Avaliação da sobrevida de cinco anos em hemodiálise no Brasil: uma coorte de 3.082 pacientes incidentes

Assessment of a five-year survival on hemodialysis in Brazil: a cohort of 3,082 incident patients

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RESUMO

O Brasil tem o terceiro maior contingente de pacientes em hemodiálise (HD) no mundo. Todavia, pouco conhece-se sobre a taxa de sobrevida e os preditores do risco de mortalidade nessa população, que são os objetivos deste estudo. Um total de 3.082 pacientes incidentes em HD, de 2000 a 2004, em 25 unidades de diálise distribuídas por 7 dos 26 estados do Brasil, foi acompanhado até 2009. Os pacientes tinham entre 52 ± 16 anos de idade, 57,8% eram homens e 20,4%, diabéticos. O desfecho primário foi de mortalidade por todas as causas. Os dados foram censurados aos cinco anos de seguimento. A taxa global de sobrevida em cinco anos foi de 58,2%. No modelo proporcional de Cox, as variáveis associadas ao risco de óbito foram: a idade (risco relativo – RR = 1,44 por década; p < 0,0001), diabetes (RR = 1,51; p < 0,0001), albumina sérica (RR = 0,76 por g/dL; p = 0,001), creatinina (RR = 0,92 por mg/dL; p < 0,0001) e fósforo (RR = 1,06 por mg/dL; p = 0,04). Os resultados mostram que a taxa de mortalidade em HD nesta coorte brasileira foi relativamente baixa, mas a população é mais jovem e com prevalência de diabetes mais baixa do que aquela descrita nos países desenvolvidos.

Palavras-chave: Diálise Renal. Análise de Sobrevida. Insuficiência Renal Crônica. Estudos de Coortes. Hemodiálise. Mortalidade.

ABSTRACT

Brazil has the third largest contingent of patients on maintenance hemodialysis (HD) worldwide. However, little is known regarding survival rate and predictors of mortality risk in that population, which are the purposes of this study. A total of 3,082 patients incident on HD, from 2000 to 2004, at 25 dialysis facilities distributed among 7 out of 26 states of Brazil were followed-up until 2009. Patients were 52 ± 16 years-old, 57.8% men, and 20.4%, diabetics. The primary outcome was all causes of mortality. Data were censored at five years of follow-up. The global five-year survival rate was 58.2%. In the Cox proportional model, variables associated with risk of death were: age (hazard ratio – HR = 1.44 per decade, p < 0.0001), diabetes (HR = 1.51, p < 0.0001), serum albumin (HR = 0.76 per g/dL, p = 0.001), creatinine (HR = 0.92 per mg/dL, p < 0.0001), and phosphorus (HR = 1.06 per mg/dL, p = 0.04). The present results show that the mortality rate on HD in this Brazilian cohort was relatively low, but the population is younger and with a lower prevalence of diabetes than the ones reported for developed countries.

Keywords: Renal Dialysis. Survival Analysis. Renal Insufficiency, Chronic. Cohort Studies. Hemodialysis. Mortality.

INTRODUCTION

Developed countries are the virtually source of all epidemiological studies regarding outcomes of patients on hemodialysis (HD). Most nephrologists in developing countries make their decisions based on those studies. However, we still do not know if the conclusions of those studies are appropriate in the setting of HD in impoverished nations, with different demographic and clinical profiles.[1]

Brazil has the third largest contingent of patients on maintenance HD worldwide.[2] However, little is known regarding survival rate and predictors of mortality risk in that population. It is estimated that about 70,000 patients are on maintenance HD and 8,000 on peritoneal dialysis in the country.[3] Previous studies suggest important differences between the profile of the population on HD, in Brazil, and the one in developed countries.[1,3-5]

The objectives of the present study were to draw the profile of a large HD population in a developing country, and to define the long-term predictors of death risk in this setting.

Methods

This is a retrospective analysis of all incident patients on HD at every dialysis center franchised by Fresenius Medical Care in Brazil, from January 1, 2000 to June 30, 2004. The 25 dialysis facilities were distributed among 7 out of 26 states of Brazil: Rio de Janeiro (n = 13), Brasília (n = 3), Ceará (n = 3), Pernambuco (n = 2), Piauí (n = 2), Minas Gerais (n = 1), and São Paulo (n = 1). Patients included in this study were followed-up until June 30, 2009. Data were censored at five years of follow-up. Primary outcome was all cause mortality. Patients younger than 18 years-old and those who died before 90 days on HD were excluded from the analysis.

Data source

Data were extracted from Latin America Fresenius Medical Care database. Information at every dialysis facility were collected using the same electronic record, which was called Fresenius Medical Care Register, and was monthly sent to the headquarter of the Registry in Buenos Aires, Argentina. Demographic, clinical and laboratory data, on a monthly basis, from all patients, were collected.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median and interquartiles range. Categorical variables were presented as frequencies. The survival rate was calculated by Kaplan-Meier method; curves were compared by the Log-Rank test. Hazard ratio for death was estimated by a Cox proportional model with adjustment for demographic, clinical, and laboratory variables. Only laboratory variables that showed p-values lower than 0.10 in the univariate assessment were included in the multivariate analysis. At the end, p-values lower than 0.05 were considered significant. The software SPSS, version 18.0 for Windows, was used for statistical analysis.

Results

A total of 3,221 incident patients were initially included in this analysis, but 77 were excluded due to missing data, and 62 were younger than 18 years-old. The baseline characteristics of the remaining 3,082 patients are presented in Table 1. Patients were 52 ± 16 years-old, 57.8% were men and 20.4% were diabetics. The prevalence of hepatitis C and B and human immunodeficiency virus (HIV) positive serology were 4.2, 1.3 and 0.5%, respectively. Native arteriovenous fistula, graft and double-lumen catheter were the initial vascular access in 50.2, 0.4 and 49.4% of patients, respectively. However, such

Table 1 Characteristics of the incident patients (n = 3,082)

Gender (% males)	57.8
Age (years-old)	52 ± 16
< 40 (%)	22.1
40 to 49 (%)	20.5
50 to 59 (%)	22.9
≥ 60 (%)	34.5
Primary renal disease (%)	
Diabetic Nephropathy	20.4
Hypertensive Nephrosclerosis	17.9
Chronic Glomerulonephritis	8.5
Others	18.6
Unknown	34.6
Body mass index (kg/m^2)	22.7 ± 4.4
Positive anti-HCV (%)	4.2
Positive HBsAg (%)	1.3
Positive HIV (%)	0.5
Hematocrit (%)	30.6 ± 6.2
Serum albumin (g/dL)	3.8 ± 0.5
Creatinine (mg/dL)	8.2 ± 3.0
Phosphorus (mg/dL)	5.0 ± 1.7
Calcium (mg/dL)	9.0 ± 1.1
Intact PTH (pg/mL)	154 (49 – 272)

Anti-HCV: antibodies to hepatitis C virus; HBsAg: hepatitis B surface antigen; HIV: human immunodeficiency virus; PTH: parathyroid hormone. Values are expressed as frequencies, mean ± standard deviation, or median and interquartiles range.

variable was not considered in further analysis, since only 60.9% of the patients had data regarding initial vascular access.

A total of 2,061 patients dropped out before completing the five-year follow-up (47.4% died, 30.8% were transferred to other center, 15.3% had a kidney transplant, 2.5% were shift to peritoneal dialysis, 1.4% were recovering from renal function, and 1.3% abandoned the treatment).

The global five-year survival rate was 58.2%. Diabetic patients presented a poorer survival compared to nondiabetics (41.1 *versus* 62.7%; p < 0.0001), as seen in Figure 1. Survival rate decreased significantly for each decade increment. Five-year survival rates for patients < 40 years-old, 40 to 49 years-old, 50 to 59 years-old and ≥ 60 years-old were 83.5, 73.5, 54.3 and 37.9%, respectively (Figure 2). Serum albumin values at entrance were available in 2,846 cases (92.3%). Patients with serum albumin below the median (3.8 g/dL) at initiation of dialysis also presented survival rates lower than those with serum albumin ≥ 3.8 g/dL (52.5 *versus* 66.0%; p < 0.0001), as seen in Figure 3.

In the univariate analysis, age (hazard ratio – HR = 1.50; 95% confidence interval – CI: 1.44 - 1.57 per decade; p < 0.0001), diabetes (HR = 1.83; 95%CI: 1.59 - 2.10; p < 0.0001), female gender (HR = 1.16; 95%CI: 1.03 - 1.33; p = 0.015), serum creatinine at admission (HR = 0.85 per mg/dL; 95%CI: 0.83 - 0.87; p < 0.0001), serum albumin (HR = 0.59 per g/dL; 95%CI: 0.52 - 0.67; p < 0.0001), and serum phosphorus (HR = 0.95 per mg/dL; 95%CI: 0.91 - 0.99; p = 0.011) were associated with the risk of mortality (Table 2).

After adjustment, in a Cox proportional model, the only variables that persisted associated with the risk of death were age (HR = 1.44; 95%CI: 1.35 - 1.53 per decade; p < 0.0001), diabetes (HR = 1.51; 95%CI: 1.25 - 1.82; p < 0.0001), serum creatinine (HR = 0.92 per mg/dL; 95%CI: 0.88 - 0.95; p < 0.0001), serum albumin (HR = 0.76 per g/dL; 95% CI: 0.64 - 0.90; p = 0.001), and serum phosphorus (HR = 1.06 per mg/dL; 95%CI: 1.01 - 1.13; p = 0.04), as seen in Table 3.

Figure 1. Survival curves according to diabetes status.

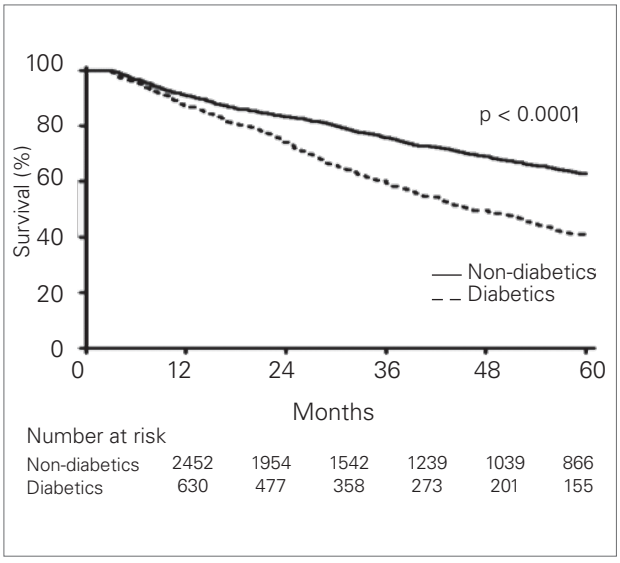

Figure 2. Survival curves according to age ranges. All survival rate comparisons by Log Rank were significantly different (p < 0.001).

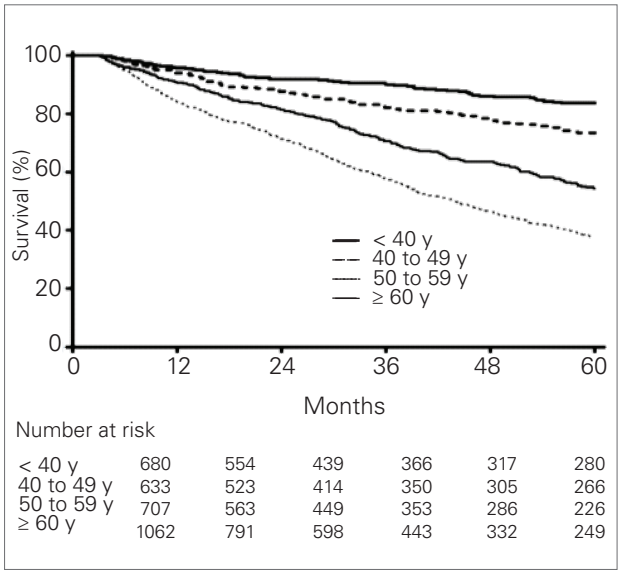

Figure 3. Survival curves according to baseline serum albumin.

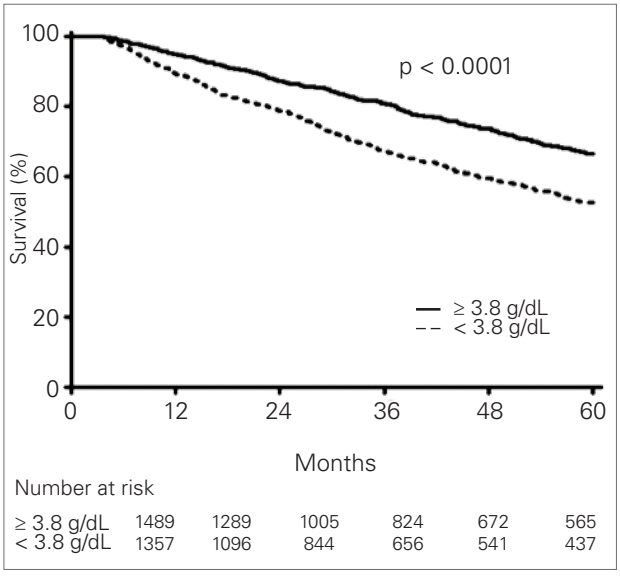

Table 2 Univariate analysis of death risk

Variable	Hazard ratio	95% confidence interval	P value
Gender (male *versus* female)	0.86	(0.75 – 0.97)	0.015
Age (decade)	1.50	(1.44 – 1.57)	< 0.0001
Diabetes (yes *versus* no)	1.83	(1.59 – 2.10)	< 0.0001
Body mass index (kg/m^2)	0.99	(0.97 – 1.01)	0.156
Hematocrit (%)	0.99	(0.98 – 1.00)	0.167
Creatinine (mg/dL)	0.85	(0.83 – 0.87)	< 0.0001
Serum albumin (g/dL)	0.59	(0.52 – 0.67)	< 0.0001
Phosphorus (mg/dL)	0.95	(0.91 – 0.99)	0.011
Calcium (mg/dL)	1.03	(0.97 – 1.10)	0.281
Intact PTH (per 100 pg/mL)	0.97	(0.94 – 1.00)	0.051

PTH: parathyroid hormone.

Table 3 Multivariate analysis of death risk by a Cox regression model

Variable	Hazard ratio	95% confidence interval	P value
Gender (male *versus* female)	0.98	(0.82 – 1.16)	0.776
Age (decade)	1.44	(1.35 – 1.53)	< 0.0001
Diabetes (yes *versus* no)	1.51	(1.25 – 1.82)	< 0.0001
Body mass index (kg/m^2)	0.98	(0.96 – 1.01)	0.125
Creatinine (mg/dL)	0.92	(0.88 – 0.95)	< 0.0001
Serum albumin (g/dL)	0.76	(0.64 – 0.90)	0.001
Phosphorus (mg/dL)	1.06	(1.01 – 1.13)	0.035
Intact PTH (per 100 pg/mL)	1.00	(0.97 – 1.03)	0.767

PTH: parathyroid hormone.

Discussion

The survival rate seen in our population was higher than the one in the United States, similar to several European countries and close to the outstanding outcomes seen in Japan.[4-6] Such low mortality rate could be partially explained by the age of our HD population and a lower proportion of diabetics when compared to HD patients in developed countries.[4-7] Only 33.8% of patients were more than 60 years-old, in accordance with the relatively young profile of Brazilian population. In 2000, for instance, only 8.6% (14.5 million people) of general Brazilian population were older than 60.[8] Thus, the profile of HD patients is a mirror of the national demographic pyramid. It should be pointed that the age profile of Brazilian population seems to be quickly changing, due to the persistent low-birth rate and progressive increase of life expectancy in Brazil.[9]

The low prevalence of diabetes is also a plausible explanation for the good outcome. The percentage of diabetes in the studied population was less than half the one reported in United States and slight lower than in most European countries.[4,5]

Other factors that could contribute to the low mortality rate are the almost universal use of native fistula as definitive vascular access, the accomplishment of at least 240 minutes per session by a vast majority of the patients, and the full time presence of nephrologists at all dialysis facilities, which is a legal local obligation.[10]

Most of the practices and procedures regarding safety on dialysis are the legacy of the reaction coordinated by the Minister of Health and Brazilian Society of Nephrology, following a tragedy that shocked the country. In 1996, 50 patients on maintenance HD in a single dialysis center at Caruaru, Pernambuco state, died after being exposed to microcystin-contaminated

water.[11] Since then, strict rules for dialysis providers were implemented,[10] which, probably, have contributed to improve the outcome on dialysis nationwide.

The profile of our HD population and long-term survival are similar to the findings of another cohort study with 1,009 incident patients from Southern Brazil.[12]

Regarding the variables associated with the risk of death, we confirmed several of the well-known risk factors as strong predictors of death, like age and diabetes. The adjusted risk of death increased 44% per each additional decade of life, and it was 51% higher for diabetic patients. The prevalence of obesity and consequently of diabetes are increasing faster in developing countries like Brazil than in industrialized nations.[13] Thus, one can anticipate a new challenge for the near future to keep the survival rate in HD in the current level.

In contrast to previous studies addressing populations from developed countries,[14] body mass index was not found to be a predictor of survival in our HD population.

Serum albumin and serum creatinine were inversely associated with the mortality risk. Such laboratory variables are dependent on clinical conditions and body muscle mass, respectively, and they are not modifiable factors in most cases. Increased serum phosphorus was associated with a higher risk of death. Even though such risk associated with serum phosphorus was not found to be as strong as that associated with serum albumin or creatinine, the former is a modifiable factor, and early attention to the control of hyperphosphatemia should be paid.

This study presents several limitations. The analysis was restricted to patients who survived the first three months on HD. We excluded early mortality from the analysis, because most patients were admitted in the clinics only after discharge from hospital where they started HD. Moreover, we would not be able to estimate the actual early mortality rate since many patients died just after initiating dialysis in the hospitalization period. Thus, the mortality rate would be higher if deaths that occurred in the first 90 days of dialysis had been considered. However, the same criteria have been used in most epidemiological studies of HD population, including those we used as reference.[4,5] Finally, we should consider that the studied population could not be completely representative of a nationwide feature, since near half of the patients are from Rio de Janeiro State.

As far as we know, this is the largest cohort of incident patients on HD from a developing country. We believe that while a national registry is not available, this study can provide important information regarding the profile and predictors of survival in maintenance HD in Brazil.

In conclusion, the mortality rate on HD in this Brazilian cohort was found to be relatively low, but the population is younger and has a lower prevalence of diabetes than the ones reported for developed countries.

Appendix

The dialysis facilities that participated in the study are the following ones:

- *Clínica de Doenças Renais* (CDR), Ingá and São Lourenço affiliates- Niterói, Rio Bonito – Rio de Janeiro, Macaé, Três Rios, Barra do Piraí, Barra Mansa, Santo Antônio de Pádua, Nova Iguaçu, São João de Meriti, Botafogo, Anil – Rio de Janeiro, Cascadura – Rio de Janeiro, Rio de Janeiro States;
- *Centro de Terapia Nefrológica* (Cetene) – São Paulo (SP);
- *Instituto Mineiro de Nefrologia* – Belo Horizonte (MG);
- *Clínica do Rim* – Petrolina (PE), *Nefroclínica* – Recife (PE);
- *Clínica Pró-Nefron* – Fortaleza (CE), Protorim – Fortaleza (CE), Prorim – Fortaleza (CE);
- Clinefro – *Clínica Nefrológica do Piauí* – Teresina (PI), Unirim – Parnaíba (PI);
- *Nephron Serviços Médicos,* Mix Park Sul, Gama and Taguatinga affiliates, Brasília *(DF)*;
- *Unidades Mix Park Sul, Gama e Taguatinga*.

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