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Impact of clinical, sociodemographic and quality of life factors on dialysis patient survival: a nine-year follow-up cohort study

Impacto de fatores clínicos, sociodemográficos e de qualidade de vida na sobrevida de pacientes em diálise: um estudo de coorte com nove anos de seguimento

Impacto clínico, sociodemográfico y factores de calidad de vida en la supervivencia de pacientes con diálisis: estudio de cohorte durante un periodo de nueve años

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Abstract

Although renal replacement therapy has contributed to the survival of chronic kidney failure (CKF) patients, mortality remains a major concern. This study aimed to identify the factors associated with mortality in a prospective cohort of CKF patients. Sociodemographic, clinical, nutritional, lifestyle and quality of life data were collected from 712 patients. The instruments used were the Short-Form Health Survey *(SF-36),* Global Subjective Assessment *(GSA) and Charlson Comorbidity Index (CCI) questionnaires. A total of 444 patients died during the study. After five years of follow-up, factors such as not being married (hazard ratio – HR = 1.289, 95%CI: 1.001; 1.660), a low frequency of leisure activities (HR = 1.321; 95%CI: 1.010; 1.727) and not being transplanted (HR = 7.246; 95%CI: 3.359; 15.630) remained independently associated with the risk of mortality. At the end of the follow-up period, factors such as not being married (HR = 1.337, 95%CI: 1.019; 1.756), not being transplanted (HR = 7.341, 95%CI: 3.829; 14.075) and having a worse nutritional status (HR = 1.363, 95%CI: 1.002; 1.853) remained independently associated with an increased risk of mortality, whereas a high schooling level (10 to 12 years, HR = 0.578, 95%CI: 0.344; 0.972; and over 12 years, HR = 0.561, 95%CI: 0.329; 0.956) and a better SF-36 physical functioning score (HR = 0.992, 95%CI: 0.987; 0.998) were protective factors associated with survival. The survival of patients with CKF is associated with factors not restricted to the clinical spectrum. The following factors were associated with high mortality: not being married, low schooling level, a limited social routine, a longer time on dialysis, worse nutritional status, and worse physical functioning.*

Survival; Mortality; Quality of Life; Chronic Kidney Failure; Renal Replacement Therapy

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Introduction

Chronic kidney disease (CKD) is a severe public health problem worldwide, leading to millions of deaths every year due to associated clinical complications or no accessibility to available treatments [1]. All over the world, approximately 1.4 million individuals with CKD require renal replacement therapy (RRT), with an annual incidence of approximately 8% [2].

Although technological advances of the required RRT techniques have contributed to better treatment and survival quality for chronic kidney failur (CKF) patients, high mortality rates remain a major concern [1]. According to the United States Renal Data System, in 2016 mortality rates of CKF patients rose with age, particularly in the elderly [3]. Regarding RRT modalities, a shorter survival time is observed for dialysis, with lower rates at the first, second and fifth years of treatment, compared to renal transplant (Tx) [4]. In addition to posing a lower risk of mortality, Tx leads to better clinical and psychological conditions, better quality of life (QoL) and has a lower cost compared to dialysis [5,6,7].

Other factors are also related to RRT patients life expectancy. Sociodemographic characteristics, such as male sex, advanced age, and residing in the lowest HDI (Human Development Index) countries, with limited access to healthcare services [6,7,8,9,10,11,12,13,14,15,16,17], were observed as variables associated with short survival. The coexistence of low QoL scores with cardiovascular diseases, diabetes and infections has been shown to be a predictor of increased mortality in different patient groups, regardless of RRT [6,18,19,20,21].

In recent years, there has been a growing interest in understanding CKF patients survival, not only in favor of better management and more effective care but also for the implementation of precise public health policies. The growing CKF patients population has implications for planning and allocating health expenditures, since the impact of kidney treatment modalities on total health financing is relatively high compared with other diseases [22]. In Brazil, the growing CKF patients population represents a burden to public budget, since 85% to 95% of therapies are subsidized by the Brazilian Unified National Health System (SUS) [23]. Thus, several measures are necessary to reduce the economic and social effects triggered by the high prevalence of CKD in dialysis phase. In addition to health promotion and prevention actions carried out in primary care, especially for risk groups, it is necessary to include more effective and comprehensive interventions for patients who are already on RRT, considering this condition's multiple impacts on the lives of general patients. Knowledge of main QoL and survival determinants can favor better adaptation and coping with the disease and its treatment, in addition to maintaining the patient's general physical and emotional health and strengthening social and relational bonds.

Internationally, several studies have been conducted to investigate the survival of dialysis patients [8,9,10,11,12,13,14]. There is a methodological diversity regarding the study design, sample size and population groups [11,24,25]. In Brazil, population-based studies assessing the survival of patients on RRT are rare [13,19,26]. Most survival studies found in Brazilian literature use secondary data from specific CKF populations and have short follow-up [13,18,19,27,28,29,30]. To enhance causal inference capacity and results generalization, we need longitudinal studies with Brazilian population representative samples and follow-up durations long enough to capture sufficient events. A better understanding of the factors associated with the mortality of CRF patients undergoing treatment at SUS – an universal, public and free health system – can allow us to develop actions aiming health care improvement, as well as contributing to current scientific knowledge. Thus, this study sought to identify the main factors associated with mortality in different treatment periods, in a prospective cohort of CKF patients who initiated dialysis therapy at SUS.

Methods

Study design and setting

A longitudinal, 9-year follow-up study (January 2008 to May 2017) was conducted in a RRT patients cohort from twelve dialysis units of the public health system in the city of Belo Horizonte, Minas Gerais State, Brazil [31,32] (Figure 1). The Research Ethics Committee of the Minas Gerais Federal

University (UFMG) approved the research protocol (decisions 397/2006 and 1.747.336/2016), and all participants signed an Informed Consent Form.

Population

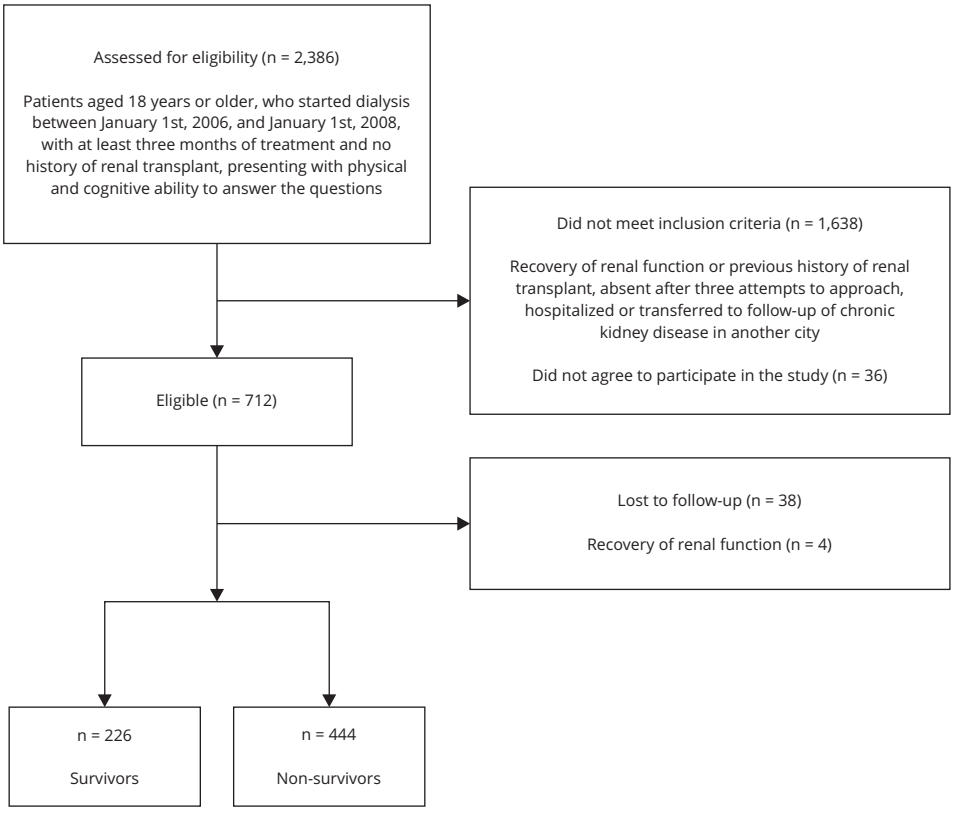
The initial cohort included all patients who matched the eligibility criteria (Figure 1). The exclusion criteria are also presented in Figure 1. Based on medical records of the dialysis units, all patients who met the inclusion criteria were contacted by the interviewers and invited to participate. Out of 2,386 patients assessed for eligibility, 748 were considered eligible for the survey, 36 refused to participate, and the final sample comprised 712 participants.

Follow-up

Data were collected between January and April 2008 through interviews conducted during dialysis sessions. Mortality data were collected in the medical records and by consulting the Mortality Information System. Survival time was calculated from the date of the interview. Three different follow-up intervals were used for the survival analysis: 1-year, 5-year and 9-year follow-up.

Figure 1

Flowchart of the study design with chronic kidney failure patient who initiated therapy in dialysis in Belo Horizonte, Minas Gerais State, Brazil, 2008.



Variables and measures

Box 1 presents a list of the variables used in this study. The data were obtained through a structured interview and by consulting medical records at the participating units.

(1) The Charlson Comorbidity Index (CCI) was used to assess the severity of comorbidity. This index comprises 19 comorbidity conditions, with scores varying from 1 to 6. The higher the total score, the more severe the clinical condition [33]. The included comorbidities, as well as their scores, are presented in Box 1.

(2) The nutritional status (nourished, suspected malnutrition and severe malnutrition) was assessed using the Global Subjective Assessment (GSA) method, which is based on the clinical and physical history of the patient [34]. This assessment addresses several aspects related to the patient´s general

Box 1

Variables used in the study with chronic kidney failure patients who initiated dialysis therapy in Belo Horizonte, Minas Gerais State, Brazil, 2008.

SOCIODEMOGRAPHIC	CLINICAL
Age (years)	**Baseline time on dialysis** (months)
Sex (female, male)	**Total time on dialysis** (months)
Skin color (black, brown, yellow, indigenous, white, others)	**Transplant** (yes, no)
Marital status (single, married, *de facto* relationship, divorced, widowed, others)	**Time on transplant** (months)
Schooling (illiterate, up to 9, 10 to 12, over 12 years)	**Renal graft loss** (yes, no)
Source of income (work, benefits, others)	**Charlson Comorbidities Index – CCI**
Has a job (yes, no)	(1) myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer, mild liver disease, diabetes; (2) hemiplegia, moderate or severe renal disease, diabetes with target-organ damage, any tumors, leukemia, lymphoma; (3) moderate or severe liver disease; (6) metastatic solid tumor, AIDS
Income (number of minimum wages)	**Medications prescribed**
Religion (yes, no)	**Global Subjective Assessment – GSA** (nourished, suspected malnutrition, severe malnutrition)
	Type of treatment (hemodialysis, peritoneal dialysis, transplant)
QUALITY OF LIFE	**LIFE HABITS**
Physical components of SF-36	**Recreational activities** (yes, no)
Physical functioning; Role physical; Bodily pain; General health status	Bars and dance clubs, street festivals, sports and cultural events, leisure associations
Mental components of SF-36	**Social groups participation** (yes, no)
Vitality; Social functioning; Role emotional; Mental health	Non-governmental organizations, workers unions, religious congregations, political parties, philanthropic organizations, sports associations and others community groups

Reported by the patient;

Obtained from the medical records at the participant units;

SF-36: *36-Item Short-Form Health Survey*.

nutritional status, such as weight loss in the last six months, changes in food intake, presence of gastrointestinal symptoms (nausea, vomiting, diarrhea and poor appetite) and functional capacity, with good diagnostic accuracy [35].

(3) Quality of life (QoL) was measured by the validated Portuguese version of the 36-*Item Short-Form Health Survey* (SF-36) [36,37,38]. The SF-36 is a tool that assesses general health status and QoL based on eight scales and two measures (Box 1). Scores range from 0 to 100, and scores nearest to 100 indicate higher QoL.

Statistical analysis

The patients' characteristics were described as frequencies for the categorical variables and as mean and standard deviation for the quantitative variables, if the normality assumption was considered valid; otherwise, median and interquartile range were used. The differences between survivor and non-survivor groups were analyzed using the unpaired Student's t test and the Mann-Whitney test to compare normally and not normally distributed quantitative variables, respectively, and the chi-squared test was used for categorical variables. Univariate and multivariate analyses were conducted using Cox proportional hazard models to assess the influence of sociodemographic variables, type of treatment (transplant or no) and QoL, on the risk of mortality. The models were adjusted for sex, age and time on dialysis before the interview. All variables with significance $p < 0.20$ in the Cox univariate regression were tested in the multivariate model, and only those with significance of $p < 0.05$ remained in the final model. The assumption of proportional hazards was tested by adjusting the model with a time-dependent variable. The SPSS version 6.0 (https://www.ibm.com/) was used for analyses.

Results

Sample characteristics: of 712 initial participants, 4 patients (0.5%) recovered renal function, 38 (5.3%) were considered lost to follow-up due to moving from the city or not being found, and the remaining 670 were analyzed (Figure 1). Regarding mortality data, 51 (7.6%) patients died in the first year of follow-up, 264 (34.5%) died up to the fifth year, and 129 (18.1%) died up to the ninth years, totaling 444 (62.3%) deaths throughout the follow-up period. The baseline characteristics of the study population are displayed in Table 1. The mean age of the sample was 53.9±15.2 years, and most were male, married or in de facto relationships, had up to 9 years of schooling, and their main source of income was government allowances. Regarding the clinical aspects, 78.7% were well nourished, and the main diseases related to the CCI were diabetes, congestive heart failure and chronic pulmonary disease. The comparison between the survivor and non-survivor groups differed in the following aspects: age ($p < 0.01$), schooling ($p < 0.01$), presence in the labor market ($p < 0.01$), social activities ($p = 0.02$) and recreational activities ($p < 0.01$). Regarding the clinical variables and type of treatment, differences were also observed between the groups, and the survivors who were more likely to receive a Tx ($p < 0.01$), remained on dialysis for less time ($p < 0.01$), had a smaller CCI score ($p < 0.01$) and had better nutritional status ($p < 0.01$). Moreover, the survivors showed better QoL in the physical component ($p < 0.01$) and in the scales physical functioning ($p < 0.01$), role physical ($p < 0.01$), bodily pain ($p = 0.01$) and social functioning ($p < 0.01$).

After one-year follow-up, the results of Cox univariate regression analysis showed survival associated factors were: Tx (HR = 27.185, 95%CI: 1.185; 63.43), physical components (HR = 0.962; 95%CI: 0.935; 0.990) and the physical functioning scales (HR = 0.982, 95%CI: 0.973; 0.992) and bodily pain (HR = 0.989, 95%CI: 0.980; 0.999) of SF-36 (Table 2). The Cox regression models adjusted for sex, age and time on dialysis before interview did not show any mortality associated factors (Table 3).

After five years follow-up, the Cox univariate regression showed survival associated factors were: schooling (HR = 1.721, 95%CI: 1.081; 2.741), employment (HR = 1.480, 95%CI: 1.032; 2.123), Tx (HR = 10.545, 95%CI: 5.223; 21.291), CCI (HR = 1.092, 95%CI: 1.046; 1.141), nutritional status (HR = 1.667, 95%CI: 1.301; 2.134), frequency of leisure activities (HR = 1.781, 95%CI: 1.418; 2.235) and physical component scores (HR = 0.971, 95%CI: 0.959; 0.982); additionally, almost all SF-36

Table 1

Sociodemographic and clinical characteristics at baseline of CKF patients who initiated therapy in dialysis in Belo Horizonte, Minas Gerais State, Brazil, 2008, according to survival status considering the 9-year period.

Variables	Total population (n = 712)	Survivors (n = 226)	Non-survivors (n = 444)	p-value
Sociodemographic variables				
Age [mean±SD]	53.9±15.2	45.0±13.3	58.7±13.8	< 0.01
Sex (female) [n (%)]	301 (42.3)	107 (47.3)	179 (40.3)	0.82
Skin color (brown/black) [n (%)]	406 (57.7)	139 (61.5)	241 (55.3)	0.27
Married/de facto relationship [n (%)]	411 (57.7)	140 (61.9)	242 (54.5)	0.06
Religion (yes) [n (%)]	659 (92.7)	210 (92.9)	409 (92.3)	0.78
Schooling (years) [n (%)]				
Illiterate	61 (8.6)	11 (4.9)	47 (10.7)	< 0.01
Up to 9	418 (59.1)	127 (56.2)	268 (61.0)	
10 to 12	154 (21.8)	64 (28.3)	79 (18.0)	
Over 12	74 (10.5)	24 (10.6)	45 (10.3)	
Has a job	95 (13.3)	42 (18.6)	46 (10.4)	< 0.01
Number of monthly minimum wages [mean±SD]	3.9±5.5	1.9 (1.2; 3.9)	2.1 (1.3; 4.0)	0.13
Source of income [n (%)]				
Work	81 (13.6)	33 (18.4)	42 (11.0)	0.01
Benefits	506 (84.8)	146 (81.6)	332 (86.9)	
Others	10 (1.7)	0	8 (2.1)	
Clinical variables				
Baseline time on dialysis (months) [mean±SD]	13.9±8.4	14.4±8.2	13.0 (7.0; 21,0)	0.47
Total time on dialysis (months) [mean±SD]	68.0±37.7	91.9±39.5	51.0 (32,0; 79.0)	< 0.01
Total time on transplant (months) [mean±SD]	69.2±86.7	66.6±31.1	11.0 (2.0; 72.0)	< 0.01
Transplant (yes) [n (%)]	109 (16.8)	94 (42.9)	13 (3.1)	< 0.01
Renal graft loss (yes) [n (%)]	18 (17.3)	13 (14.0)	5 (50.0)	< 0.01
CCI [mean±SD]	3.3±1.7	2.0 (2.0; 3.0)	3.0 (2.0; 4.0)	< 0.01
Medications prescribed [mean±SD]	5.9±4.3	5.0 (4.0; 7.0)	6.0 (4.0; 8.0)	0.17
GSA (well nourished) [n (%)]	560 (78.7)	194 (85.8)	331 (74.5)	< 0.01
Habits				
Recreational activities * (no) [n (%)]	502 (70.5)	182 (80.5)	291 (65.5)	< 0.01
Social group * (no) [n (%)]	203 (28.6)	76 (33.6)	112 (25.3)	0.02
SF-36 scores				
Physical components [mean±SD]	40.8±9.9	42.6±9.2	39.7±10.1	< 0.01
Physical functioning	54.6±29.9	70.0 (50.0; 90.0)	45.0 (20.0;70.0)	< 0.01
Role physical	40.0±39.9	50.0 (0.0; 100)	25.0 (0.0; 75.0)	< 0.01
Bodily pain	67.0±29.6	72.0 (51.0; 100)	62.0 (41,0; 100)	0.01
General health status	59.3±22.7	61.5±20.3	60.0 (40.0; 77.0)	0.09
Mental components [mean±SD]	49.4±12.5	53.0 (43.4; 58.5)	51.5 (39.6; 60.1)	0.44
Vitality	62.4±25.1	70.0 (50.0; 77.0)	65.0 (40.0; 80.0)	0.05
Social functioning	71.2±27.9	75.0 (55.0; 80.0)	75.0 (50.0; 100)	< 0.01
Emotional role	59.8±41.9	66.6 (33.3; 100)	66.6 (66.6; 100)	0.09
Mental health	71.5±23.3	80.0 (60.0; 92.0)	76.0 (54.0; 88.0)	0.11

CCI: Charlson Comorbidity Index; GSA: Global Subjective Assessment method; SD: standard deviation; SF-36: *36-Item Short-Form Health Survey*.
Note: recreational activities and social group: participation in some social activity at least once a month. Values for categorical variables are given as number (percentage) and compared by the chi-square test. Continuous variables, presumed to have a normal distribution, were summarized by the mean±SD and compared by the t test. For other quantitative variables, median and interquartile range were used as a summary measure, and the Mann-Whitney test was used to make comparisons in the group.
* As described in Box 1.

Table 2

Cox univariate regression analyses according to follow-up intervals of chronic kidney failure patients who initiated dialysis therapy in Belo Horizonte, Minas Gerais State, Brazil, 2008, considering the 9-year period.

Variables	1-year follow-up (n = 670)		5-year follow-up (n = 264)		9-year follow-up (n = 129)	
	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
Sociodemographic variables						
Age	1.024 (1.004; 1.044)	0.01	1.034 (1.026; 1.042)	< 0.01	1.038 (1.031; 1.045)	< 0.01
Sex (female)	1.100 (0.634; 1.909)	0.73	0.923 (0.738; 1.156)	0.48	0.871 (0.720; 1.052)	0.15
Skin color (brown/black)	1.175 (0.456; 3.029)	0.73	1.159 (0.799; 1.681)	0.43	1.077 (0.784; 1.479)	0.64
Married/de facto relationship (no)	1.393 (0.804; 2.412)	0.23	1.170 (0.940; 1.461)	0.15	1.213 (1.006; 1.462)	0.04
Religion (no)	1.060 (0.382; 2.943)	0.91	1.119 (0.749; 1.671)	0.58	1.074 (0.757; 1.524)	0.69
Schooling (years)						
Over 12 (reference)						
Illiterate	1.202 (0.388; 3.728)	0.74	1.721 (1.081; 2.741)	0.02	1.648 (1.094; 2.482)	0.01
Up to 9	0.995 (0.418; 2.371)	0.99	1.028 (0.707; 1.496)	0.88	1.061 (0.773; 1,453)	0.71
10 to 12	0.399 (0.122; 1.306)	0.12	0.708 (0.455; 1.101)	0.12	0.753 (0.522; 1.087)	0.13
Has a job (no)	1.853 (0.668; 5.143)	0.23	1.480 (1.032; 2.123)	0.03	1.581 (1.165; 2.145)	< 0.01
Monthly minimum wages (n)	1.012 (0.957; 1.069)	0.68	1.012 (0.990; 1.034)	0.29	1.016 (0.997; 1.034)	< 0.01
Clinical variables						
Transplant (no)	27.185 (1.185; 63.430)	0.03	10.545 (5.223; 21.291)	< 0.01	11.177 (6.427; 19.439)	< 0.01
CCI	1.091 (0.973; 1.224)	0.13	1.092 (1.046; 1.141)	< 0.01	1.078 (1.038; 1.118)	< 0.01
Number of prescribed medications	0.996 (0.927; 1.070)	0.91	0.993 (0.965; 1.023)	0.65	1.008 (0.992; 1.025)	0.30
GSA (malnourished)	1.521 (0.833; 2.779)	0.17	1.667 (1.301; 2.134)	< 0.01	1.612 (1.302; 1.997)	< 0.01
Habits						
Recreational activities * (no)	1.727 (0.989; 3.016)	0.05	1.781 (1.418; 2.235)	< 0.01	1.643 (1.351; 2.001)	< 0.01
Social group * (no)	1.293 (0.677; 2.470)	0.43	1.261 (0.975; 1.631)	0.07	1.281 (1.034; 1.588)	0.02
SF-36						
Physical components	0.962 (0.935; 0.990)	< 0.01	0.971 (0.959; 0.982)	< 0.01	0.977 (0.967; 0.986)	< 0.01
Physical functioning	0.982 (0.973; 0.992)	< 0.01	0.985 (0.981; 0.989)	< 0.01	0.985 (0.982; 0.989)	< 0.01
Role physical	0.995 (0.988; 1.002)	0.16	0.995 (0.992; 0.998)	< 0.01	0.996 (0.993; 0.998)	< 0.01
Bodily pain	0.989 (0.980; 0.999)	0.02	0.992 (0.988; 0.996)	< 0.01	0.994 (0.991; 0.997)	< 0.01
General health status	0.994 (0.982; 1.006)	0.29	0.995 (0.991; 1.001)	0.03	0.995 (0.991; 0.999)	0.02
Mental components	0.997 (0.975; 1.019)	< 0.01	0.996 (0.987; 1.005)	0.34	0.996 (0.988; 1.003)	0.28
Vitality	0.992 (0.981; 1.003)	0.15	0.994 (0.991; 0.998)	< 0.01	0.995 (0.991; 0.998)	< 0.01
Social functioning	0.997 (0.988; 1.007)	0.55	0.995 (0.991; 0.998)	< 0.01	0.995 (0.992; 0.998)	< 0.01
Role emotional	0.998 (0.992; 1.005)	0.58	0.997 (0.995; 1.001)	0.04	0.998 (0.996; 1.001)	0.07
Health mental	0.992 (0.981; 1.003)	0.14	0.996 (0.991; 1.002)	0.06	0.995 (0.992; 0.999)	0.02

95%CI: 95% confidence interval; CCI: Charlson Comorbidity Index; GSA: Global Subjective Assessment method; HR: hazard ratio;
SF-36: *36-Item Short-Form Health Survey*.

Note: recreational and social group activities: participation in some social activity at least once a month. HR > 1.000 indicates an increasing risk of death with increasing predictive values (continuous predictor) or with the presence of one condition (binary predictor).

* As described in Box 1.

Table 3

Cox regression models per follow-up time and including factors associated with survival of chronic kidney failure patients who initiated therapy dialysis therapy in Belo Horizonte, Minas Gerais State, Brazil, 2008, considering the 9-year period.

Models	ß	HR	95%CI	p-value
1-year follow-up	-	-	-	-
5-year follow-up				
Married/de facto relationship (no)	0.254	1.289	1.001; 1.660	0.04
Recreational activities * (no)	0.278	1.321	1.010; 1.727	0.04
Transplant (no)	1.980	7.246	3.359; 15.630	< 0.01
9-year follow-up				
Married/de facto relationship (no)	0.291	1.337	1.019; 1.756	0.03
Schooling (years)				
Illiterate (reference)				
Up to 9	-0.585	0.557	0.284; 1.091	0.08
10 to 12	-0.547	0.578	0.344; 0.972	0.03
Over 12	-0.578	0.561	0.329; 0.956	0.03
Transplant (no)	1.993	7.341	3.829; 14.075	< 0.01
GSA (malnourished)	0.309	1.363	1.002; 1.853	0.04
Physical functioning (SF-36)	-0.008	0.992	0.987; 0.998	< 0.01

95%CI: 95% confidence interval; HR: hazard ratio; GSA: Global Subjective Assessment method; SF-36: *36-Item Short-Form Health Survey*.
Note: Cox regression analysis adjusted for age, sex and initial time on dialysis. Recreational activities: participation in some social activity at least once a month. HR > 1 indicates an increasing risk of death with increasing predictive values (continuous predictor) or with the presence of one condition (binary predictor).
* As described in Box 1.

scales, except mental health, which showed no significance, were associated with survival (Table 2). The Cox regression models adjusted for sex, age and time on dialysis before the interview indicated that not being married or not being in a de facto relationship (HR = 1.289, 95%CI: 1.001; 1.660), low frequency of recreational activities (HR = 1.321, 95%CI: 1.010; 1.727) and not being transplanted (HR = 7.246, 95%CI: 3.359; 15.630) remained independently associated with mortality (Table 3).

After nine years of follow-up: the univariate analysis showed that survival associated factors were: being married or in a de facto relationship (HR = 1.213, 95%CI: 1.006; 1.462), schooling (HR = 1.648, 95%CI: 1.094; 2.482), employment (HR = 1.581, 95%CI: 1.165; 2.145), Tx (HR = 11.177, 95%CI: 6.427; 19.439), CCI (HR = 1.078, 95%CI: 1.038; 1.118), nutritional status (HR = 1.612, 95%CI: 1.302; 1.997), frequency of social activities (HR = 1.281, 95%CI: 1.034; 1.588) and of leisure activities (HR = 1.643, 95%CI: 1.350; 2.001), physical components (HR = 0.977, 95%CI: 0.967; 0.986) and almost all SF-36 scales (Table 2). The Cox regression models adjusted for sex, age and time on dialysis before the interview indicated that not being married or not being in a de facto relationship (HR = 1.337, 95%CI: 1.019; 1.756), not being transplanted (HR = 7.341, 95%CI: 3.829; 14.075) and worse nutritional status (HR = 1.363, 95%CI: 1.002; 1.853) remained independently associated with increased mortality (Table 3). High schooling level (10 to 12 years, HR = 0.578, 95%CI: 0.344; 0.972; and over 12 years, HR = 0.561, 95%CI: 0.329; 0.956), as well as better physical functioning scores on SF-36 (HR = 0.992, 95%CI: 0.987; 0.998), were protective factors associated with survival.

Discussion

From our results, we observed that as period of disease increased, mortality risk factors were added and correlated with deterioration of the patient's general health status and their permanence on dialysis. CKF is associated with a broad range of complications, resulting in adverse effects on health, and it is recognized as an independent risk factor for cardiovascular and bone diseases, in addition to impairing physical, nutritional, emotional and cognitive functions [39]. In a national study carried out in the United States, the comorbidities of 1,039 patients on RRT, aged over 18 years, were assessed at the beginning of dialysis treatment and during a five-year follow-up, and the association between comorbidity and survival was verified at different intervals. They concluded that clinical worsening, as well as progressive severity of comorbidities, were independent risk factors for mortality [40]. Despite the evidence in literature, in our study, we did not find mortality associated factors in the first-year follow-up, probably due to the lack of specific clinical and laboratory parameters at baseline. Different risk factors have been related to death after the first year on RRT, such as advanced age, coexistence of cardiovascular diseases, diabetes as primary cause of CKD, no venous access for dialysis and inappropriate access to health care services at predialysis period [9,10,11,12,13,40,41].

In this study, sociodemographic characteristics and lifestyle, such as being married or being in a de facto relationship, higher schooling and participating in leisure activities, were associated with longer survival in the 5- and 9-year follow-up intervals. These factors can be included in the concepts of social support and social capital, both described as important sources of protection for physical and emotional health, as well as welfare and QoL [42,43,44,45,46,47].

Social support can be defined as the individual's social relation structures, including affective or instrumental involvement [42,43]. Various studies showed that individuals with poor social support are at higher risk of hospitalization, getting sick and mortality, both in the general population and in specific morbidity groups [44,45,46,47,48,49]. A cohort study conducted in seven countries (France, Germany, Italy, Japan, Spain, the United Kingdom and the United States) investigated the influence of social support and other psychosocial factors on mortality, compliance with medical care and QoL in 32,332 patients on hemodialysis (HD). They observed that poorer social support was associated with a higher risk of mortality, less adhesion to medical care and worse QoL [45]. Restrictions in social participation were associated with increased risk of graft loss and of all-cause mortality during a ten-year follow-up in a sample of 331 renal-transplanted patients from a university transplant center in Slovakia between 2003 and 2009 [46].

Limited social engagement results from deterioration of the patient´s clinical and emotional conditions and from being avoided by some members of his social network, who avert disease related issues. Consequently, the patient's network and family may shrink, and the closest members available may take on an increasing relevance, which may often be exclusive. In this context, marital status is considered an important social support for CKF patients. The literature shows the association between marital status and mortality and has consistently identified that single individuals usually report worse health conditions and higher risk of death than their married peers do, and men are particularly affected [48,49]. An American retrospective cohort study assessed the survival of 13,400 patients with stage 2 or more advanced CKD, and being married was one of the factors associated with better survival [48]. It is believed that married people are more likely to have healthier behaviors, given that the spouses represent a positive support to encourage the patients as they face life changes imposed after starting RRT. Moreover, it is suggested that individuals in a significant affective relationship may benefit from an extra pair of eyes to monitor their health status and keep their commitment to treatment [49].

Social capital includes economic values added by the social network, such as employment, income, schooling, and access to services. These socioeconomic factors can affect the health and well-being of the general population and have been related to the prevalence and progression of CKD [13,48,50]. In our study, higher schooling levels were predictors of longer survival, and similar results were found in cohorts of CKF patients [47,50,51]. In a nationally representative sample from the United States of incident dialysis patients, those with higher schooling presented lower waiting list times and threefold higher Tx rates, and although mortality was not associated with schooling level, increased graft loss rates were observed in the group with less schooling in this study [50]. In a Japanese cohort of

7,974 patients on HD, employment status and education were inversely associated with mortality, and only employment was associated with admissions to the hospital [52]. Employment and education are strongly associated factors, being considered income markers and, consequently, related to life expectancy. Low schooling may lead to poor compliance with treatment, partly due to communication barriers among patients and professionals, difficulty with handling medications, diet and other types of care, thus negatively impacting control of the disease. In dialysis and Tx patients, limited health knowledge has been related to lower socioeconomic status, comorbidity and mortality [50,51].

In our study, we found an association between nutritional status and survival; malnutrition assessed by GSA was an independent risk factor for mortality after a 9-year follow-up. CKF, as well as the available RRT, are major conditions for nutritional deterioration of patients over time, primarily those on dialysis [52,53,54,55]. An United States study explored the relationship between time on dialysis, nutritional status and survival in a prevalence cohort of 3,009 adult patients who underwent at least three months of dialysis treatment. They concluded that a longer time of treatment was related to worse nutritional status, with a significant decline in all nutrition parameters assessed [52]. Patients progressive malnutrition is also a predisposing factor to complications, such as coronary artery diseases and diabetes, which cause a high proportion of deaths in this population. On the other hand, low serum albumin levels, a strong marker of malnutrition, may be secondary to acute or chronic infectious and inflammatory processes, which, in turn, contribute to an increased mortality risk [53,54]. More severe malnutrition stages were also related to reduced QoL. In a study in the United States, data collected using the SF-36 and GSA instruments, added to laboratory and clinical nutritional values, showed inverse significant correlations among QoL scores and body fat percentage, anemia and low serum albumin levels in 65 patients on dialysis [55]. It is of utmost importance to monitor the nutritional status and subjective condition of well-being in CKD patients on RRT. The reason for this is the physical debilitation experienced due to malnutrition, which may be insidious and progressive, can lead to negative consequences in the functional and mental health of patients and negatively impact their survival.

After a 9-year follow-up, we found an association between the physical functioning scale of the SF-36 physical components and an increased risk of death in our cohort. This finding is consistent with data shown in the international literature, in which worse scores related to QoL physical and mental domains were associated with increased general mortality rates of CKF patients [6,7,16,17,20,21,55,56]. In recent decades, the QoL of patients on RRT has been extensively studied, since it impacts their physical and psychic capacities and vitality, in addition to limiting social and occupational interactions. Even with medicine advances, better control of CKD symptoms was not able to avoid deterioration in patients QoL [7]. There are several factors associated with this decreased QoL, including sex, age, number of comorbidities, nutritional status, dialytic parameters, compliance with treatment and mental health [6,17,55]. Time on treatment and type of RRT have also been described as risk factors for worse quantification, since the longer the period on HD or peritoneal dialysis (PD), the greater the risk of having comorbidities and physical deterioration, whereas Tx results in better clinical and emotional conditions [5,31,32]. In a Brazilian cohort with 205 incident dialysis patients followed up for 10 years, the QoL measured at baseline and at the end of follow-up was dynamic throughout the years on RRT and presented better scores after Tx. This study also demonstrated that a longer time on dialysis and limited social and occupational routines were risk factors for reduced scores on the SF-36 [32]. A poor QoL was associated with different complications in patients, including a greater risk of hospitalizations and of mortality [6,7,16,17,18,19,20,21,55].

Being transplanted was the main condition related to survival in our sample, both in the 5- and 9-year follow-up intervals. It is a consensus that among RRTs, transplantation refers to a modality of treatment that is closer to a more functional life for promoting better QoL and less mortality, in addition to other benefits, such as reduced cost of health and fewer comorbidities [5,6,7,17,23,56,57]. After Tx, the lifestyle of patients will very likely change due to no longer having the strict routine of dialysis sessions, thus having more time for occupational, social and leisure activities; moreover, there is increased vitality and well-being, resulting from improved general health conditions [32]. A systematic review of the literature compared social participation among adult CKF patients under different RRT modalities and demonstrated that renal-transplanted patients experienced better possibilities of participation in social and leisure activities when compared to those on HD or PD, and presented better

QoL and mental health [56]. In another systematic review of 110 studies – including studies conducted in African, European and Asian countries and totaling 1,961,904 participants with CKD – transplantation was associated with a reduced risk of mortality and cardiovascular events, as well as with better QoL, compared to dialytic treatment. These results were consistent for different modalities of dialysis, for deceased and living donor transplants and among countries with different health systems [57].

Some limitations of the present study should be addressed. First, there was no assessment of uremic parameters. Such data would be very relevant in our study, due to the association between increased mortality and glomerular filtration rate, in addition to other clinical parameters already demonstrated in previous studies. Second, there was data loss due to changes in the participating clinics. Some of them were closed and incorporated into larger dialysis centers, and others reopened after a long inactive period, which hindered access to both patients and mortality data. Third, there was a possible survival bias, as the 712 participants represented the patients who survived between 2006 and 2008. Regarding this potential survival bias, we also considered the best clinical condition that patients achieved after Tx when compared to those who remained on dialysis.

Conclusion

Studies on the analysis of RRT patient survival are considered fundamental tools for the care team and health care managers, since they contribute to improvement of care conditions and to a broader understanding of treatment program results. Based on the early identification of morbidity and mortality risks for this group of patients, it is possible to implement specific strategies for more positive outcomes regarding QoL and years of life.

In this study, the primary protection factors for longer survival of CKD patients on RRT were Tx and presence of a more active routine and social life, and a better QoL. Not being married or not being in a de facto relationship, lower schooling, a limited social routine, more time on dialysis, worse nutritional status and worse physical functioning were associated with increased mortality. These results indicated that better survival was associated with factors that go beyond the patient's clinical condition, encompassing personal, relational and social aspects. The treatment for CKF includes a series of precautions, and the disease itself and its treatment cause consequences that radically alter the person's global functioning. As the prolongation of survival is achieved through more advanced treatment techniques, the health care of these patients needs to transcend the physical aspect and move towards more comprehensive, singular and humanized care, as recommended in SUS fundamentals and guidelines. Therefore, we reinforce the importance of building and strengthening therapeutic projects that include a multidisciplinary team, in addition to the active participation of patients and their families in the assistance basis from health services.

Contributors

D. C. S. Brito, E. L. Machado, I. A. Reis and M. L. Cherchiglia contributed in the study conception and design; data collection; data analysis and interpretation; statistical analysis; supervision or mentoring

Additional informations

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Resumo

Embora a terapia de substituição renal tenha contribuído para a sobrevida de pacientes renais crônicos, a mortalidade ainda é preocupante. O estudo teve como objetivo identificar os fatores associados à mortalidade em uma coorte prospectiva de pacientes renais crônicos. Foram coletados dados sociodemográficos, clínicos, nutricionais de estilo de vida e qualidade de vida em 712 pacientes. Os instrumentos utilizados foram os questionários da Short-Form Health Survey *(SF-36),* Global Subjective Assessment e Charlson Comorbidity Index*. Um total de 444 pacientes morreram durante o estudo. Depois de cinco anos de seguimento, o estado civil sem parceiro (*hazard ratio *– HR = 1,289; IC95%: 1,001; 1,660), baixa frequência de atividades de lazer (HR = 1,321, IC95%: 1,010; 1,727) e não ser transplantado (HR = 7,246; IC95%: 3,359; 15,630) mantiveram associação independente com risco de mortalidade. No final do período de seguimento, não ter parceiro (HR = 1,337; IC95%: 1,019; 1,756), não ser transplantado (HR = 7,341; IC95%: 3,829;14,075) e estado nutricional ruim (HR = 1,363; IC95%: 1,002; 1,853) mantiveram associação independente com risco aumentado de mortalidade, enquanto maior escolaridade (de 10 a 12 anos, HR = 0,578; IC95%: 0,344; 0,972; e de mais de 12 anos, HR = 0,561; IC95%: 0,329;0,956) e melhor funcionalidade física na escala SF-36 (HR = 0,992; IC95%: 0,987; 0,998) apareceram como fatores de proteção para sobrevida mais longa. A sobrevida de pacientes renais crônicos está associada a fatores que não se limitam ao espectro clínico. O estado civil sem parceiro, baixa escolaridade, rotina social limitada, tempo maior em diálise, estado nutricional ruim e funcionamento físico ruim mostraram associação com alta mortalidade.*

Sobrevida; Mortalidade; Qualidade de Vida; Falência Renal Crônica; Terapia de Substituição Renal

Resumen

A pesar de que la terapia de reemplazo renal ha contribuido a la supervivencia de pacientes con problemas de insuficiencia renal crónica (IRC), la mortalidad continúa siendo un motivo de preocupación. El objetivo de este estudio fue identificar los factores asociados a la mortalidad en una cohorte prospectiva de pacientes con IRC. Se recogieron datos de carácter sociodemográfico, clínico, nutricional, de estilo y calidad de vida, procedentes de 712 pacientes. Las herramientas utilizadas fueron las siguientes encuestas: Short-Form Health Survey *(SF-36),* Global Subjective Assessment y Charlson Comorbidity Index*. Un total de 444 pacientes murieron durante el estudio. Tras cinco años de seguimiento, el hecho de no estar casado (HR = 1,289; IC95%: 1,001; 1,660), tener una frecuencia baja de actividades de ocio (HR = 1,321; IC95%: 1,010; 1,727) y no haber sufrido un trasplante (HR = 7,246; IC95%: 3,359; 15,630) estuvieron independientemente asociados con el riesgo de mortalidad. Al final del período de seguimiento, no estar casado (HR = 1,337; IC95%: 1,019; 1,756), no haber sufrido un trasplante (HR = 7,341; IC95%: 3,829; 14,075), así como contar con un peor estado nutricional (HR = 1,363; IC95%: 1,002; 1,853) estuvieron independientemente asociados con un aumento en el riesgo de mortalidad, mientras que un alto nivel de escolaridad (10 a 12 años, HR = 0,578; IC95%: 0,344; 0,972; y más de 12 años, HR = 0,561; IC95%: 0,329; 0,956) y una mejor puntuación en el SF-36 de desempeño físico (HR = 0,992; IC95%: 0,987; 0,998) fueron factores protectores, asociados a la supervivencia. La supervivencia de pacientes con IRC tiene factores asociados que no se restringen al espectro clínico. No estar casado, un bajo nivel de escolaridad, una rutina social limitada, un periodo más prolongado de tiempo con diálisis, un peor estado nutricional, así como una peor actividad física estuvieron asociados con una alta mortalidad.*

Sobrevida; Mortalidad; Calidad de Vida; Fallo Renal Crónico; Terapia de Reemplazo Renal

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