Association of Comorbid Conditions and Mortality in Hemodialysis Patients in Europe, Japan, and the United States: The Dialysis Outcomes and Practice Patterns Study (DOPPS)

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Abstract. Mortality rates among hemodialysis patients vary greatly across regions. Representative databases containing extensive profiles of patient characteristics and outcomes are lacking. The Dialysis Outcomes and Practice Patterns Study (DOPPS) is a prospective, observational study of representative samples of hemodialysis patients in France, Germany, Italy, Japan, Spain, the United Kingdom, and the United States (US) that captures extensive data relating to patient characteristics, prescriptions, laboratory values, practice patterns, and outcomes. This report describes the case-mix features and mortality among 16,720 patients followed up to 5 yr. The crude 1-yr mortality rates were 6.6% in Japan, 15.6% in Europe, and 21.7% in the US. After adjusting for age, gender, race, and 25 comorbid conditions, the relative risk (RR) of mortality was 2.84 ($P < 0.0001$) for Europe compared with Japan (reference group) and was 3.78 ($P < 0.0001$) for the US compared with Japan. The adjusted RR of mortality for the US *versus* Europe was 1.33 ($P < 0.0001$). For most comorbid diseases, prevalence was highest in the US, where the mean age (60.5 ± 15.5 yr) was also highest. Older age and comorbidities were associated with increased risk of death (except for hypertension, which carried a multivariate RR of mortality of 0.74 [$P < 0.0001$]). Variability in demographic and comorbid conditions (as identified by dialysis facilities) explains only part of the differences in mortality between dialysis centers, both for comparisons made across continents and within the US. Adjustments for the observed variability will allow study of association between practice patterns and outcomes.

Outcomes among dialysis patients differ considerably between and within countries. One of the most concerning differences is the varying mortality rate across countries with large populations of dialysis patients. Held *et al.* (1) reported the mortality risk for the renal replacement population in the United States (US), adjusted for age and diabetes mellitus, to be 15% higher than the European risk and 33% higher than the Japanese risk. It has not been possible to determine how much of these differences in mortality are related to demographic and comorbid disease variability because of limitations with the international registries of patients with end-stage renal disease (ESRD).

The Dialysis Outcomes and Practice Patterns Study (DOPPS) is a prospective, observational study of hemodialysis patients across seven countries: France, Germany, Italy, Japan, Spain, the United Kingdom, and the US (2). The study is designed to characterize the case-mix of representative samples of hemodialysis facilities and patients and to relate them to four outcomes: mortality, hospitalization, quality of life, and vascular access events. The aim is to determine which practices are associated with the best outcomes for hemodialysis patients, after adjusting for the effects of demographic and comorbid characteristics. The DOPPS is designed to address some of the limitations of previous registry studies, which often have depended on voluntary reporting and have collected limited information on patient characteristics and unit prac-

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tices. For example, the response rate for the European Renal Association/European Dialysis and Transplant Association (ERA/EDTA) Registry was only 66% by center and 55% by patient questionnaire in 1994 (3). The DOPPS is unique in its enrollment of representative prevalent hemodialysis samples and prospective, uniform data collection.

The goal of this study was to compare demographic characteristics and comorbid conditions of the hemodialysis patients enrolled in the DOPPS across Europe, Japan, and the US and to explore the relationships between case mix and mortality.

Materials and Methods

Patient Selection and Data Collection

A detailed description of the DOPPS design, facility sampling, patient sampling, data collection, sample size determinations, and data management has been reported previously (2). In brief, representative random samples of hemodialysis centers were selected in the US (n = 142), Europe (n = 101), and Japan (n = 61). The study included patients who were 18 yr or older. Selections were stratified to reflect the distribution of academic *versus* non-academic and satellite *versus* central dialysis units within a given nation. The disposition of all patients at participating centers (including death, transfer, and transplantation) was tracked.

At each dialysis facility, a random sample of individual patients was selected for detailed study. Data were collected regarding patient demographic characteristics, comorbid diseases, laboratory values, and medical history. All deaths, hospitalizations, and vascular access events or procedures were recorded, and quality-of-life questionnaires were completed yearly. Mortality and other patient outcomes were carefully tracked. Patients who departed during the study were replaced by randomly selected patients new to the same unit. The prevalence of demographic and comorbid characteristics was determined for the original cross-sectional cohort of 3856 patients in the US, 2590 patients in Europe, and 2169 patients in Japan (total = 8615 patients). The analysis of the association between mortality and patient characteristics was based on the original enrollment cohort and replacement patients, amounting to 9432 patients in the US, 4563 patients in Europe, and 2725 patients in Japan (total = 16,720 patients). Data collection began in the US in June 1996, in Europe in May 1998, and in Japan in February 1999. For the mortality analyses, patients were followed until January 2002 in the US, November 2000 in Europe, and October 2001 in Japan.

Data on comorbid conditions were abstracted from medical records at patient entry using a standardized data collection instrument. Study coordinators at each facility, who were usually nurses, performed data abstraction. Responses of "yes" and "suspected" were pooled to represent presence of the 25 comorbid conditions listed in Appendix A.

Statistical Analyses

Comparisons among continents were performed using χ^2 tests for proportions (prevalence) and t tests for means. The association between mortality and case-mix factors was analyzed using the Cox proportional hazards model. Patients were censored at the time of renal transplantation or transfer from the facility. The association between mortality and patient factors was determined for each characteristic ("univariate" models) and in a combined model. In the Cox models examining the effect of patient characteristics on mortality, stratification by continent was used to control for regional differences in mortality. In a separate model, continental differences in the association between mortality and comorbidities were tested with interaction terms between continent and comorbidity. Significant interactions were explored further in continent-specific models. The sandwich estimator was used to account for patient clustering within dialysis facilities, yielding unbiased variance estimates and P-values. An association was considered statistically significant when the P-value was < 0.05. Separate mortality models were fitted for the first 12 mo on hemodialysis and for time beyond 12 mo on hemodialysis to identify factors that have different short- and long-term effects on mortality (non-proportional hazards). Adjusting for such factors in the Cox models as though they were proportional hazards effects led to no important differences in results compared with adjusting for them as non-proportional hazards effects.

Variation in mortality between US facilities was investigated with and without adjustment for comorbidities. Cox proportional hazards regression was used to compute the expected number of deaths in each facility based on the patient mix at the facility and the overall average patient-mix of the sample. Cox survival curves were created without and with adjustment for patient comorbidities. Mixed Poisson models were employed to compute the variation due exclusively to case-mix.

Results

Demographic Characteristics

Baseline patient demographic characteristics for the prevalent cohorts of patients (n = 8,615) enrolled at study start at each facility are listed in Table 1. Japan's hemodialysis pop-

Table 1. Baseline demographic characteristics by continent

	Europe (n = 2590)	Japan (n = 2169)		US (n = 3856)	
	Mean	Mean	P-value[a]	Mean	P-value[a]
Age (yr) (SD)	60.2 (15.2)	58.6 (12.5)	0.001	60.5 (15.5)	0.02
% 65+	47.1	33.1	<0.0001	44.7	0.08
% 75+	16.8	10.1	<0.0001	20.2	<0.0001
Male (%)	57.6	61.9	0.002	53.4	<0.0001
Black (%)	1.6	0.0	<0.0001	38.3	<0.0001
Years on hemodialysis (SD)	5.1 (5.6)	7.4 (6.4)	<0.001	3.4 (3.8)	<0.001

[a] P-value for comparison with Europe.

ulation was younger and had a higher proportion of males; Japanese patients had been receiving hemodialysis longer than the patients in the US or Europe. Nearly 96% of the dialysis population in Europe was white, compared with 54% in the US and 0% in Japan. Black patients made up 38.3% of the US hemodialysis population, compared with 1.6% in Europe and 0% in Japan.

Comorbid Conditions

The prevalence of comorbid conditions present at baseline is shown by continent in Table 2. The prevalence of cardiovascular disease, particularly coronary artery disease, congestive heart failure, hypertension, cerebrovascular disease, and peripheral vascular disease, was substantially higher in the US compared with Europe or Japan ($P < 0.001$). Cardiovascular disease was generally least prevalent among Japanese hemodialysis patients, except for cerebrovascular disease (12.5%), which was similar to the European prevalence (13.7%). Left ventricular hypertrophy (LVH), cardiomegaly by x-ray, and other cardiac conditions were most prevalent in Europe. Diabetes mellitus was considerably more prevalent in the US (45.7%) than in Europe (20.1%) or Japan (25.6%). The prevalence of HIV/AIDS was higher in the US (1.1%) compared with Europe (0.2%) or Japan (0%). Neurologic disease was also present in a higher proportion of patients in the US (12.4%) than in Europe (6.1%) or Japan (4.0%). Hepatitis B was most common in Europe (4.1%), whereas hepatitis C was most common in Japan (13.4%). While the US *versus* European prevalences were similar for lung disease (13.0% *versus* 10.7%), cancer (9.6% *versus* 9.0%), and psychiatric disorders (24.2% *versus* 24.7%), the prevalences of these diseases were markedly lower in Japan (1.4% lung disease, 5.3% cancer, 2.5% psychiatric disorders). Dyspnea and recurrent cellulitis/gangrene were most common in the US (29.6% and 11.3%, respectively), followed by Europe (19.8% and 6.4%), and markedly lower in Japan (2.7% and 2.1%). Deep venous thrombosis was most prevalent in Europe (4.9%). Japan had the highest percentages of patients with carpal tunnel syndrome and beta-2-microglobulin disease (10.8% and 14.8%, respectively), compared with Europe (7.8% and 7.4%) or the US (4.9% and 1.3%).

Influence of Case-Mix Factors on Mortality

The associations between baseline characteristics and mortality risk for all patients combined are presented in Table 3, based on univariate and multivariate analyses. Age significantly predisposes to mortality, with the risk of death increasing by 3% to 4% per year. This effect was consistent through-

Table 2. Prevalences (%) of comorbid conditions at baseline by continent[a]

	Europe	Japan	*P*-value[b]	US	*P*-value[b]
Coronary artery disease	29.4	19.2	<0.001	49.8	<0.001
Congestive heart failure	25.0	6.1	<0.001	45.8	<0.001
Other cardiac disease	36.5	23.9	<0.001	36.3	0.89
Left ventricular hypertrophy	55.2	28.1	<0.001	34.4	<0.001
Cardiomegaly by x-ray	34.4	29.4	<0.001	34.9	0.67
Hypertension	72.7	55.9	<0.001	83.2	<0.001
Cerebrovascular disease	13.7	12.5	0.22	18.4	<0.001
Peripheral vascular disease	22.5	11.5	<0.001	26.1	0.01
Diabetes mellitus	20.1	25.6	<0.001	45.7	<0.001
Lung disease	10.7	1.4	<0.001	13.0	0.005
Dyspnea	19.8	2.7	<0.001	29.6	<0.001
Smoking	16.6	24.7	<0.001	17.6	0.34
Cancer	9.0	5.3	<0.001	9.6	0.42
HIV/AIDS	0.2	0.0	0.05	1.1	<0.001
Gastrointestinal bleed	5.2	3.6	0.01	9.9	<0.001
Peptic ulcer disease	17.6	9.3	<0.001	16.2	0.14
Hepatitis B	4.1	2.2	<0.001	2.4	<0.001
Hepatitis C	11.5	13.4	0.04	7.4	<0.001
Neurological disorder	6.1	4.0	<0.001	12.4	<0.001
Psychiatric disease	24.7	2.5	<0.001	24.2	0.67
Recurrent cellulitis or gangrene	6.4	2.1	<0.001	11.3	<0.001
Vision problems	31.2	17.9	<0.001	27.6	<0.001
Deep venous thrombosis	4.9	0.5	<0.001	3.2	<0.001
Carpal tunnel syndrome	7.8	10.8	<0.001	4.9	<0.001
Beta-2-microglobulin disease	7.4	14.8	<0.001	1.3	<0.001

[a] See Appendix for definitions of comorbid conditions.
[b] *P*-value for comparison with Europe.

Table 3. Associations between case-mix variables and mortality for all patients in the DOPPS, pooled[a]

	Univariate Models		Multivariate Model	
	RR	*P*-value	RR	*P*-value
Age (per year)	1.04	<0.0001	1.03	<0.0001
age 65+	2.26	<0.0001	—	—
age 75+	2.24	<0.0001	—	—
Male (*versus* female)	1.01	0.7071	1.03	0.4247
Black (*versus* other)	0.63	<0.0001	0.80	<0.0001
Coronary artery disease	1.51	<0.0001	1.13	0.0012
Congestive heart failure	1.60	<0.0001	1.22	<0.0001
Other cardiac disease	1.43	<0.0001	1.15	0.0002
Left ventricular hypertrophy	1.17	<0.0001	0.92	0.0261
Cardiomegaly by x-ray	1.34	<0.0001	1.07	0.0829
Hypertension	0.85	<0.0001	0.74	<0.0001
Cerebrovascular disease	1.47	<0.0001	1.21	<0.0001
Peripheral vascular disease	1.63	<0.0001	1.21	<0.0001
Diabetes mellitus	1.38	<0.0001	1.27	<0.0001
Lung disease	1.53	<0.0001	1.29	<0.0001
Dyspnea	1.84	<0.0001	1.20	<0.0001
Smoking	1.17	<0.0001	1.05	0.3156
Cancer	1.25	<0.0001	1.28	<0.0001
HIV/AIDS	2.71	<0.0001	2.96	<0.0001
Gastrointestinal bleed	1.55	<0.0001	1.25	<0.0001
Peptic ulcer disease	1.32	<0.0001	1.06	0.1885
Hepatitis B	1.20	0.0760	1.12	0.2771
Hepatitis C	1.18	0.0085	1.17	0.0159
Neurological disorder	1.73	<0.0001	1.39	<0.0001
Psychiatric disease	1.64	<0.0001	1.30	<0.0001
Recurrent cellulitis or gangrene	2.01	<0.0001	1.48	<0.0001
Vision problems	1.22	<0.0001	0.91	0.0107

[a] Deep venous thrombosis, carpal tunnel syndrome, β_2-microglobulin disease, and number of years on dialysis are not statistically significant variables and have been excluded.

out the age range. In univariate analysis, patients older than 65 yr had more than double the risk of dying compared with patients younger than 65. There was no significant difference in mortality risk between men and women. Black patients had a 20% lower mortality risk than did patients of other races ($P < 0.0001$). All of the comorbid factors in Table 3, except for hepatitis B, are significantly associated with mortality in the univariate analyses, but multivariate analysis suggests that cardiomegaly by x-ray and peptic ulcer disease were not significantly associated with mortality independent of other factors. Most comorbidities predicted significantly increased RR of death among hemodialysis patients (RR range, 1.06 to 2.96) in both univariate and multivariate analyses. However, hypertension was associated with significantly decreased mortality risk in both univariate (RR = 0.85) and multivariate (RR = 0.74) analyses. The diagnoses of LVH and vision problems were each associated with increased mortality in the univariate analyses but with lower mortality in the multivariate model, indicating confounding with other comorbid conditions.

The reported risks in Table 3 represent average associations across all continents using a continent-stratified Cox model. Potential differences in mortality-comorbidity associations by continent were tested in separate Cox models adjusted for continent and continent-comorbidity interaction terms. Statistically significant interactions were found for lung disease, cancer, and dyspnea, indicating geographic differences in the association between mortality and these comorbidities. Table 4 shows the continent-specific mortality risks associated with these conditions. Lung disease was comparably associated with mortality in Japan and the US but not in Europe. The magnitude of the association between mortality and cancer varied by continent, being greatest in Japan and smallest in the US. Similarly, dyspnea had a greater impact in Japan than in Europe or the US.

Four case-mix variables had associations with mortality that differed significantly ($P < 0.01$) between the initial year on hemodialysis *versus* subsequent years. Black race (RR = 0.75) and the diagnosis of hypertension (RR = 0.59) were associated with markedly diminished RR of mortality for incident dialysis patients, but these benefits were dramatically reduced after the first year of treatment (RR = 0.99 and 0.92, respectively; *P*-values > 0.05). The increased risk of mortality associated

Table 4. Multivariate analysis of associations between case-mix variables and mortality, by continent[a]

	Europe		Japan		US	
	RR	*P*-value	RR	*P*-value	RR	*P*-value
Lung disease	1.01	0.8994	1.30	0.4922	1.36	<0.0001
Dyspnea	1.45	<0.0001	2.42	0.0005	1.16	0.0003
Cancer	1.74	<0.0001	2.35	<0.0001	1.17	0.0022

[a] These three conditions are the only ones for which the relation to mortality varied significantly by continent.

with HIV infection was significantly greater during the first year of dialysis (RR = 5.60) compared with subsequent years (RR = 2.27). In contrast, peripheral vascular disease (RR = 1.27) was associated with increased risk of death only after a year of hemodialysis. The RR of mortality did not differ significantly between the first year and subsequent periods for any of the other variables in Table 3.

Crude and Adjusted Mortality Rates

The crude 1-yr mortality rates among hemodialysis patients were 6.6% in Japan, 15.6% in Europe, and 21.7% in the US. Table 5 shows the RR of mortality by continent for the facilities sampled in the DOPPS. The crude risk of mortality was significantly higher in Europe than in Japan, and higher still in the US. After adjusting for case-mix, the magnitudes of these differences were reduced, but not eliminated. Figure 1A shows unadjusted survival curves by continent. Figure 1B shows adjusted survival curves, illustrating reduced but persistent survival differences by location.

Figure 2 shows the distribution of RR of mortality across the 142 participating hemodialysis centers in the US. Crude mortality rates varied considerably (by ± 29.5%). Adjusting for case-mix clearly narrowed the spread of the RR, but this adjustment fails to explain variability in mortality between units, which remained at 21.2%. This represents a 28% reduction in the variance between units.

Discussion

The characteristics of hemodialysis patients and their clinical outcomes varied across countries and facilities. The crude 1-yr mortality rate among European DOPPS patients, 15.6%, is similar to the 14.4% reported by the ERA/EDTA Registry for 1995 (4). The US rate of 21.7% in the DOPPS is similar to the 22.7% rate reported by the United States Renal Data System (USRDS) for 1996–1998 (5). The 6.6% mortality rate in Japan, however, was lower than the rate of 9.4% reported for 1996 by the Japanese Society for Dialysis Therapy (6). In Japan in 1998, approximately 23% of dialysis facilities were public and university-based, and such units have been inaccessible to the DOPPS to date. It is possible that sicker patients are transferred to these university-based units and subsequently die, falsely lowering the mortality rate for the Japanese dialysis facilities enrolled in the DOPPS. Future DOPPS research will include all the varieties of facilities in Japan.

Table 5. Relative risks of mortality by continent

	Europe		Japan	US	
	RR	*P*-value[a]	RR	RR	*P*-value[a]
Crude	3.12	<0.0001	1.00	5.34	<0.0001
Adjusted[b]	2.84	<0.0001	1.00	3.78	<0.0001

[a] *P*-value for comparison with Japan.
[b] Adjusted for covariates listed in Table 3.
Note: Mortality is significantly higher ($P < 0.0001$) for the US *versus* Europe, both crude (RR = 1.71) and adjusted (RR = 1.33).

Mean age varied (Table 1), with the US and Europe having older hemodialysis populations (mean ages of 60.5 and 60.2 yr, respectively) compared with Japan (58.6 yr). The gender distribution also varied, with the highest proportion of males in Japan (61.9%), followed by Europe (57.6%) and the US (53.4%). The US had greater racial diversity, with 54.0% of patients being white, 38.3% black, and 3.7% Asian. In comparison, 95.6% of patients in Europe were white and 99.8% of patients in Japan were Asian. As shown in other studies (5,7,8), older age was associated with increased risk of mortality in the DOPPS (34% increased risk per 10 yr of age in multivariate analysis, $P < 0.0001$). Black hemodialysis patients experienced a survival benefit (RR = 0.80, $P < 0.0001$), as reported in other studies (5, 9). The survival advantage for black patients applies to the US, as the vast majority of patients from Europe or Japan were non-black. The mechanism underlying racial predisposition to mortality risk is not known, but it also has been observed that Asian Americans experience lower ESRD mortality than do whites in the US (10). In the DOPPS, gender did not predict survival, in contrast to studies that have noted survival benefits among women (8).

Coronary artery disease, congestive heart failure, hypertension, peripheral vascular disease, lung disease, HIV/AIDS, neurologic disease, and gastrointestinal bleeding were each significantly more prevalent in the US than in Europe and least prevalent in Japan. These findings indicate that US patients carry the highest burden of the most important and highly prevalent diseases that predict poor outcome. LVH and cardiomegaly by x-ray were most prevalent in Europe. The study design of the DOPPS (chart review, not interventional) leaves open the possibilities that LVH is screened/diagnosed more often in Europe or that it truly occurs more often. In the US, 45.7% of hemodialysis patients had diabetes mellitus, compared with 20.1% and 25.6% in Europe and Japan, respectively

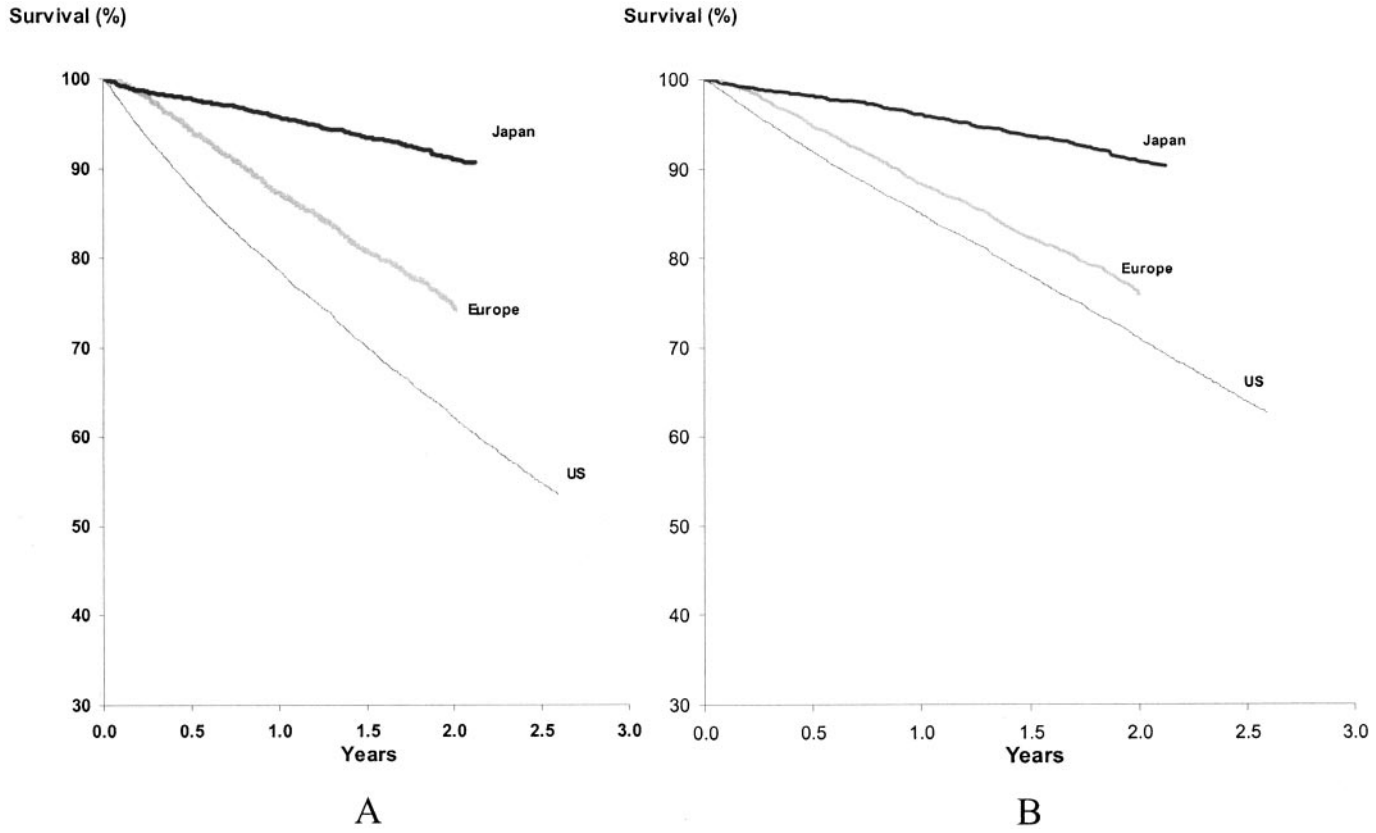

Figure 1. Cox survival curves by continent: (A) unadjusted and (B) adjusted for patient demographics and comorbidities listed in Table 3.

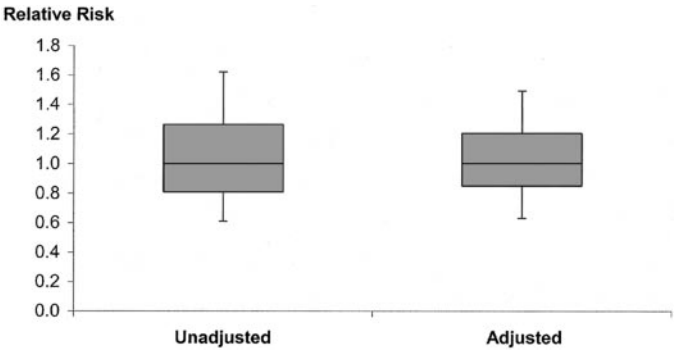

Figure 2. Relative risks of mortality across 142 hemodialysis centers in the United States, before and after adjustment for patient demography and comorbid disease prevalences (see Table 3 for list of covariates). The horizontal lines designate the median values, the boxes delineate 25th and 75th percentiles, and the whiskers extend to the 5th and 95th percentiles. A relative risk of 1.0 corresponds to the median facility mortality rate in the United States.

(Table 2). The country-specific prevalences of diabetes reported here are difficult to compare with published reports from the registries of the USRDS, the EDTA, and the Japanese Society for Dialysis Therapy because of differences in the definition of diabetes in the populations surveyed (3,5,6,11). Registry data often record diabetes as the cause of renal failure but fail to tabulate the coexistent presence of diabetes among patients with other primary etiologies of ESRD. The higher prevalences of carpal tunnel syndrome and β_2-microglobulin disease in Japan likely are consequences of increased survival and prolonged years on dialysis. A report on the first 1,000 patients enrolled in the US HEMO study finds prevalence rates of comorbidities comparable to the US portion of our study (12). HEMO uses similar, but not identical, definitions of comorbid conditions.

Multivariate analysis of data pooled from all patients identified a number of comorbidities that were significantly associated with increased risk of death (Table 3), ranging from a 5% higher adjusted mortality risk among patients who smoke to a nearly threefold greater mortality risk among those with HIV infection. Most cardiovascular comorbidities were associated with substantially increased risk of death. Hypertension, however, was associated with a 26% decreased risk of mortality ($P = 0.0001$). This finding is consistent with other reports, not fully understood, that high predialysis BP is protective in ESRD patients (13–16). LVH was associated with an increased risk of mortality in univariate analysis (RR = 1.17) but a decreased risk in multivariate analysis (RR = 0.92). The confounding effects of other coexistent cardiovascular comorbidities, such as congestive heart failure, likely explain the reversed direction of LVH risk in the multivariate analysis. In effect, LVH does not appear to be an independent risk factor for mortality in hemodialysis patients. Similarly, the reversed direction of risk associated with vision problems in the multivariate model is likely attributable to adjustment for the con-

founding effects of other comorbidities. The mortality risk associated with most comorbid conditions was not significantly different by continent. Geographic differences in risk were noted for three comorbid conditions (Table 4). This finding may reflect variable reporting, severity, or treatments. Black patients and hypertensive patients experienced marked survival benefits during the initial year of hemodialysis, but no significant benefit thereafter, whereas peripheral vascular disease was significantly linked to increased mortality after one year of treatment.

Adjustment for demographic status and comorbid diseases accounted for some, but by no means all, of the differences in RR of mortality between the three regions (Table 5, Figure 1). Approximately 30% of the increased risk of death in the US compared with Japan and Europe was because of the greater burden of comorbid disease and increased age in the US. The difference in mortality risk between Europe and Japan changed less after case-mix adjustment. It is likely that other factors, such as differences in practice patterns, contributed to differing outcomes, and we will examine the associations between practice patterns and outcomes in subsequent research. Furthermore, the DOPPS cannot fully account for case-mix differences or for other non–practice-related influences on mortality. The comorbidity data do not include all diseases and are limited in their discrimination of disease severity (although one study has found that grading severity of comorbid diseases fails to improve prognostic power of mortality risk modeling for ESRD patients) (17). A greater proportion of US patients have "do not resuscitate in the event of cardiac arrest" orders on their charts (data not shown). Countries vary in their rates of acceptance of patients onto hemodialysis, which likely results in sicker patients receiving treatment and dying in certain nations, and the DOPPS cannot adjust for these differences completely. Additionally, renal transplantation rates differ substantially across regions, and it is possible that healthier patients leave the dialysis population for transplantation in some areas but remain on dialysis and improve overall dialysis outcomes in others (6,8). Finally, the death rates for the general population differ across regions, and factors such as diet, air quality, poverty, crime, substance abuse, etc. may alter survival of dialysis patients, unrelated to hemodialysis procedures.

Figure 2 shows that crude mortality outcomes also vary widely across hemodialysis centers within the US. The variability narrows but does not disappear after adjustment for comorbidity. The DOPPS aims to identify practice patterns associated with patient benefits rather than simply portray a competitive contrast of regional outcomes. Adjustment for case-mix explains a considerable amount of the variability in outcome, but not all, reinforcing the likelihood that differences in practice patterns further account for outcomes.

In conclusion, this study shows that increasing age and a variety of comorbid conditions (coronary artery disease, congestive heart failure, cardiomegaly, other cardiac diseases, diabetes mellitus, peripheral vascular disease, cerebrovascular disease, lung disease, cancer, HIV infection, gastrointestinal bleeding, neurologic disease, psychiatric disease, cellulitis/gangrene, hepatitis, and smoking) were significantly associated with mortality among hemodialysis patients. Furthermore, this study quantified the prevalences and risks across Europe, Japan, and the US. Adjusting for demographic and comorbid conditions accounted for only part of the differences in death rates among hemodialysis patients on the three continents.

Appendix A

Comorbid conditions were defined in the DOPPS questionnaire as follows:

1. Coronary artery disease: Prior diagnosis of coronary artery disease, or history of angina pectoris or myocardial infarction any time in the past, an abnormal coronary artery angiogram, or a history of coronary angioplasty or bypass surgery

2. Congestive heart failure (CHF): A prior diagnosis of CHF, a history of pulmonary edema, or a history of hospitalization for CHF within the past 12 mo

3. Other cardiovascular conditions: A history of cardiac arrest or arrhythmia (including atrial fibrillation), pericarditis, or placement of a permanent pacemaker or prosthetic heart valve

4. Left ventricular hypertrophy: By echocardiography, electrocardiography, or unspecified

5. Cardiomegaly: By x-ray

6. Hypertension: A diagnosis of hypertension documented in the medical record

7. Cerebrovascular disease: A history of cerebrovascular accident, transient ischemic attack, or carotid endarterectomy

8. Peripheral vascular disease: A prior diagnosis of peripheral vascular disease, a history of aortic aneurysm or its surgical repair, claudication or rest pain in the extremities from peripheral vascular disease, arterial bypass surgery, or amputation due to peripheral vascular disease

9. Diabetes mellitus: A diagnosis of diabetes mellitus, a history of diabetic gastroparesis, or the use of insulin or oral medications for diabetes any time before enrollment

10. Lung disease: A history of chronic obstructive lung disease or the use of home oxygen for a primary respiratory disorder

11. Dyspnea: Shortness of breath at rest or with minimal exertion

12. Smoking: Active smoker or stopped <1 yr ago

13. Cancer: Any history of malignancy, excluding skin cancer

14. HIV/AIDS: A positive serum HIV antibody titer or the diagnosis of AIDS

15. Gastrointestinal bleed: Gastrointestinal bleed from any cause within the last 12 mo

16. Peptic ulcer disease

17. Hepatitis B: Hepatitis B surface antigen–positive

18. Hepatitis C: Hepatitis C antibody–positive

19. Neurologic disease: A history of seizure disorder, dementia, or Parkinson disease

20. Psychiatric disorder: A history of alcohol or substance abuse within the past 12 mo, or a history of depression or other psychiatric disorder (*e.g.*, schizophrenia, bipolar disorder)

21. Recurrent cellulitis or gangrene

22. Vision disturbances: A history of diabetic or hypertensive retinopathy, or being legally blind from any cause

23. Deep venous thrombosis

24. Carpal tunnel syndrome: Diagnosis of carpal tunnel syndrome or history of surgery for carpal tunnel syndrome

25. β_2-microglobulin disease: Diagnosis of β_2-microglobulin disease or dialysis-associated amyloidosis

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