



Severe acute respiratory syndrome coronavirus 2 antibody prevalence in adult patients with short bowel syndrome—A German multicenter cross-sectional study

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Abstract

Background: Not all patients suffer from a severe course of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, demanding a definition of groups at risk. Short bowel syndrome (SBS) has been assumed to be a risk factor, because of the complexity of disease, the need for interdisciplinary care, and frequent contact with caretakers. We aimed to establish data on the course of infection and prevalence of SARS-CoV-2 seropositivity in SBS patients in Germany.

Methods: From January 2021 until January 2022 a total of 119 patients from three different tertiary care centers with SBS were included. All patients received an antibody test against the nucleocapsid (N) antigen and were asked to fill out a questionnaire, which included frequency of contact with medical personnel, risk behavior and worries.

Results: Sixty-seven percent of SBS patients received parenteral nutrition with a median of 6 days per week. The seroprevalence of SARS-CoV-2 antibodies was 7.6% ($n = 9$). Seven patients with positive antibodies had coronavirus disease 2019 (COVID-19) with a mild course. None of the patients were hospitalized or needed further treatment. There was no difference in willingness to take risks in SARS-CoV-2 antibody-positive and -negative patients ($P = 0.61$). Patients were predominantly worried about the economy (61%) and transmitting COVID-19 (52%), less frequent (26%) about receiving insufficient medical treatment.

Conclusion: These are the first clinical results concerning SARS-CoV-2 seropositivity and COVID-19 disease in patients with SBS. The seropositivity is comparable to national data, which we attribute to increased risk awareness and avoidance. Further studies are warranted to investigate effects of COVID-19 infection in SBS patients.

KEYWORDS

COVID-19, N protein, risk behavior, SARS-CoV-2, seroprevalence, short bowel syndrome (SBS)

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CLINICAL RELEVANCY STATEMENT

Patients with short bowel syndrome (SBS) are proposed to be a group at high-risk for a severe course of coronavirus disease 2019. This multicenter cross-sectional study analyzes the prevalence of antibodies against the nucleocapsid antigen in patients with SBS, their risk behavior and frequency of contact with medical personnel. The overall severe acute respiratory syndrome coronavirus 2 seropositivity in SBS patient was comparable to national data, possibly attributed to increased risk awareness and avoidance.

BACKGROUND

Patients with a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection do not all suffer from a severe course of coronavirus disease 2019 (COVID-19) and can be asymptomatic in some cases.^{1,2} Therefore, adequate calculations concerning the rate of infections in a distinct population remain difficult. Several studies have therefore tried to analyze representative population samples with the help of SARS-CoV-2 antibody screening. SARS-CoV-2 infection, symptomatic or asymptomatic, causes a rapid antibody response.³ Measurement of the nucleocapsid (N) antigen against SARS-CoV-2 is therefore an adequate tool to quantify the spread of the virus in a population.⁴

Of particular clinical relevance are seroprevalence studies concerning patient groups at risk, which tend to have more severe cases of COVID-19, potentially requiring intensive care or even dying from COVID-19. Patient groups at higher risk of a severe course of COVID-19 are people of older age, people living in long-term care facilities, and people with underlying health conditions such as diabetes, chronic kidney disease, or a chronic respiratory disease. Several national and international guidelines^{5,6} have highlighted the need for prioritization of vaccination in these subgroups as well as allocation of medical care. Although these risk groups have been adequately researched thus far,⁷ data on orphan diseases such as short bowel syndrome (SBS) and SARS-CoV-2 seroprevalence are lacking.

SBS is a result of surgical reduction of the small intestine and consequently of the absorptive surface area. The majority of SBS patients require long-term parenteral nutrition if oral autonomy cannot be achieved.⁸ Complications of parenteral nutrition include catheter-associated bloodstream infections, thrombosis, and intestinal failure-associated liver disease.⁹ Furthermore, individual parenteral nutrition is vital to adequately manage nutrition and metabolic needs of the patients. Patients with SBS require interdisciplinary care and therefore frequent contact with caretakers, even in times of contact restrictions to prevent the spread of COVID-19.

The combination of malnourishment in some cases, frequent caretaker contact and SBS as a disturbance of the immune system itself result in patients with SBS being categorized as high-risk

patients regarding COVID-19, although reliable data are missing.^{10,11} Therefore, we aimed to establish data on prevalence of seropositivity for SARS-CoV-2 antibodies in a subgroup of SBS patients in Germany and assess data on their clinical course of COVID-19. Additionally, we tried to identify risk factors as well as protective factors in SBS patients with a previous case of COVID-19.

MATERIALS AND METHODS

Study design

Patients with SBS managed at three tertiary care centers across Germany were included in the study between January 1, 2021, and of January 31, 2022. The study centers were the Department of Hepatology and Gastroenterology at Charité—Universitätsmedizin Berlin, Internal Medicine and Gastroenterology at Asklepios Clinic St. Georg and the Medical Clinic 1 at the University Clinic Frankfurt. Patients were recruited during routine outpatient clinic visits, where blood is also routinely drawn. Written informed consent was obtained from all participants. Patient blood was then tested for antibodies against the N antigen for SARS-CoV-2 by the respective clinic laboratory (Elecsys Anti-SARS-CoV-2; F. Hoffmann-La Roche Ltd). Published false-positive rates were between 0% and 0.2%.^{12,13} Patients filled out a questionnaire with information regarding their digestive anatomy, parenteral support, frequency of medical personnel visits, current respiratory symptoms, course of potential or proven COVID-19 disease, occupation, household situation, the willingness to take risks (on a scale of 0–10, where high scores indicate riskier behavior) and level of worry due to COVID-19 concerning the economy, personal finances, transmission of SARS-CoV-2, insufficient treatment, and lack of medical or general supplies. The status of vaccination was documented at the time of presentation and patients were defined as fully vaccinated 2 weeks after the second dose. Study data were collected and managed using REDCap electronic data capture tools hosted at the Charité—Universitätsmedizin Berlin.

Statistical analysis

Statistical analysis was performed with R version 4.1.2 and R Studio version 1.4 for macOS (R Foundation for Statistical Computing). Additional required packages were tidyverse and gtsummary. For descriptive analysis, data were analyzed using the Welch two-sample *t* test for continuous variables and the Fisher exact test for categorical variables. Categorical variables are reported as counts and proportions, continuous variables as median and interquartile range (IQR). Adjustment for multiple testing was performed by Benjamini and Hochberg and are reported as *q*-values. Overall, two-sided *P* values ≤ 0.05 were considered statistically significant.

RESULTS

Patient population

Over the 13-month study period, 119 patients from three different German tertiary care centers were included in the study. More patients were female (67%). Median patient age was 60 years (IQR, 25.5 years), and the median patient BMI, 20.99 kg/m² (IQR, 5.15 kg/m²). Most common etiology for SBS was ischemia (20%) followed by ileus and surgical complications (Table 1). A third of patients (36%) had a stoma, and 67% of patients required parenteral nutrition with 6 days (IQR, 7 days) per week on average.

Sixty-six percent of patients were retired or disabled, and of those who worked, 32% performed exclusive home office at study time. Only few patients had respiratory symptoms such as a cough or running nose at time of presentation or within the last 6 months prior to the routine visit at the SBS center.

SARS-CoV-2 seropositivity and vaccination

The seroprevalence of SARS-CoV-2 antibodies against the N antigen was 7.6% ($n = 9$). Seven patients (77.8%) with positive antibodies had COVID-19 with a mild course and two patients had an asymptomatic SARS-CoV-2 infection. None of the patients was hospitalized because of COVID-19 or needed further medical treatment. Overall vaccination rate was 31% over the study period of January 2021 until January 2022, with equal distribution (30% vs 44%, $P = 0.50$) between the SARS-CoV-2 antibody-positive and antibody-negative group.

Risk behavior and patient worries

There was no significant difference in willingness—as assessed by the standardized questionnaire—to take risks in patients that were SARS-CoV-2 antibody-positive and those that were not (4.5 [IQR, 1.5] vs 6.0 [IQR, 2.0], $P = 0.61$). Overall, there was a trend for a subjectively reported reduced willingness to take risks in our patients (Figure 1). When asked about which aspects of life patients worried most about, 61% were very worried about the economy, 52% very worried about transmitting COVID-19, and 26% of receiving insufficient medical treatment due to the COVID-19 pandemic. There were no differences in degree of worry between both groups (Figure 2). When evaluating household situation and visits from medical personnel, SARS-CoV-2 antibody-positive patients had slightly more contact with their family members. Patients lived with more than one adult in 78% vs 71% of cases ($P = 0.90$) and with more than one child in 11% vs 2.7% ($P = 0.30$). 56.6% of patients received more than one visit of medical personnel per week, not differing, however, in between groups.

DISCUSSION

Not all patients with a SARS-CoV-2 infection suffer from a severe course of COVID-19. SBS has been assumed to be a risk factor for severe course of SARS-CoV-2 infection, due to the complexity of disease, the need for interdisciplinary care and therefore frequent contact with caretakers.

We here present one of the first antibody prevalence study against SARS-CoV-2 N antigen in patients with SBS and show a seroprevalence of 7.6% over the course of the year 2021. Despite previous studies showing an association with the rate of community-acquired COVID-19 and frequency of contact with nursing staff in patients with intestinal failure in the United Kingdom, our seroprevalence was within the German national average, which was 4.1%–11.6% measured in antibodies against the spike (S) antigen for the first half of 2021.^{14,15} More recent data from July 2021 to October 2021 suggest a seroprevalence of up to 7.9% (KoCo19 Study).^{16,17}

All the infections in our SBS cohort had mild clinical courses, with two patients having no symptoms at all. This would be unexpected in a group of high-risk patients. There has been discussion about an improvement of micronutrient supplementation, that is, with zinc, selenium, and vitamin D to reduce low-grade inflammation and therefore raising antiviral resistance against COVID-19.^{18–20} Although highly speculative, it is possible, that adequate parenteral nutrition with a heightened awareness for micronutrition contributed to milder courses of COVID-19 in our study population.

Worrying was a relevant topic for patients with SBS. With high and very high subjective worry concerning the economy, COVID-19 transmission, and receiving insufficient medical treatment. Especially reassuring patients that they will get adequate treatment can be difficult due to changing contact restrictions and, in some cases, delayed outpatient appointments. Financial aspects played a further role for our SBS patients. With many patients in early retirement and currently rising costs of living in many major German cities. These aspects were, however, not associated with seropositivity for SARS-CoV-2.

Seroprevalence studies vary greatly depending on study region, study population and study time point.^{14,21} Our study duration of one year saw the appearance of two new SARS-CoV-2 variants, namely Delta and Omicron, both with their individual infection peaks.²² Furthermore, severity of disease varied greatly with the emergence of the omicron variant. The relatively small sample size of nine infected patients and their mild course of disease might therefore not adequately represent the severity of disease. Additionally cross-sectional data on vaccination, at a time of new implementation, may not adequately reflect the status quo. Nevertheless, we managed to achieve a formidable sample size despite SBS being an orphan disease and propose at least some transferability of our study data.

TABLE 1 Patient data

Variable	Overall, N = 119	Negative, N = 110	Positive, N = 9	P-value ^a	q-value ^b
Sex, female (%)	80 (67)	75 (68)	5 (56)	0.5	>0.9
Age, years, median (IQR)	60 (25.5)	59.5 (27.5)	63 (16)	0.7	>0.9
BMI, kg/m ² , median (IQR)	20.99 (5.2)	20.79 (4.9)	21.22 (3.2)	0.4	>0.9
Etiology, n (%)				>0.9	>0.9
Ischemic	24 (20)	22 (20)	2 (22)		
Surgical	19 (16)	17 (16)	2 (22)		
Ileus	18 (15)	17 (16)	1 (11)		
Tumor	18 (15)	17 (16)	1 (11)		
IBD	14 (12)	13 (12)	1 (11)		
Trauma	6 (5.1)	6 (5.5)	0 (0)		
Radiation	4 (3.4)	3 (2.8)	1 (11)		
Other	15 (13)	14 (13)	1 (11)		
Stoma, n (%)	43 (36)	39 (35)	4 (44)	0.7	>0.9
Type of SBS, n (%)				>0.9	>0.9
Type 1 (end-enterostomy)	39 (33)	36 (33)	3 (33)		
Type 2 (jejunocolic anastomosis)	43 (36)	40 (36)	3 (33)		
Type 3 (jejunoleocolic anastomosis)	37 (31)	34 (31)	3 (33)		
Length of remaining Intestine, cm, median (IQR)	85.0 (70)	80.0 (70)	120.0 (22.5)	0.052	0.5
Days receiving parenteral support, n (%)				0.6	>0.9
0	39 (33)	33 (30)	6 (67)		
1	0 (0)	0 (0)	0 (0)		
2	3 (2.5)	3 (2.7)	0 (0)		
3	5 (4.2)	5 (4.5)	0 (0)		
4	11 (9.2)	11 (10)	0 (0)		
5	11 (9.2)	11 (10)	0 (0)		
6	8 (6.7)	8 (7.3)	0 (0)		
7	42 (35)	39 (35)	3 (33)		
Administration of parenteral nutrition, n (%)				>0.9	>0.9
With care Service	28 (35)	27 (36)	1 (33)		
Without care Service	47 (59)	45 (59)	2 (67)		
Changing	4 (5.1)	4 (5.3)	0 (0)		
Symptomatic COVID-19 infection, n (%)	7 (5.9)	0 (0)	7 (78)	<0.001	<0.001
Occupation, n (%)				0.8	>0.9
Looking for work	2 (1.7)	2 (1.8)	0 (0)		
In training	12 (10)	11 (10)	1 (11)		
Retired	79 (66)	73 (66)	6 (67)		
On sick leave	7 (5.9)	6 (5.5)	1 (11)		
Part time job	10 (8.4)	9 (8.2)	1 (11)		
Full time job	9 (7.6)	9 (8.2)	0 (0)		

(Continues)

TABLE 1 (Continued)

Variable	Overall, N = 119	Negative, N = 110	Positive, N = 9	P-value ^a	q-value ^b
Home Office, n (%)				>0.9	>0.9
Yes	6 (32)	6 (33)	0 (0)		
No	10 (53)	9 (50)	1 (100)		
Changing	3 (16)	3 (17)	0 (0)		
Adults in household, n (%)				>0.9	>0.9
>1	85 (71)	78 (71)	7 (78)		
≤1	34 (29)	32 (29)	2 (22)		
Children in household, n (%)				0.3	>0.9
>1	4 (3.4)	3 (2.7)	1 (11)		
≤1	115 (97)	107 (97)	8 (89)		
Doctor visits, n (%)	1 (0.8)	0 (0)	1 (11)	0.076	0.5
Care service visits, n (%)	45 (38)	40 (36)	5 (56)	0.3	>0.9
Provider visits, n (%)	20 (17)	18 (16)	2 (22)	0.6	>0.9
Ostomy care visits, n (%)	1 (0.8)	1 (0.9)	0 (0)	>0.9	>0.9
Smoking, n (%)				0.2	>0.9
Nonsmoker	63 (53)	60 (55)	3 (33)		
Ex-smoker	33 (28)	28 (25)	5 (56)		
Smoker	23 (19)	22 (20)	1 (11)		
Complete vaccination, n (%)	37 (31)	33 (30)	4 (44)	0.5	>0.9

Abbreviations: COVID-19, coronavirus disease 2019; IBD, inflammatory bowel disease; SBS, shortbowel syndrome.

^aFisher exact test; Welch two-sample t test.

^bFalse discovery rate correction for multiple testing.

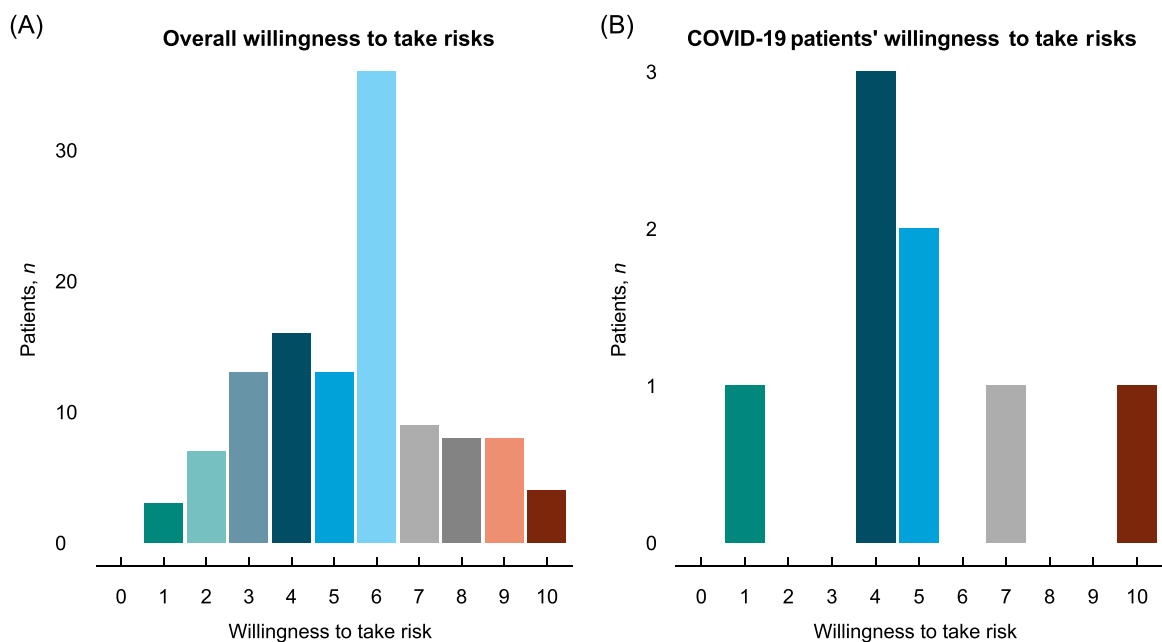


FIGURE 1 (A) Overall willingness to take risks on a scale of 0–10; (B) willingness to take risks in subgroup of severe acute respiratory syndrome coronavirus 2 seropositive patients

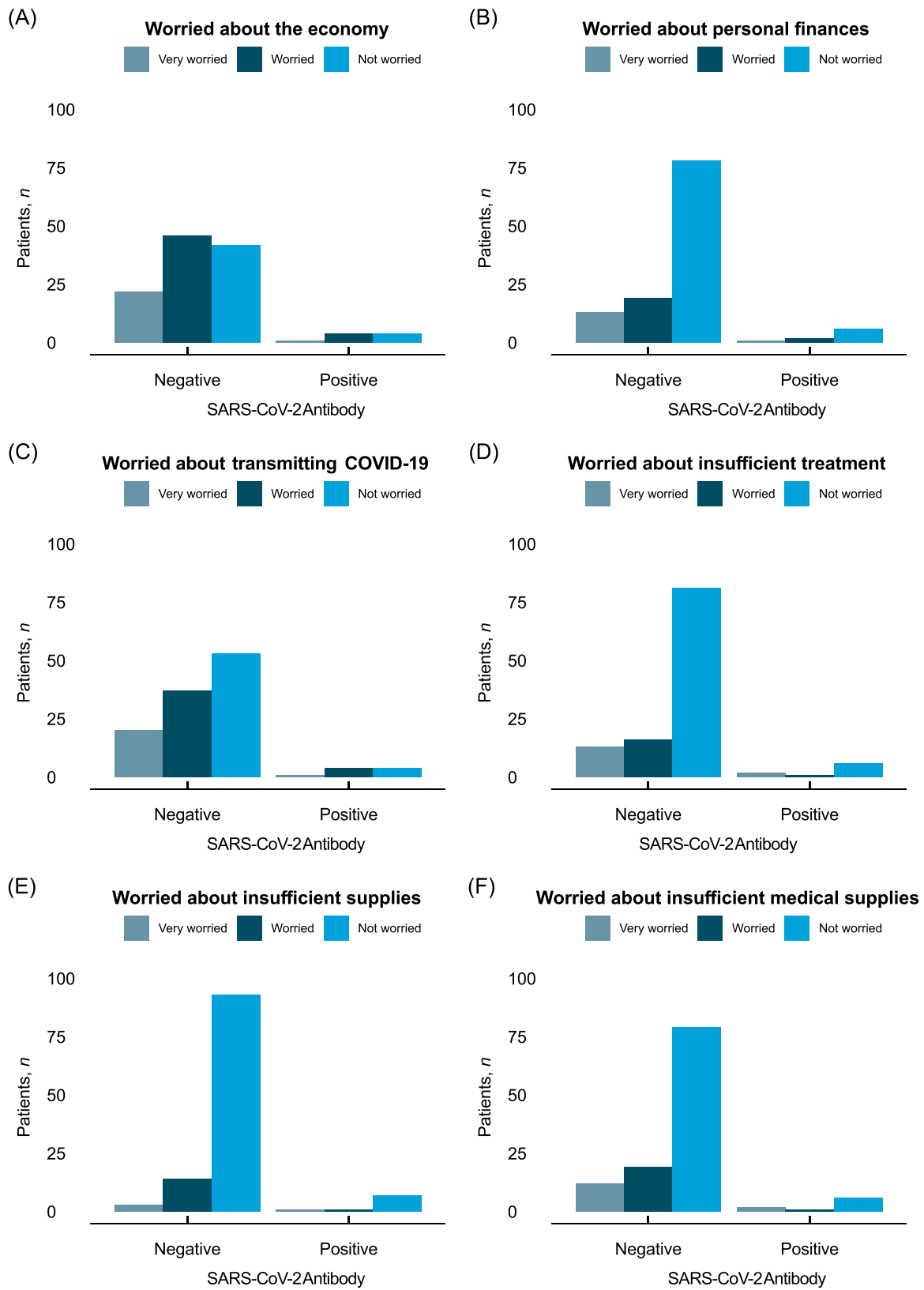


FIGURE 2 Worry about aspects of life in patients: (A) economy, (B) personal finances, (C) transmission of severe acute respiratory syndrome coronavirus 2, (D) insufficient treatment, (E) insufficient general supplies, (F) insufficient medical supplies

CONCLUSION

We here report on SARS-CoV-2 seropositivity and COVID-19 disease in patients with SBS. The seropositivity is comparable to German national data, despite frequent caretaker contact due to complexity of SBS. We assume increased risk awareness and avoidance may have attributed to comparable seroprevalence. Infections were only mild and did not require hospitalization. Further studies are warranted to investigate effects of COVID-19 infection in SBS patients.

AUTHOR CONTRIBUTIONS

Elisabeth Blüthner and Simon Moosburner equally contributed to the conception and design of the research. Ulrich-Frank Pape and Frank Tacke contributed to the design of the research. Ulrich-Frank Pape, Irina Blumenstein, and Jeanette Wichmann contributed to acquisition of data. Elisabeth Blüthner, Simon Moosburner, and Frank Tacke contributed to the interpretation and analysis of data and drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work as well as read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICS STATEMENT

The institutional ethics board approved the study (EA4/199/20).

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