Psychological Responses to the Coronavirus Disease 2019 Pandemic in Renal Transplant Recipients

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ABSTRACT

Background. Renal transplant recipients are at increased risk for an adverse course of coronavirus disease 2019 (COVID-19), most likely due to immunosuppression and the high level of cardiovascular comorbidity. Many transplant recipients are aware of these facts. The psychological effects of this knowledge, however, remain elusive.

Methods. Cross-sectional study on 62 renal transplant recipients. Fifty cardiovascular outpatients without immunosuppression and 55 healthy subjects served as control. We performed a focused psychological assessment during the pandemic (April 2020) and compared the data with a time 6 months before. Additionally, an intergroup analysis was performed for the data during the pandemic. The analysis was performed by means of a questionnaire derived from KPD-38. We extracted 5 questions focusing on the parameters "life satisfaction" and perceived "action competence." Life satisfaction score ranged from 2 to 8, and the score for action competence from 5 to 20.

Results. Both life satisfaction and perceived action competence were significantly lower during the pandemic than 6 months before in all the 3 groups ($P < .005$ each). During the pandemic median levels of life satisfaction did not significantly differ between the 3 groups (transplant recipients 6, interquartile range [IQR] 4-7; cardiovascular patients 5, IQR: 4-6; healthy controls 6, IQR 5-7; Kruskal-Wallis $P > .05$). In contrast, the perceived action competence was higher in healthy subjects (15, IQR 12-17) than in both renal transplant recipients (13, IQR 10-15) and cardiovascular patients (13, IQR 8-14, Kruskal-Wallis $P = .0003$).

Conclusion. The COVID-19 pandemic has negative effects on life satisfaction and perceived action competence in renal transplant recipients, cardiovascular patients without immunosuppression, and healthy subjects. The effects on life satisfaction in transplant recipients did not differ from nonimmunocompromised patients or healthy controls. In contrast, the feeling of reduced action competence exceeded healthy controls, most likely due to a subjective need for stricter social distancing to avoid infection.

HEALTH status has an important impact on quality of life [1]. Health-related quality of life measurements are part of a multidimensional concept including domains related to physical, emotional, mental, and social functioning [2,3]. Many studies have shown that mean health-related quality of life of renal transplant recipients is superior to hemodialysis patients [4]. In some cases it

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reached levels similar to healthy controls. The current coronavirus disease 2019 (COVID-19) pandemic, however, may influence crucial changes in life satisfaction of renal transplant recipients. Because of their comorbidities and immunosuppressive therapy, they are supposed to be at increased risk for adverse outcomes.

Indeed, there is an increasing number of reports on the clinical course of COVID-19 in solid organ transplant recipients, most of them showing a substantially increased number of severe and fatal courses [5–7]. In a cohort of transplant patients in New York City, mortality was 28% compared with 0.5% to 5% in the general population [6]. Because risk factors for adverse outcomes in COVID-19 have been transparently presented by the media, transplant recipients may suffer from increased levels of anxiety. Many of them might maintain social distancing in a rigid manner beyond lockdown measures in order to avoid infection. Thus, it may be speculated that the perceived competence to act and quality of life of renal transplant recipients may be extraordinarily affected. To date, there are no data on the psychological effects of the COVID-19 pandemic on transplant recipients.

The present cross-sectional study investigates the perceived change of life satisfaction and competence to act from October 2019 to April 2020. In order to differentiate the impact of immunosuppression, results are compared with patients with cardiovascular disease without immunosuppressive medication and to healthy controls.

PATIENTS AND METHODS
Study Population and Protocol

A cross-sectional survey was performed in April 2020 at the transplant center of Ruhr-University Bochum. Questionnaires were sent to 150 renal transplant recipients who were currently managed in the outpatient clinic of the transplant center. They were informed that the survey was being done for research only and that their privacy would be protected. Inclusion criteria were age >18 years, successful transplantation (defined as no current need for dialysis) >6 months ago, and capability to understand the questionnaire. There were 2 control groups: the first group consisted of subjects admitted to an outpatient clinic for nephrology, hypertensiology, and lipidology at Ruhr-University Bochum, the other one comprised a group of healthy subjects. Data on age, sex, time of transplantation, transplant function, cardiovascular comorbidities, immunosuppressive medication, and hospitalizations within the last 12 months were recorded. Ethical approval was obtained by the ethics committee of Ruhr-University Bochum (No. 20-6895). Patients provided written informed consent to participate in the study.

Questionnaire

The study aimed at an assessment of life satisfaction and perceived competence to act during the pandemic (April 2020) and 6 months before the pandemic. The questionnaire was derived from "The Clinical Psychological Diagnosis System 38" (KPD-38). It was developed for the purpose of quality assurance and outcome monitoring in psychotherapy and psychosomatic medicine in Heidelberg [8]. The KPD-38 encompasses the following 6 scales with a total of 38 items: 1. physical impairment, 2. mental impairment, 3.

social problems, 4. action competence, 5. general life satisfaction, and 6. social support. In order to reduce the patients' expenditure of time and thereby to increase the rate of participation, we extracted formulated 6 questions focusing on the following 2 parameters: "action competence" and "general life satisfaction." The corresponding scales ranged from 1 to 4 (2 questions on life satisfaction, 5 questions on perceived action competence). Patients were asked to answer questions with regard to the current state and 6 months before the pandemic. Questionnaires that were returned within 4 weeks were analyzed and included in the study.

Statistics

Data were presented as median and interquartile range (IQR). Intragroup comparison of questionnaire data from the 2 time points was performed by Wilcoxon paired test. Kruskal-Wallis test with Dunn's post hoc analysis were used for comparison of data between transplant recipients, cardiovascular patients, and healthy controls. Dichotomous parameters were compared by χ^2/Fisher's exact test. All statistical analyses were done using SPSS Statistics 25 (SPSS Inc, Chicago, Illinois, United States) and Prism 5 (GraphPad Software, La Jolla, California, United States).

RESULTS

Questionnaires were completed and returned by 62 renal transplant recipients (41.3%). Fifty cardiovascular outpatients without immunosuppression and 55 healthy persons were enrolled as control groups. All of them completed the questions of the questionnaire. Table 1 and Table 2 summarize the characteristics of all the 3 groups including epidemiologic data, transplant data, immunosuppression, prevalence of cardiovascular comorbidity, underlying renal disease, serum creatinine concentration/estimated glomerular filtration rate, and events necessitating hospitalization in the past 12 months. The majority (n = 53, 85.5%) of the renal transplant patients had a triple immunosuppressive regime consisting of a calcineurin inhibitor, mycophenolic acid, and prednisolone.

Median age of the transplant population was 57 (IQR 48-67). The majority of the patients were male (n = 37, 59.7%). Mean time after transplant was 77 months (IQR 37.3-164). The most frequent cardiovascular comorbidities were hypertension (n = 54, 87.1%), diabetes (n = 8, 13%), hyperlipidemia (n = 44, 71%), and coronary artery disease (n = 6, 1%). The cardiovascular patients without immunosuppression did not differ from the renal transplant population in terms of age (median 58, IQR 39-67; P = .90), gender (male n = 21 (42%), female n = 29 (58%); P = .087), the prevalence of hyperlipidemia (n = 28, 56%; P = .116), and diabetes (n = 11, 22%; P = .217). In contrast, serum creatinine concentrations (median 1.0, IQR 0.8-1.1) and proteinuria (median 0.09, IQR 0.09-0.12) were lower than in the transplant population (P < .001; P = .006). The prevalence of the cardiovascular comorbidities, hypertension (n = 34, 68%; P = .02) and coronary artery disease (n = 16, 32%; P = .004), was statistically different from the transplant population. The number of hospitalizations were

Table 1. Epidemiologic and Clinical Characterization of the Renal Transplant Population, the Cardiovascular Patients Without Immunosuppression, and the Healthy Controls

	Renal Transplant Recipients (n = 62)	Control Group 1 (Cardiovascular Patients, n = 50)	Control Group 2 (Healthy Controls, n = 55)	P
Number of subjects included	62	50	55	
Age (y)	58 (IQR 48-57)*	58 (IQR 39-67)*	39 (IQR 29-56)	<.001
				.90*
Male	37 (59.7%)*	21 (42%)*	21 (38.1%)	.045
Female	25 (40.3%)*	29 (58%)*	34 (61.8%)	.09*
Concomitant diseases				
Coronary heart disease	6 (1.0%)	16 (32%)	-	.004*
Hyperlipidemia	44 (71.0%)	28 (56%)	-	.12
Diabetes	8 (1.3%)	11 (22%)	-	.22
Hypertension	54 (87.1%)	34 (68%)	-	.020*
Number of hospitalizations	38 (61.2%)	2 (4%)	-	<.001*

Abbreviation: IQR, interquartile range.
*P value without control group 2.

higher in renal transplant recipients than in the cardiovascular patients (n = 38 [61.2%] vs n = 2 [4%]; P < .001).

The healthy population differed in age (median 39, IQR 28-56; P < .001) and gender (male n = 21 [38.1%], female n = 34 [61.8%]; P = .045). None of them suffered of hypertension, diabetes, hyperlipidemia, chronic kidney disease, and coronary artery disease. There were no numbers of hospitalizations.

The parameter "action competence" included 5 questions with 20 points as maximal score. Figure 1A illustrates the results in transplant recipients, cardiovascular outpatients, and healthy controls for April 2020 and October 2019. The renal transplant recipients reached a median of 13 (IQR 10-15) in April 2020. Assessment of the state 6 months before yielded a significantly higher score of 15 (IQR 12-17; P = .0001). The mean difference was 2.0 ± 3.0. The cardiovascular patients revealed a median score of 13 (IQR 8-14) during the pandemic and a median score of 14 (IQR 12-16) 6 months before. Scores were significantly lower during the pandemic (P < .0001) with a mean

Table 2. Transplant-related Data

	Transplant Recipients (n = 62)	Control Group 1 Cardiovascular Patients (n = 50)	P
Time on dialysis (mo)	40.5 (IQR 8.9-82.8)	-	
Mean time after transplantation (mo)	77 (IQR 37.3-164)	-	
Live donor transplantation (%)	11 (17.7%)	-	
Creatinine (mg/dL)	1.5 (IQR 1.1-1.9)	0.9 (IQR 0.8-1.1)	<.001*
eGFR (mL/min)	46.5 (IQR 35.3-58.8)	87.5 (IQR 68.8-101.8)	<.001*
U-PCR (mg/g Krea)	0.13 (IQR 0.09-0.22)	0.09 (IQR 0.09-0.12)	.006*
Immunosuppression			
Triple immunosuppression	53 (85.5%)	-	55 with CNI
			7 without CNI
Mono/dual immunosuppression	9 (14.5%)	-	
(Methyl-)prednisolone	60 (97.8%)	-	
Mycophenolic acid	52 (83.9%)	-	
Tacrolimus	53 (85.5%)	-	
Cyclosporine	2 (3.2%)	-	
Azathioprine	4 (6.5%)	-	
mTOR inhibitors	5 (8.1%)	-	
Belatacept	1 (1.6%)	-	
Cause of CKD			
Glomerulonephritis	19 (30.6%)	0	<.001*
Vascilitis	4 (6.4%)	0	.127
Hereditary dysplasia/reflux	4 (6.4%)	0	.127
Polycystic kidney disease	7 (11.3%)	0	.016*
Benign nephrosclerosis	6 (9.6%)	1 (2%)	<.001*
Alport syndrome	2 (3.2%)	0	<.001*
Diabetic nephropathy	17 (27.4%)	1 (2%)	<.001*

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; mTOR, mammalian target of rapamycin; U-PCR urine-protein-creatinine-ratio.
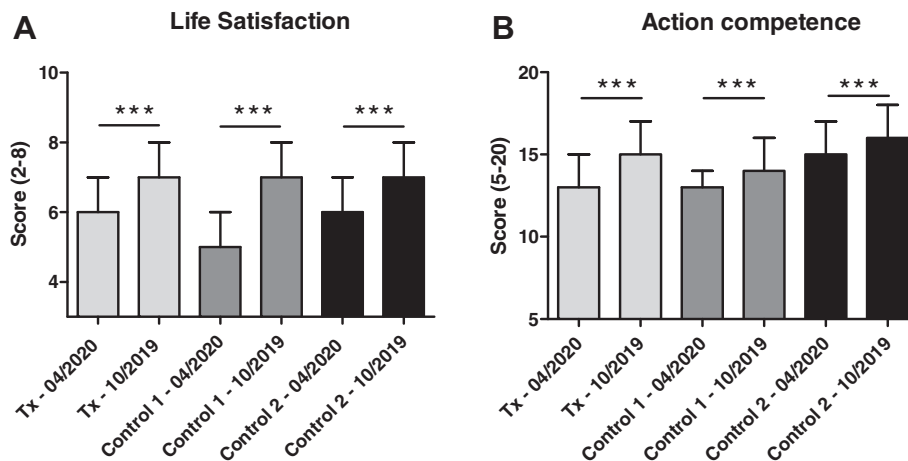*P value without control group 2.

A   Life Satisfaction

B   Action competence

Fig 1. **(A)** Life satisfaction scores (range: 2-8) and **(B)** Perceived action competence scores (range: 5-20) at April 2020 during the SARS-CoV-2 pandemic vs 6 months before in renal transplant recipients (Tx), patients with cardiovascular disease without immunosuppression (Control 1), and healthy subjects (Control 2).

change of 2.5 ± 3.8. Healthy controls reached a median score of 15 (IQR 12-17) during the pandemic and a significantly higher score of 16 (IQR 15-18) 6 months before ($P < .0001$).

Comparing the scores of action competence during the pandemic, there was a statistically significant difference between the groups ($P = .0003$). Dunn's post hoc analysis showed a significant difference between the transplant population and the healthy control group (13 vs 15, $P = .0003$) and between the group of cardiovascular patients and healthy controls (13 vs 15, $P = .0003$). Figure 1B provides a comparison of action competence and general life satisfaction of the 3 groups during the pandemic.

The parameter "general life satisfaction" encompassed 2 items (maximum score 8). The time-dependent change of this parameter is presented in Fig 1B. The median score was significantly lower during the pandemic than 6 months before (6, IQR 4-7 vs 7, IQR 5-8) in the transplant group ($P = .0001$) and a delta value of 1.0 ± 1.8. In analogy, the group of cardiovascular patients revealed a significant difference in the score for life satisfaction as well; whereas the median score was 5 (IQR 4-6) in April 2020, they reached a score of 7 (IQR 5-8) with a delta value of 2.2 ± 3.0 for the time point 6 months ago ($P < .0001$). The healthy control group reached a median score of 6 (IQR 5-7) in April 2020 and 7 (IQR 6-8) 6 months before ($P = .0028$). The general life satisfaction during the pandemic did not significantly differ between the transplant population, the group of cardiovascular patients, and the healthy control group (6 vs 5 vs 6, $P = .057$). Concordant chronological change of the score showed significant differences between all groups (15 vs 14 vs 16, $P = .0028$).

DISCUSSION

The present analysis provides the first insight into psychological responses to the COVID-19 pandemic in renal transplant recipients. Renal transplant recipients are at substantially increased risk for an adverse course of COVID-19 due to both immunosuppression and the high level of cardiovascular comorbidity. Our findings show that general life satisfaction and the perceived action competence are indeed lower during the pandemic than 6 months before. This finding was observed in the same way, however, in cardiovascular outpatients without immunosuppression and in the healthy control group.

Using the KPD-38 questionnaire as a validated measurement for health-related quality of life we focused on the items "action competence" and "general life satisfaction," since these were likely affected by menacing circumstances associated with the COVID-19 pandemic. In order to differentiate the impact of immunosuppression and cardiovascular comorbidities on perceived health threat, we made use of a control group with cardiovascular diseases but without immunosuppression and a group with neither immunosuppression nor cardiovascular diseases. The transplant and cardiovascular patients were homogeneous for age, sex, and cardiovascular comorbidities like hyperlipidemia and diabetes as well.

The participation rate of 41.3% among transplant patients is comparable to the majority of health surveys with participants suffering from chronic or severe illness [9]. This is of importance, as the participation rate may have substantial impact on the findings of a survey. The higher the rate of participation, the lower the anticipated selection bias.

In accordance with the basic hypothesis, general life satisfaction was significantly reduced during the COVID-19 pandemic in renal transplant recipients. The individual reasons are beyond the scope of this investigation. This phenomenon occurred in the same way in non-immunocompromised subjects, however, immunosuppression does not appear to be the primary driver of this emotional disturbance. The analogous findings in the control group of cardiovascular outpatients and healthy controls implicate a more generalized concern. The question arises if the impairment of life satisfaction may merely be the consequence of lockdown-associated restrictions in daily

life activities. Very likely, these restrictions indeed contribute to the reduced satisfaction. It should be kept in mind, however, that the questionnaire focuses on health-related quality of life not overall quality of life.

The perceived action competence depends on both the individual predispositions to conduct an activity and the external limitations to do so. The lockdown-associated restrictions in social activities will thereby have a strong impact on action competence. Subjects with risk factors for a severe course of COVID-19 might extend the social distancing beyond the requested lockdown regulations due to anxiety of infection. The present findings show that the reduction in perceived action competence is indeed more pronounced in subjects with risk factors than in healthy persons. Interestingly, it did not matter whether these risk factors consisted of immunosuppression or cardiovascular comorbidities. Thus, the general knowledge of belonging to a risk population for a severe course of COVID-19 is of greater determinative significance for the degree of anxiety during the pandemic than individual variations in comorbidities.

Before the pandemic, many reports showed a superior life satisfaction in transplant patients compared with patients with end-stage renal disease [10–12]. In a representative sample of 1424 renal transplant recipients from 5 kidney centers in France, the need for medication for cardiovascular diseases had a negative impact on life satisfaction. However, there was no association between immunosuppressive drugs and quality of life [13]. Somewhat surprising, this finding remained unchanged during the pandemic in the present population. In fact, the role of immunosuppression in the clinical course of COVID-19 is still incompletely understood. A comparative study on patients with and without rheumatological diseases from Erlangen, Germany did not show more severe courses in subjects with immunosuppression [14]. Moreover, the results on tocilizumab in subjects with severe COVID-19 pneumonia show that immunosuppression may even provide positive effects in the later course of infection [15].

The present analysis is limited by several aspects. First, the sample size is small. Second, the present work is limited by evaluation of only 2 items of KPD-38. On the other hand, the participation rate was high enough and the timeline of the pandemic urgently necessitates to address questions beyond somatic issues.

The present findings show for the first time that the COVID-19 pandemic has a significant impact on the quality of life in renal transplant recipients. Whereas the impairment of life satisfaction is comparable to the general population, the perceived restrictions on acting freely are higher. On the one hand rigid compliance with measures of social distancing has to be welcomed during lockdown phases in order to reduce the risk of infection. On the other hand, the knowledge of belonging to a high-risk population may lead to anxiety-driven social isolation beyond the lockdown. Thus, the pandemic constitutes a psychological challenge to the transplant population. Transplant physicians should openly discuss this problem with their patients.

REFERENCES

[1] Finkelstein FO, Wuerth D, Finkelstein SH. Health related quality of life and the CKD patient: challenges for the nephrology community. Kidney Int 2009;76:946–52.

[2] Aarnio M, Winter T, Kujala U, Kaprio J. Associations of health related behaviour, social relationships, and health status with persistent physical activity and inactivity: a study of Finnish adolescent twins. Br J Sports Med 2002;36:360–4.

[3] Revicki DA, Kleinman L, Cella D. A history of health-related quality of life outcomes in psychiatry. Dialogues Clin Neurosci 2014;16:127–35.

[4] Tamura Y, Urawa A, Watanabe S, Hoosegow T, Ogura T, Nishikawa K. Mood status and quality of life in kidney recipients after transplantation. Transplant Proc 2018;50:2521–5.

[5] Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in solid organ transplant recipients: initial report from the US epicenter. Am J Transplant 2020;20:1800–8.

[6] Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. N Engl J Med 2020;382:2475–7.

[7] Husain SA, Dube G, Morris H, et al. Early outcomes of outpatient management of kidney transplant recipients with coronavirus disease 2019. Clin J Am Soc Nephrol 2020;15:1174–8.

[8] Percevic R, Gallas C, Wolf M, Haug S, Hünerfauth T, Schwarz M, et al. Das klinisch psychologische diagnosesystem. Diagnostica 2005;3851:134–44.

[9] Mindell JS, Giampaoli S, Goesswald A, Kamtsiuris P, Mann C, Männistö S, et al. Sample selection, recruitment and participation rates in health examination surveys in Europe–experience from seven national surveys. BMC Med Res Methodol 2015;15:78.

[10] Overbeck I, Bartels M, Decker O, Harms J, Hauss J, Fangmann J. Changes in quality of life after renal transplantation. Transplant Proc 2005;37:1618–21.

[11] Olbrisch ME, Benedict SM, Ashe K, Levenson JL. Psychological assessment and care of organ transplant patients. J Consult Clin Psychol 2002;70:771–83.

[12] Painter PL, Luetkemeier MJ, Moore GE, Dibble SL, Green GA, Myll JO, et al. Health-related fitness and quality of life in organ transplant recipients. Transplantation 1997;27:1796–800.

[13] Mouelhi Y, Jouve E, Alessandrini M, Pedinielli N, Moal V, Meurette A, et al. Factors associated with health-related quality of life in kidney transplant recipients in France. BMC Nephrol 2018;19:99.

[14] Schett G, Sticherling M, Neurath MF. COVID-19: risk for cytokine targeting in chronic inflammatory diseases? Nat Rev Immunol 2020;20:271–2.

[15] Xu X, Han M, Li T, Sun W, Wang D, Fu B, et al. Effective treatment of severe COVID-19 patients with tocilizumab. Proc Natl Acad Sci U S A 2020;117:10970–5.