

COVID-19 outcomes in MS

Observational study of early experience from NYU Multiple Sclerosis Comprehensive Care Center

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Abstract

Objective

To report outcomes on patients with multiple sclerosis (MS) and related disorders with coronavirus disease 2019 (COVID-19) illness.

Methods

From March 16 to April 30, 2020, patients with MS or related disorders at NYU Langone MS Comprehensive Care Center were identified with laboratory-confirmed or suspected COVID-19. The diagnosis was established using a standardized questionnaire or by review of in-patient hospital records.

Results

We identified 76 patients (55 with relapsing MS, of which 9 had pediatric onset; 17 with progressive MS; and 4 with related disorders). Thirty-seven underwent PCR testing and were confirmed positive. Of the entire group, 64 (84%) patients were on disease-modifying therapy (DMT) including anti-CD20 therapies (n = 34, 44.7%) and sphingosine-1-phosphate receptor modulators (n = 10, 13.5%). The most common COVID-19 symptoms were fever and cough, but 21.1% of patients had neurologic symptom recrudescence preceding or coinciding with the infection. A total of 18 (23.7%) were hospitalized; 8 (10.5%) had COVID-19 critical illness or related death. Features more common among those hospitalized or with critical illness or death were older age, presence of comorbidities, progressive disease, and a nonambulatory status. No DMT class was associated with an increased risk of hospitalization or fatal outcome.

Conclusions

Most patients with MS with COVID-19 do not require hospitalization despite being on DMTs. Factors associated with critical illness were similar to the general at-risk patient population. DMT use did not emerge as a predictor of poor COVID-19 outcome in this preliminary sample.

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From the NYU Langone Multiple Sclerosis Comprehensive Care Centers (E.P., I.K., L.C., C.S., V.S., R.E.C., J.H., J.M.G., M.G., N.A.-F., R.W., M.K., L.B.K., L.Z.R.), New York, NY; and Cohen's Children Medical Center Northwell Health (C.F.-C.), Lake Success, NY.

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Glossary

CAD = coronary artery disease; **COVID-19** = coronavirus disease 2019; **DMT** = disease-modifying therapy; **ICU** = intensive care unit.

At present, we do not know whether multiple sclerosis (MS) or disease-modifying therapies (DMTs) for MS increase the risk of acquiring coronavirus disease 2019 (COVID-19) or worsen the course (hospitalizations, intensive care unit [ICU], and death). DMT medications have immunosuppressive effects that could hamper mounting an effective immune response to the infection.¹ On the other hand, immunosuppression could offer protection by downregulating hyperinflammation and the cytokine storm associated with COVID-19.²

New York City emerged as the epicenter of the COVID-19 pandemic in the United States in March 2020. Given the widespread prevalence of COVID-19 in our community, clinicians at the NYU Multiple Sclerosis Comprehensive Care Center (MSCCC) received numerous reports of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2) infection from patients and began systematically collecting symptom data and the clinical course. This timely, real-world observational study on outcomes of COVID-19 in actively treated patients with MS help inform clinicians as they counsel patients with MS and guide treatment decisions during the pandemic.

Methods

For this observational study, demographic and clinical features were collected on patients currently followed at MSCCC and its 4 affiliated sites in the greater New York area (2 in Long Island and 2 in Brooklyn) with a history of COVID-19 from March 16 through April 30, 2020. All patients who contacted the center with infectious symptoms or were seen during routine teleneurology visits were queried regarding COVID-19 exposure using a standardized instrument. Inclusion criteria were any patient with MS or related disorders who was diagnosed with COVID-19 by a health care provider (based on symptoms, course, radiographic findings consistent with CDC COVID-19 criteria,³ and/or positive SARS-COV2 PCR when available). For hospitalized patients, in-patient records were reviewed. NYU School of Medicine Institutional Review Board approval was obtained for the study.

Descriptive statistics were used to summarize the demographic and clinical characteristics of patient. Continuous variables were described in terms of means and SDs, and categorical variables were summarized as counts and percentages. No imputation was made for missing data. Differences between hospitalized vs nonhospitalized patients were compared by the *t* test, χ^2 test, or Fisher exact test as indicated, with CIs set at 95%.

Data availability

Anonymized data can be made available on request for research purposes by submitting a request to the corresponding author. No deidentified patient data or study-related documents will be shared.

Results

A total of 76 patients met the inclusion criteria, 72 (93%) with MS, and 4 (7%) with related disorders (neuromyelitis optica spectrum disorder, chronic relapsing inflammatory optic neuropathy, neurosarcoidosis, and myelin oligodendrocyte glycoprotein-immunoglobulin G-associated disorder). The average age of the full sample was 44.9 ± 15.2 years (range 13–71 years), and 61.8% were female. The disease duration was 15.2 ± 10.7 years (range 1–52 years). Racial breakdown was 50 (65.8%) white, 21 (27.6%) black, 3 (3.9%) Asian, 1 (1.3%) Pacific Islander, and 1 (1.3%) other. Hispanic ethnicity was reported by 15 (19.7%). Of the 72 patients with MS, 55 (76.4%) had a relapsing-remitting subtype and 17 (23.6%) primary or secondary progressive subtypes. Sixty-five patients (84%) were on DMT. One patient resided in a nursing facility. He had an uncomplicated course.

Common symptoms reported included fever (68.4%), cough (68.4%), fatigue (38.2%), shortness of breath (31.6%), and myalgias/arthralgias (26.3%). Other frequent symptoms included anosmia (22%), ageusia (19.7%), and headache (21.1%). A subset reported neurologic symptom recrudescence (21.1%) suggestive of relapse. In some cases, neurologic symptoms preceded viral symptoms by several days.

Of the 84% of patients on DMTs, 44.7% were treated with anti-CD20 therapies (rituximab *n* = 18; ocrelizumab *n* = 16), 13.5% on sphingosine-1-phosphate (S1P) modulators (fingolimod *n* = 8; siponimod *n* = 2), 7.9% (*n* = 6) on glatiramer acetate, 5.3% (*n* = 4) each on natalizumab and dimethyl fumarate, and 3.9% (*n* = 3) on beta-interferons. Table 1 summarizes outcomes by DMT class. There were no observed differences between DMT use among those who were and were not hospitalized or between those specifically treated with anti-CD20 therapies (43% vs 50%, OR = 0.76 [CI 0.26–2.18]).

As shown in table 2, of the full sample, 18 (23.7%) were hospitalized. The hospitalized vs nonhospitalized patients were more likely to be older (CI 1.22–17.11, *p* = 0.03), have progressive MS subtype (OR 4.11 [CI 1.21–13.97], *p* = 0.04), required ambulatory assistance or were nonambulatory (OR 4.27 [CI 1.38–13.27], *p* = 0.01), and have comorbid obesity (OR 6.25 [CI 1.90–20.50], *p* = 0.003). Coronary artery disease (CAD) was observed in *n* = 3 hospitalized patients and no cases in nonhospitalized patients.

Table 1 Disease-modifying therapy specific outcomes

Demographics	Anti-CD20	S1P inhibitors	Glatiramer acetate	Natalizumab	Dimethyl fumarate	Interferon	IVIG	None
n	34	10	6	4	4	3	3	12
Age, years (SD)	38.72 (SD 14.9)	44.90 (SD 11.2)	53.3 (SD 14.8)	37.8 (SD 17.9)	52.8 (SD 7.2)	57.6 (SD 16.7)	57 (SD 12.8)	49.8 (SD 15.8)
Female n (%)	20 (62.5%)	6 (60%)	4 (66.7%)	2 (50%)	2 (50%)	1 (33.3%)	3 (100%)	8 (66.7%)
Ambulation status, n (%)								
Ambulatory	27 (79.4%)	9 (90%)	2 (33.3%)	4 (100%)	3 (75%)	3 (100%)	—	8 (66.7%)
Ambulatory with assistance	4 (11.8%)	1 (10%)	3 (50%)	—	—	—	2 (66.7%)	1 (8.3%)
Nonambulatory	3 (8.8%)	—	1 (16.7%)	—	1 (25%)	—	1 (33.3%)	3 (25%)
Hospitalization								
Not hospitalized	25 (73.5%)	9 (90%)	5 (83.3%)	3 (75%)	2 (50%)	3 (100%)	3 (100%)	8 (66.7%)
Hospitalized	9 (26.5%)	1 (10%)	1 (16.7%)	1 (25%)	2 (50%)	—	—	4 (33.3%)
Comorbidities associated with COVID-19								
Obesity	9 (26.5%)	3 (30%)	2 (33.3%)	2 (50%)	1 (25%)	—	1 (33.3%)	6 (50%)
Hypertension	4 (11.8%)	3 (30%)	1 (16.7%)	1 (25%)	2 (50%)	—	2 (66.7%)	4 (33.3%)
Diabetes	1 (2.9%)	1 (10%)	1 (16.7%)	1 (25%)	1 (25%)	—	1 (33.3%)	2 (16.7%)
CAD	1 (2.9%)	—	1 (16.7%)	1 (25%)	—	—	—	—
COVID-19 outcomes								
Death	2 (5.8%)	—	1 (16.7%)	1 (25%)	—	—	—	2 (16.7%)
Ongoing treatment/still recovering	8 (23.5%)	3 (30%)	1 (16.7%)	—	—	—	1 (33.3%)	2 (16.7%)
Recovered	24 (70.6%)	7 (70%)	4 (66.7%)	3 (75%)	4 (100%)	3 (100%)	2 (66.7%)	8 (66.7%)

Abbreviations: Anti-CD20 = ocrelizumab and rituximab; COVID-19 = coronavirus disease 2019; Interferons = interferon beta-1a and interferon beta-1b; IVIG = IV immunoglobulins; S1P inhibitors = fingolimod and siponimod. One 58-year-old woman with a history of hypertension on leflunomide had a mild course.

Table 2 Demographics of hospitalized vs nonhospitalized patients with COVID-19

Demographics	Hospitalized (n = 18)	Nonhospitalized (n = 58)
Age, years (range, SD)	52.0 (17–71, 14.6)	42.7 (13–71, 14.8)
Sex (% female)	10 (55.6%)	37 (63.8%)
Race, n (% white)	12 (66.7%)	38 (65.5%)
Ethnicity, n (% Hispanic)	6 (33.3%)	9 (15.5%)
Clinical diagnosis		
RRMS	8 (44.4%)	47 (81.0%)
Progressive MS	7 (38.8%)	10 (17.2%)
Other demyelinating syndrome	3 (16.7%)	1 (1.7%)
Disease duration, years (range, SD)	17.2 (5–36, 10.5)	14.6 (1–52, 10.8)
Ambulation status, n (%)		
Ambulatory	9 (50%)	47 (81%)
Ambulatory with assistance	5 (27.8%)	6 (10.3%)
Nonambulatory	4 (22.2%)	5 (8.6%)
Comorbidities associated with COVID-19		
Obesity	11 (61%)	12 (20.7%)
Hypertension	5 (27.8%)	12 (20.6%)
CAD	3 (16.6%)	—
Diabetes	2 (11.1%)	6 (10.3%)
Venous thromboembolism	3 (16.6%)	1 (1.7%)
COVID-19 outcomes		
Death, n (%)	5 (27.7%)	1 (1.7%)
Ongoing treatment/still recovering	4 (22.2%)	10 (17.2%)
Recovered, n (%)	9 (50.0%)	47 (81.0%)

Abbreviations: CAD = coronary artery disease; COVID-19 = coronavirus disease 2019; DMT = disease-modifying therapy.

History of venous thromboembolism was recorded in n = 3 hospitalized and n = 1 nonhospitalized patient.

Eight patients (10.5%) had critical illness defined by ICU admission (n = 5) and/or death (n = 6) (table 3). Compared with the entire MS sample, the critically ill patients were older (mean of 57.7 ± 10.5 years, range 42–71 years), more likely to have a progressive subtype (50.0%), and or required assistance for ambulation/nonambulatory (62.5% requiring assistance or nonambulatory). Following the pattern observed in those who were hospitalized, the critically ill group had had high rates of comorbid obesity (62.5%), CAD (25%), and venous thromboembolism (37.5%). There were no reports of stroke. One patient had hypercoagulability resulting in multiple venous thromboembolisms and ultimately died.

Nine patients with pediatric-onset MS were identified as the center has a large pediatric MS sample (table 4). Ages ranged from 13 to 26 years; 8 were female, and all had

relapsing-remitting MS. Noted comorbidities were obesity (n = 3), type I diabetes (n = 1), or both (n = 1). Two of the 9 were hospitalized requiring supplemental oxygen. None required invasive ventilation. Eight patients were either fully recovered or recovering at censoring date. One remains hospitalized.

Discussion

Patients with MS and related disorders often seek guidance regarding the impact of the disease and medication on their risk of COVID-19. This observational study—although subject to sampling and ascertainment biases—provides some insights regarding COVID-19 disease course in actively treated patients with MS and related disorders.

The rate of hospitalization in our patients (24%) and mortality (7.9%) are in line with the data of another published MS

Table 3 Critically ill and deceased patient outcomes

Age/ sex	Race/ ethnicity	Diagnosis and disease duration (y)	DMT	Ambulation status	Comorbidities	COVID course and outcome
42/ M	Black/non-Hispanic	RRMS—18 y	Rituximab	Nonambulatory	Chronic anticoagulation for VTE, Hodgkin lymphoma, and ITB	Several weeks of fevers, cough, and dyspnea. A family member in the home was also sick with similar symptoms. Died at home.
46/ M	Black/non-Hispanic	SPMS—26 y	None	Nonambulatory	Diabetes, morbid obesity, hypertension, chronic anticoagulation for VTE, and hyperlipidemia	Hospitalized with dyspnea, fever, and cough and received high-flow oxygen. Discharged to a rehabilitation facility on supplemental oxygen
50/F	White/non-Hispanic	RRMS—13 y	None	Ambulatory	Hypertension, obesity, and hypothyroid	Hospitalized with respiratory failure following treatment with 5 d of IVMP for MS exacerbation. Received ventilator and ECMO support. Deceased.
60/F	Black/non-Hispanic	RRMS—19 y	Natalizumab	Ambulatory	CAD with cardiac stents, hypertension, and obesity	Hospitalized with fatigue, cough, fever, and respiratory failure. Found to have DVT and PE. Had cardiac arrest. Deceased.
62/ M	White/ Hispanic	NMOSD—7 y	Rituximab	Ambulatory	Obesity	Hospitalized with dyspnea and fever and on high-flow oxygen. Remains hospitalized.
65/F	White/non-Hispanic	SPMS—31 y	None	Nonambulatory	ITB and neurogenic bladder with indwelling Foley	Hospitalized with fever, dyspnea, and code status DNR/DNI. Deceased
66/ M	White/non-Hispanic	SPMS—33 y	Ocrelizumab	Nonambulatory	Remote history of testicular and prostate cancer and ITB	Hospitalized with respiratory failure and received ventilator support. Deceased.
71/ M	Black/non-Hispanic	SPMS—30 y	Glatiramer acetate	Ambulatory with assistance	Chronic anticoagulation for VTE obesity	Hospitalized with dyspnea and fever and had cardiac arrest. Deceased.

Abbreviations: CAD = coronary artery disease; COVID-19 = coronavirus disease 2019; DMT = disease-modifying therapy; DNR/DNI = do not resuscitate/do not intubate; DVT = deep venous thrombosis; ECMO = extracorporeal membrane oxygenation; ITB = intrathecal baclofen pump; IVMP = IV methylprednisolone; PE = pulmonary embolus; RRMS = relapsing-remitting MS; SPMS = secondary progressive MS; VTE = venous thrombosis.

Of the 8 patients, 7 tested positive for COVID-19. The patient who died at home was not tested for COVID as he did not receive any hospital care before expiration. Both he and a family member he resided with had symptoms of fever, cough, and dyspnea for several weeks prior. The family member has since recovered.

Table 4 Demographics of patients with pediatric-onset MS with COVID-19

	Full sample (n = 9)
Demographics	
Age, years (range, SD)	19.44 (13–26, 4.12)
Sex (% female)	7 (77.7%)
Race, n (% white)	6 (66.6%)
Ethnicity, n (% Hispanic)	5 (55.5%)
Clinical history	
MS subtype, n (% RRMS)	9 (100%)
Disease duration, years (range, SD)	6.11 (2–12, 3.55)
DMT, n (%)	
Glatiramer	1 (11.1%)
Ocrelizumab	2 (22.2%)
Rituximab	4 (44.4%)
Natalizumab	1 (11.1%)
None	1 (11.1%)
Ambulation status, n (% fully ambulatory)	9% (100)
COVID-19 testing, comorbidities, and hospitalization	
Tested for COVID-19, n (%)	5 (55.5%)
Positive, n (% tested)	4 (80%)
Diabetes, type I	2 (22.2%)
Obesity	3 (33.3%)
Asthma	1 (11.1%)
Hospitalized, n (%)	2 (22.2%)

Abbreviation: DMT = disease-modifying therapy.

patient survey⁴ and for the general population of patients with COVID-19.⁵ Similar risk factors were identified including older age, male sex, and high number of comorbidities such as obesity, diabetes, hypertension, and CAD.^{6–8} MS-specific features associated with more severe COVID-19 included nonambulatory status and progressive disease course. Given the small sample size, we could not determine whether these patients were at higher risk, given their advanced age and other comorbidities, or whether worse disability in and of itself represents an additional risk factor.

We did not observe an association between DMT class and COVID-19 outcome in univariate comparisons; however, our sample size is small, and these preliminary findings should be interpreted with caution. There is a relatively high proportion

of COVID-19–infected patients on anti-CD20 therapies (44.7%) compared with our MSCCC population in which 33.1% of patients take anti-CD20 therapies. This observation could be an artifact of sampling bias or might represent an increased susceptibility to COVID-19 infection as anti-CD-20 therapies increase the risk of non-COVID-19 infections in general.¹ It is worth noting that although we had a larger-than-expected portion of patients on anti-CD20 therapies, there is no evidence to suggest worse outcomes.

As a note of caution in the care of patients with MS, a subgroup of individuals reported worsening of preexisting neurologic symptoms before or at onset of COVID-19 symptoms. One such patient was treated with several days of high-dose steroids after which they presented with respiratory and circulatory failure and ultimately died (table 3). Infections are a well-known cause of pseudoexacerbations, and in areas with high prevalence of COVID-19, testing for SARS-COV2 should be considered in patients with acute worsening of preexisting symptoms before steroid treatment is initiated.

Our study has several limitations. This was a convenience sample and not randomly selected, nor was the entire practice systematically surveyed. Patients were identified during routine teleneurology visits, if they notified the office, or if hospitalized—likely leading to an overrepresentation of more symptomatic individuals. Patients on higher potency infusible DMTs were more likely to have frequent follow-up and may have been more readily captured. In contrast, patients in nursing homes, who would be expected to be most severely affected by COVID-19, visit specialized centers less frequently and could be underrepresented in our cohort. Although we used a systematic questionnaire to collect relevant data, we could not verify these data independently unless the patient was seen by an NYU Langone-affiliated physician or hospital. Another problem was lack of access to COVID-19 testing in our area. Less than half of our patients (48.7%) underwent SARS-COV2 PCR testing. As shown in table 5, subgroup analysis showed that this group was not different from the overall sample with respect to demographic or MS-related features.

Our early experience with COVID-19 at NYU Langone MSCCC could inform clinicians taking care of patients with MS during the pandemic. Our findings suggest that individuals with MS who experience COVID-19 have similar disease course, outcomes, and risk factors for complications as the general population. Rigorous, population-based studies are needed to confirm our preliminary findings and better define the risk of COVID-19 infection with respect to individual DMTs. Future studies should assess the role of baseline lymphocyte counts and immunoglobulin levels with respect to viral susceptibility and course as well as examine the frequency of serologies to COVID-19 according to DMT class. As we and others collect more data and contribute to larger MS registries, we expect more answers will be forthcoming to further guide patient management.

Table 5 Demographics and outcomes of all patients vs COVID-19 PCR confirmed positive

	All patients (n = 76)	COVID PCR positive (n = 37)
Demographics		
Age, years (range, SD)	44.9 (13–71, 15.2)	47.5 (13–71, 15.15)
Sex, F/M (% female)	47/29 (61.8%)	23/14 (62.2%)
Race, n (%)		
White	50 (65.8%)	24 (64.9%)
Black	21 (27.6%)	12 (32.4%)
Asian	3 (3.9%)	—
Pacific Islander	1 (1.3%)	—
Other	1 (1.3%)	1 (2.7%)
Ethnicity, n (%)		
Non-Hispanic	59 (77.6%)	28 (75.7%)
Hispanic	15 (19.7%)	8 (21.6%)
Other	2 (2.6%)	1 (2.7%)
Smoking status, n (%)		
Never	52 (68.4%)	25 (67.5%)
Former	20 (26.3%)	10 (27.02)
Current	2 (2.6%)	1 (2.7%)
Unknown	2 (2.6%)	1 (2.7%)
Clinical		
MS, n (%)		
RRMS	55 (72.3%)	25 (67.6%)
SPMS	15 (19.7%)	10 (27.0%)
PPMS	2 (2.6%)	—
Other demyelinating syndrome, n (%)	4 (5.2%)	2 (5.4%)
Disease duration, years (range, SD)	15.2 (1–52, 10.7)	16.9 (2–52, 11.46)
DMT, n (%)		
Anti-CD20	34 (44.7%)	14 (37.8%)
S1P Inhibitors	10 (13.2%)	4 (10.8%)
Glatiramer acetate	6 (7.9%)	4 (10.8%)
Natalizumab	4 (5.3%)	3 (8.1%)
Dimethyl fumarate	4 (5.3%)	2 (5.4%)
Leflunomide	1 (1.3%)	1 (2.7%)
Interferons	3 (3.9%)	1 (2.7%)
IVIG	3 (3.9%)	1 (2.7%)
None	12 (15.8%)	7 (18.9%)
Ambulation status, n (%)		
Ambulatory	56 (73.7%)	24 (64.9%)
Ambulation with assistance	11 (14.4%)	7 (18.9%)

Continued

Table 5 Demographics and outcomes of all patients vs COVID-19 PCR confirmed positive (continued)

	All patients (n = 76)	COVID PCR positive (n = 37)
Nonambulatory	9 (11.8%)	6 (16.2%)
Comorbidities associated with COVID-19		
Hypertension	17 (22.4%)	11 (29.7%)
Obesity	23 (30.3%)	11 (29.7%)
Diabetes	8 (10.5%)	5 (13.5%)
VTE	4 (5.3%)	3 (8.1%)
CAD	3 (3.9%)	3 (8.1%)
History of cancer	4 (5.3%)	2 (5.4%)
Baclofen pump	3 (3.9%)	2 (5.4%)
Indwelling Foley	3 (3.9%)	2 (5.4%)
None	24 (31.6%)	12 (32.4%)
COVID-19 outcomes		
Death, n (%)	6 (7.9%)	5 (13.5%)
Ongoing treatment/still recovering	14 (18.4%)	7 (18.9%)
Recovered, n (%)	56 (73.7%)	25 (67.6%)

Abbreviations: Anti-CD20 = ocrelizumab and rituximab; CAD = coronary artery disease; COVID-19 = coronavirus disease 2019; DMT = disease-modifying therapy; Interferons = interferon beta-1a and interferon beta-1b; IVIG = IV immunoglobulins; S1P inhibitors = fingolimod and siponimod; VTE = venous thromboembolism.

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Appendix Authors

Name	Location	Contribution
Erica Parrotta, DO	NYU Langone Comprehensive Care Center, New York, NY	Organization and acquisition of data; analyzed and interpreted data; drafted results; and revised the manuscript for intellectual content
Ilya Kister, MD	NYU Langone Comprehensive Care Center, New York, NY	Interpreted the data; drafted the discussion; and revised the manuscript for intellectual content
Leigh Charvet, PhD	NYU Langone Comprehensive Care Center, New York, NY	Analyzed the data; performed statistical analysis; and revised the manuscript for intellectual content
Carrie Sammarco, DNP	NYU Langone Comprehensive Care Center, New York, NY	Major role in acquisition of data
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Appendix (continued)

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Malcolm Gottesman, MD	NYU Langone MS Comprehensive Care Center, Mineola, NY	Acquisition of data
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Cristina Fernandez-Carbonell, MD	Cohen's Children Medical Center Northwell Health, Lake Success, NY	Acquisition of data

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Appendix (continued)

Name	Location	Contribution
Lauren B. Krupp, MD	NYU Langone Comprehensive Care Center, New York, NY	Interpreted the data and drafted and revised the manuscript for intellectual content
Lana Zhovtis Ryerson, MD	NYU Langone Comprehensive Care Center, New York, NY	Designed and conceptualized the study; analyzed the data; and drafted and revised the manuscript for intellectual content

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