Death by Withdrawal From Dialysis: A 20-Year Clinical Experience^{1,2}

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ABSTRACT

The reasons for withdrawal from dialysis are not well understood. The goals of this study were to determine the risk of dying by withdrawal from dialysis over time and to elucidate pertinent clinical correlates in 716 long-term dialysis patients. These patients were monitored from the initiation of dialysis through the time of death, transplant or transfer to another program during a 20-yr period from 1970 through 1989. The causes of death in the 340 deceased patients were analyzed. Clinical correlates and associated risk factors were evaluated in the patients who died from withdrawal from dialysis. Withdrawal from dialysis was defined as: "Death with manifestations of uremia because of withdrawal from dialysis. Underlying medical conditions should not have been active, leading to rapid deterioration with imminent death." Withdrawal from dialysis and cardiac events were the second leading cause of death, each accounting for 18.5% of the deaths. Patients stopping dialysis were older at the start of dialysis than were patients dying of other causes (P < 0.0006; Kruskal-Wallis test), with 65.1% of these patients 61 yr of age and older. Cancer, malnutrition, catabolism, and "dissat-

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isfaction with life" were important associations with the decision to withdraw. More than 50% of patients withdrawing from dialysis had either diabetic nephropathy or atherosclerotic renal vascular disease. Withdrawal from dialysis was a common cause of death in these dialysis patients especially if they were over 61 and had systemic diseases such as diabetes mellitus and renal vascular disease. The reasons for a higher incidence of withdrawal in certain programs deserve further study.

Key Words: Dialysis, causes of death, withdrawal, diabetes mellitus, renal vascular disease, elderly

ardiovascular mortality has been reported to be the most frequent cause of death among longterm dialysis patients (1-20). In our program, to the contrary, infections have been the most common cause of death (21). Withdrawal from dialysis has been the second most frequent cause of death and equaled cardiac causes (21). Although previous studies have linked withdrawal to socioeconomic status, age at start of dialysis, and the renal diagnosis, this phenomenon has been poorly understood and reported to occur with a varying frequency (22-35). There have been numerous reports in the literature about withdrawal from dialysis, but most have emanated from the same authors describing a particular subset of dialysis patients (22,26-31). The goals of this study were to determine the risk of dying by withdrawal from dialysis over time and to elucidate the pertinent clinical correlates. This report expands our prior experience with mortality and emphasizes the importance that withdrawal from dialysis has assumed during the 20 yr from 1970 through 1989.

MATERIALS AND METHODS

Patient Population

A computerized database was established to store demographic, clinical, and survival data of all patients with ESRD above age 15 yr who were on dialysis at North Shore University Hospital for over 90 days (36). Entries into the database were made at the initiation of dialysis and continuously over the ensuing years if there was any change in the patient's status; a new entry was made if there was a dialysis

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modality switch. The current study covers all 716 patients beginning dialysis from January 1, 1970, through December 31, 1989, with a follow-up through December 31, 1990. No patient has been denied entry into the dialysis program during these 20 yr unless there was obvious advanced metastatic neoplastic disease. The dialysis unit is based in a tertiary-care university hospital in a predominantly white, middle-class, suburban community with over 98% of the patients covered by health insurance before starting dialysis. The same physicians have been caring for these patients since 1970. All dialysis treatments were performed by the use of accepted protocols to maintain normal blood pressures, dry weights, and a clinical sense of well-being. Our hemodialysis prescription has consisted of three 4.0- to 5.0-h treatments weekly with blood flows of 250 to 400 mL/min and dialysate flows of 500 mL/min. "Rapid dialysis" protocols have not been used in our units. Intermittent peritoneal dialysis treatments were performed with 40 2-L exchanges twice weekly. The patients on continuous ambulatory peritoneal dialysis performed at least four 2-L exchanges daily.

A specific renal diagnosis was entered into the database for each patient starting dialysis. These were then grouped into five categories: chronic glomerulonephritis, polycystic kidney disease, diabetes mellitus, renal vascular disease, and "other," as previously described (21,36).

The cause of death was established by the nephrologists at the time of the death. The causes of death were then grouped into six categories: cardiac, infectious, withdrawal, sudden, vascular, and "other." Since 1970, the same definition for each cause of death has been in use: infectious, death either from sepsis with proven bacteremia or as the sequelae of acute fulminant hepatitis; withdrawal, death with manifestations of uremia because of withdrawal from dialysis and underlying medical conditions should not have been active, leading to rapid deterioration and with imminent death; cardiac, death due to the manifestations of a well-documented acute myocardial infarction (typical chest pain associated with electrocardiographic changes and enzyme elevations) or from overt congestive cardiac failure; sudden, sudden and without explanation, but not related to a preexisting cardiac condition or in a patient with known hyperkalemia; vascular, death as the result of either a cerebrovascular accident, mesenteric artery thrombosis, ruptured aneurysm, or generalized ischemic ("low-flow") state; and "other," all other causes of death, including respiratory failure, hyperkalemia, gastrointestinal bleeding, and other miscellaneous or unknown causes (trauma, etc.) (21).

The database was updated when associated conditions developed including cancer, malnutrition, dementia, and catabolism with weight loss. Proximate risk factors were defined as the immediate condition and precipitating factor leading the patients and their families to make the decision to withdraw from dialysis. The causes of death by age at the start of dialysis were further analyzed according to the age group of patients. These age groups were based on the results of our previous study of survival on dialysis (36). We reviewed the clinical course, causes of death, and comorbid risk factors of all patients who began dialysis from January 1, 1970, through December 31, 1989. All deaths were reviewed, and the clinical diagnosis was compared with autopsy results when available.

Statistical Methods

All statistic analyses were performed on an IBM/ PS2 computer (IBM, Armonk, NY) with the SAS PC software package (SAS Institute, Inc., Cary, NC). The time until death was measured as the time from the start of the first dialysis treatment until death.

Cause-specific survival distributions for the six causes of death were estimated. A patient's survival time was considered censored for a given cause of death if the patient was still alive, died of a cause other than the one under study, received a transplant, or was transferred alive to another facility. For example, when withdrawals were analyzed, the survival time of a patient who died of an infectious cause was considered censored. The hazard function was used to describe the likelihood of dying just after time t, given that the patient had survived through time t (37).

RESULTS

There were 716 patient entries onto maintenance dialysis from January 1, 1970, through December 30, 1989. There were 393 males, 70 blacks, 548 patients on in-center hemodialysis, 58 patients on home hemodialysis, and 71 patients on continuous ambulatory peritoneal dialysis. There were 340 deaths through December 1990.

The overall causes of death during the 20 yr are presented in Figure 1. Infectious causes accounted for more than 32% of all deaths in this chronic dialysis population. Withdrawal from dialysis and cardiac causes each accounted for 18.5% of the deaths.

The median starting age has increased significantly from 47 yr in the 1970–1973 group to 61 yr of age in the 1986–1989 starting group (P < 0.0001; Kruskal-Wallis test). In addition, 40% of entering patients have either diabetic nephropathy or renal vascular disease as the cause of their ESRD during the last 8 yr of study (Table 1). There were 180 patients 40 yr of age or younger, 255 patients from

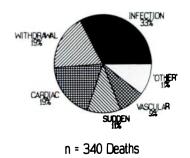


Figure 1. The distribution of all 340 deaths by cause from 1970 through 1989 is shown.

41 to 60 yr of age, and 281 patients 61 yr of age or older, making the oldest age group the largest segment of our dialysis population. More than 65% of patients withdrawing from dialysis were 61 yr of age or older. The patients withdrawing from dialysis were significantly older at the start of dialysis than were the patients dying from other causes of death (P < 0.0006; Kruskal-Wallis test) (Table 2). There was a difference in dialysis modality for the patients withdrawing compared with that for the total dialysis population, with fewer of these patients being on home hemodialysis and CAPD (χ^2 goodness of fit; P < 0.05) (Table 3).

The pattern of the causes of death changed as the patients aged. The patients were separated into two groups, ≤ 60 yr of age at start and >61 yr of age. Withdrawal deaths nearly doubled in patients over 60 yr of age compared with those under 60 yr (Figure 2). Cardiac deaths and total deaths also increased in this older group, whereas infectious deaths decreased.

The renal diagnoses as a percentage of the 63 withdrawal deaths ranged from 3.2% for polycystic kidney disease to 27.0% for diabetes mellitus and 23.8% for atherosclerotic renal vascular disease. More than 50% of patients withdrawing from dialysis

Diagnosesª			Start Years		
	1970-1973 (N = 63)	1974–1977 (N = 152)	1977-1981 (<i>N</i> = 138) (%)	1982-1985 (N= 183)	1986-1989 (N= 180)
CGN	49	34	26	29	27
PKD	11	10	8	9	6
DIAB	7	18	29	25	26
RVD	8	8	7	17	14
"Other"	25	30	30	20	27

TABLE 1. Renal diagnoses and year started

^a CGN, chronic glomerulonephritis; PKD, polycystic kidney disease; DIAB, diabetes mellitus; RVD, renai vascular disease; "Other" renai diagnoses include: amyloidosis, tubulointerstitial nephritis, chronic pyelonephritis, obstructive uropathy, collagen vascular disease, malignant hypertension, miscellaneous, and unknown renai disorders.

Cause of Death	Media	n Age ^a (yr)	N
Infectious	60	(20-83)	111
Withdrawal	67	(19-86)	63
Cardiac	65	(31-80)	63
Sudden	62	(28-83)	38
Vascular	62	(35-82)	29
"Other"		(22-77)	36

 $^{\circ}P$ < 0.0006 (Kruskal-Wallis test). The median age at start of the 376 living patients was 48.0 yr (those patients not dead as of December 31, 1990).

TABLE	3.	Dialysis	modality	and	patient
distribu	oitu	n—197	0-1989		

Type of Dialysis	% Patients Withdrawing ^a (N = 63)	% Total Dialysis Population (N = 716)
In-Center Hemodialysis	89	77
Home Hemodialysis	0	8
CAPD	3	10
In-Center Peritoneal	8	5

^a χ^2 goodness of fit; P < 0.05.

had either diabetes mellitus or atherosclerotic renal vascular disease as the cause of ESRD—the two renal diagnoses that carry the highest mortality rates (Table 4).

In 58 of the 63 patients withdrawing from dialysis, several proximate risk factors and existing comorbid conditions were identified (Table 5). Most often, these factors were related to the underlying condition, *e.g.*, gastropathy or neuropathy in diabetes mellitus, to the need for upcoming surgery, or to pain in the

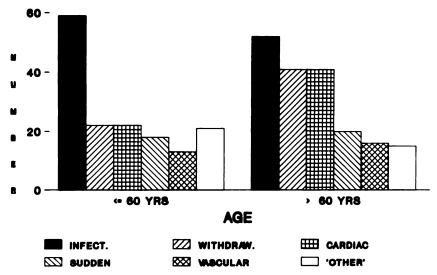


Figure 2. The different pattern of deaths in patients below and over 60 yr of age is shown.

TABLE 4.	Renal diagnoses	as a percentage of	f each cause of death

Di ag nosesª	N	Infection $(N = 111)$	Withdrawal (N = 63)	Cardiac (<i>N</i> = 63)	Sudd e n (<i>N</i> = 38)	Vascular (N = 29)	"Oth er" (N = 36)
				(%)		
CGN	74	23.4	19.0	17.5	23.7	17.2	30.6
PKD	16	4.5	3.2	0.0	7.9	6.9	11.1
DIAB	99	26.1	27.0	38.1	47.4	27.6	8.3
RVD	56	9.0	23.8	25.4	7.9	31.1	8.3
"Other"	95	37.0	27.0	19.0	13.1	17.2	41.7

^a CGN, chronic glomerulonephritis; DIAB, diabetes mellitus; RVD, renai vascular disease; PKD, polycystic kidney disease; "Other," transplant rejection, amyloidosis, tubulointerstitial nephritis, chronic pyelonephritis, obstructive uropathy, collagen vascular disease, malignant hypertension, miscellaneous, and unknown renail disorders.

presence of cancer. Other proximate factors were related to "quality of life" issues. Pain, either from peripheral neuropathy or related to cancer, was present in one third of the patients. Progressive dissatisfaction with the type of lifestyle, dementia, and an urgent need for surgery, usually orthopedic or vascular, were prominent precipitating factors leading to the decision to withdraw from dialysis. At least 40 patients volunteered that they were "at peace with themselves" and felt an inner calm after making the decision to withdraw.

An examination of the hazard function for deaths by withdrawal, cardiac causes, and infectious causes revealed different patterns of death. However, the relatively small number of deaths in each group may limit formal inference from these curves. Although the risk of death from withdrawal appears to be steady during the first 8 yr on dialysis, we do notice a later change with an increased risk of death due to withdrawal existing between 102 and 162 months on dialysis, compared with cardiac and infectious causes of death. Cardiac causes displayed decreased risk after 126 months, and the risk of infectious deaths was level throughout the study period.

DISCUSSION

Dialysis is a readily accessible life-sustaining treatment for patients with ESRD. There have been several publications from individual programs and a few network registries about survival, the relationship to particular diseases, and other comorbid conditions all highlighting the increasing age of entering dialysis patients and the rising number of diabetics (10,15– 19,21,23,27,28,36,38–40). Only a few studies, however, have addressed causes of death, in general, and, in particular, withdrawal from dialysis. The reports describing withdrawal from dialysis have emanated mainly from Kjellstrand and his associates (22–32).

Withdrawal from dialysis has become more impor-

Factors	N۵	Comment
Weight Loss or Malnutrition	48	
Pain	21	9 with cancer
"Quality of Life"	16	7 with diabetes mellitus
Dementia	14	
Cancer	12	2 with multiple myeloma
Peripheral Vascular Disease with Need for Surgery/Ampu- tation	11	
Stated Wishes	11	
Imminent Surgery	8	5 with diabetes mellitus
Immobility	7	
Gastropathy	5	5 with diabetes mellitus
Fractures Requiring Surgery	3	
Total	156	

TABLE	5.	Comorbid conditions and precipitating
factor	s a	ssociated with withdrawal

^a Most patients had more than one associated risk factor or comorbid condition.

tant as patients and physicians have to deal with the concepts of the right to die with dignity, quality of life issues, and the increasing use of health care proxies and living wills (22,41-43). At times, patients with severe pain, physical impairment, or neurologic disability request that dialysis be stopped, after a discussion with the nephrologists. Both the patient care team and family members were closely involved in the process leading to withdrawal from dialysis. Almost always, the patients mentioned their thoughts first to the nephrologists. Frequent discussions were then held between the patient, family, and health care team to assure ourselves that there was no acute depressive reaction. On occasion, we considered the family's wishes or even suggested that dialysis could be discontinued, if there had been an advance directive or if a clear decision made by the patient, especially in the presence of significant physical impairment or neurologic disability. In addition, physician and/or patient bias could lead to an inability to consider voluntary withdrawal from dialysis. We have allowed open discussion about the initiation and withdrawal of dialysis therapies since the inception of our program. This experience is supported by the results of a recently published survey of nephrologists' attitudes (44).

We have suspected that the educational and socioeconomic levels of these patients are above average because of the census tract of the catchment area of our hospital and interactions with the patients. In support of these thoughts, Kjellstrand has suggested that withdrawing patients are more sophisticated and have higher socioeconomic status (27).

Despite numerous reports that cardiovascular diseases are the leading cause of death in dialysis patients, we have shown that infections have been the most frequent cause of death, in this 20-yr experience as in our prior report (21). However, the time patterns of cardiac and withdrawal deaths have differed from one another, with the majority of cardiac deaths occurring early with none after 10.5 yr compared with a late peak of withdrawal deaths at 8.5 to 13.0 yr. Our experience has differed from Canadian reports that show no difference in age or comorbid conditions in withdrawing patients but that suggest that chronic heart failure with poor exercise tolerance was the major proximate precipitating factor (32). There was only one diabetic (9.1%) in that withdrawing population compared with the higher proportion of diabetics in Kjellstrand's and our patients (27,28). The older patients and those with diabetes mellitus and renal vascular disease withdrew most frequently. Reports by Neu and Kjellstrand concur that most withdrawals occurred in the older and diabetic patients (22,26-31).

It should be noted that dialysis patients who were doing well did not withdraw from dialysis. Patients on home modalities, who tend to have longer survivals, did not withdraw from dialysis. There were few diabetics and patients with renal vascular disease on home hemodialysis. As the patients aged, the proportion of deaths due to infections decreased as the proportion of deaths due to withdrawal and cardiac deaths increased (Figure 2). We speculate that voluntary withdrawal might become more common in the future as the age of patients initiating dialysis increases.

As expected, several concurrent comorbid conditions and proximate factors were present. At the time of withdrawal, 12 patients had cancer, 14 had dementia, 39 had known cardiovascular disease, and 38 had recent significant weight loss. Dissatisfaction with lifestyle, pain, and the upcoming need for surgery were prominent reasons given for deciding to withdraw from dialysis. Many of these patients expressed subjective thoughts that they were doing very poorly.

The recent airing of medical ethical issues has led to more open discussions about initiation and withdrawal from dialysis. As long as we accept every dialysis patient regardless of age, diagnosis, socioeconomic status, or chance for survival, we should be prepared to allow patients to withdraw from dialysis. The advancing age of new dialysis patients with more serious medical problems has led to frequent discussions about the wisdom of even initiating dialysis. We believe that dialysis resources must be treated as unlimited until we can better predict who will do well on dialysis. Similar principles have been espoused by Kjellstrand and Kilner (27,42,43). Therefore, both acceptance and withdrawal policies must be liberal and discussed openly with prospective patients. The sense of "peace of mind" and "inner calm" that followed such decisions suggested that the patient made the proper and correct decision.

In summary, withdrawal from dialysis is a frequent cause of death, accounting for 18.5% of all deaths. Patients over 61 yr of age have the highest proportion of deaths due to voluntary withdrawal. More than 50% of patients withdrawing from dialysis had either diabetes mellitus or renal vascular disease. Withdrawal from dialysis may be a common cause of death, especially in the older patients and in those with the more serious renal diagnoses of diabetes mellitus and renal vascular disease. Our experience, as reported here, suggests that more investigation into the attitudes about the acceptability to patients and staff of withdrawal from dialysis may be warranted.

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