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Dialysis, time and death: comparisons of two consecutive decades among patients treated at the same Brazilian dialysis center

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Abstract

The survival of hemodialysis patients is likely to be influenced not only by well-known risk factors like age and comorbidity, but also by changes in dialysis technology and practices accumulated along time. We compared the survival curves, dialysis routines and some risk factors of two groups of patients admitted to a Brazilian maintenance hemodialysis program during two consecutive decades: March 1977 to December 1986 (group 1, N = 162) and January 1987 to June 1997 (group 2, N = 237). The median treatment time was 22 months (range 1-198). Survival curves were constructed using the Kaplan-Meier method and compared using the log-rank method. The Cox proportional hazard regression model was used to investigate the more important variables associated with outcome. The most important changes in dialysis routine and in patient care during the total period of observation were the progressive increase in the dose of dialysis delivered, the prohibition of potassium-free dialysate, the use of bicarbonate as a buffer and the upgrading of the dialysis equipment. There were no significant differences between the survival curves of the two groups. Survival rates at 1, 5 and 10 years were 84, 53 and 29%, respectively, for group 1 and 77, 42 and 21% for group 2. Patients in group 1 were younger (45.5 ± 15.2 *vs* 55.2 ± 15.9 years, P<0.001) and had a lower prevalence of diabetes (11.1 *vs* 27.4%, P<0.001) and of cardiovascular disease (9.3 *vs* 20.7%, P<0.001). According to the Cox multivariate model, only age (hazard ratio (HR) 1.04, confidence interval (CI) 1.03-1.05, P<0.001) and diabetes (HR 2.55, CI 1.82-3.58, P<0.001) were independent predictors of mortality for the whole group. Patients of group 2 had a lower prevalence of sudden death (19.1 *vs* 9.7%, P<0.001). After adjusting for age, diabetes and other mortality risk factors, the risk of death was 17% lower in group 2, although this difference was not statistically significant. We conclude that the negative effects of advanced age and of higher frequency of comorbidity on the survival of group 2 patients were probably offset by improvements in patient care and in the quality and dose of dialysis delivered, so that the survival curves did not undergo significant changes along time.

Key words
- Chronic renal failure
- Hemodialysis
- Kaplan-Meier survival curves
- Risk factors

Introduction

In 1987 we reported the outcome of all patients admitted to a maintenance dialysis program in our Service during the previous decade (1). Since that time, many changes have been introduced in the dialysis routine and in patient care intended to reduce patient mortality and morbidity. In addition, shifts in the demographic characteristics of the dialysis population have possibly also influenced the outcome. The purpose of the present study was to compare the survival rates and some risk factors observed in patients initiating dialysis during that period with those of patients admitted to the program during the following decade. We believe that the data collected here will allow a better understanding of the consequences of our past and current dialysis routines and will serve as a basis for future improvements and corrections of these practices. Moreover, they will also be of interest as a comprehensive description of some dialysis practices and results outside North America and Europe, considering the paucity of data on the subject in the literature.

Material and Methods

Subjects

Between March 28, 1977, and June 30, 1997, 399 terminal renal failure patients were admitted to our maintenance dialysis program. No selection criteria were applied for enrollment in the program and no patient was excluded from analysis. Fifty-two patients (13%) had started dialysis at other centers. For those patients, the average duration of dialysis before admission to our Service was 7 months. Only 15 (4%) of the patients transferred from other centers had been on dialysis for more than 1 year. The causes of renal failure were the following: diabetic nephropathy, 21%; hypertensive kidney disease, 18.8%; chronic glomerulonephritis, 12.8%; interstitial nephropathy, 10%; polycystic kidney disease, 5.8%; others, 7.3%, and undetermined, 24.3%. Less than 15% of the diagnoses were based on biopsies. Necropsies were not performed.

Patients were divided into two groups: those initiating dialysis between March 28, 1977 and December 31, 1986 (group 1, N = 162) and those initiating dialysis between January 1, 1987 and June 30, 1997 (group 2, N = 237). Follow-up ranged from 1 to 198 months and the observation period ended on July 31, 1997. The mean duration of follow-up for the entire cohort was 37 ± 40 months and the median 22 months. The corresponding data for group 1 were 46 ± 46 and 28, while those for group 2 were 32 ± 35 and 20, respectively. The follow-up ended when patients died, were transplanted, changed to peritoneal dialysis or were transferred to other dialysis facilities. Data were collected from the dialysis center medical records. The following data were recorded: gender, race (white/nonwhite), age at the initiation of dialysis, presence of diabetes, cardiovascular disease (angina, myocardial infarction, cerebrovascular accident, congestive heart failure, arteriopathy), hypertension (predialysis systolic blood pressure >160 and/or diastolic blood pressure >90 mmHg at three different times) and of other comorbid conditions, dialysis duration and causes of death (cardiac, cerebrovascular accident, malnutrition, infection, gastrointestinal bleeding, hepatic insufficiency, cancer and others).

During the first decade, antihypertensive treatment was based on propranolol and methyl-dopa. After 1990, ACE-inhibitors and calcium-blocking drugs were frequently used alone or in combination with the aforementioned drugs. Treatment with calcitriol and erythropoietin was initiated in 1988. Roughly 70% of our patients are currently taking at least one of these medications. Until May 1995, all patients were under the direct care of the authors, and this responsibility has been shared with doctors contracted thereafter.

Dialysis

The study was conducted in a community hospital-based dialysis center that initiated its activities on March 28, 1977. The hospital serves an area near downtown São Paulo with a population of 1,400,000 inhabitants. Initially, hemodialysis was performed using a cuprophane coil dialyzer and a recirculating delivery system. Water treatment equipment was limited to particulate filters until August 1984. Since then, softeners and deionizers have been used, together with cuprophane hollow-fiber dialyzers. A single-pass delivery system was introduced in September 1987. Polysulphone dialyzers (1.4 to 2.0 m^2 of surface area, reused 6 to 10 times) replaced those made of cuprophane in May 1995. Hollow-fiber dialyzer disinfection was initially performed with formaldehyde. Since 1995 this procedure has been carried out using a peroxyacetic acid disinfectant. Sodium bicarbonate replaced sodium acetate as the buffer in August 1984. Potassium concentration in the dialysate (mEq/l) was 2.5 (1977 to 1983), 0 (1984 to 1988) and 1.5 (from 1989 onward). Proportional delivery systems were never employed.

Hemodialysis was performed through an arteriovenous fistula or a subclavian catheter. Some patients were started on intermittent peritoneal dialysis before a suitable vascular access was available. Continuous ambulatory peritoneal dialysis (CAPD) was never employed. During the first 5 years, 1/4 of our patients, usually women and males of low body weight, were dialyzed for 4 h twice a week, while all the other patients were dialyzed for 4 h three times a week. Since then, the proportion of individuals dialyzed twice a week was gradually reduced so that, after 1989, all our patients were dialyzed for a minimum of 12 h per week. Kt/V calculations were employed after 1994 as a base to increase, but never to decrease the duration of the dialysis section. The lowest acceptable Kt/V was 1.2. Mean current Kt/V in our service is 1.36.

Statistical analysis

Unless otherwise indicated, all values are reported as means ± SD. The unpaired Student *t*-test and chi-square test were used to compare continuous and categorical variables, respectively. Patient survival was calculated from the date of admission to dialysis to the date of death. Crude mortality estimates were obtained by dividing the number of patients who died during a period of 12 months by the number of patients at risk during the same period. Survival curves were constructed using the Kaplan-Meier method (2). Differences between curves were determined using the log-rank test. The Cox proportional hazard regression model (BMPD-PC Statistical Software, Los Angeles, CA) was used to determine independent associations of several prognostic variables with patient survival. Initially, univariate models were constructed. The variables found to significantly affect patient survival were then included in multivariate models. All statistical tests were two-sided. A P value of less than 0.05 was considered to be statistically significant.

Results

Although there was a considerable overlap in terms of the dialysis routines and technology employed in the two groups, some trends could be identified. Patients of group 1 were dialyzed during shorter periods of time using less advanced dialysis equipment and inadequate water treatment. They were also exposed to potassium-free dialysate and to acetate for longer periods of time. Finally, they did not have access to dialysis modeling or to treatment with calcitriol and erythropoietin.

Table 1 - Clinical characteristics of the patients in the present study.

NS, Nonsignificant. The Student *t*- and chi-square tests were used to compare groups.

Clinical characteristics	Group 1 (N = 162)	Group 2 (N = 237)	P
Age (years)	45.5 ± 15.2	55.2 ± 15.9	<0.001
Whites (%)	87.0	90.3	NS
Males (%)	53.1	57.0	NS
Diabetes	18 (11.1%)	65 (27.4%)	<0.001
Cardiovascular diseases	15 (9.3%)	49 (20.7%)	<0.001
Coronary artery disease	7	18	
Congestive heart failure	1	9	
Cerebrovascular accident	4	12	
Pericarditis	3	4	
Peripheral vascular disease	0	6	
Hypertension	79 (48.8%)	102 (42.8%)	NS
Gastrointestinal disease	12 (7.4%)	8 (3.4%)	NS
Liver disease	4 (2.5%)	5 (2.1%)	NS
Malnutrition	5 (3.1%)	5 (2.1%)	NS
Chronic obstructive lung disease	3 (1.8%)	5 (2.1%)	NS
Tuberculosis	5 (3.1%)	3 (1.3%)	NS
Cancer	2 (1.2%)	4 (1.9%)	NS
Others	17 (10.5%)	22 (9.3%)	NS

Table 2 - Number of patients at risk per year of observation and crude annual death rate.

*P<0.05 (Student *t*-test).

Year	Patients at risk (N)	Crude mortality (%)
1977	15	17
1978	24	15
1979	31	16
1980	35	9
1981	42	7
1982	48	10
1983	53	11
1984	57	10
1985	67	16
1986	67	21
Mean ± SD	43.9 ± 17.7	13.2 ± 4.4
1987	62	10
1988	79	16
1989	82	12
1990	84	14
1991	81	14
1992	87	18
1993	83	13
1994	87	16
1995	92	18
1996	97	20
Mean ± SD	83.4 ± 9.2*	15.1 ± 3.1

Table 1 shows the clinical characteristics of the patients. Patients in group 1 were 10 years younger (45.5 ± 15.2 *vs* 55.2 ± 15.9 years, P<0.001) and had a lower prevalence of diabetes (11.1 *vs* 27.4%, P<0.001) and of cardiovascular diseases (9.3 *vs* 20.7%, P<0.001) compared to group 2. The prevalence of the other variables tested did not differ between groups.

During the periods of observation, there were 96 deaths in group 1 (59.2%) and 105 in group 2 (44.3%). Median survival was 63 ± 10 and 51 ± 6 months for groups 1 and 2, respectively. The number of patients at risk per year of observation with the respective crude annual mortality rates is shown in Table 2. The number of patients at risk was almost two times higher during the second treatment decade (44 ± 18 *vs* 83 ± 9, P<0.05), while the mean crude mortality rates for the two periods were closely similar (13 ± 4 *vs* 15 ± 3%, NS).

The survival curves did not differ between groups (Figure 1). The survival rates tended to be slightly better in group 1, but the difference did not reach statistical significance. Actuarial survival at 1, 5 and 10 years was 84, 53 and 29% for group 1 and 77, 42 and 21%, for group 2, respectively. The mean annual actuarial mortality was 6.1 and 7.9 for groups 1 and 2, respectively. In both groups, the actuarial mortality was about 15% during the first two years of observation and fell to 10% or less during the subsequent years. Table 3 shows the causes of death of the two groups. Patients of group 1 had a higher prevalence of sudden death (19.1 *vs* 9.7%, P<0.001) and of overall cardiovascular death (28.4 *vs* 16.9%, P<0.01). There were no significant differences between groups for the other causes of death.

Considering all patients, the variables that interfered significantly with the outcome as determined by univariate analysis were age (hazard ratio (HR) 1.05, confidence interval (CI) 1.04-1.06, P<0.001), white race (HR 1.58, CI 1.01-2.47, P = 0.04), the presence of cardiovascular disease (HR 2.32, CI 1.64-3.29, P<0.001) and diabetes (HR 3.53, CI 2.56-4.89, P<0.001) (Table 4). Multivariate analysis showed that only age (HR 1.04, CI 1.03-1.05, P<0.001) and diabetes (HR 2.55, CI 1.82-3.58, P<0.001) were independent predictors of higher mortality (Table 5). Each additional year of age at initiation of dialysis increased the risk of death by 4%, while diabetics faced a probability of death 2.5 times higher. After adjusting for age, diabetes and for other risk factors, the probability of death for group 2 was 17% lower, but the difference was not statistically significant (HR 0.83, CI 0.61-1.14, P = 0.25). Race, gender and the presence of hypertension, cardiovascular disease and other comorbid conditions also did not independently influence outcome.

Discussion

This study provides a detailed description of the dialysis routines and the results achieved by a typical community hospital-based dialysis facility located in the most affluent region of Brazil.

The main finding of this investigation was the lack of a significant difference in the survival rates of the two populations studied. Indeed, the actuarial survival tended to be lower in group 2, although the difference was not statistically significant. The lack of improvement in outcome with time is somewhat surprising, considering the important progress in dialysis technology and in patient care over the years covering the period of study. This is true even assuming that the dialysis equipment in use at most Brazilian dialysis centers, including our own, is outmoded by international standards (3). A likely explanation for this result lies in the fact that patients of group 2 were a decade older, had three times more diabetes and two times more cardiovascular diseases compared with patients of group 1. It is well known that age, diabetes and cardiovascular diseases have a strong negative influence on the prognosis of dialysis patients (4-6). Moreover, our data show that age and diabetes were independent risk factors for the whole population of patients. Therefore, it seems that improvement brought about by treatment during the last decade was counterbalanced by the increase in the prevalence of risk factors, the

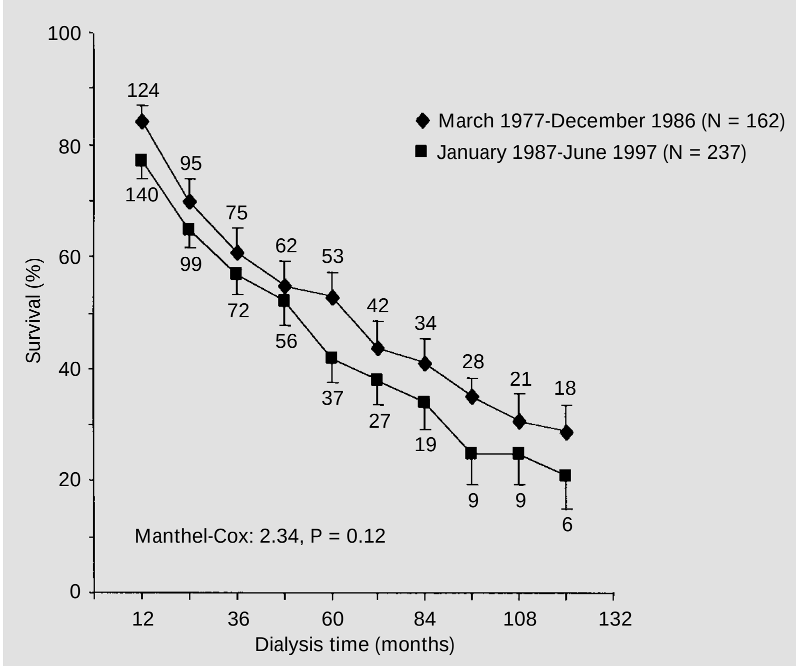

Figure 1 - Kaplan-Meier survival curves for patients on dialysis from March 1977 to December 1986 (N = 162; lozenges) and from January 1987 to June 1997 (N = 237; squares). Bars indicate the SEM. Numbers over or under the bars indicate number of patients at risk at the beginning of each time interval for each group.

Table 3 - Causes of death.

Cause of death	Group 1	Group 2	P
Sudden death	31 (19.1%)	23 (9.7%)	<0.01
Others, cardiac	6 (3.7%)	6 (2.5%)	NS
Cerobrovascular accident	9 (5.5%)	11 (4.6%)	NS
Cardiovascular deaths (global)	46 (28.4%)	40 (16.9%)	<0.01
Malnutrition	11 (6.8%)	17 (7.2%)	NS
Infection	16 (9.9%)	23 (9.7%)	NS
Gastrointestinal bleeding	4 (2.5%)	2 (0.8%)	NS
Hepatic failure	3 (1.8%)	0 (0%)	NS
Cancer	3 (1.8%)	3 (1.3%)	NS
Miscellaneous	10 (6.2%)	19 (8.0%)	NS

NS, Nonsignificant (chi-square test).

Table 4 - Univariate proportional hazard analysis of variables associated with mortality in dialysis patients.

Cox proportinal regression analysis.

Variable	Regression coefficient	Standard error	Hazard ratio	95% Confidence interval	P
Group (2)	-0.2635	0.1484	1.30	0.97-1.74	0.08
Age	0.0458	0.0052	1.05	1.04-1.06	<0.001
Gender (male)	0.0159	0.1430	1.02	0.77-1.34	0.91
Race (white)	0.4548	0.2278	1.58	1.01-2.47	0.04
Diabetes	1.2622	0.1653	3.53	2.56-4.89	<0.001
Cardiovascular diseases	0.8438	0.1766	2.32	1.64-3.29	<0.001
Hypertension	-0.0857	0.1467	0.92	0.69-1.22	0.56
Comorbidity (others)	0.1184	0.1517	1.13	0.84-1.52	0.43

Table 5 - Multivariate proportional hazard analysis of variables associated with mortality in dialysis patients.

Cox proportinal regression analysis.

Variable	Regression coefficient	Standard error	Hazard ratio	95% Confidence interval	P
Group (2)	-0.1828	0.1594	0.83	0.61-1.14	0.25
Age	0.0414	0.0057	1.04	1.03-1.05	<0.001
Race (white)	0.0855	0.2351	1.09	0.69-1.73	0.30
Diabetes	0.9375	0.1719	2.55	1.82-3.58	<0.001
Cardiovascular diseases	0.3493	0.1861	1.42	0.98-2.04	0.08

net result being the stabilization of the survival curves. It should, however, be emphasized that some dialysis practices and routines were common to both periods, an almost unavoidable problem when dealing with retrospective studies. This makes it impossible to pinpoint which practices influenced the results but does not invalidate the general idea that the quality of dialysis improved along the years. That some improvement in treatment did occur is indicated by the important reduction in the prevalence of sudden and global cardiovascular death of group 2 despite the increase in age and in the prevalence of diabetes and of cardiovascular disease. Also, the probability of death for group 2, after adjusting for age, diabetes and other variables, was 17% lower, but the difference was not statistically significant.

The survival rates reported here are intermediate between those in Europe and in the United States, while the causes of death and their proportion were not different from those reported in the literature in general (7). In Europe, the average actuarial 1-year and 5-year survival rates are 85 and 60%, respectively (8,9). In the United States, the respective figures are 75 and 49% (6). The crude annual mortality rate in the US is also higher than that reported here, reaching 22% during the first year of dialysis (6). However, comparisons between our results and those of the literature should be interpreted with caution because the data have not been adjusted for age or for other factors known to influence survival. For instance, the mean age of patients initiating dialysis in the United States is 59.6 years, roughly 5 years more than our patients of group 2 and 15 years more than our patients of group 1 (6). Also, the proportion of dialysis patients with diabetes in the United States is higher (37.3%) (6). On the other hand, individuals who die within the first 90 days of dialysis are excluded from US national ESRD mortality rates, in contrast to the procedures followed in the present investigation. Taken together, these data indicate that the results achieved by our Service are probably closer to those reported in the United States than to those reported in Europe. As mentioned above, there are few data concerning the survival rates of patients on dialysis in Brazil. Sesso et al. (10) reported an actuarial first-year survival of 80% and a crude mortality rate of 17% among 1483 individuals admitted to dialysis facilities in the State of São Paulo in 1991. Their patients were of similar age but presented a lower prevalence of diabetes (8%) compared to the individuals in our investigation.

In conclusion, the present study shows a stable long-term survival rate of hemodialysis patients during 20 years of observation despite an increase in the prevalence of risk factors. It also provides a detailed description of dialysis routines over the last twenty years at a typical hospital-based dialysis facility in southeast Brazil.

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