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Coronavirus Disease 2019 Associated Risk Score, Behavior, and Symptom Prevalence in German Transplant Recipients

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ABSTRACT

Background. Transplant recipients are prone to developing severe infections because of immunosuppression. Therefore, studying the manifestation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in transplant recipients is of particular importance.

Methods. One hundred twelve transplant patients consecutively visiting the outpatient department of 2 German transplant centers were included in this study after providing written informed consent. The patients were interviewed about coronavirus disease 2019 (COVID-19) symptoms and history. Nasopharyngeal swabs were analyzed by SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR). SARS-CoV-2 IgG and IgA were measured concomitantly in patient sera by enzyme-linked immunosorbent assay.

Results. The risk of severe COVID-19 according to 2 recent scores differed among the analyzed patients. All patients were well educated about their presumed higher risk of a severe COVID-19 and described performing self-isolation wherever possible. Nevertheless, 20 patients reported contact with someone suspected of having COVID-19 or who tested positive shortly thereafter (18%). Despite this relatively high exposure, no clinically relevant case of COVID-19 was reported. Though SARS-CoV-2 IgG and IgA were found in 3 patients (3%); 2 patients were asymptomatic and only 1 had mild COVID-19 symptoms and positive RT-PCR 4 weeks earlier. There were no occult SARS-CoV-2 infections, as demonstrated by negative PCR tests.

Conclusion. Despite the high exposure level, the incidence of COVID-19 remained very low. Because of the differences in COVID-19 risk, balancing risk exposure and quality of life should be recommended.

SOLID organ transplant recipients are prone to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection because of frequent contact with medical staff and facilities. Additionally, patients are regarded to be at high risk of a critical coronavirus disease 2019 (COVID-19) course because of immunosuppression and

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Table 1. Characteristics and Results of 112 Monitored Transplant Recipients With COVID-19

	Number		Percentage	
Age				
Median (IQR)	51 (41-62)			
<50	52		46.4	
50-59	31		27.7	
60-69	15		13.4	
70-79	14		12.5	
≥80	0		0.0	
Sex				
Male	69		61.6	
Female	43		38.4	
Underlying kidney disease				
Glomerulonephritis	32		28.6	
Diabetes mellitus	23		20.5	
Hypertensive kidney disease	9		8.0	
Cystic kidney disease	12		10.7	
Alport syndrome	8		7.1	
Other	15		13.4	
Unknown	13		11.6	
Transplant age				
Months; median (IQR)	38 (7-112)			
Type of transplant				
Kidney	95		84.8	
Kidney-pancreas	12		10.7	
Pancreas	3		2.7	
Kidney-liver	2		1.8	
Type of donation				
Deceased donor	70		62.5	
Living donor	41		36.6	
Unknown	1		0.9	
Previous transplant				
None	98		87.5	
Kidney	12		10.7	
Pancreas	1		0.9	
Small intestine	1		0.9	
Immunosuppression				
Triple (CNI MPA steroid)	78		69.6	
Triple (including belatacept)	7		6.3	
Triple (including AZA)	7		6.3	
Triple (including mTORi)	4		3.6	
Double (CNI MPA)	6		5.4	
Double (CNI steroid)	7		6.3	
Mono (CNI)	3		2.7	
Creatinine (mg/dL)				
Median (IQR)	1.58 (1.2-2.1)			
GFR (mL/min/1.73 m²)				
>90	7		6.3	
60-89	25		22.3	
30-59	57		50.9	
15-29	19		17.0	
<15	4		3.6	
Leukocytes				
<4/nL	15		13.4	
4-10/nL	80		71.4	
>10/nL	17		15.2	
COVID-19 risk score*	Score I	Score II	Score I	Score II
Low-risk category	24	36	21.4	32.1
Moderate-risk category (high risk)	76	47	67.9	42.0
High-risk category (very high risk)	12	29	10.7	25.9

Table 1. (continued)

	Number		Percentage	
COVID-19 Score I vs Score II				
Same category	81		72.3	
Score I > Score II	13		11.6	
Score II > Score I	18		16.1	
Symptoms associated with COVID-19	Currently	Recently	Currently	Recently
Cough	3	16	3	14
Sore throat	3	11	3	10
Anosmia and lack of taste	1	8	1	7
Shortness of breath	0	7	0	6
Fever	0	10	0	9
At least 2 of the above (currently or recently)	13		12	
Headache	4	15	4	13
Limb pain	2	12	2	11
Fatigue	6	35	5	31
Nausea, vomiting	3	6	3	5
Diarrhea	3	12	3	11
Rhinitis, sinusitis	6	18	5	16
COVID-19 history				
Previously tested positive	1		0.9	
Contact with person with COVID-19 symptoms/positive test	20		18	
RT-PCR test results				
Negative	112		100	
Positive	0		0	
SARS-CoV-2 IgG test result				
Test performed	99		88.4	
Negative	96		97	
Positive	3		3	
SARS-CoV-2 IgA test result				
Test performed	99		88.4	
Negative	90		90.9	
Positive	9		9.1	
SARS-CoV-2 IgA and IgG positive	3		3	

Abbreviations: AZA, azathioprine; COVID-19, coronavirus disease 2019; CNI, calcineurin inhibitor (tacrolimus/cyclosporine); GFR, glomerular filtration rate; IQR, interquartile range; MPA, mycophenolic acid (mycophenolate mofetil/mycophenolate sodium); mTORi, mTOR inhibitor; RT-PCR, reverse transcription-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

*COVID-19 Score I: Dagan et al [8]; COVID-19 Score II: Schnake-Mahl et al [9].

comorbidities [1]. Therefore, studying transplant recipients is of special importance during the COVID-19 pandemic.

METHODS

One hundred twelve transplant patients consecutively visiting the outpatient department of 2 German transplant centers for scheduled visits in April and May 2020 were included. The patients were interviewed about COVID-19 symptoms, history, and behavior. Nasopharyngeal swabs were collected and analyzed by SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR). SARS-CoV-2 IgG and IgA were measured concomitantly in patient sera by enzyme-linked immunosorbent assay. Clinical data and results are presented in Table 1. Ethical approval (Nos. 20-6886 and 20-9214-BO) and written informed consent were obtained.

RESULTS

Most patients had received a kidney transplant (85%); the other patients received combined pancreas-kidney (11%), liver-kidney (1.8%), or single pancreas (3%) transplants. The median transplant age was 38 months (interquartile

range = 7-112). Seventy patients received organs from deceased donors (63%) and 41 received organs from living donors (37%). Fourteen patients had previously received another transplant (12.5%). Ninety-six patients received triple immunosuppression (85.7%), 13 received double immunosuppression (11.6%) and 3 received mono immunosuppression (2.7%).

Many transplant patients described chronic or frequently recurring complaints on the COVID-19 symptom questionnaire. Thirteen patients reported at least 2 recent common cold symptoms such as coughing, sore throat, or fever (12%).

All patients were well educated about their presumed higher risk of severe COVID-19 infection and described self-isolation wherever possible. Nevertheless, 20 patients reported contact with someone suspected of being infected with COVID-19 or who tested positive shortly thereafter (18%). Despite this relatively high exposure risk, there were no occult SARS-CoV-2 infections as demonstrated by negative SARS-CoV-2 RT-PCR performed on nasopharyngeal swabs. Serologic testing performed in 99 patients

(88.4%) by enzyme-linked immunosorbent assay showed that 3 patients were positive for SARS-CoV-2 IgG and IgA (3%). One patient had had RT-PCR-confirmed mild COVID-19 4 weeks earlier, but the other 2 IgG/IgA-positive patients did not report any past COVID-19 symptoms. SARS-CoV-2 seroprevalence in blood bank donors in Germany was 1.35% in a recent report of the Robert Koch Institute [2]. Although the incidence in this cohort is more than twice as high, the small number of patients impedes definite conclusions. Interestingly, 9 patients were only SARS-CoV-2 IgA positive (9%), of whom 1 had a cough and sore throat for 1 week several weeks earlier. The other patients reported no COVID-19 symptoms. The lower specificity of SARS-CoV-2 IgA, however, limits the interpretation of test results [3].

Transplant patients are perceived as a high-risk population for critical COVID-19 according to the US Centers for Disease Control and Prevention, British National Health Service, and German Robert Koch Institute [4–6]. However, this classification might not reflect the individual situation, which has important implications for daily life for many patients during this pandemic. The few studies assessing the actual risk of transplant patients report diverse results [1,7]. We assessed the risk according to 2 recently published, but not yet validated, scores [8,9]. Twenty-one and 32% of patients were in the lowest risk category, 68% and 42% were in the moderate-risk category (risk of severe illness), and 11% and 26% were in the high-risk category (risk of the need for critical care) according to COVID-19 scores I and II, respectively (Table 1). The main reasons for a higher score, notwithstanding chronic kidney disease and immunosuppression, were older age, cardiovascular disease, diabetes mellitus, hypertension, and recent hospitalization. The IgG/IgA-positive patient with mild COVID-19 had a low risk, and the 2 asymptomatic IgG/IgA-positive patients were of moderate and high risk.

DISCUSSION

Overall, our findings show that asymptomatic COVID-19 courses can occur in transplant recipients. This is in line with case reports of transplant patients infected with COVID-19 that report a diverse symptomatology [10–13]. Common cold symptoms typical of COVID-19 were frequent, making symptom-based testing less useful. Despite self-isolation, contact with others infected with COVID-19 was frequent, though the COVID-19 incidence remained low. The risk of severe COVID-19 was diverse in the patient

cohort, indicating the need for nuanced recommendations for balancing risk exposure and quality of life, especially for younger patients with few comorbidities.

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