

Influence of spirituality on renal function of kidney transplant patients

Influência da espiritualidade sobre a função renal em pacientes transplantados renais

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Abstract

Objective: To evaluate influence of spirituality on renal function of kidney transplant patients.

Methods: This cross-sectional study included 81 kidney transplant patients who had undergone transplantation between 30 and 60 months previously. Patients were followed up for 12 months. The analysis was carried out in a large public hospital in the countryside of São Paulo, Brazil. Based on the Duke University Religion Index-religiosity and spirituality scale, we divided patients into two groups (spiritualized [n=52] and less spiritualized [n=29]), considering the median spirituality. For statistical analysis, we used inductive tests and analysis with linear mixed models, with a level of significance of 5% (p<0.05).

Results: Clinical characteristics, immunosuppression, social support, adherence to drug therapy, quality of life, and depression did not differ between groups. Renal function after 12 months was significantly higher in the spiritualized group from 9 months on. After 12 months, the percentage of patients with creatinine clearance higher than 60 ml/min was 61.5% in the spiritualized group and 34.5% in the less spiritualized group (p=0.02). Multivariate analysis showed that the less spiritualized group had a 4.7 times greater risk [1.4 - 16.8] for worsening in renal function (p=0.01).

Conclusion: More spiritualized patients had better renal function after 1 year of transplantation. This result was independent of clinical features, social support, and adherence to immunosuppressive therapy. A holistic approach in health with emphasis on spirituality is encouraged.

Resumo

Objetivo: Avaliar a influência da espiritualidade na função renal de pacientes transplantados renais.

Métodos: Estudo transversal, conduzido em um hospital de clínicas, público e de grande porte, situado no interior do Estado de São Paulo, Brasil, que incluiu 81 pacientes transplantados renais, entre 30 dias e 60 meses de pós-transplante, seguidos por 12 meses. Com base na Escala de Religiosidade de DUREL os pacientes foram divididos em dois grupos considerando-se a mediana da espiritualidade, sendo estes o grupo espiritualizado (n=52) e o menos espiritualizado (n=29). Para a análise estatística foram utilizados testes indutivos e a análise de modelos lineares mistos, com nível de significância de 5% (p<0,05).

Resultados: As características clínicas, de imunossupressão, apoio social, adesão ao tratamento medicamentoso, qualidade de vida e depressão não apresentaram diferenças entre os grupos. A função renal ao longo de um ano foi significativamente maior no grupo espiritualizado a partir do nono mês. Ao fim de 12 meses, a porcentagem de pacientes com *clearance* de creatinina superior a 60ml/min. foi de 61,5% no grupo espiritualizado e 34,5% no grupo menos espiritualizado (p=0,02). A análise multivariada mostrou que o grupo menos espiritualizado apresentou um risco de 4,7 vezes [1,4 - 16,8] maior para pior função renal (p=0,01).

Conclusão: Pacientes mais espiritualizados apresentaram melhor função renal no decorrer de um ano de transplante. Esse efeito foi independente de características clínicas, do apoio social e da adesão à terapia imunossupressora. Assim, uma abordagem holística no atendimento, com ênfase no cuidado espiritual, é encorajada.

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Conflicts of interest: none to report.

Introduction

Chronic renal disease constitutes a world health problem.⁽¹⁾ In Brazil an estimated 123,000 patients are undergoing dialysis. The incidence of this disease in Brazil grows annually.⁽²⁾

Hemodialysis, peritoneal dialysis and renal transplantation are the available treatment approaches. However, these approaches are considered replacement therapies and not curative. Renal transplantation is pointed out as best therapy because it promotes better quality of life, lower mortality, and reduction in health system costs.⁽³⁾

Although the number of kidneys transplantations in Brazil is growing, the number of procedures done is far from the ideal.⁽⁴⁾ Despite advantages of this therapy, patients face challenges and they must adhere to a number of recommendations after the procedure, including changes in daily life activities, continuous use of immunosuppressive drugs, preventions of infections (because they often have changes in immunologic function), periodic medical consultations, changes in diet and regular exercise.^(3,5)

For this reason, the development or establishment of strategies is needed. Among these strategies, the spirituality and religion are highlighted.^(6,7) Important studies on this subject have shown the relevance of this topic in clinical practice.⁽⁸⁻¹⁰⁾

A study showed a correlation between religiosity and reduction in mortality.⁽¹¹⁾ The same benefit was seen in patients with chronic renal disease, although religion was associated with better social support.⁽¹²⁾ Other studies have pointed out benefits of spirituality and/or religiosity for general health among patients with chronic renal disease.⁽¹³⁻¹⁵⁾

Another study found that after kidney transplantation, spirituality was correlated with adherence to treatment and suggested a possible relationship between these variables.⁽¹⁶⁾ Still, higher religiosity was related with lower behavior risk and better adherence to treatment.⁽¹⁷⁾

To the best of our knowledge, no studies so far have focused on spirituality and evolution of renal function of kidney transplant patients, thereby justifying our research. The hypothesis of this

study is that spirituality is associated with better renal function of patients who have undergone kidney transplantation.

This study evaluates the influence of spirituality in renal function of kidney transplant patients.

Methods

This cross-sectional study was carried out in a multidisciplinary kidney transplantation service of a large public hospital in the countryside of São Paulo, Brazil.

Samples was composed of 81 kidney transplant patients assisted in the hospital. Inclusion criteria were age 18 years or older and time since transplantation of more than 30 days and earlier than 60 days. We excluded those with double transplants, such as pancreas and kidney and other organs. Patients were divided into two groups based on the mean spirituality of the total sample. Groups were terms “spiritualized” (n=52) and “less spiritualized” (n=29).

Data were collected after the Institutional Ethical and Research Committee approved the study (CAAE number 20869413.8.0000.5411). All participants provided written informed consent. This study adhered to principles for research on human subjects of resolution 466/2012 of the National Health Council.

Patients were invited to participate between October 2013 and July 2014, and their renal function was followed-up through July 2015.

For the primary outcome, we sought to evaluate and compare evolution of renal function for 12 months in both groups. We analyzed changes from baseline at 3, 6, 9, and 12 months after the study began. Renal function was estimated by the Cockcroft-Gault formula and adjusted for body surface. For the secondary outcome, we evaluated in both groups the incidence of allograft time, acute cellular rejection, and death. Correlations with the religiosity/spirituality scale were assessed. In addition the following variables were considered: age, sex, time since transplantation, level of formal education and religion.

We evaluated possible confounding factors associated with worsening of renal function, including donor type (living or deceased), panel-reactive class 1 antibody, number of HLA mismatches arising from incompatibility, time since transplantation, immunosuppressive therapy and proven acute rejection by biopsy during the 12-month period.

Creatinine was evaluated at baseline and after 3, 6, 9 and 12 months from the first assessment. We evaluated serum levels of immunosuppressive medications used in the same period, including cyclosporine, tacrolimus, sirolimus and everolimus.

For data collection we used six validated questionnaires: the Duke University Religion Index (DUREL)-religiosity and spirituality scale,⁽¹⁸⁾ Beck Depression Inventory,⁽¹⁹⁾ State-Trait Anxiety Inventory (STAI),⁽²⁰⁾ Social Support Scale (SSS),⁽²¹⁾ World Health Organization Quality-of-Life Scale (WHOQOL-BREF)⁽²²⁾ and Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS).⁽²³⁾

The DUREL scale is composed of five items used to measure religiosity. This scale aims at measuring three greater domains of religiosity (organizational religious activity, non-organizational religious activity, and intrinsic religiosity). To compare groups, each dimension was analyzed separately because summing up scores from different dimensions is not recommended.⁽¹⁸⁾

The Beck Depression Inventory was used to evaluate depression symptoms. The higher the value the greater the presence of depressive symptoms. A cut-off point above 15 has been used as an indication for depression.^(19,24)

The STAI was used to evaluate anxiety. This inventory has two different scales to measure two concepts of anxiety (state and trait). Its total score ranges from 20 to 80, and higher values indicate higher anxiety.⁽²⁰⁾

The SSS was used to evaluate social support. This is composed of four dimensions: material, affective, emotional and positive social interaction. Indexes of these dimensions include scores between 20 and 100. The higher the score, the greater the social support.⁽²¹⁾

To assess quality of life, the WHOQOL-BREF was used. This instrument has 26 questions related to four domains: physical health, psychological health, social relationships and environment. The higher the score, the better the quality of life.⁽²²⁾

The BAASIS was used to evaluate adherence to immunosuppressive medications. This scale has four questions that assess the use of medications in the last 4 weeks of treatment. A positive response to any question is defined as non-adherence.⁽²³⁾

For statistical analysis of parametric variables, we used the Student t test. For non-parametric variables, we used the Mann-Whitney test. The chi-squared test or Fisher's exact test was used for categorical variables when appropriate. For analysis of primary endpoints, we applied analysis with linear mixed models throughout the months of the study. Repetitive measures were considered during five evaluations (0, 3, 6, 9 and 12 months), with estimated creatinine clearance as the dependent variable and time and group (spiritualized and less spiritualized) as the fixed variables.

Multivariate binary logistic regression analysis was constructed for risk factors associated with worse renal function at the end of 12 months. We considered as a dependent variable estimated creatinine clearance lower than 60 ml/min, and as covariables, those with a p value <0.20 in the univariate analysis and others included for being strongly related to worse outcome, the following: age of the receipt, group, induced therapy type, time since transplantation, donor type, panel-reactive class 1 antibody, presence of acute rejection and non-adherence. For secondary outcomes, we used the Spearman's test to analyze correlation between religiosity and spirituality scales and adherence scale. The correlations between religiosity and spirituality scales and non-adherence with creatinine clearance were performed using the Pearson's test. The significance level adopted for all tests was 5% (p<0.05).

Results

First, we evaluated 114 patients. Of these, we excluded 21 individuals because time since transplantation was longer than 60 months, 7 because they declined to participate, and 5 because they were younger than 18 years. For this reason, the final sample consisted of 81 patients. Participants' mean age was 42 (± 12) years. The majority of them were women (53%) and mean time since undergoing transplantation was 8 months.

Sample was divided into two groups based on the mean spirituality, which had value of 4. Groups were divided into spiritualized (n=51) and less spiritualized (n=29) groups.

Most patients underwent renal transplantation from a deceased donor (63.5%) with low panel-reactive class 1 antibody titer; the rate of retransplantation in both groups was low. Predominant induction therapy was basiliximab, and the most common combination was tacrolimus with mycophenolate, with no difference between groups. The baseline disease was undetermined in both groups, without a difference between them. Percentage of biopsy-proven acute cellular rejection was 9.8% in the spiritualized group and 7.1% in the less spiritualized group. Initial creatinine and creatinine clearance were similar in both groups (Table 1).

Both groups had a similar level of formal education and most of them had finished high school (Table 2).

The DUREL scale showed higher organization religion in spiritualized group, with a mean score of 2 (1-3) compared with a median score 2 (2-4) in the less spiritualized group ($p=0.001$). Organized religiosity also was higher in the spiritualized group [2; 2-2] than in the less spiritualized group (2; 2-5) ($p=0.01$). Religiosity/spiritualized scale was used to divide groups. Remaining variables (depression, anxiety, quality of life, social support and adherence to immunosuppressive treatment) did not differ between groups (Table 2).

Percentage of patients considered non-adherent did not differ in the groups, at 19.2% in the spir-

Table 1. Basal characteristics and immunological and immunosuppressive risk in spiritualized and less spiritualized groups (n=81)

Variables	Spiritualized (n=52)	Less spiritualized (n=29)	p-value
Women n (%)	31(59.6)	12(41.4)	0.16*
Mean age (SD) (years)	43 \pm 11	41 \pm 15	0.61 [§]
Deceased donor n (%)	33(63.5)	20(69)	0.80*
Median time of transplantation (months) Median (P)	6[2-24]	12[1-26]	0.98*
Median panel (%) (P)	0[0-34]	0[0-1]	0.10*
Median mismatches (P)	3[2-3]	3[2-4]	0.63*
Retransplantation n (%)	2(3.9)	0(0)	0.53*
Type of induction			
Without induction n (%)	10(19.2)	4(13.8)	
Basiliximab n (%)	27(51.9)	19(65.5)	0.49*
Thymoglobulin n (%)	15(28.8)	6(20.7)	
Used immunosuppression:			
Tacrolimus n (%)	45(88.2)	29(100)	0.08*
Everolimus or sirolimus n (%)	10(19.6)	4(13.8)	1*
Azathioprine n (%)	1(2)	0(0)	1*
Mycophenolate n (%)	46(90.2)	25(86.2)	0.71*
Prednisone n (%)	51(100)	29(100)	1*
Acute rejection n (%)	5(9.8)	2(7.1)	1*
Median initial creatinine (mg/dL) (P)	1.3[1-1.9]	1.4[1.2-1.8]	0.13*
Mean initial creatinine clearance (SD) (ml/min)	65.06 \pm 25.2	56.36 \pm 24.5	0.14 [§]
Evolution in 12 months			
Loss of allografts n (%)	0(0)	2(6.9)	0.12*
Baseline disease			
Diabetes	2(5.9)	4(8)	0.61*
Hypertension	10(29.4)	9(18)	
Glomerulonephritis	8(23.5)	16(32)	
Undetermined	14(41.2)	21(42)	
Deaths n (%)	1(1.9)	0(0)	1*

*Chi-squared test; +Fisher's exact test; §Student t test; #Mann-Whitney test; SD - standard deviation; p - percentile 25% and 75%

itualized group and 27.6% in the less spiritualized group ($p=0.41$) (Table 2).

For the primary outcome, the analysis of measures did not show differences in creatinine over time and between groups. At the end of 12 months, the mean creatinine value in the spiritualized group was 1.47 (± 0.6) and 1.95 (± 1.7) in the less spiritualized group (Table 3).

The analysis of creatinine clearance showed no differences between groups in the assessment period (12 months). The spiritualized group showed significantly higher creatinine clearance after the ninth month ($p=0.009$) (Table 3). At the end of 12 months, the percentage of patients with creatinine clearance higher than 60 ml/min was 61.5% in the spiritualized group and 34.5% in the less spiritualized group ($p=0.02$) (Table 3).

Table 2. Level of formal education, religion and baseline questionnaire in spiritualized and less spiritualized group (n=81)

Variables	Spiritualized (n=52)	Less spiritualized (n=29)	p-value
Formal education n (%)			
Illiterate	0(0)	0(0)	
Elementary	22(42.3)	10(34.5)	0.74*
High School	24(46.2)	16(55.2)	
Higher education or above	6(11.5)	3(10.3)	
Religion n(%)			
Atheist	0(0)	0(0)	
Catholic	29(55.8)	19(65.5)	0.34*
Protestant	22(42.3)	8(27.6)	
Spiritualist	0(0)	1(3.4)	
Others	1(1.9)	1(3.4)	
Religiosity/Spirituality Median (P)			
Non-organizational religion.	2[1-3]	2[2-4]	0.001#
Organizational religion	2[2-2]	2[2-5]	0.01#
Spiritualism	3[3-4]	6[5-6]	0.0001#
Median depression (P)	7[4-11]	10[4-17]	0.42#
Anxiety			
Trait	40±8	42±9	0.24 ^a
Mean (SD)			
State	40±8	42±9	0.40 ^a
Quality of life			
Physical	67.8[58.9-75.5]	67.8[53.6-75]	0.58#
Median (P)			
Psychological	75[68.7-83.3]	75[66.36-83.3]	0.50#
Social relationships	75[66.6-83.3]	75[66.6-83.3]	0.66#
Environment	67.2[57.8-75]	68.7[62.5-5]	0.78#
Social support			
Material	95[75-100]	95[90-100]	0.72#
Median (P)			
Affective	100[90-100]	95[85-100]	0.34#
Social interaction	90[70-97.5]	80[67.5-100]	0.98#
Emotional	93[73-100]	80[70-100]	0.49#
Adherence to immunosuppressive therapy Median(P)	0[0-0]	0[0-1]	0.48#
Non-adherence (BAASIS > 0) n(%)	10(19.2)	8(27.6)	0.41+

*Chi-squared test; +Fisher's exact test; &Student t test; #Mann-Whitney test; SD - standard deviation; p - percentile 25% and 75%

The multivariate analysis of risk factors associated with creatinine clearance lower than 60 ml/min at the end of 12 months belonged to the less spiritualized group and was associated with a risk 4.7 times higher (1.4 - 16.8) and worsened renal function (p=0.01). Still, worsening in renal function after 12 months was associated with patients' age (odds ratio [OR] =1.01; 1.001 - 1.13) per year of life, time since transplantation (OR = 1.09; 1.03 - 1.15) per additional months and organ received from deceased donor (OR=12.4; 7.17 - 88.3).

For secondary outcomes, the loss of allograft was zero in the spiritualized group and 6.9% in the

less spiritualized group (p=0.12). No difference was seen in relation to death in either group (Table 1).

Non-organizational religiosity was correlated with spirituality (r=0.449; p<0.001). Organizational religiosity was correlated with spirituality (r=0.328; p=0.003). We did not observe a correlation with adherence to immunosuppressive agents and spirituality (r=-0.259; p=0.02). Spirituality was inversely correlated with creatinine clearance at 12 months (r=-0.259; p=0.02). Adherence to immunosuppressive medications was inversely correlated with creatinine clearance at 12 months (r=-0.381; p<0.001). Multivariate analysis of factors associated with creatinine clearance at 12 months showed that spiritualization was inversely and independently correlated to renal function (beta =-3.701; p=0.03) and time since transplantation (beta=-0.627; p=0.001).

Table 3. Analysis of repetitive measures of creatinine clearance at baseline, three, six, nine and twelve months after the first assessment in spiritualized and less spiritualized group (n=81)

Variables	Spiritualized (n=52) Mean (SD) ^a	Less spiritualized (n=29) Mean (SD) ^a
Creatinine (mg/dL)		
Baseline	1.58±0.76	2.05±2.09
Month 3	1.57±0.75	1.76±0.80
Month 6	1.60±0.75	1.61±0.40
Month 9	1.61±0.86	1.65±0.57
Month 12	1.47±0.64	1.95±1.7
Creatinine clearance (ml/min)		
Baseline	65.06±25.2	56.36±24.5
Month 3	64.29±25.4	57.97±18.4
Month 6	62.47±24.3	59.13±17.1
Month 9	64.44±27.0	60.00±18.6*
Month 12	67.13±26.9	56.66±20.9*
Creatinine clearance > 60 ml/min at the end of 12 months. n(%) ^b	32(61.5%)	10(34.5%)**

a. Analysis of linear mixed models; b. Fisher's exact test; SD - standard deviation; *p<0.009 x spiritualized group; **p=0,02

Discussion

Limitations of this study are the fact that it took place in a single center and its cross-sectional design, which did not allow us to extrapolate results and establish casual relationships. Therefore, further studies are warranted to better understand relationship between religiosity and result of renal transplantation.

However, contributions of this study are clear and include a detailed report of clinical features and immunologic profiles of study participants, data not often observed in studies on religiosity. In addition to the control for potential confounding factors associated with poor results, such as non-adherence, depression, anxiety, and social support. Another positive aspect of this study is the religiosity scale used, which is easy to apply and reproduce.

The main contributions of this investigation to clinical practice are related to the strengthening of the hypothesis that spirituality can positively influence renal function in patients who underwent transplantation: Results showed improvement after 12 months since the procedure. However, assistance focused on spiritual well-being is needed.

We observed that the level of religiosity was high among kidney transplant patients who participated in the study. About 67% of participants had higher indexes of intrinsic religiosity and, therefore, they were considered the group with higher spirituality. This finding suggests that patients with chronic diseases present higher religiosity/spirituality than general population.

To have faith or belief in a higher power helps patients confront and, consequently, manage the process involved in a kidney transplantation, mainly regarding the ability to overcome fear and anxiety and other negative feelings.⁽¹⁰⁾

Religiosity/spirituality are considered important resources during management of stressful situations that require individuals to face the situation.^(25,26) To be close to God, church, and its members favors the emotional support to individuals who underwent transplantation.⁽¹⁰⁾

The less spiritualized group had worsened renal function at 12 months. The multivariate analysis showed that this result persisted regardless of their adherence to immunosuppressive therapy and clinical factors associated with poor results. Therefore, the worsening in renal function observed in this group is not explained by clinical features.

Both groups, spiritualized and less spiritualized, showed predominance of moderate immunological risk, organ from a deceased donor and low reactivi-

ty antibody panel; in most cases they received similar maintenance of immunosuppression (tacrolimus combined with prednisone and mycophenolate) and induction therapy (basiliximab).

Better social support and better quality of life, traditionally associated with religiosity/spirituality,^(8,9) do not explain the improvement in renal function observed in participants who were spiritualized, mainly because depression score, anxiety, social support and quality of life did not differ between groups.

A strong characteristic associated with poor result in renal transplantation is the adherence to immunosuppressive therapy.⁽²⁷⁾ Non-adherence has been associated with rejection due to late antibody and, consequently, worsening renal function.⁽²⁸⁾ For this reason, among confounding factors approached in this study, adherence has special importance when the study period considered includes the initial period after transplantation; during this period non-adherence poses a higher risk.⁽²⁹⁾

Adherence scale did not differ between groups. In addition, no correlation between intrinsic relation and adherence scores was seen, although scores on both scales were inversely correlated with renal function at 12 months. Our findings suggest that spirituality can indirectly reflect the sum of factors such as social support, adherence, and quality of life, and these factors might lead to better renal function.

It is well known that patients tend to deny any non-adherence to drug therapy when answering questionnaires. However, when religiosity/spirituality questionnaires are applied, patients seem to answer them more adequately, possibly because these questionnaires are not related to an obligation to do something.

Our study found no differences in mortality between both groups. This result can be explained by the low rate of adverse reactions observed after 12 months of follow-up. Previous studies that approached mortality in patients who were on a waiting list for liver transplantations, had chronic renal diseases, and were undergoing dialysis also associated higher religiosity/spirituality with lower mortality.⁽¹²⁾

Our study suggests that religiosity and spirituality should be considered in patients who are at risk of worse evolution after renal transplantation. In addition, there is a need to integrate these variables into health care delivery for these patients.

Conclusion

Kidney transplant patients had a higher degree of religiosity and spirituality. Patients who were spiritualized presented improvement in renal function 1 year after transplantation. This result was seen regardless of clinical characteristics, social support and immunosuppressive therapy. A holistic approach to health care with emphasis on spirituality is encouraged.

Collaborations

Bravin AM, Trettene AS, Cavalcante RS, Banin VB, Padula NAMR, Saranholi TL, Popim RG e Andrade LGM contributed with conception of the Project, analysis and interpretation of data, drafting the manuscript, and approval of final version to be published.

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