

# Early Death in Dialysis Patients: Risk Factors and Impact on Incidence and Mortality Rates<sup>1</sup>

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## ABSTRACT

Patients who die within the first 90 days after beginning dialysis are not included in mortality rates and may be absent from incidence counts. To identify factors associated with mortality within 3 months of the initiation of dialysis for ESRD and to estimate the impact of early deaths on ESRD incidence and mortality rates, this study investigated 15,245 patients who began dialysis in Georgia, North Carolina, and South Carolina over a 5-yr period. Data were collected by dialysis facility staff and reported to an ESRD registry. Six percent of all new patients died within 90 days of dialysis initiation (32% of all deaths occurring in the first year of treatment). Characteristics independently associated with increased risk of early death included older age, white race, male gender, physical and nutritional impairment, smoking, and the presence of cancer, congestive heart failure, clinical depression, and history of myocardial infarction. Depending on race-gender group, age-adjusted mortality rates based on this cohort were underestimated by 3 to 12% when patients who died early were excluded. These results suggest that certain patient characteristics—some potentially modifiable—confer increased risk of early death, and that the systematic exclusion of patients who die early from the U.S. national registry substantially influences ESRD mortality rates.

**Key Words:** *Kidney failure, early mortality, incidence, risk factors, survival*

**I**ndividuals who die within the first 90 days of dialysis treatment are excluded from U.S. national ESRD mortality rates and may be missing from inci-

dence counts (1). Consequently, little is known about the initial survival of patients with ESRD or of the risk factors associated with early mortality.

The identification of modifiable characteristics associated with the risk of death during the first 90 days of treatment could lead to improved survival during this interval. Further, information about early survival probabilities might help patients and their families make informed choices about the benefit to be expected from renal replacement therapy. Finally, the exclusion of early deaths from published survival and incidence rates may influence risk comparisons among different groups of ESRD patients.

The purpose of this study is to identify factors associated with mortality at the onset of dialysis and to estimate the impact of these deaths on survival and incidence rates.

## METHODS

### Study Population

All patients starting dialysis treatment between January 1, 1989 and December 31, 1992 in Georgia, North Carolina, and South Carolina were identified through an ESRD registry (Network 6). Because of small numbers for other race/ethnic categories, we limited our analyses to the 15,245 new patients who were white or black.

### Data Collection

Information about patient characteristics was collected at the onset of treatment by dialysis facility staff and included age; primary cause of renal disease (categorized as diabetic or other); gender; years of education; student and employment status; type of housing; and whether the patient lived alone, with family, or with others. The most recent serum albumin level was reported and facility staff indicated the patients' activity level, based on a modified Karnofsky scale (2). Staff reviewed patient records for a history of the following comorbid conditions: alcoholism, angina pectoris, blindness, cancer, comorbid diabetes (diabetic patients without diabetic ESRD), congestive heart failure, clinical depression, hypertension, myocardial infarction, peripheral neuropathy, peripheral vascular disease, renal osteodystrophy, smoking, and substance abuse. Initial treatment modality was defined as hemodialysis (HD), continuous ambulatory peritoneal dialysis (CAPD), continuous cycling peritoneal dialysis (CCPD), and intermittent peritoneal dialysis (IPD). Patients who received renal transplants or who transferred out of the network were identified by a bimonthly census. Patient deaths were reported by facility staff, using a special form.

### Analysis

The distributions of characteristics among patients dying within 90 days of dialysis initiation were compared with those of all new patients beginning dialysis, using chi-squared tests. Crude rates of death were calculated by dividing the number of deaths occurring among patients with a characteristic by the follow-up time in years for all patients

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with the characteristic and multiplying by 100 (deaths per 100 dialysis yr).

Associations between patient characteristics (including initial treatment modality) and death were first examined in univariate analyses stratified individually for age, race, and gender (3). The characteristics independently associated with death within 90 days were then identified using unconditional logistic regression (4,5). Terms for statistical interactions identified in the stratified analyses were assessed for significance using log-likelihood ratio tests (4). After elimination of all nonsignificant interactions, main-effect variables that were not associated with outcome at the 0.05 significance level were removed one at a time to yield the most parsimonious risk model.

We assessed whether deaths were evenly distributed during the first year of dialysis by calculating a death hazard for each month of follow-up, using actuarial survival analysis (6). The hazard is the rate of death, expressed as deaths per

patient-month, and is based on the probability of dying in the month for patients who survived to the beginning of the month. Follow-up began at the first reported date of dialysis and continued until death, renal transplantation (*N* = 549), transfer from the Network, or 365 days of follow-up.

We estimated the impact of excluding early deaths on incidence and mortality rates by calculating two sets of rates: one that included and one that excluded patients who died within 90 days. Incidence rates of ESRD treated with dialysis during the 4-yr interval used the population of states that comprise Network 6 obtained from the 1990 Census and were standardized to the age distribution of the U.S. population in 1990 by a direct method (7,8).

First-year mortality rates were calculated by dividing the number of deaths occurring in the intervals 1 to 365 days and 91 to 455 days by the total patient follow-up time for the interval in years and multiplying by 1000 (deaths per 1000 patient yr at risk). The latter interval was used to conform to

TABLE 1. Patient characteristics and early death<sup>a</sup>

Factor	New Patients		Deaths <91 Days			P Value <sup>c</sup>
	N	%	N	%	Rate <sup>b</sup>	
Mean Age (SD)	56.8 (16.2)		65.4 (13.2)			
Age Level						
<45	3730	24	87	9	9.7	<0.001
45 to 64	5989	39	274	30	19.1	
65 to 74	3744	25	355	39	40.7	
75+	1782	12	206	22	50.5	
Race						
Black	8973	59	411	45	19.2	<0.001
White	6272	41	511	55	34.9	
Gender						
Male	7527	49	485	53	27.2	0.04
Female	7718	51	437	47	23.9	
Diabetic ESRD						
Yes	5122	34	292	32	24.0	0.20
No	10123	66	630	68	26.3	
Dialysis Begun						
1989	3307	21	241	26	31.0	0.009
1990	3472	23	200	22	24.4	
1991	3947	26	221	24	23.4	
1992	4519	30	260	28	24.3	
Dialysis Modality						
Hemodialysis	12240	80	779	85	26.9	<0.001
CAPD	2251	15	104	11	19.3	
CCPD	670	4	29	3	17.9	
IPD	84	1	10	1	51.1	
Activity Level <sup>d</sup>						
Normal	1662	13	24	5	5.9	<0.001
Mildly impaired	4830	37	82	18	6.9	
Moderately impaired	4050	31	163	36	16.6	
Severely impaired	2341	18	183	40	33.0	
Albumin Level (g/L) <sup>d</sup>						
41 to 50	1879	15	25	6	5.5	<0.001
35 to 40	5401	43	124	29	9.4	
31 to 34	2899	23	121	28	17.3	
10 to 30	2278	18	162	38	29.6	

<sup>a</sup> CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cycling peritoneal dialysis; IPD, intermittent peritoneal dialysis.

<sup>b</sup> Crude mortality rate in deaths per 100 dialysis yr.

<sup>c</sup> P compares distribution of patients dying within 90 days of dialysis initiation to that of all new dialysis patients.

<sup>d</sup> Total is less than 15,245 because of missing data.

the U.S. Renal Data System (USRDS) convention (1). Death rates were age-adjusted (10-yr intervals) by direct standardization to a population that had equal weights assigned to each age interval (7).

## RESULTS

The mean (SD) age of the 15,245 patients starting dialysis was 56.8 (16.2) yr. There were 922 (6%) deaths among new patients within the first 90 days of dialysis. Characteristics of all new patients and of patients who died during the first 90 days of treatment are shown in Tables 1 through 3. Compared with all new patients, people who died during this period were older, white, male, poorly educated, without social support, and were more impaired physically and nutritionally, and a higher proportion had cancer or a history of myocardial infarction.

Characteristics independently associated with death within 90 days of dialysis initiation are shown in Table 4. Older age, white race, male gender, physical and nutritional impairment, smoking, and the pres-

ence of cancer, congestive heart failure, clinical depression, and history of myocardial infarction were independently associated with an increased risk of very early death. Patients with hypertension were at decreased risk of death. A history of myocardial infarction was associated with increased risk of very early death among the youngest patients only.

The death rate was not constant during the first year of treatment. Thirty-two percent of all first-year deaths occurred during the first 3 months of treatment. The monthly hazard rate increased from 0.24 deaths per patient-month in the first month to 0.27 in the second, and then declined until the seventh month of treatment, thereafter leveling off (Figure 1).

Incidence rates of ESRD treated with dialysis were between 4.5 and 8.8% higher when all patients starting dialysis, rather than only those surviving past 90 days on dialysis, were considered (Table 5). The discrepancy in incidence rates was greater for white than black patients. In addition, the incidence rate ratio, a

TABLE 2. Socioeconomic characteristics and early death

Factor	New Patients		Deaths <91 Days			P Value <sup>b</sup>
	N	%	N	%	Rate <sup>a</sup>	
Education (yr) <sup>c</sup>						
0 to 8	4638	35	277	50	25.2	<0.001
9 to 12	6342	48	182	33	11.8	
>12	2210	17	93	17	17.3	
Student Status						
Yes	223	2	1	1	1.8	<0.001
No	15022	98	921	99	25.9	
Social Support						
Lives alone	4188	27	509	56	53.9	<0.001
With family	8670	57	307	33	14.6	
With others	2372	16	105	11	18.4	
Housing						
Owns home	9222	60	739	80	34.3	<0.001
Rents home	2560	17	52	6	8.3	
Subsidized rent	978	6	15	2	6.3	
Other	2470	16	115	12	19.3	
Employed <sup>c</sup>						
Yes	1276	9	23	4	7.4	<0.001
No	12324	91	544	96	18.4	
Alcoholism						
Yes	736	5	25	3	14.0	0.002
No	14509	95	897	97	26.1	
Clinical Depression						
Yes	2774	18	139	15	20.9	0.01
No	12471	82	783	85	26.6	
Smoking						
Yes	2163	14	75	8	14.1	<0.001
No	13082	86	847	92	27.5	
Substance Abuse						
Yes	241	2	5	1	8.5	0.009
No	15004	98	917	99	25.8	

<sup>a</sup> Crude mortality rate in deaths per 100 dialysis yr.

<sup>b</sup> P compares distribution of patients dying within 90 days of dialysis initiation to that of all new dialysis patients.

<sup>c</sup> Total is less than 15,245 because of missing data.

TABLE 3. Comorbidity and early death

Factor	New Patients		Deaths <91 Days			P Value <sup>b</sup>
	N	%	N	%	Rate <sup>a</sup>	
<b>Angina Pectoris</b>						
Yes	2007	13	117	13	24.4	0.66
No	13238	87	805	87	25.7	
<b>Blindness</b>						
Yes	862	6	27	3	12.9	<0.001
No	14383	94	895	97	26.3	
<b>Cancer</b>						
Yes	715	5	59	6	34.8	0.01
No	14530	95	863	94	25.1	
<b>Comorbid Diabetes</b>						
Yes	1487	10	52	6	14.4	<0.001
No	13758	90	870	94	26.8	
<b>Congestive Heart Failure</b>						
Yes	3293	22	197	21	25.0	0.86
No	11952	78	725	79	25.7	
<b>Hypertension</b>						
Yes	10138	66	319	35	13.0	<0.001
No	5107	34	603	65	51.9	
<b>Myocardial Infarction</b>						
Yes	1449	10	92	10	26.6	0.61
No	13796	90	830	90	25.4	
<b>Peripheral Neuropathy</b>						
Yes	2570	17	97	10	15.6	<0.001
No	12675	83	825	90	27.6	
<b>Peripheral Vascular Disease</b>						
Yes	2862	19	143	16	20.8	0.009
No	12383	81	779	84	26.6	
<b>Renal Osteodystrophy</b>						
Yes	494	3	16	2	13.4	0.008
No	14751	97	906	98	25.9	

<sup>a</sup> Crude mortality rate in deaths per 100 dialysis yr.

<sup>b</sup> P compares distribution of patients dying within 90 days of dialysis initiation to that of all new dialysis patients.

measure of the relative risk for blacks compared with whites, was overestimated by nearly 4% when patients who died very early were excluded.

On the other hand, when only patients who survived past 90 days on dialysis were considered, age-adjusted, first-year mortality rates were underestimated by between 2.9 and 12.1% (Table 6). The mortality of whites compared with that of blacks was underestimated by almost 7% when only patients with survival past 90 days were included in the analyses.

## DISCUSSION

We were interested in the possibility that deaths during the first year of treatment would be uniformly distributed during the year and that risk factors measured at the onset of treatment would identify patients at increased risk of early mortality. Our choice of 90 days was prompted, in part, by the USRDS convention, which reports ESRD mortality rates only for patients who survive to Day 91 of dialysis treatment,

at which time Medicare eligibility for all patients ensures more complete case reporting (9).

We found that the risk of death among new dialysis patients was not uniform and decreased during the first year. A USRDS study of patients aged 65 to 69 comparing 1- and 2-yr survival measured from Day zero versus Day 90 of dialysis also indicated a higher death rate early during treatment (9). These findings suggest that there is a high-risk population of patients who die early after the initiation of dialysis treatment.

Overall, 6% of new dialysis patients in our study died within the first 90 days. Other researchers have also reported high rates of death early during treatment. Among 2396 patients starting dialysis in Michigan between 1974 and 1978, approximately 10% died within 3 months (10). Smaller, local studies have reported 90-day death rates of 12% (11-13) and 16% (14). Our lower rates may reflect better early survival in recent years.

We know of only one other study that has examined

**TABLE 4. Factors independently associated with deaths occurring within 90 days of dialysis initiation, by logistic regression**

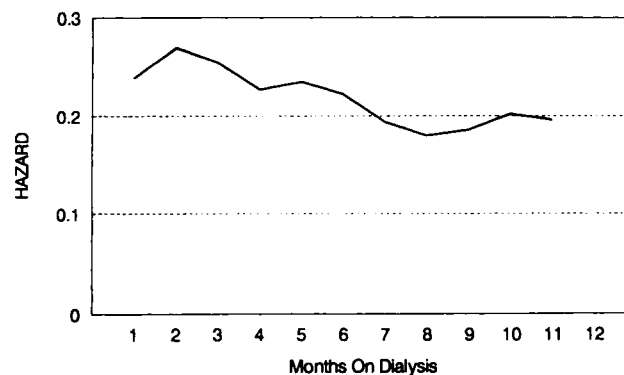
Factor	Level	Deaths <91 Days <sup>a</sup> (Odds Ratio)
Age (yr)	45 to 64	2.1 (1.4, 3.3)
	65 to 74	4.3 (2.8, 6.6)
	75+	5.0 (3.2, 7.8)
Race	White	1.6 (1.3, 1.9)
Gender	Male	1.6 (1.3, 1.9)
Activity Impairment	Mild	0.9 (0.6, 1.4)
	Moderate	1.5 (0.9, 2.3)
	Severe	2.3 (1.4, 3.6)
Albumin (g/L)	35 to 40	1.4 (0.9, 2.2)
	31 to 34	2.4 (1.5, 3.7)
	10 to 30	4.4 (2.8, 6.9)
Myocardial Infarction By Age Level	<45	8.8 (4.2, 18.6)
	45 to 64	1.4 (0.8, 2.4)
	65 to 74	1.2 (0.8, 1.9)
	75+	1.0 (0.6, 1.6)
Cancer	Yes	1.5 (1.1, 2.0)
Congestive Heart Failure	Yes	1.5 (1.2, 1.9)
Hypertension	Yes	0.7 (0.6, 0.9)
Depression	Yes	1.3 (1.0, 1.6)
Smoking	Yes	1.3 (1.0, 1.7)

<sup>a</sup> Stratum-specific odds ratios are presented for those factors in which the strength of the association with mortality varied across levels of (interacted with) another factor. 95% confidence intervals are listed in parentheses.

factors associated with death within 90 days. Khan *et al.* (13) compared the data (collected over a 22-yr period) of 42 Scottish patients who had died within 3 months of dialysis initiation to that of 42 age- and gender-matched control subjects. Patients who died early had lower mean albumin levels, a higher proportion of these patients were smokers, and more of them had multiple comorbid conditions or diabetes, placing them in a "high-risk" group. Mean blood pressure measurements were not different between groups.

Differences in methodology make it difficult to compare our results with those of Khan *et al.* The positive influence that we observed of older age and male gender on early mortality could not be assessed by Khan *et al.* because patients were matched on these variables. Also, no mention was made of racial differences.

In the study presented here, smoking and certain comorbid conditions—including cancer, congestive heart failure, and, in young patients, a history of myocardial infarction—were each associated with early death. On the other hand, a diagnosis of hypertension was protective among members of our cohort. We can only speculate about the reasons for this latter finding. Perhaps patients treated for hypertension had better access to care for ESRD. Alternatively, low blood pressure may be a marker for poor left ventric-



**Figure 1.** The hazard rate in deaths per patient-month for deaths occurring within the first year among 15,245 patients beginning dialysis in ESRD Network 6 between 1989 and 1992. The hazard rate is based on the probability that a patient will die in a specific month, given that the patient has survived to the beginning of that month calculated using life-table analysis.

**TABLE 5. Influence of patients with early death (<91 days) on age-adjusted incidence rates of dialysis**

Race-Gender	All New Patients		New Patients Surviving ≥91 Days		% Error
	N	Incidence <sup>a</sup>	N	Incidence <sup>a</sup>	
White Men	3500	160	3205	146	8.8
White Women	2772	104	2556	96	7.7
All Whites	6272	128	5761	117	8.6
Black Men	4027	671	3837	636	5.2
Black Women	4946	641	4725	612	4.5
All Blacks	8973	655	8562	624	4.7
Incidence Rate Ratio (Blacks:Whites)		5.1		5.3	3.8

<sup>a</sup> Incidence rate per million population, age-adjusted by direct standardization to the U.S. population in 1990.

ular function. The association we observed may also have been the result of residual confounding by race in our data.

The severity of some risk factors was greater among patients who died within the first 3 months of treatment compared with those dying later in the first year. In our study, compared with patients who died between 91 and 365 days after dialysis initiation, individuals dying within the first 90 days were more likely to be moderately or severely functionally impaired (results not shown). Also, consistent with Khan *et al.*, the average serum albumin level was lower among patients who died within 90 days than among those dying later (31.9 versus 32.6 g/L;  $P = 0.04$ ). These observations suggest that early deaths occurred among individuals who were more frail at the time of onset of treatment.

We have previously reported that the perceived ab-

**TABLE 6. Influence of patients with early death (<91 days) on first-year, age-adjusted mortality rates<sup>a</sup>**

Race-Gender	All New Patients		New Patients Surviving ≥91 Days		% Error
	Deaths	Mortality <sup>b</sup>	Deaths	Mortality <sup>c</sup>	
White Men	855	260	682	232	10.8
White Women	642	240	533	211	12.1
All Whites	1497	250	1215	222	11.2
Black Men	603	173	535	162	6.4
Black Women	805	173	731	168	2.9
All Blacks	1408	173	1266	165	4.6
Standardized Rate Ratio (White:Black)	1.45		1.35		6.9

<sup>a</sup> Deaths per 1000 yr at risk, age-adjusted by direct standardization to a standard population, giving equal weight to each of eight age categories (0 to 19, 20 to 29, . . . , 80+).

<sup>b</sup> Based on number of deaths and years at risk in the interval 1 to 365 days.

<sup>c</sup> Based on number of deaths and years at risk in the interval 91 to 455 days.

sence of social support is a risk factor for mortality among new dialysis patients (15). The study presented here suggests that new dialysis patients who are reported by staff as living alone (as one measure of decreased social support) may be at increased risk of early death. However, in our multivariate risk model, living alone was not independently associated with this increased risk. This may be a result of the different measurements of social support used in the two studies (self-report versus staff-report). It is also possible that socially isolated elderly patients are more likely to be functionally impaired and malnourished, two conditions that are very strongly associated with increased risk of death in patients on dialysis.

Our findings suggest that people who are contemplating dialysis treatment, particularly older individuals with ESRD, might benefit from a modification of factors associated with early mortality, such as nutritional status. However, in the absence of clinical trials, potential benefits are speculative and interventions to improve nutrition or functional status may not be justified solely by an expected improvement in the likelihood of survival.

On the other hand, patients with risk factors for early death (or their families) might make different choices when advised of the likelihood of a poor outcome from treatment for ESRD. Predictors of early survival identified by this study and others (16) may also prove useful to those evaluating the costs and benefits of ESRD treatment.

Mortality rates were high during the first year of dialysis and, as expected, the effect of excluding individuals who died during the first 90 days of dialysis treatment resulted in underestimates of mortality and

incidence rates. However, because mortality was especially high during the initial months of dialysis treatment, the magnitude of the underestimates was greater than expected. In addition, the degree of underestimation was not uniform among race-gender groups. The high rate of early deaths among whites resulted in age-adjusted mortality and incidence rates that were underestimated to a greater extent for whites than for blacks. An important consequence of these variations in early mortality is that national estimates of the black:white relative risk of beginning dialysis treatment for ESRD may be overestimated and those of the white:black relative risk of mortality with ESRD may be underestimated.

Patients who die soon after starting dialysis, especially non-Medicare patients, may not be included in U.S. incidence estimates. The degree to which omissions because of early deaths influence these rates is not known. The error estimates that we present, based on including and not including all patients who died within 90 days of dialysis initiation, establish upper bounds for this error. Although the undercount is probably less, our data were not suited to further investigation of this issue.

Several limitations should be considered when interpreting the results of this study. First, we relied on dialysis facility staff to ascertain the presence or absence of the risk factors correctly. Although some patient characteristics such as age and cause of renal failure have been shown to be accurately assessed in this way (17), others, including comorbid status, have not been similarly validated. We have shown, however, that data obtained on cardiovascular risk factors from medical records by dialysis facility staff were better predictors of mortality than were data obtained by patient history or by using specialized epidemiologic questionnaires (18).

Second, the associations that we found may have been influenced by unmeasured risk factors. However, we are not aware of factors other than those that we included which have been associated with mortality in other epidemiologic studies of patients with ESRD.

The incidence rates of ESRD treated by dialysis that we report may have been slightly increased by the inclusion of patients who resided outside the three-state area monitored by the registry but who dialyzed in Network 6 facilities. However, the inclusion of these patients should not have influenced incidence rate comparisons that included and excluded patients who died early.

Our results could not have been affected by selection bias because we studied all patients beginning dialysis in a defined geographic area over a 5-yr period and our follow-up was virtually complete.

In conclusion, we found that new ESRD patients experience declining rates of mortality during the first year of treatment. The risk factors for early mortality are similar to those associated with overall mortality. Mortality rates that fail to account for early deaths

may lead to biased estimates of risk among certain groups, particularly whites, older individuals, and men.

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