Effect of Change in Vascular Access on Patient Mortality in Hemodialysis Patients

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● ***Background:*** **Hemodialysis patients using a catheter have a greater mortality risk than those using an arteriovenous (AV) access (fistula or graft). However, catheter-dependent patients also differ from those with an AV access in several clinical features, and these differences may themselves contribute to their excess mortality.** ***Methods:*** **The current study evaluates whether a change in vascular access affects risk for mortality in patients enrolled in the Hemodialysis Study. Time-dependent Cox regression was used to relate mortality risk to current type of access and change in access type during the preceding 1 year.** ***Results:*** **Compared with patients who dialyzed using an AV access at both the beginning and end of the preceding 1-year interval, relative risks for mortality were 3.43 (95% confidence interval [CI], 2.42 to 4.86) in patients who dialyzed with a catheter at both times; 2.38 (95% CI, 1.76 to 3.23) in patients switching from an AV access to a catheter, and 1.37 (95% CI, 0.81 to 2.32) in patients switching from a catheter to an AV access. Change from AV access to a catheter was associated with an antecedent decrease in serum albumin level (odds ratio, 1.25; 95% CI, 1.09 to 1.45 per 0.5 g/dL; $P = 0.002$), weight loss (odds ratio, 1.14; 95% CI, 1.06 to 1.22 per 2 kg; $P < 0.001$), and decreases in equilibrated normalized protein catabolic rate (odds ratio, 2.22; 95% CI, 1.41 to 3.57 per 0.25 g/kg/d; $P < 0.001$) and non–access-related hospitalization (odds ratio, 1.19; 95% CI, 1.06 to 1.32 per 1 additional hospitalization over 4 months; $P = 0.002$). Change from a catheter to AV access was predicted by only the antecedent non–access-related hospitalization rate (odds ratio, 0.93; 95% CI, 0.87 to 0.97 per 1 additional hospitalization over 4 months; $P < 0.001$).** ***Conclusion:*** **Change from a catheter to AV access is associated with a substantial decrease in mortality risk. *Am J Kidney Dis* 47:469-477.**

INDEX WORDS: Vascular access; fistula; graft; catheter; mortality.

VASCULAR ACCESS IS an important predictor of death in hemodialysis patients. Relative risk for death is increased 2- to 3-fold in incident patients using catheters compared with those using an arteriovenous (AV) access (fistula or graft).[1-5] This observation holds true in the United States and other countries regardless of whether one examines overall mortality or cause-specific mortality (in particular, infection-related death). Patients dialyzing with a catheter differ in several important respects from those with an AV access: they typically are older, have greater comorbidity, and have lower serum albumin levels.[1,2,4,5] These clinical features themselves are associated with a greater relative risk for mortality.[6] Thus, it is not clear whether the excess mortality in catheter-dependent hemodialysis patients is caused by complications related to the catheter or dialysis using a catheter is simply a marker of patients more likely to die.

One way to address this question is to determine whether a change in vascular access type changes the relative risk for mortality. Specifically, is change from an AV access to a catheter associated with an increased likelihood of death? Conversely, is change from a catheter to an AV access associated with decreased mortality risk? To evaluate this research question, we used a large prospective database collected for patients enrolled in the Hemodialysis (HEMO) Study.

METHODS

Study Design

The design and methods of the HEMO Study have been reported previously.[6] In brief, the HEMO Study was a multicenter, prospective, randomized, 2 × 2 factorial clinical trial that evaluated the effect of dialysis dose and flux on the morbidity and mortality of hemodialysis patients. The study was approved by the institutional review board at each

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of 15 clinical centers associated with 72 participating dialysis units, and all patients gave written informed consent.

Baseline

Subjects were enrolled in the baseline phase between March 1995 and October 2000 and randomized between May 1995 and February 2001. Eligibility requirements for baseline enrollment included age between 18 and 80 years, receiving incenter hemodialysis thrice weekly, and on hemodialysis therapy longer than 3 months. Demographic and clinical information were collected at baseline. Patients were excluded during baseline if: (1) residual urea clearance in a 24- to 46-hour urine collection was greater than 1.5 mL/min/35 L of urea volume; (2) serum albumin level (nephelometry) was less than 2.6 g/dL (<26 g/L); (3) they failed to achieve the high target dialysis dose in 4.5 hours or less on 2 of 3 consecutive monitored dialysis sessions; (4) they had serious comorbid medical conditions, including active malignancy or infection, unstable angina, or end-stage cardiac, pulmonary, or hepatic disease; or (5) they were scheduled for a living donor kidney transplantation. Several baseline factors were collected on all study patients, including age, sex, race, diabetic status, Index of Coexisting Disease score,[7,8] presence of cardiac disease, presence of peripheral artery disease, anthropometric volume (computed by using the Watson formula[9]), serum albumin level, serum creatinine level, and type of vascular access.

Interventions

Patients meeting inclusion and exclusion criteria were randomly assigned to the study interventions in a 2 × 2 factorial design with equal allocation. Each patient was randomly assigned to receive either a standard (equilibrated Kt/V, 1.05) or high (equilibrated Kt/V, 1.45) dialysis dose and to dialyze with either a low-flux (β_2-microglobulin clearance <10 mL/min) or high-flux (β_2-microglobulin clearance >20 mL/min) membrane. Target dialysis dose was achieved by manipulating dialyzer clearance, dialysis blood flow, and treatment time (minimum, ≥2.5 hours). Adherence to dose intervention was monitored by means of monthly urea kinetic modeling. Dialyzer reuse was permitted, but the number of reuses was limited in the high-flux arm to meet the target β_2-microglobulin clearance. Unmodified cellulose dialyzers were not allowed. Mean achieved equilibrated Kt/V was 1.53 ± 0.09 in the high-dose group and 1.16 ± 0.08 in the standard-dose group; single-pool Kt/Vs were 1.71 ± 0.11 and 1.32 ± 0.09, respectively. Mean achieved β_2-microglobulin clearances were 3.4 ± 7.2 and 33.8 ± 11.4 mL/min in the low-flux and high-flux groups, respectively. Other than the study interventions, dialysis and medical management of patients conformed to current standards of care. Monthly laboratory tests performed for all study patients included a serum albumin level. Data collection ended in December 2001. Mean patient follow-up for mortality was 2.84 years.

Follow-Up Data Collection

At monthly kinetic modeling sessions, clinical centers provided information about the type of vascular access (fistula, graft, or catheter) being used for dialysis. For the purpose of this analysis, fistulae and grafts were both labeled as an AV access, whereas catheters were labeled as a venous access. This prospective information was used to track changes in vascular access. In addition, during the monthly kinetic sessions, we collected information about patients' postdialysis weight, protein catabolic rate, and serum albumin level. Monthly C-reactive protein (CRP) levels were determined starting on September 1, 1999. Finally, clinical centers determined the cause of death for each patient, and their classifications were reviewed by the Outcomes Committee.[3]

Analyses of this report are based on a data set consisting of 54,841 kinetic modeling sessions conducted in 1,826 of 1,846 randomized patients in which valid kinetic modeling data were obtained and which were restricted to the first kinetic modeling session conducted within each calendar month. In Cox regression analyses, values of predictor variables during months with missing kinetic modeling were input from the most recent nonmissing value. Analyses of baseline and follow-up factors that predicted access type were restricted further to 48,081 of these kinetic modeling sessions, which were conducted after 4 months of follow-up.

Statistical Analyses

Generalized estimating equations for a dichotomous response variable were used to relate type of access at each month during follow-up to baseline and follow-up factors. Factors first were evaluated univariately (controlling for clinical center and randomized treatment group) and then jointly in a multivariable model.

Time-dependent Cox regression next was used to relate the relative risk for mortality at each time to the patient's most recently recorded access type while controlling for different sets of baseline factors to evaluate potential confounding relationships. First, relative risk associated with use of a venous versus AV access was evaluated with only the case-mix variables age, sex, race, diabetic status, and years on dialysis therapy included as covariates. Relative risk was evaluated next after controlling for both case-mix factors and baseline levels of serum albumin and serum creatinine, comorbidity index, cardiac disease, peripheral vascular disease, and anthropometric volume, and then again after controlling for these factors plus mean values of serum albumin, anthropometric volume, systolic blood pressure, and rate of non–access-related hospitalizations during the preceding 4-month period. Patients dialyzing with fistulae and grafts were treated as a single group for the purpose of this analysis because our preliminary data analysis showed no difference in mortality risk between the 2 types of vascular access. Specifically, relative risks for mortality for patients with grafts versus fistulae were 1.00 (95% confidence interval [CI], 0.83 to 1.20) controlling for case-mix variables only and 0.97 (95% confidence interval, 0.80 to 1.18) controlling for the full set of covariates listed.

Separate time-dependent Cox regression analyses were used to relate risk for mortality at each follow-up time beginning 1 year after randomization to change in type of access between the patient's most recently recorded access type and type of access 1 year earlier. These analyses were performed while controlling for the baseline factors listed and mean values of serum albumin, anthropometric volume, systolic blood pressure, and rate of non–access-related hospitalizations during the 4 months preceding the 1-year period during which access change was evaluated. The 1-year intervals were classified into 1 of 5 categories: (1) an AV access at both times (88.3% of 1-year intervals), (2) switch from a catheter to an AV access (2.3% of 1-year intervals), (3) switch from an AV access to a catheter (4.1% of 1-year intervals), (4) a catheter at both times (2.8% of 1-year intervals), and (5) other or unknown access at either time (2.6%). Relative risks were obtained for the second, third, fourth, and fifth categories compared with the first category in which an AV access was used at both times.

For simplicity, the analyses described in the preceding paragraph considered only access type at the beginning and end of the preceding 1-year period regardless of type of access at specific times during this interval. Sensitivity analyses were conducted in which separate categories also were defined for patients with more than 1 change in type of access during the 1-year interval. Results of these sensitivity analyses were similar to those based on type of access at the beginning and end of 1-year intervals.

Finally, we conducted additional analyses to relate the odds of changing from an AV access to a catheter to changes in other factors. These analyses were conducted by first restricting the data set to kinetic modeling sessions that followed 6-month intervals during which an AV access was reported at each modeled dialysis. Within this restricted data set, generalized estimating equations with dichotomous responses were used to relate the odds of changing from an AV access to a catheter to changes in selected factors during the preceding 6 months, controlling for baseline covariates. Analogous analyses, restricted to kinetic modeling sessions after 6-month periods during which a catheter access was recorded at each modeled dialysis, were used to relate changes from a catheter to an AV access to changes in other factors.

All survival analyses were stratified by the 15 clinical centers and conducted with follow-up time censored at transplantation or 4 months after transfer of patients to nonparticipating dialysis units. Because of its greater familiarity, we use the expression "relative risk" when referring to hazard ratios in Cox regression analyses. Generalized estimating equation models were fit for Bernouli responses with a working compound symmetry covariance matrix, with robust SEs used for statistical inference. Two-sided *P* are reported for all hypothesis tests without adjustment for multiple comparisons.

RESULTS

Baseline characteristics of patients enrolled in the HEMO Study are listed in Table 1. There was a slight predominance of female patients and almost half the patients had diabetes. Nearly two thirds were black, reflecting the racial composition of the participating dialysis centers. Cardiac disease (coronary artery disease, congestive heart failure, arrhythmias, or left ventricular hypertrophy) was present in more than three fourths of patients. The proportion of subjects dialyzing with a catheter was approximately 5% at the time of randomization, 60% used an AV graft, and 33% used a fistula. Proportions of the 3 types of vascular access remained fairly constant for up to 3 years of patient follow-up.

Table 1. Baseline Patient Characteristics of the Study Population

Age (y)	57.6 ± 14.0
Female (%)	56.2
Black race (%)	62.6
Prior dialysis (y)	3.7 ± 4.4
Diabetes (%)	44.6
Cardiac disease (%)	80.1
Peripheral vascular disease (%)	21.0
Albumin (g/dL)	3.62 ± 0.34
Creatinine (mg/dL)	10.3 ± 2.9
Systolic blood pressure (mm Hg)	151 ± 26
Diastolic blood pressure (mm Hg)	81 ± 15
Anthropometric volume (L)	34.9 ± 6.1
Fistula (%)	33.2
Graft (%)	60.2
Venous catheter (%)	5.1

NOTE. Values expressed as mean ± SD or percent. The number of accesses adds up to less than 100% because of a small number of accesses reported as "other" or "unknown." To convert albumin in g/dL to g/L, multiply by 10; creatinine in mg/dL to μmol/L, multiply by 88.4.

The likelihood of dialysis using a catheter was associated with several baseline clinical and laboratory factors (Table 2). These included patient sex, comorbidity (Index of Coexisting Disease score), Karnofsky score, serum albumin level, serum creatinine level, urea volume, presence of peripheral vascular disease, and rate of non–access-related hospitalization. Catheter use also was associated highly with 3 follow-up variables: current serum albumin level, current urea volume, and rate of non–access-related hospitalization. On multiple variable analysis, dialysis with a catheter was associated with 3 baseline factors: serum albumin level, serum creatinine level, and urea volume (Table 3).

Risk for mortality was 3-fold greater in patients dialyzing with a catheter compared with those using an AV access (Table 4). This relative risk remained significant even after adjustment for multiple baseline factors and follow-up albumin level, anthropometric volume, systolic blood pressure, and non–access-related hospitalization rate. The excess mortality in patients with catheters was observed in patients with and without diabetes. The risk was not increased significantly

Table 2. Univariate Association of Catheter Versus AV Access Use With Designated Factors

Parameter	Odds Ratio	95% CI	*P*
Age (/10 y)	1.01	0.91-1.11	0.91
Diabetes	1.03	0.78-1.34	0.85
Black race	0.74	0.53-1.03	0.03
Sex (female)	1.92	1.45-2.54	<0.0001
Dialysis duration (y)	1.01	0.98-1.05	0.52
Base Index of Coexisting Disease score	1.24	1.04-1.47	0.014
Baseline Karnofsky (10%)	0.87	0.80-0.95	0.001
Baseline albumin (/0.5 g/dL)	0.17	0.07-0.38	<0.0001
Baseline creatinine (/mg/dL)	0.87	0.83-0.92	<0.0001
Baseline anthropometric volume (/5 L)	0.64	0.56-0.73	<0.0001
Heart disease at baseline	1.41	0.98-2.02	0.06
Peripheral vascular disease at baseline	1.18	1.03-1.37	0.02
Non–access-related hospitalization rate in last 4 mo	1.07	1.04-1.09	<0.0001
Current albumin (/0.5 g/dL)	0.05	0.03-0.08	<0.0001
Current anthropometric volume (/5 L)	0.49	0.42-0.57	<0.0001

NOTE. Odds ratios for catheter use versus AV access use during follow-up kinetic modeling sessions. Each factor is evaluated individually, controlling for clinical center and randomized dose and flux groups. The bottom 3 factors are follow-up factors; the remaining are baseline factors. To convert albumin in g/dL to g/L, multiply by 10; creatinine in mg/dL to μmol/L, multiply by 88.4.

in the subset of patients without baseline cardiac disease. The excess mortality associated with use of a catheter compared with an AV access also was observed for cause-specific mortality. After adjusting for the full set of baseline covariates and follow-up albumin level, anthropometric volume, systolic blood pressure, and non–access-related hospitalization rate, relative risks were 1.62 (95% CI, 1.16 to 2.27) for cardiac death and 2.27 (95% CI, 1.45 to 3.55) for infection-related death ($P < 0.001$ for both comparisons).

Time-dependent Cox regression analysis was used to relate mortality risk to changes in type of vascular access during the preceding year. With patients using an AV access at both the beginning and end of the 1-year interval serving as the reference, Table 5 lists relative risks for changing from an AV access to a catheter, changing from a catheter to an AV access, and for use of a catheter at both times. Change from an AV access to a catheter was associated with more than a 2-fold greater death rate compared with patients who used an AV access at both times; this was true for patients with and without diabetes and patients with or without preexisting cardiac disease. Conversely, change from a catheter to an AV access was associated with a substantially lower risk for mortality compared with use of a catheter at both times.

The association between risk for death and change in access type also was observed for cause-specific mortality. After adjusting for the full set of baseline covariates and follow-up albumin level, anthropometric volume, systolic blood pressure, and non–access-related hospitalization rate, change from an AV access to a catheter was associated with a 1.67 (95% CI, 0.96 to 2.89) relative risk for cardiac death and a 3.51 (95% CI, 1.94 to 6.35) relative risk for infection-related death compared with patients using an AV access at both times. Conversely, change from a catheter to an AV access was associated with a 0.37 (95% CI, 0.12 to 1.16) relative risk for cardiac death and a 0.28 (95% CI, 0.07 to 1.09) relative risk for infection-

Table 3. Multivariable Model for Catheter Versus AV Access Use

Parameter	Odds Ratio	95% CI	*P*
High-Kt/V group	1.01	0.77-1.32	0.94
High-flux group	0.87	0.66-1.13	0.30
Age (/10 y)	0.91	0.81-1.02	0.10
Diabetes	0.87	0.64-1.17	0.35
Black race	0.78	0.55-1.09	0.14
Sex (female)	0.90	0.59-1.38	0.64
Dialysis duration (y)	1.01	0.97-1.04	0.66
Baseline albumin (/0.5 g/dL)	0.28	0.11-0.70	0.006
Baseline creatinine (/mg/dL)	0.93	0.87-1.00	0.04
Baseline anthropometric volume (/5 L)	0.67	0.56-0.81	<0.0001
Heart disease at baseline	1.29	0.89-1.86	0.18
Peripheral vascular disease at baseline	1.12	0.97-1.30	0.12

NOTE. Odds ratios for catheter versus AV access use during follow-up kinetic modeling sessions. Multivariate model, controlling for clinical center. To convert albumin in g/dL to g/L, multiply by 10; creatinine in mg/dL to μmol/L, multiply by 88.4.

Table 4. Association of Mortality Risk With Catheter Versus AV Access Use

Group Analyzed	Covariate Adjustment	Relative Risk	95% CI
All randomized patients	Case-mix	2.97*	2.43-3.64
	Full set of baseline covariates	2.51*	2.05-3.08
	Full set of baseline covariates + follow-up albumin level, anthropometric volume, systolic blood pressure, and non–access-related hospitalization rate	1.59*	1.28-1.98
Baseline cardiac disease	Full set of baseline covariates	2.59*	2.09-3.22
No baseline cardiac disease	Full set of baseline covariates	1.90	0.88-4.07
Diabetes	Full set of baseline covariates	3.11*	2.31-4.17
No diabetes	Full set of baseline covariates	2.08*	1.52-2.84

NOTE. Case-mix factors include age, sex, race, diabetic status, and years on dialysis therapy. Full set of covariates includes case-mix factors plus the additional baseline factors albumin level, creatinine level, comorbidity index, cardiac disease, peripheral vascular disease, and Watson volume. All analyses were adjusted for randomized treatment group and stratified by clinical center.

*$P < 0.001$.

related death compared with patients using a catheter at both times.

We also evaluated clinical factors that predicted a subsequent change in vascular access. During the course of the study, change from an AV access to a catheter after at least 6 months of dialysis with an AV access occurred on 484 occasions. Conversely, change from a catheter to an AV access after at least 6 months with a catheter occurred on 172 occasions. Change from an AV access to a catheter was associated significantly with an antecedent decrease in serum albumin level, weight loss, decrease in protein catabolic rate, or increase in frequency of hospitalization (Table 6). Conversely, change from a catheter to an AV access correlated with the antecedent frequency of hospitalization, but was not associated significantly with changes in serum albumin level, weight, or protein catabolic rate (Table 7).

Table 5. Association of Mortality Risk With Change in Access Type During 1 Year

		Change From AV Access to Catheter		Change From Catheter to AV Access		Catheter at Both Times	
Group Analyzed	Covariate Adjustment	RR	95% CI	RR	95% CI	RR	95% CI
All randomized patients	Case-mix	2.38	1.76-3.23	1.37	0.81-2.32	3.43	2.42-4.86
	Full set of baseline covariates	2.15	1.58-2.92	1.31	0.77-2.22	2.73	1.92-3.87
	Full set of baseline covariates + follow-up albumin, anthropometric volume, systolic blood pressure, and non–access-related hospitalization rate	2.05	1.48-2.86	1.08	0.60-1.95	2.61	1.79-3.82
Baseline cardiac disease	Full set of baseline covariates	2.04	1.46-2.86	1.46	0.84-2.54	2.89	1.99-4.19
No baseline cardiac disease	Full set of baseline covariates	2.39	0.96-5.96	0.47	0.06-3.75	3.08	0.62-15.22
Diabetes	Full set of baseline covariates	2.40	1.57-3.68	1.12	0.48-2.60	3.96	2.32-6.77
No diabetes	Full set of baseline covariates	2.14	1.32-3.45	1.63	0.81-3.29	2.03	1.21-3.40

NOTE. Reference group consists of patients with an AV access at both times. Case-mix factors include age, sex, race, diabetic status, and years on dialysis therapy. Full set of covariates includes case-mix factors plus the additional baseline factors albumin level, creatinine level, comorbidity index, cardiac disease, peripheral vascular disease, and Watson volume. All analyses adjusted for randomized treatment group and stratified by clinical center. In the full cohort, relative risks for switches from a catheter to an AV access compared with patients using catheters at both times are 0.40 (95% CI, 0.22 to 0.74) with case-mix adjustment only, 0.48 (95% CI, 0.26 to 0.88) adjusting for the full set of baseline covariates, and 0.41 (95% CI, 0.21 to 0.81) adjusting for both the full set of baseline covariates and follow-up covariates.

Table 6. Predictors of Change From an AV Access to a Catheter After at Least 6 Months With an AV Access

Factor	Odds Ratio	95% CI	*P*
6-Month albumin change (/0.5-g/dL decrease)	1.25	1.09-1.45	0.002
6-Month posthemodialysis weight change (/2-kg decrease)	1.14	1.06-1.22	<0.001
6-Month equilibrated normalized protein catabolic rate change (/0.25-g/kg/d decrease)	2.22	1.41-3.57	<0.001
4-Month non–access-related hospitalization rate (/1 additional hospitalization over 4 mo)	1.19	1.06-1.32	0.002

NOTE. Changes in albumin level, postdialysis weight, and equilibrated normalized protein catabolic rate were calculated as the difference between the most recent monthly value (while the patient remained on an AV access) and the mean of 3 monthly values obtained 4, 5, and 6 months earlier. Patients changed from an AV access to a catheter after at least 6 months of using an AV access on 484 occasions. Each listed factor was analyzed individually, controlling for the baseline factors randomized group, age, sex, race, diabetic status, years on dialysis therapy, albumin level, creatinine level, Watson volume, cardiac disease, and peripheral vascular disease. To convert albumin in g/dL to g/L, multiply by 10.

Finally, we also related use of a catheter to CRP level during the period starting on September 1, 1999, at which point monthly CRP measurements were added to the protocol of the HEMO trial. During this period, the odds of catheter use were associated inversely with the most recent CRP measurement: each 2-fold greater CRP level was associated with a 10% reduction in the odds of catheter use (95% CI, 0.83 to 0.97; $P = 0.009$) after controlling for case-mix factors and baseline anthropometric volume. In analyses analogous to those listed in Tables 6 and 7, the slope of log-transformed CRP during 6-month periods was not associated with either the odds of switching from an AV access to a catheter ($P = 0.44$) or the odds of switching from a catheter to an AV access ($P = 0.32$).

DISCUSSION

The present study documents that patients dialyzing with catheters differ from those using an AV access in several baseline characteristics (Table 2). Although the likelihood of dialysis with a catheter was nearly 2-fold greater in women than men on univariate analysis, this association was no longer evident on multiple variable analysis (Table 3). Previous analysis of results from the HEMO Study and studies by other investigators suggested that differences in outcomes between female and male hemodialysis patients may be attributable in part to differences in anthropometric volume.[10] Thus, it is likely that the greater catheter use in female hemodialysis patients was caused by their lower urea volume.

We also confirm increased risk for mortality in patients dialyzing with a catheter compared with those using an AV access (fistula or graft), in agreement with other investigators.[1-5] Several factors associated with catheter use (sex, race, comorbidity, serum creatinine level, anthropometric volume, and baseline serum albumin level)

Table 7. Predictors of Change From a Catheter to an AV Access After at Least 6 Months With a Venous Catheter

Factor	Odds Ratio	95% CI	*P*
6-Month albumin change (/0.5-g/dL increase)	0.97	0.93-1.01	0.17
6-Month posthemodialysis weight change (/2-kg increase)	0.99	0.97-1.01	0.41
6-Month equilibrated normalized protein catabolic rate change (/0.25-g/kg/d increase)	0.87	0.76-1.01	0.06
4-Month non–access-related hospitalization rate (/1 additional hospitalization over 4 mo)	0.93	0.89-0.97	<0.001

NOTE. Changes in albumin level, postdialysis weight, and equilibrated normalized protein catabolic rate were calculated as the difference between the most recent monthly value (while the patient remained using a venous catheter) and the mean of 3 monthly values obtained 4, 5, and 6 months earlier. Patients changed from a venous catheter to an AV access after at least 6 months of using a venous catheter on 172 occasions. Each listed factor was analyzed individually, controlling for the baseline factors randomized group, age, sex, race, diabetic status, years on dialysis therapy, albumin level, creatinine level, Watson volume, cardiac disease, and peripheral vascular disease. To convert albumin in g/dL to g/L, multiply by 10.

are themselves associated with patient mortality.[6,11-13] Thus, the increased risk for mortality in catheter patients could be caused by either catheter-related complications or other patient factors associated with having a catheter. The relative risk for mortality associated with catheters was attenuated from 2.97 with adjustment for only case-mix factors to 1.59 after adjustment for the full set of baseline factors and follow-up serum albumin level, systolic blood pressure, anthropometric volume, and non–access-related hospitalization rate. However, persistence of a significant association between mortality and catheter use after adjustment for these factors (Table 4) suggests that catheter use is an independent predictor of patient mortality.

To further evaluate this question, we investigated the association of mortality risk with change in type of vascular access during the preceding 1-year interval. Our analysis shows that change from an AV access to a catheter was associated with increased risk for mortality compared with patients who used an AV access at both times. Conversely, change from a catheter to an AV access was associated with decreased risk for mortality compared with patients using a catheter at both times (Table 5). This association does not prove a causal effect of access type on mortality risk because it is possible that changes in access type are a marker for changes in other factors that influence mortality risk. However, by relating mortality risk to change in access, our analyses should decrease the risk for confounding from patient characteristics that are consistent over time. Thus, the finding that mortality risk is associated with change in access type adds additional support to the body of observational evidence suggesting that the catheter itself, at least in part, contributes to excess mortality in hemodialysis patients.

Finally, to evaluate the possibility that change in access type is a marker for changes in other factors, we undertook additional analyses to understand which factors are predictive of change in access. Change from an AV access to a catheter was associated with antecedent (during the previous 6 months) changes in markers of malnutrition or inflammation (serum albumin level, protein catabolic rate, and patient weight), as well as an increase in hospitalization rate (Table 6). A decrease in serum albumin level or body mass index during a 6-month period is predictive of increased hemodialysis patient mortality.[12] Thus, development of malnutrition is associated simultaneously with both increased AV access failure and patient mortality. Conversely, change from a catheter to an AV access was predicted by a lower hospitalization rate, but not by nutritional or inflammatory markers (Table 7).

How might catheter use impact on patient mortality? It is well documented that infections are much more common in catheter-dependent patients than those using an AV access.[3,14,15] Catheter-related bacteremia and its metastatic complications (eg, endocarditis) can result in infection-related death.[16] However, dialysis with a catheter also was associated with an increase in noninfectious causes of mortality, in particular, cardiovascular deaths. Hemodialysis patients frequently have increased levels of inflammatory markers, which, in turn, predict increased risk for death or cardiovascular events.[17] One could postulate that the presence of a catheter in itself increases inflammation, thereby contributing to an increase in mortality. However, the inverse relationship between CRP level and the likelihood of catheter use that we observed appears to argue against such a mechanism. Similarly, lack of change in CRP levels when patients switched from an AV access to a catheter is inconsistent with this hypothesis. Thus, the precise mechanism by which change in access type influences patient mortality remains to be elucidated.

The proportion of patients in the HEMO Study using a catheter (~5%) was considerably less than that present in the prevalent and incident US hemodialysis populations (~25% and 65%, respectively).[18,19] This discrepancy is explained primarily by the requirement to achieve the high target Kt/V within 4.5 hours and the lower dialysis blood flow that can be achieved with a catheter than with an AV access.

To simplify the time-dependent Cox regression analyses, we used access type recorded at the beginning and end of the 1-year period regardless of access changes in the course of that time. Sensitivity analyses designating separate categories of patients for different patterns of multiple changes did not alter the conclusions of the analyses presented in this report.

The possible implications of catheter use for patient survival are staggering. Changing a patient's access from a catheter to an AV access may decrease the patient's mortality risk by more than 50% compared with patients who remain using a catheter (Table 5). This magnitude of risk reduction is similar to that attributed to increases in Kt/V[13,20] or hemoglobin level[21] or decreases in serum phosphorus level.[22] This observation also should provide a strong motivation for establishing an AV access in predialysis patients. The excess mortality of US hemodialysis patients compared with those in Europe and Japan may be attributable in part to greater catheter use in the United States.

Aggressive efforts to increase the proportion of US patients dialyzing with a fistula resulted in a concurrent increase in catheter-dependent patients. Specifically, although the prevalence of fistula use increased from 27% to 33% between 1998 and 2002, the proportion of catheters increased from 19% to 27%.[23] Decreasing the prevalence of catheters requires both increased predialysis placement of fistulae and concerted efforts to salvage immature fistulae with radiological or surgical interventions.[24] A number of recent investigations observed a relatively high success rate in converting immature fistulae to ones usable for dialysis by using this approach.[25-28] Widespread implementation of such approaches can substantially decrease dialysis catheter use.

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