) formula (ml/min)[17], adjusted to the standard body surface area of 1.73 m^2, which was calculated using the Du Bois and Du Bois equation.[18] The second is the four-variable formula from the 'Modification of Diet in Renal Disease' (MDRD) study, which involves black ethnicity. We used the four-variable MDRD formula, because black ethnicity is an independent predictor of GFR (due to the increased muscle mass of blacks compared to whites).[19;20] The results of the following laboratory tests at the start of dialysis were collected: haematocrit, calcium, phosphorus, albumin, and for diabetes mellitus patients HbA1c. Adequacy of initial dialysis treatment was obtained by collecting Kt/Vurea values per week, determined 3 months after the start of dialysis treatment. In addition, we collected date and reason for the end of dialysis treatment.

Statistical analysis

Differences in baseline characteristics among natives and immigrants were analysed with *t*-tests for continuous variables and chi-square tests for categorical variables. Continuous data are described as mean ± standard deviation (SD). The endpoint for survival was death. Patients were treated as censored when they had a transplantation, return of kidney function, a relocation to an unknown dialysis centre or when they reached the end of the study period. We ascribed death to patient's initial treatment modality (intention-to-treat analysis). Survival analysis was performed using the Kaplan-Meier method with the log-rank test.[21] The univariate Cox proportional hazards model was used to determine the influence of baseline characteristics on mortality. The multivariate Cox proportional hazards model was used to adjust the association of ethnicity with mortality for gradually more potential explanatory variables. On account of the missing values, each model was built both with and without replacing the missing values by the mean of the known values. As these were not materially different, the relative mortality risks (RRs) presented here are computed with mean substitution. For all analyses, the *P*-value <0.05 was considered statistically significant. All analyses were carried out with SPSS 14.0 for Windows statistical software.

RESULTS

Baseline and adequacy characteristics

Three hundred one patients started dialysis treatment in the Sint Lucas Andreas Hospital between 1 January 1996 and 31 December 2005 for at least 30 days. During this decade, 13 patients started chronic dialysis treatment in another hospital for at most 30 days and were transferred to the Sint Lucas Andreas Hospital to continue dialysis treatment for at least 1 month. Of these 314 patients, 11 medical records got lost. Of 303 patients included in the study, 177 (58%) were natives and 126 (42%) were immigrants. One hundred four (59%) natives and 68 (54%) immigrants had haemodialysis (HD) as initial treatment modality. Of the immigrant dialysis patients, 36 were black, 25 Moroccan, 22 Suriname Hindustani, 18 from an East-Asian origin, 8 Turkish and 17 categorized as other (9 Caucasians).

To evaluate whether natives and immigrants started dialysis under the same conditions, demographic, clinical and laboratory characteristics at baseline and adequacy characteristics determined 3 months after the start of dialysis treatment are listed in Tables 1 and 2.

Table 1. Baseline characteristics of 172 haemodialysis patients and 131 peritoneal dialysis patients by ethnic background.

Characteristics	Native (n = 177)	Immigrant (n = 126)	*P* value *
Demographic			
Age (years; mean [SD])	67.6 (12.4)	54.5 (15.1)	<0.001
Male gender (%)	59	63	NS
Clinical			
Body mass index (kg/m2; mean [SD])	26.3 (5.3)	25.8 (4.5)	NS
Predialysis treatment (%) †	82	81	NS
Glomerular filtration rate			
Cockcroft-Gault formula (ml/min/1.73m², mean [SD])	8.3 (3.0)	8.3 (3.2)	NS
MDRD formula (ml/min/1.73m², mean [SD]) ‡	6.7 (2.9)	6.3 (2.6)	NS
Haemodialysis modality (%) §	59	54	NS
Primary cause of renal failure (%)			
Diabetes mellitus	20	29	NS
Hypertension / vascular	24	18	NS
Glomerulonephritis	5	11	0.03
Interstitial nephritis ‖	16	10	NS
Polycystic kidney disease	7	6	NS
Other	11	12	NS
Cause uncertain	18	15	NS
Comorbidity (%)			
Diabetes mellitus	31	37	NS
Vascular disease ¶	37	22	0.005
Coronary artery disease #	32	21	0.04
Congestive heart failure	18	21	NS
Hypertension	73	86	0.01
Malignancy	21	3	<0.001

* Native *versus* immigrant, NS = non-significant.
† Six months or more under the care of a nephrologist before the initiation of dialysis.
‡ MDRD formula = 4-variable formula from the 'Modification of Diet in Renal Disease' study.
§ Dialysis modality defined as treatment being used 6 months after the start of dialysis or the most recent treatment if the patient is already dropped out after 6 months.
‖ Including pyelonephritis, drug induced nephropathy and urolithiasis.
¶ Peripheral vascular disease and/or cerebrovascular accident.
\# Angina pectoris and/or myocard infarct and/or percutaneous transluminal coronary angioplasty and/or coronary artery bypass graft.

Racial differences between these characteristics were evaluated. At the start of treatment, native patients were older (natives, 68 ± 12 years versus immigrant, 55 ± 15 years; $P < 0.001$), and had a higher prevalence of vascular diseases ($P = 0.005$), coronary artery diseases ($P = 0.04$) and malignancy ($P < 0.001$) than immigrants, whereas hypertension was more common among immigrants ($P = 0.01$) (Table 1). Differences in the distribution of primary causes of renal failure between natives and immigrants were statistically non-significant, except for more glomerulonephritis for immigrants (*P* = 0.03) (Table 1). The mean haematocrit level of natives was significantly higher than that of immigrants at the start of dialysis (0.32 l/l versus 0.30 l/l, *P* = 0.03), as well as the mean calcium level (2.15 mmol/l versus 2.06 mmol/l, *P* = 0.03) (Table 2). There were no other significant differences in demographic, clinical and laboratory characteristics at baseline, and in adequacy characteristics (Tables 1 and 2).

Table 2. Laboratory characteristics at baseline and adequacy characteristics of 172 haemodialysis patients and 131 peritoneal dialysis patients by ethnic background.

Characteristics (mean [SD])	Native (n = 177)	Immigrant (n = 126)	*P* value *
Laboratory			
Haematocrit level (L/L)	0.32 (0.05)	0.30 (0.06)	0.03
Calcium level (mmol/L)	2.15 (0.30)	2.06 (0.37)	0.03
Phosphorus level (mmol/L)	2.09 (0.81)	2.13 (0.67)	NS
Serum albumin level (g/L)	33.7 (5.6)	34.4 (5.4)	NS
HbA1c (%) †	7.0 (1.3)	7.2 (1.1)	NS
Adequacy ‡			
Weekly Kt/Vurea *hemodialysis*	3.42 (1.03)	3.42 (1.16)	NS
Weekly Kt/Vurea *peritoneal dialysis*	1.95 (0.39)	2.04 (0.55)	NS

* Native *versus* immigrant, NS = non significant.

† Includes only diabetes mellitus patients.

‡ Determined 3 months after the start of dialysis.

Survival analysis for natives versus immigrants

The unadjusted Kaplan-Meier survival curves for all native and immigrant dialysis patients, as well as for HD and peritoneal dialysis (PD) patients separately, are demonstrated in Figure 1. The curves present a better survival for immigrant compared to native dialysis patients, for all dialysis patients together, as well as for HD and PD patients separately (log-rank test $P < 0.001$). The unadjusted patient survival at 1, 2, and 5 years was 80%, 62% and 27% for natives and 94%, 86% and 63% for immigrants, respectively.

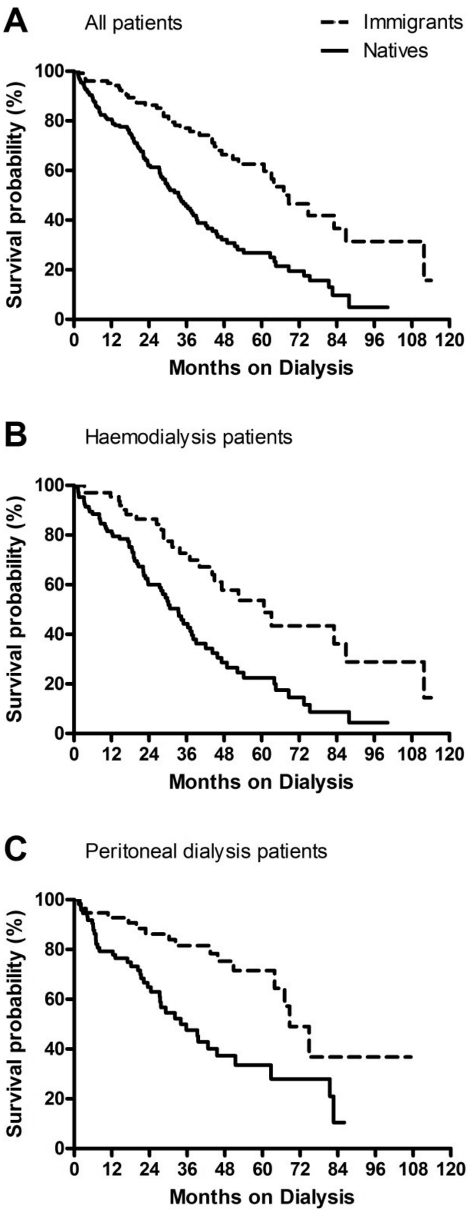

Figure 1. Kaplan-Meier survival curves of native and immigrant dialysis patients. Follow-up censored at renal transplantation, return of kidney function and relocation to an unknown dialysis centre. *P* < 0.001 by log rank test. **(A)** All patients: solid line, natives (n = 177) and dashed line, immigrants (n = 126). **(B)** Haemodialysis patients: solid line, natives (n = 104) and dashed line, immigrants (n = 68) and **(C)** peritoneal dialysis patients: solid line, natives (n = 73) and dashed line, immigrants (n = 58).

To investigate the influence of different baseline parameters on mortality, the univariate Cox proportional hazards models demonstrated the following: older age was associated with increased mortality; higher GFR calculated using the four-variable MDRD formula was associated with increased mortality, while higher level of serum albumin was associated with a lower risk of death. Furthermore, the presence of diabetes mellitus, vascular disease, coronary artery disease, congestive heart failure and malignancy in the medical history were each associated with increased mortality; conversely, hypertension seemed to be protective. Diabetic nephropathy was associated with a higher risk of death and end-stage polycystic kidney disease was associated with a large decrease in risk of death (data not shown).

The crude RR for mortality [95% confidence interval (CI)] is 2.72 (CI 1.88-3.92) times higher for natives compared to immigrants (Table 3, model 1). After adjusting for age, the RR for natives compared to immigrants attenuates to 1.87 (CI 1.27-2.74) (Table 3, model 2). After adjusting for gradually more extensive multivariable models, the RRs remain ~2 (CI >1) (Table 3, models 3-6).

Table 3. Gradually more extensive multivariable models for the connections of ethnic background with mortality: native *versus* immigrant (n = 303). Multivariate analysis with the Cox proportional hazards model.

Model	**Relative risk for mortality**	**Confidence interval (95%)**	**Variables tested**
1. Unadjusted	2.7	1.9 – 3.9	Ethnicity
2. Age	1.9	1.3 – 2.7	Model 1 plus age
3. Demographics and clinical characteristics	2.1	1.4 – 3.1	Model 2 plus gender, body mass index, predialysis treatment, Cockcroft-Gault formula, MDRD formula *, dialysis modality, primary cause of renal failure
4. Comorbidity	2.0	1.3 – 3.1	Model 3 plus vascular disease, hypertension, diabetes mellitus, malignancy, congestive heart failure, coronary artery disease
5. Laboratory characteristics	2.0	1.3 – 3.0	Model 4 plus haematocrit, calcium, albumin, phosphorus
6. Adequacy characteristics	2.0	1.3 – 3.0	Model 5 plus Kt/Vurea 3 months after the start

* MDRD formula = 4-variable formula from the ‘Modification of Diet in Renal Disease’ study.

A sub-analysis by age group (patients ≤55 years old, 56-70 years old, >70 years old) revealed a higher crude RR for mortality for natives compared to immigrants in the highest age group than in the middle age group [RR 2.26 (CI 1.11-4.57) versus RR 1.85 (CI 1.05-3.25)]. In the lowest age group, there was no significant difference in mortality between native and immigrant dialysis patients [crude RR 1.29 (0.50-3.31)].

Computing Table 3 for HD patients, the unadjusted RR is 2.50 for natives compared to immigrants. After adjusting for age, the RR decreases to 1.83. The RRs of progressively more extensive multivariable models are 1.67, 1.72, 1.62 and 1.84 (respectively models 3-6, Table 3). Doing the same for PD patients, the unadjusted RR is 2.76 and 1.80 adjusted for age. After adjusting for variables in models 3-6 in Table 3, RRs are 2.71, 2.28, 2.46 and 2.43, respectively.

To clarify the effect of including patients who dropped out after 30 days and before 90 days, we performed an additional analysis. In this period 11 patients died and one had a return of kidney function. After excluding those patients, the results of the characteristics and models presented in Tables 1-3 were not substantially different from those of the primary analysis (data not shown). Also, an extra analysis was performed to determine the effect of including Caucasian immigrants. After excluding nine immigrant Caucasians, immigrants had statistically significant more diabetic nephropathy (P = 0.031, instead of P = 0.053) and the difference in end-stage glomerulonephritis as a primary cause of renal failure was no longer significant (P = 0.06, instead of P = 0.03). Furthermore, results of the characteristics and models shown in Tables 1-3 were not materially different from those of the primary analysis (data not shown).

Results of the multivariable models predicting the association of ethnicity with mortality were obtained with mean substitution for missing values. Each variable had <5% missing values, except for HbA1c, BMI, GFR calculated with the CG formula, and Kt/Vurea, with missing values varying between 11% and 22% of patients. After building models 1-6 presented in Table 3 without mean substitution, results are approximately the same compared to those obtained with mean substitution (Models 1-6 in Table 3: 2.72, 1.87, 2.00, 1.92, 1.64 and 1.89. For HD patients: 2.50, 1.83, 1.78, 1.80, 1.58 and 2.10. For PD patients: 2.76, 1.80, 2.74, 2.59 and 1.90 for models 1-5, while model 6 could not be executed because of the small patient number).

Follow-up and causes of death

The duration of follow-up and the outcomes are listed in Table 4. The duration of follow-up was significantly longer for immigrants compared to natives (38 months versus 28 months, *P* < 0.001). A significantly higher proportion of native patients died while on dialysis (61% natives versus 33% immigrants, *P* < 0.001). Significantly more immigrants received a renal transplant (23%) compared to natives (10%) (*P* = 0.002). The average period between the start of dialysis treatment and the time of renal transplantation was 43.6 months (± 22.1) for natives and 46.3 months (± 23.8) for immigrants (*P* = non-significant). To evaluate the effect of censoring patients at the time of renal transplantation, we also did an analysis without censoring for transplantation. The RR for mortality for native compared to immigrant dialysis patients hardly modified from 2.72 (CI 1.88-3.92) with censoring for transplantation to 2.65 (CI 1.86-3.76) without censoring for transplantation.

Table 4. Mean follow-up and outcomes of 172 haemodialysis patients and 131 peritoneal dialysis patients.

	Native (n = 177)	**Immigrant (n = 126)**	***P v*alue ***
Follow–up (monts; mean [SD])	27.8 (20.6)	37.6 (25.6)	<0.001
Transplanted	18 (10%)	29 (23%)	0.002
Transferred	-	3 (2%)	0.04
Return of kidney function	1 (1%)	3 (2%)	NS
Death	107 (60%)	41 (33%)	<0.001

* Native *versus* immigrant, NS = non-significant.

The major causes of death in the two groups are described in Table 5. One hundred seven natives (61% of natives) and forty-one immigrants (33% of immigrants) died during the follow-up time. There were no statistically significant differences in the cause of death between natives and immigrants. Cardiovascular disease was the primary cause of death in both groups.

Table 5. Causes of death of 107 native patients and 41 immigrant patients during follow-up.

	Native		**Immigrant**		***P* value ***
	n	**Percentage**	**n**	**Percentage**	
Cardiovascular	42	39	13	32	NS
Sepsis	19	18	10	24	NS
Malignancy	4	4	1	2	NS
Withdrawal from treatment	4	4	2	5	NS
Others	16	15	6	15	NS
Unknown	22	21	9	22	NS

* Native *versus* immigrant, NS = non significant.

DISCUSSION

In this study, differences in survival between native and immigrant dialysis patients in an urban setting in the Netherlands were examined. During a decade, 42% of incident patients in the dialysis programme of an Amsterdam dialysis centre were immigrants. The RR for death for native compared to immigrant dialysis patients was 2.7. After adjusting for age, the RR for mortality remains 1.9. After additional adjustment for gradually more potential explanatory variables, immigrant dialysis patients remain to have approximately two times better survival compared to native dialysis patients. Consequently, besides age, these other factors do not appear to explain the difference in survival between natives and immigrants substantially.

Although we included a considerable number of possible risk factors in our models to explain survival advantage of immigrants, some other factors were not available. For instance, genetic factors were not attainable. However, to be an explanation, these genes should operate through intermediating clinical parameters. A great part of the clinical parameters currently known to be important have been adjusted for in our models, making it less likely that genetic factors fully account for survival advantage of immigrants. Furthermore, lifestyle data (physical activity, smoking, use of alcohol and drugs) and psychosocial factors were not available. Some of these are independent risk factors for mortality in dialysis patients. They might be a partial explanation for the better survival of immigrant dialysis patients; therefore, differences in these factors between natives and immigrants have to be explored further.[7;22;23]

A second limitation of this study is the single-centre setting. To generalize results to a larger population and to extensively examine possible explanations for the survival advantage of immigrants, the study should be replicated in a multicentre setting. However, for the purpose of this study, the single-centre setting was appropriate, given the 10-year follow-up time and the large number of included patients in this study. Moreover, there are not many among the 52 dialysis units in the Netherlands with such a high proportion of immigrant patients.

In addition to the limitations mentioned above, censoring observations at the time of transplant could have influenced our results as well. Censoring patients at the time of renal transplantation eliminates the survival period that is expected to follow on transplantation. Because in general only the healthiest dialysis patients get a renal transplant, this may affect survival estimates. In our study, immigrants were more likely to receive kidney transplants. However, not censoring for transplantation did not materially change our results as the crude RR for mortality in natives versus immigrants was 2.72 when we censored for transplantation, while this RR was 2.65 without censoring for transplantation.

To find explanations for the better survival for immigrant compared to native Dutch dialysis patients, mortality in the general population is an important factor to be taken into account. For example, one study found that 26% of the difference in European north-south mortality among patients on renal replacement therapy could be attributed to differences in general population mortality.[24] In the general population in Amsterdam, differences in mortality between natives and immigrants exist. Life expectancy appears to be lower among native Dutch people compared to other nationality groups.[25] For example, at the age of 50, life expectancy is 4.4 and 6.9, and 2.5 and 1.7 years higher for Mediterranean males and females and Caribbean males and females, respectively, compared to native Dutch males and females. This could partly explain the better survival of immigrant dialysis patients.

Racial differences in survival could also be caused by other phenomena. At first, selective migration of immigrants may play a role. For some immigrants, favourable health conditions are required to migrate. Despite their renal failure, other health benefits of immigrants could still be present at the start of dialysis treatment.[26;27] Secondly, differences in survival may also be clarified by differences in treatment. However, to explain survival differences, immigrant patients would need to have received better treatment than native Dutch patients. On the basis of our clinical impression, we consider it not plausible that there was an important treatment difference favouring immigrants.

Like most American and Canadian studies, in our study differences in survival persist after case-mix adjustment. In these American and Canadian studies, white dialysis patients were compared to non-whites, blacks or Asian dialysis patients. The unadjusted and adjusted RR for mortality in most of these studies is less than 2 and 1.5 respectively. In our study this is 2.7 and 2.0 respectively. However, it is hard to compare the results of these studies since each study adjusted for different factors.[1-7;9-11]

In the first phase of the American arm of the Dialysis Outcomes and Practice Patterns Study (DOPPS), in which only HD patients were included, the effect of race/ethnicity on survival was no longer significant after case-mix adjustment.[8] Three differences between our study and the DOPPS should be noted. Firstly, we included incident patients while DOPPS included prevalent patients. Including prevalent patients might be a selection bias, because patients who die in the first period of dialysis treatment will not be represented in the study. Secondly, the relatively high unadjusted RR in our study could be the reason for the persistent difference in survival after case-mix adjustment. Our unadjusted RR of 2.7 decreased to 2.0 after adjustment for a range of variables. In the DOPPS the unadjusted RR for mortality for non-Hispanic whites compared to blacks was only 1.6. After adjustment for variables included in their study, this RR for mortality attenuated to 1.0. Lastly, the DOPPS adjusted for some factors that were not available in our study (mainly medical events and social characteristics). However, adjusting for these factors in the DOPPS did not influence the RR for mortality.

CONCLUSION

In an urban setting in the Netherlands, immigrant HD and PD patients have better survival compared to native Dutch dialysis patients. The survival advantage of immigrants is only partly explained by the younger age of immigrants at the start of dialysis. As provided medical care is not likely to be better for immigrants, lifestyle or psychosocial factors may play a role. Further investigation is needed to determine factors that influence survival for all dialysis patients.

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