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Supplementary appendix

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Supplementary Material

Content

COVID-19 Associated Risks and Effects in Myasthenia Gravis (CARE-MG): Development of an International Physician Registry and Initial Data

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Author Contributions:

Authors SM, JTG and RJK helped with design of the study protocol and manuscript preparation. All other authors helped with design of study protocol and important suggestions to manuscript.

All authors have full access to data and accept responsibility and accept responsibility for the decision to submit for publication. Authors SM and YL verify the underlying data in table 1.

This study is approved by central IRB and additional local IRBs as required.

Author Disclosures:

Muppidi S: Dr Muppidi reports no conflicts directly related to this publication. Dr. Muppidi reports other from Alexion, other from argenx, other from Ra Pharma, outside the submitted work; .

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CARE-MG Registry Details

We request that physicians report patients with Autoimmune Myasthenia gravis who developed COVID-19 irrespective of severity.

Inclusion Criteria:

1. MG diagnosis (as per antibody criteria or electrodiagnostic criteria or response to acetylcholine esterase inhibitor therapy)
2. COVID-19 diagnosis both laboratory-confirmed or clinically suspected
    - Laboratory Confirmed COVID-19 - Positive viral RNA tests or positive serology for SARS-CoV-2
    - Suspected COVID-19 but not confirmed - Fever with Dry cough, +/- anorexia, myalgias, dyspnea, anosmia/ageusia, potential exposure, Chest imaging suggestive of COVID-19

Critical elements requested in registry:

1. MG clinical characteristics including MG antibody status, thymectomy or thymoma status, preceding immunosuppression, and MGFA status.
2. Details related to COVID-19 diagnosis including diagnostic testing, severity, validated measures of sepsis or respiratory status, and any treatment given for COVID-19
3. MG worsening/crises with COVID-19 and any MG-specific treatment given for worsening and crises.
4. Overall outcomes during or soon after COVID-19 diagnosis including death.

Research Study Approval:

This study was reviewed by the Advarra central institutional review board (IRB) and was given 'exempt' status as per U.S Department of Health and Human Services regulations found at 45 CFR (code of federal regulations) 46.104(d)(4). Further information on Advarra can be obtained at https://www.advarra.com/about-advarra/the-advarra-review-board/ (accessed on September 3, 2020).

We recommend physicians to follow local regulations regarding research study protocol and submitting de-identified information. Registry is specifically designed to avoid any identifying information and minimize or eliminate the burden on reporting physicians or faculty.

Case Report Forms:

The registry remains open and active accrual continues through electronic or paper case report form submission.

Case submission can be completed at https://myasthenia.org/For-Professionals/Resources-for-Professionals/CARE-MG).

Data Storage:

All submitted data electronically (by REDCap) or paper form is stored at Duke Clinical and Translational Science Institute.

CARE-MG Registry commitment and goals:

CARE-MG registry represents the commitment of neurologists and neuromuscular specialists from across the globe to collect key information necessary to ensure evidence-based practices for our patients with MG in a dynamic public health environment. We encourage clinicians to report all their COVID-19 MG cases irrespective of outcomes and to join the CARE-MG Study Group.

Only with robust international collaboration can we ensure our data represent the true experience of patients with MG and address critical unanswered questions related to the pandemic. Responsive real-world data updates will be made available as cases continue to be reported by the neurology community.

Table 1:

Table 1: Demographic and Disease Characteristics of Patients with Myasthenia Gravis Diagnosed with Coronavirus Disease 2019 in the CARE-MG Registry, as of October 5th, 2020

Cohort Characteristics	
No. of patients with MG	91(100%)
Demographics	
Age, mean (SD), yrs	56.24 (±16.1)
Age >65 years, n (%)	30 (32%)
Women, n (%)	49 (53%)
Men, n (%)	42 (47%)
Antibody Status	
AChR+, n (%)	72 (79%)
MuSK+, n (%)	7 (8%)
Seronegative or Unknown, n (%)	12 (13%)
Clinical Phenotype	
Ocular, n (%)	9 (10%)
Generalized, n (%)	82 (90%)
MGFA Clinical Class prior to COVID-19	
Asymptomatic, n (%)	21 (23%)
I, n (%)	16 (17%)
IIa/IIb, n (%)	35 (38%)
IIIa/IIIb, n (%)	11 (12%)
IVa/IVb, n (%)	5 (6%)
V, n (%)	1 (1%)
Unknown, n (%)	2 (2%)
MG Therapy prior to COVID-19	

Immunosuppressive therapy, n (%)	81 (89%)
Symptomatic or no therapy, n (%)	10 (11%)
Co-morbid conditions	
Cardiovascular disease	11 (12%)
Pulmonary disease	10 (11%)
HTN	23 (25%)
Diabetes	24 (26%)
Obesity (BMI>30)	11 (12%)
Former or current smoker	14 (15%)
COVID-19 Diagnosis	
Laboratory confirmed, n (%)	80 (88%)
Clinically suspected, n (%)	11 (12%)
COVID-19 Clinical Course	
Hospitalization required, n (%)	63 (69%)
Outpatient management, n (%)	28 (31%)
COVID-19 specific treatments	
Remdesivir	4 (4%)
Hydroxychloroquine	16 (18%)
Azithromycin	16 (18%)
Tocilizumab	3 (3%)
Oseltamivir	4 (4%)
Lopinavir	4 (4%)
Tocilizumab	3 (3%)
Corticosteroids	11 (12%)
MG Clinical Course during COVID-19	
No. with MG exacerbation/crisis	36 (40%)

Worst MGFA Clinical Class during or immediately following COVID-19	
Asymptomatic, n (%)	14 (15%)
I, n (%)	11(12%)
IIa/IIb, n (%)	30 (33%)
IIIa/IIIb, n (%)	15 (16%)
IVa/IVb, n (%)	11 (12%)
V, n (%)	4 (4%)
Unknown, n (%)	6 (7%)
Treatment for MG exacerbation/crisis	36 (40%)
PLEX	4 (4%)
IVIG	16 (18%)
Corticosteroids	18 (20%)
Other (change in pyridostigmine dose)	2 (2%)
Clinical Outcome	
Death	22 (24%)
Recovered/Discharged Home	39 (43%)
Recovering/Unknown	30 (33%)

Author Appendix: CARE-MG Study Group

Steering Committee

Srikanth Muppidi* (Stanford University, USA)

Saiju Jacob* (University Hospitals Birmingham NHS Foundation Trust, UK)

Jeffrey T. Guptill* (Duke University, USA)

Henry Kaminski* (George Washington University, USA)

James F. Howard Jr* (University of North Carolina, USA)

Gary Cutter (University of Alabama, USA)

Heinz Wiendl* (University of Münster, Germany)

Richard J. Nowak* (Yale University, USA)

Steering committee members actively participated in the development of study protocol and design of case reporting form and formulate overall goals of the registry. We hope to expand the study group in future to improve the gender balance and have more international representation in future as we expand the study.

All clinicians who report cases are automatically included in the investigator group and we hope to acknowledge the effort by researchers.

Investigators (listed alphabetically)

First name, middle initial	Last name
Amanda C Guidon*	Guidon*
Alok	Tyagi
Ana Paula	Sousa
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Ashwin	Pinto
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Stuart Viegas	Viegas
Victoria	Marshall
Yingkai Li	Li

***Member of the International MG/COVID-19 Working Group**

Cases reported from different countries (alphabetically)- as of Oct 5st, 2020

Country	**91 (100%)**
Canada	1(1%)
Iran	22(24%)
Israel	1(1%)
Italy	3(3%)
Japan	1(1%)
Portugal	1(1%)
Spain	1(1%)
Trinidad and Tobago	1(1%)
United Kingdom	33(36%)
United States of America	28(31%)