# Neuro-COVID-19: sintomi e sindromi 

Università di Pisa
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## OUTLINE

$\checkmark$ History
$\checkmark$ Pathomechanisms
$\checkmark$ What neurological manifestations?
$\checkmark$ Changing perspective: from neurological manifestations in Covid to Covid impact in care of neurological patients: the past, the present, the future
173.730 casi di COVID-19 ${ }^{\circ}$ di cui:
18.553 operatori sanitari ${ }^{\text {\$ }}$
22.586 deceduti


Età mediana dei casi: 62 anni

## Overview

ISS 22.04.2020-Sorveglianza Integrata COVID-19 Italia

Decessi per Covid al 22 aprile 2020



Rate of published articles from Jan 1, 2000, to July 7


Review Article
Neurological complications of coronavirus infection; a comparative review and lessons learned during the COVID-19 pandemic
Maryam Sharifian-Dorche ${ }^{a, b}$, Philippe Huot ${ }^{a}$, Michael Osherov ${ }^{a}$, Dingke Wen ${ }^{a, c}$,

# Overview of public health and social measures in the context of COVID-19 

Interim guidance
18 May 2020
https://www.who.int/publications/i/item/overview-of-public-health-and-social-measures-in-the-context-of-covid-19

# Response of the multiple sclerosis community to COVID-19 

Mult Scler. 2020 Sep;26(10):1134-1136.
Olga Ciccarelli, Jeffrey A Cohen and Alan Thompson

# COVID-19 and Multiple Sclerosis: Predisposition and Precautions in Treatment <br> SN Compr Clin Med 2020 Sep 3;1-6 <br> Shaghayegh Sadeghmousavi ${ }^{1,2} \cdot$ Nima Rezaei $^{3,4,5}$ (D) 

## Neuromuscular diseases and Covid-19: Advices from scientific societies and early observations in Italy

## Corrado Angelini (1), Gabriele Siciliano (2)

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Are people with neuromuscular disease (NMD) at higher risk?
What do people with NMD need to do to avoid infection?
What consequences does the risk of Covid-19 infection have for treatments
    used in people with NMD?
What needs to be done to assure ventilatory services during self-isolation
    (LVR bags, home ventilators etc.)
When should people with NMD seek admission if they develop symptoms of
    infection?
Can treatments for Covid-19 have effects on neuromuscular disease?
What should neuromuscular specialists do to assist Emergency Medical and
    Intensive Care decisions on admission to units, escalation of treatment, and
    ceilings of care in neuromuscular patients?
#2 What patient support should neuromuscular centres provide?
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Dealing with immune-mediated neuropathies during COVID-19 outbreak: practical recommendations from the task force of the Italian Society of Neurology (SIN), the Italian Society of Clinical Neurophysiology (SINC) and the Italian Peripheral Nervous System Association (ASNP)
$>$ Neurol Sci. 2020 May 4;1-4. doi: $10.1007 /$ s10072-020-04448-9.
Raffaele Dubbioso ${ }^{1}$ (D) Eduardo Nobile-Orazio ${ }^{2}$ • Fiore Manganelli ${ }^{1} \cdot$ Lucio Santoro $^{1}$ • Chiara Briani ${ }^{3}$ • Dario Cocito ${ }^{4}$. Gioacchino Tedeschi ${ }^{5}$ • Vincenzo Di Lazzaro ${ }^{6}$. Gian Maria Fabrizi ${ }^{7}$ • on behalf of SIN, SINC and ASNP

Do patients with immune-mediated neuropathy have an increased risk of contracting SARS-CoV-2 infection?

What to do if a patient is on immunoglobulin therapy?

What to do if a patient is treated with plasmapheresis?

What to do if a patient

with immune-mediated neuropathy is positive for SARS-CoV-2?

Can I start treatment in a patient with/immune-mediated neuropathy?


Neurological manifestations of COVID-19 caused by SARS-CoV-2

> J Intern Med. 2020 Apr 30;10.1111/joim.13089. doi: 10.1111/joim.13089. Online ahead of print.

## Clinical and Epidemiological Characteristics of 1,420 European Patients With Mild-To-Moderate Coronavirus Disease 2019

| Characteristic | All patients <br> $(\mathrm{N}=1420)$ | Cured patients <br> $(\mathrm{N}=264)$ | $15-39$ yo <br> $(\mathrm{N}=793)$ | $40-59$ yo <br> $(\mathrm{N}=551)$ | $>60$ yo <br> $(\mathrm{N}=76)$ |
| :--- | :---: | :---: | :---: | :---: | :---: |
| Age |  |  |  |  |  |
| Mean (SD) - yo | $39.17 \pm 12.09$ | $34.1 \pm 12.4$ | $30.14 \pm 4.8$ | $48.4 \pm 5.5$ | $66.9 \pm 6.9$ |
| Gender (N - \%) | $458(32.3)$ | $168(63.6)$ | $231(29.0)$ | $190(34.5)$ | $37(48.7)$ |
| Male | $962(67.7)$ | $96(36.4)$ | $562(71.0)$ | $361(65.5)$ | $39(51.3)$ |
| Female |  |  |  |  |  |
| Ethnicity (N - \%) | $1298(91.4)$ | $242(91.7)$ | $715(90.2)$ | $512(92.9)$ | $71(93.4)$ |
| European/Caucasian | $514(63.3)^{*}$ | $200(76.0)^{*}$ | $264(59.7)^{*}$ | $215(65.7)^{*}$ | $35(81.4) *$ |
| Symptoms (N - \%) | $887(62.5)$ | $154(58.3)$ | $480(60.5)$ | $370(67.2)$ | $37(48.7)$ |
| Asthenia | $274(19.3)$ | $39(14.8)$ | $163(20.6)$ | $97(17.6)$ | $14(18.4)$ |
| Myalgia |  |  |  |  |  |
| Dysphagia |  |  |  |  |  |
| Comorbidities | $13(0.9)$ | $0(0)$ | $3(0.4)$ | $4(0.7)$ | $6(7.9)$ |
| Neurological diseases |  |  |  |  |  |

Exploring the clinical association between neurological symptoms and COVID-19 pandemic outbreak: a systematic review of current literature

Davide Tiziano Di Carlo ${ }^{1,2}$. Nicola Montemurro ${ }^{1,2}$. Giandomenico Petrella ${ }^{1,2}$. Gabriele Siciliano ${ }^{3}$. Roberto Ceravolo ${ }^{3}$. Paolo Perrini ${ }^{1,2}{ }^{2}$

| $\rightarrow 19$ studies |
| :--- |
| (from March $1^{\text {th }}$ to May 29 |


|  | Raw data | Rate (95\% CI) | N of articles |
| :--- | :--- | :--- | :--- |
| Demographic data <br> N patients included in the analysis | 12157 |  |  |
| Male patients | $2261 / 4460$ | $50.6 \%(49.2-51.6 \%)$ | 19 |
| Age (median, IQR) | $50.3(11.9)$ | - | 9 |
| Comorbidity |  |  |  |
| Hypertension | $1969 / 6321$ | $31.1 \%(30-32.3 \%)$ | 10 |
| Diabetes | $384 / 6321$ | $13.5 \%(12.3-14.8 \%)$ | 8 |
| Cardiovascular disease | $297 / 2842$ | $10.5 \%(9.3-11.6 \%)$ | 7 |
| Malignancy | $85 / 2561$ | $3.3 \%(2.6-4 \%)$ | 6 |
| Smoking | $277 / 3082$ | $9 \%(8-10 \%)$ | 6 |
| Neurological symptoms |  |  |  |
| CNS | $136 / 2227$ | $6.1 \%(5.1-7.1 \%)$ | 3 |
| $\quad$ Dizziness | $237 / 3163$ | $7.5 \%(6.6-8.4 \%)$ | 10 |
| Headache |  |  |  |
| PNS | $407 / 869$ | $46.8 \%(43.5-50.2 \%)$ | 5 |
| Hypo/anosmia | $402 / 769$ | $52.3 \%(48.7-55.8 \%)$ | 4 |
| Gustatory disorders |  |  |  |
| Muscular injury manifestation | $441 / 2806$ | $15.7 \%(14.4-17.1 \%)$ | 7 |
| Myalgia | $667 / 2732$ | $24.8 \%(23.2-26.4 \%)$ | 6 |
| Fatigue | $117 / 384$ | $30.5 \%(25.9-35.1 \%)$ | 3 |
| Fatigue or myalgia | $3222 / 3999$ | $80.6 \%(79.3-81.8 \%)$ | 13 |
| Other symptoms | $1908 / 3964$ | $48.1 \%(46.6-49.7 \%)$ | 12 |
| Fever | $1009 / 2976$ | $33.9 \%(32.2-35.6 \%)$ | 98 |
| Cough | $124 / 1502$ | $8.3 \%(7-9.8 \%)$ | 7 |
| Dyspnea | $357 / 1320$ | $27.1 \%(24.7-29.5 \%)$ | 10 |
| Pharyngodynia |  |  |  |
| Digestive symptoms |  |  |  |
|  |  |  |  |


|  | Nonsever | 95\% CI | Severe | 95\% CI | $P$-value | N. studies |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Comorbidity |  |  |  |  |  |  |
| Hypertension | 151/973 | 15.5\% (13.4-17.9\%) | 121/371 | 32.6\% (28-37.6\%) | < 0.01 | 6 |
| Cardiovascular disease | 41/1127 | 3.6\% (2.7-4.9\%) | 40/465 | 8.6\% (3.4-11.5\%) | < 0.01 | 5 |
| Diabetes | 66/973 | 6.8\% (5.4-8.6\%) | 64/371 | 17.3\% (13.7-21.4\%) | < 0.01 | 6 |
| Malignancy | 19/915 | 2\% (1.3-3.2\%) | 24/346 | 6.9\% (4.7-10.2\%) | < 0.01 | 5 |
| Smoking | 35/447 | 7.8\% (5.7-10.7\%) | 18/164 | 11\% (7-16.8\%) | 0.26 | 2 |
| Neurological symptoms |  |  |  |  |  |  |
| CNS |  |  |  |  |  |  |
| Dizziness | 24/228 | 10.5\% (7.2-15.2\%) | 25/124 | 20.1\% (14-28.1\%) | 0.02 | 2 |
| Headache | 67/837 | 8\% (6.3-10\%) | 40/308 | 13\% (9.7-17.2\%) | 0.01 | 6 |
| PNS |  |  |  |  |  |  |
| Hypo/anosmia | 8/126 | 6.4\% (3.1-11\%) | 3/88 | 3.4\% (0.7-9\%) | 0.5 | 1 |
| Gustatory disorders | 9/126 | 7.1\% (36.4-13.2\%) | 3/88 | 3.4\% (0.7-9\%) | 0.7 | 1 |
| Muscular injury manifestation |  |  |  |  |  |  |
| Myalgia or fatigue | 140/1189 | 11.8\% (10.1-13.7\%) | 127/432 | 29.4\% (25.3-33.9\%) | $<0.01$ | 7 |

## Infezione Covid19- Severa o non severa

## PUTATIVE MECHANISMS

## 4) Effects on CNS:

- Neuroinflammation
- Neurodegeneration
- Demyelination
$\rightarrow$ Azione diretta del virus a livello di SNC e SNP
$\rightarrow$ Effetto mediato da azione del virus su endotelio
$\rightarrow$ Effetto della tempesta citochinica
$\rightarrow$ Effetto immuno-mediato

3) Lymphocyte and monocyte infiltration

4) Disrupted blood-brain barrier integrity

## Understanding the Immunologic Characteristics of Neurologic Manifestations of SARS-CoV-2 and Potential Immunological Mechanisms



FLAIR image shows cortical hyperintensity in the right gyrus (yellow arrowheads) in both axial and coronal sections and subtle hyperintensity in the bilateral olfactory bulbs (white arrowheads) in the coronal section.


Electron microscope images of crown-shaped SARS-CoV-2 with protein spikes (red arrows) 22/09/2020

## The spectrum of neuropathology in COVID-19

Neuropathol Appl Neurobiol. 2020 Sep 16.
Safa Al-Sarraj ${ }^{1,2 \#^{*}}$, Claire Troakes ${ }^{2 *}$, Brian Hanley ${ }^{3}$, Michael Osborn ${ }^{3}$, Mark P. Richardson ${ }^{4}$, Matthew
Hotopf ${ }^{4,5}$, Edward Bullmore ${ }^{6}$, Ian Everall ${ }^{4}$.


Figure 1: A: Perivascular T lymphocyte infiltration in the frontal lobe (CD3). B: occasional T lymphocytes in the white matter of the frontal lobe (CD3). C: activated mieroglial cells in the white matter and perivascular spaces in the frontal lobe (CD68), D: activated microglial cells in the white matter frontal lobe (CD68) (A, B $\times 640, \mathrm{C}, \mathrm{D} \times 400$ )

Figure 2: A: Haemorrhagic infarction demonstrating necrotic areas and areas of recent haemorrhages associated with focal macrophage infiltration and mild proliferation of capillaries (haematoxylin and eosin stain) $\times 100, \mathrm{~B}$ and C higher power of necrotic and haemorrhagic areas in A showing macrophage

## The spectrum of neuropathology in COVID-19

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Safa Al-Sarraj ${ }^{1,2 \#^{*}}$, Claire Troakes ${ }^{2 *}$, Brian Hanley ${ }^{3}$, Michael Osborn ${ }^{3}$, Mark P. Richardson ${ }^{4}$, Matthew Hotopf ${ }^{4,5}$, Edward Bullmore ${ }^{6}$, Ian Everall ${ }^{4}$.


Figure 3: A and B: focal heavy infiltration of the parenchyma of the medulla by inflammatory cells typical of what is called micro glial nodule but with no necrosis x 400 . C: The inflammatory cells are T lymphocytes in the same spot as A (CD3) and D: intense microglial cell activation in the same spot as B (CD68) $\times 400$.

COVID-19 associated myositis with severe proximal and bulbar weakness.
Muscle Nerve 2020 Sep;62(3):E57-E60.
Hui Zhang ${ }^{1, *}$, MD, PhD; Zeinab Charmchi ${ }^{1, *}$, MD; Roberta J Seidman ${ }^{2}$,
M.D. Yaacov Anziska ${ }^{1}$, MD; Vinodkumar Velayudhan ${ }^{3}$, DO; Jonathan Perk ${ }^{1, \#}$, MD, PhD


Biopsy of the left quadriceps muscle. Hematoxylin and eosin cryostat sections demonstrate multifocal predominantly perimysial perivascular lymphocytic inflammation (C and yellow arrows in D), with focal endomysial extension (black arrows in D). Multiple regenerating myofibers (white arrows in E) are recognized by their mild sarcoplasmic basophilia and enlargement of visible nuclei. There is upregulation of human leucocyte antigen (HLA) Class ABC on myofiber surfaces and sarcoplasmic staining by immunohistochemistry are identified by the brown staining of myofibers which was most consistent with an inflarmpatary myopathy (F). (scale bar $=50$ microns)


Coronavirus invasion



Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy Thrombosis Research 191 (2020) 9-14
Corrado Lodigiani ${ }^{\mathrm{a}, \mathrm{b}, *}$, Giacomo Iapichino ${ }^{\mathrm{c}}$, Luca Carenzo ${ }^{\mathrm{c}}$, Maurizio Cecconi ${ }^{\mathrm{d}, \mathrm{c}}$, Paola Ferrazzi ${ }^{\mathrm{a}}$,
Tim Sebastian ${ }^{\text {d }}$, Nils Kucher ${ }^{\text {d }}$, Jan-Dirk Studt ${ }^{c}$, Clara Sacco ${ }^{\text {a }}$, Bertuzzi Alexia ${ }^{\text {f }}$,
Maria Teresa Sandri ${ }^{\mathrm{g}}$, Stefano Barco ${ }^{\mathrm{d}, \mathrm{h}}$, on behalf of the Humanitas COVID-19 Task Force

|  | Intensive care unit$(n-61)$ |  | General ward$(n=327)$ |  | $\begin{aligned} & \text { Total } \\ & (N=388) \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Age (years), median (Q1-Q3) | 61 (55-69) |  | 68 (55-7 |  | 66 (55-75) |  |
| Men | 49/61 | 80.3\% | 215/327 | 65.7\% | 264/388 | 68.0\% |
| Body mass index (kg/m2) |  |  |  |  |  |  |
| $\leq 25$ | 20/57 | 35.1\% | 110/306 | 35.9\% | 130/361 | 36.0\% |
| 25-30 | 20/57 | 35.1\% | 126/306 | 41.2\% | 144/361 | 39.9\% |
| $\geq 30$ | 17/57 | 29.8\% | 70/306 | 22.9\% | 87/361 | 24.1\% |
| Overall duration of hospitalization (days), median (Q1-Q3) | 18 (14-24) |  | 9 (6-13) |  | 10 (7-15) |  |
| Cardiovascular risk factors |  |  |  |  |  |  |
| Arterial hypertension on treatment | 27/61 | 44.3\% | 156/327 | 47.7\% | 183/388 | 47.2\% |
| Dabetes mellitus on treatment | 11/61 | 18.0\% | 77/327 | 23.5\% | 88/388 | 22.7\% |
| Dysilipidemia on treatment | 7/61 | 11.5\% | 69/327 | 21.1\% | 76/388 | 19.6\% |
| Chronic renal dysfunction | 9/61 | 14.8\% | 52/327 | 15.9\% | 61/388 | 15.7\% |
| Smoking | 3/61 | 4.9\% | 42/327 | 12.8\% | 45/388 | 11.6\% |
| Active cancer | 2/61 | 3.3\% | 23/327 | 7.0\% | 25/388 | 6.4\% |
| Solid | 1 |  | 16 |  | 17 |  |
| Hematological | 1 |  | 9 |  | 10 |  |
| Ongoing cancer therapy | 1/61 | 1.6\% | 10/327 | 3.1\% | 11/388 | 2.8\% |
| Hormonal therapy | 1 |  | 3 |  | 4 |  |
| Chemo/immuno-therapy | 0 |  | 5 |  | 5 |  |
| Radiotherapy | 0 |  | 2 |  | 2 |  |
| History of cancer | 0/61 | 0\% | 2/327 | 0.6\% | 2/388 | 0.5\% |
| Chronic obstructive pulmonary disease | 1/61 | 1.6\% | 34/327 | 10.49\% | 35/388 | 9.0\% |
| Prior thromboembolic events |  |  |  |  |  |  |
| Coronary artery disease | 7/61 | 11.5\% | 47/327 | 14.4\% | 54/388 | 13.9\% |
| Prior stroke | 1/61 | 1.6\% | 19/327 | 5.8\% | 20/388 | 5.2\% |
| Peripheral atherosclerosis | 5/61 | 8.2\% | 48/327 | 14.7\% | 53/388 | 13.7\% |
| Prior venous thromboembolism | 0/61 | 0.0\% | 12/327 | 3.7\% | 12/388 | 3.1\% |
| Use of co-medications |  |  |  |  |  |  |
| Aspirin | 17/61 | 27.9\% | 77/320 | 24.1\% | 93/379 | 24.5\% |
| Vitamin K antagonists | 0/61 | 0\% | 16/329 | 4.9\% | 16/388 | 4.1\% |
| Difect oral anticoagulants | 2/61 | 3.3\% | 15/329 | 4.5\% | 17/388 | 4.4\% |
| ACE-inhibitors | 6/61 | 9.8\% | 47/329 | 14.3\% | 53/388 | 13.7\% |

Venous and arterial thromboembolic events in hospitalized COVID-19 patients.

| Thromboembolic events | Intensive care unit |  |  | General ward |  |  | Total |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | n | \% of closed cases $(n=48)$ | \% of imaging tests performed* | n | $\%$ of closed cases $(\mathrm{n}=314)$ | \% of imaging tests performed* | n | \% of closed cases $(\mathrm{n}-362)$ | \% of imaging tests performed |
| At least one thromboembolic event | 8 | $16.7 \%$ ( $95 \% \mathrm{Cl}$ <br> 8.7\%-29.6\%) | - | 20 | $\begin{aligned} & 6.4 \%(95 \% \mathrm{Cl} \\ & 4.2 \%-9.6 \%) \end{aligned}$ | - | 28 | $7.7 \%(95 \% \mathrm{Cl}$ <br> 5.4\%-11.0\%6) | - |
| VTE | 4 | 8.3\% | 22\% | 12 | 3.8\% | 46\% | 16 | 4.4\% | 36\% |
| PE ( $\pm$ DVT) | 2 | 4.2\% | 25\% | 8 | 2.5\% | 36\% | 10 | 2.8\% | 33\% |
| Isolated pDVT | 1 | 2.1\% | 7\% | 3 | 1.0\% | 44\% | 4 | 1.1\% | 21\% |
| Isolated dDVT | 0 | - | - | 1 | 0.3\% | 13\% | 1 | 0.3\% | 13\% |
| Catheter-related <br> DVT | 1 | 2.1\% | 50\% | 0 | - | - | 1 | 0.3\% | 50\% |
| Ischemic strone 09/2020 | 3 | 6.3\% | - | 6 | 1.9\% | - | 9 | 2.5\% | - |
| ACS/MI | 1 | 2.1\% | - | 3 | 1.0\% | - | 4 | 1.1\% | - |

Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy > Neurology. 2020 May 22;10.1212

| ALL PATIENTS | Total <br> $(\mathbf{n}=\mathbf{1 7 3})$ | non-COVID-19 <br> $(\mathbf{n}=\mathbf{1 1 7})$ | COVID-19 <br> $(\mathbf{n}=\mathbf{5 6})$ | $\boldsymbol{p}$-value |
| :--- | :---: | :---: | :---: | :---: |
| Admitting neurological diagnosis |  |  |  | 0.035 |
| Cerebrovascular disease | $111(64.2 \%)$ | $68(58.1 \%)$ | $43(76.8 \%)$ |  |
| Epilepsy | $23(13.3 \%)$ | $19(16.2 \%)$ | $4(7.1 \%)$ |  |
| Inflammatory/Infectious disease | $9(5.2 \%)$ | $9(7.7 \%)$ | $0(0.0 \%)$ |  |
| Neoplastic | $3(1.7 \%)$ | $3(2.6 \%)$ | $0(0.0 \%)$ |  |
| Other | $27(15.6 \%)$ | $18(15.4 \%)$ | $9(16.1 \%)$ |  |
|  |  |  |  |  |


| PATIENTS WITH <br> CEREBROVASCULAR DISEASE | Total <br> $(\mathbf{n}=\mathbf{1 1 1 )}$ | non-COVID-19 <br> $(\mathbf{n}=68)$ | COVID-19 <br> $(\mathbf{n}=\mathbf{4 3})$ | $\boldsymbol{p}$-value |
| :--- | :---: | :---: | :---: | :---: |
| Cerebrovascular event |  |  |  | 0.560 |
| Transient ischemic attack | $13(11.7 \%)$ | $8(11.8 \%)$ | $5(11.6 \%)$ |  |
| Ischemic stroke | $85(76.6 \%)$ | $50(73.5 \%)$ | $35(81.4 \%)$ |  |
| Hemorrhagic stroke | $13(11.7 \%)$ | $10(14.7 \%)$ | $3(7.0 \%)$ |  |

$\rightarrow$ COVID-19 and non-COVID patients with stroke had similar baseline characteristics
 with a significantly lower number of patients with a good outcome ( $n=11,25.6 \%$ vs $n=48,70.6 \%, p<0.001$ ).

## Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young

Oaxley et al

| Variable | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Age - yr | 33 | 37 | 39 | 44 | 49 |
| Sex | Female | Male | Male | Male | Male |
| Medical history and risk factors for stroke $\dagger$ | None | None | Hyperlipidemia, hypertension | Undiagnosed diabetes | Mild stroke, diabetes |
| Medications | None | None | None | None | Aspirin ( 81 mg ), atorvastatin $(80 \mathrm{mg})$ |
| NIHSS score $\ddagger$ |  |  |  |  |  |
| On admission | 19 | 13 | 16 | 23 | 13 |
| At 24 hr | 17 | 11 | 4 | 19 | 11 |
| At last follow-up | $\begin{gathered} 13 \\ \text { (on day 14) } \end{gathered}$ | $\begin{gathered} 5 \\ \text { (on day } 10 \text { ) } \end{gathered}$ | NA; intubated and sedated, with multiorgan failure | $\begin{gathered} 19 \\ \text { (on day 12) } \end{gathered}$ | $\begin{gathered} 7 \\ \text { (on day 4) } \end{gathered}$ |
| Outcome status | Discharged to rehabilitation facility | Discharged home | Intensive care unit | Stroke unit | Discharged to rehabilitation facility |
| Time to presentation -hr | 28 | 16 | 8 | 2 | 8 |
| Signs and symptoms of stroke | Hemiplegia on left side, facial droop, gaze preference, homonymous hemianopia, dysarthria, sensory deficit | Reduced level of consciousness, dysphasia, hemiplegia on right side, dysarthria, sensory deficit | Reduced level of consciousness, gaze preference to the right, left homonymous hemianopia, hemiplegia on left side, ataxia | Reduced level of consciousness, global dysphasia, hemiplegia on right side, gaze preference | Reduced level of consciousness, hemiplegia on left side, dysarthria, facial weakness |
| Vascular territory | Right internal carotid artery | Left middle cerebral artery | Right posterior cerebral artery | Left middle cerebral artery | Right middle cerebral artery |
| Imaging for diagnosis | CT, CTA, CTP, MRI | CT, CTA, MRI | CT, CTA, CTP, MRI | CT, CTA, MRI | CT, CTA, CTP |
| Treatment for stroke | Apixaban ( 5 mg twice daily) | Clot retrieval, apixaban ( 5 mg twice daily) | Clot retrieval, aspirin ( 81 mg daily) | Intravenous t-PA, clot retrieval, hemicraniectomy, aspirin (81 mg daily) | Clot retrieval, stent, aspirin ( 325 mg daily), clopidogrel ( 75 mg daily) |
| Covid-19 symptoms 22/09/2020 | Cough, headache, chills | No symptoms; recently exposed to family member with PCR-positive Covid-19 | None | Lethargy | Fever, cough, lethargy |

## A first case of meningitis/encephalitis associated with SARS-Coronavirus-2

Takeshi Moriguchia, ${ }^{\text {a, }}$, Norikazu Harii ${ }^{\text {b }}$, Junko Goto ${ }^{\text {a }}$, Daiki Harada ${ }^{\text {a }}$, Hisanori Sugawara ${ }^{\text {a }}$, Junichi Takamino ${ }^{a}$, Masateru Ueno ${ }^{a}$, Hiroki Sakata ${ }^{a}$, Kengo Kondo ${ }^{a}$, Natsuhiko Myose ${ }^{a}$, Atsuhito Nakao ${ }^{c}$, Masayuki Takeda ${ }^{\text {d }}$, Hirotaka Haro ${ }^{\text {e }}$, Osamu Inoue ${ }^{f}$,
Katsue Suzuki-Inoue ${ }^{\mathrm{g}}$, Kayo Kubokawa ${ }^{\text {h }}$, Shinji Ogihara ${ }^{\mathrm{i}}$, Tomoyuki Sasakig ${ }^{\text {² }}$,
Hiroyuki Kinouchỉ, Hiroyuki Kojin ${ }^{\mathrm{k}}$, Masami Ito ${ }^{\mathrm{k}}$, Hiroshi Onishil, Tatsuya Shimizul, Yu Sasaki', Nobuyuki Enomoto ${ }^{\mathrm{m}}$, Hiroshi Ishihara ${ }^{\mathrm{n}}$, Shiomi Furuya ${ }^{\mathrm{k}}$, Tomoko Yamamoto ${ }^{\mathrm{k}}$, Shinji Shimada ${ }^{0}$


## Neuromuscular presentations in patients with COVID-19

Vimal Kumar Paliwal ${ }^{1} \odot \cdot$ Ravindra Kumar Garg ${ }^{2}$ © $\cdot$ Ankit Gupta ${ }^{1} \cdot$ Nidhi Tejan $^{3}$

Neurol Sci, Sep 2020
GBS

Table 4 Frequency of various demographic, clinical, and electrophysiological features and good outcome in patients with COVID-19-related GBS

| Feature | Frequency |
| :--- | :--- |
| Number | 39 |
| Age (data available in 36 patients) | $21-85$ years, mean $=60.55$, |
|  | median $=61$, mode $=70$ |
| Males (data available in 35 patients) | $26(74.28 \%)$ |
| Hyposmia/ageusia | $6(15.4 \%) / 7(17.9 \%)$ |
| Time to onset of GBS (data available in 35patients) | $3-28$ days, mean $=13.91$ days, |
|  | median $=14$, mode $=10$ |
| Bifacial paralysis | $18(46.15 \%)$ |
| Other cranial neuropathies | $9(23.07 \%)$ |
| Respiratory involvement | $17(43.58 \%)$ |
| Demyelinating/axonal (data available in 32 patients) | $24(75 \%) / 7(22 \%)$ |
| Outcome (data available in 38 patients) | GOOD $=25(65.8 \%)$, POOR $=11(28.9 \%)$, DIED $=2(5.3)$ |

# Guillain-Barré syndrome: The first documented COVID-19-triggered autoimmune neurologic disease 

More to come with myositis in the offing

[^0]
## Neuromuscular presentations in patients with COVID-19

Vimal Kumar Paliwal ${ }^{1}$ © $\cdot$ Ravindra Kumar Garg ${ }^{2}$ ( - Ankit Gupta ${ }^{1}$. Nidhi Tejan ${ }^{3}$
Neurol Sci, sep 2020

## NEUROPATHIES

| Referencel country | Type | Age/ sex | Clinical presentation | Respiratory involvement | Blood parameters/ <br> RT-PCR | Electrophysiology | Neuroimaging | Treatment/outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\begin{aligned} & \text { Ghiasvand } \\ & \text { et al./Ir- } \\ & \text { an }[66] \end{aligned}$ | Symmetrical polyneuropathy | 68/F | Fever, dry cough, myalgia, B/L lower limbs hypotonia with weakness with areflexia | Ground-glass opacities | Raised creatinine, CRP, lymphopenia | Not performed | Normal | Lopinavir/ritonavir, oseltamivir, mechanical ventilation, IV methylprednisolone/died |
| Abdelnour /UK [67] | Motor neuropathy | 69/M | Lower limb weakness, knee/ankle areflexia, gait ataxia, sensory normal | Lower lobe pneumonia | Lymphocytopenia, raised CRP, LDH, ferritin | Not performed | Normal | Spontaneous recovery |
| Chaumont <br> /France <br> [68] | Encephalopathy with peripheral neuropathy | 62/M | Confusion, memory loss, dysphagia, left facial palsy, asymmetrical quadriparesis, lower limb areflexia, upper limb hyperreflexia, action myoclonus, dysautonomia | Mild ARDS | Positive $\mathrm{lgM}, \mathrm{IgG}$ for SARS-CoV-2, positive RT-PCR nasopharyngeal swab | Demyelinating asymmetric motor polyradiculoneuropathy and moderate axonal sensorimotor neuropathy | Right MCA recent stroke, spine normal | Hydroxychloroquine, azithromycin, IVIg, rehab centre after 36 days, mRS 2 |
|  |  | 72/M | Confusion, delusion, hallucinations, memory impairment, dysphagia, slow saccades, quadriparesis, hyperreflexia, dysautonomia | ARDS | Positive $\mathrm{lgM}, \mathrm{lgG}$ for SARS-CoV-2, positive RT-PCR nasopharyngeal swab | Demyelinating asymmetric motor polyradiculoneuropathy and moderate axonal sensorimotor neuropathy | $\begin{aligned} & \text { Normal } \\ & \text { brain/spine } \\ & \text { MRI } \end{aligned}$ | Hydroxychloroquine, azithromycin, IVIg, rehab center after 50 days, mRS 4 |
|  |  | 50M | Confusion, delusion, hallucinations, memory impairment, dysphagia, slow saccades, quadriparesis, hyperreflexia, dysautonomia | ARDS | Positive $\mathrm{lgM}, \mathrm{lgG}$ for SARS-CoV-2, positive RT-PCR nasopharyngeal swab | Lower motor neuron involvement, denervation of four limbs | $\begin{aligned} & \text { Normal } \\ & \text { brain/spine } \\ & \text { MRI } \end{aligned}$ | Hydroxychloroquine, azithromycin, IVIg. methyl prednisolone, rehab centre after 76 days, mRS 4 |
|  |  | 66/M | Confusion, delusion, hallucinations, memory impairment, dysphagia, slow saccades, quadriparesis, hyperreflexia, dysautonomia | ARDS | Positive IgM , IgG for SARS-CoV-2, positive RT-PCR nasopharyngeal swab | Demyelinating motor polyradiculoneuropathy | $\begin{aligned} & \text { Normal } \\ & \text { brain/spine } \\ & \text { MRI } \end{aligned}$ | Hydroxychloroquine, azithromycin, IVIg, methyl prednisolone, discharged to home after 40 days, mRS 2 |

Neuromuscular presentations in patients with COVID-19
Neurol Sci, Sep 2020


## Myositis/rhabdomyolisis

Table 2 Demographic, clinical, and laboratory parameters and outcome of patients with myositis/rhabdomyolysis secondary to COVID-19

| Referencel country | Age/sex | Clinical presentation | Respiratory involvement | Blood parameters | Chest imaging | Neuroimaging | Treatment/outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\begin{aligned} & \text { Uysal } \\ & \text { et al//Turkey } \\ & \text { [22] } \end{aligned}$ | 60/M | Myalgia, fatigue | Yes | Raised CK, CRP, LDH, ferritin | B/L ground-glass opacities | NA | HCQ, anti-viral, azithromycin |
| Valente-Acosta et al/Mexico [23] | 71/M | Fever, dyspnea, cough, myalgia, generalized weakness | Yes | CK 8720 U/L, raised myoglobin, creatinine, LDH, LL-6, ferritin | B/L ground-glass opacities | NA | Ventilator, HCQ , anti-viral, tocilizumab |
| $\begin{aligned} & \text { Beydon } \\ & \text { et al./France } \\ & {[24]} \end{aligned}$ | NA | Myalgias, lower limb proximal weakness, fever | No | Raised CPK, CRP, lymphocytopenia | B/L ground-glass opacities | B/L external obturator muscle and quadricipital oedema with contrast enhancement | NA/critical |
| Suwanwongse et al//USA [25] | 88/M | Acute onset $B / L$ thighs pain and weakness, fever, dry cough | No | Raised CPK, LDH | Left pleural effusion | Normal | IV fluids, furosemide, HCQ/improved |
| $\begin{aligned} & \text { Zhang } \\ & \text { et al./USA } \\ & {[26]} \end{aligned}$ | 38/M | Fever, dyspnoea, myalgia | Yes | Raised CPK, CRP, LDH | Right upper and middle lobe consolidation | NA | Azithromycin, IV fluids, HCQ, doxycycline/improved |
| Jin et al/China [27] | $\begin{gathered} 60 \text { years } \\ \mathrm{M} \end{gathered}$ | Fever, cough, pain, and weakness in $\mathrm{B} / \mathrm{L}$ lower limbs | Yes | Raised CPK, myoglobin, CRP, LDH, leukopenia | B/L ground-glass opacities | NA | Oxygen inhalation, opinavir, moxifloxacin, IV fluids, gamma globulin, plasma transfusion/mproved |
| Chan <br> et al./USA <br> [28] | $\begin{gathered} 75 \text { years } \\ \mathrm{M} \end{gathered}$ | Generalized weakness, reduced appetite | Yes | Elevated CK, AST, ALT, troponin, LDH, CRP, D dimer, ferritin hematuria, normal EKG | Left lower lobe patchy opacity | NA | Antibiotics, hydroxychloroquine/improved |
|  | $\begin{aligned} & 71 \text { years } \\ & \mathrm{M} \end{aligned}$ | Repetitive leg twitching, generalized weakness, tingling/numbness legs | Yes | Elevated CK, BUN, creatinine, troponin, hematuria, EKG-AF | Multifocal pneumonia | Old lacunar infarct | Antibiotics, hydroxychloroquine, heparin, IV fluids/on mechanical ventilator |
| $\begin{aligned} & \text { Gefen } \\ & \text { et al./USA } \\ & {[29]} \end{aligned}$ | $\begin{gathered} 16 \text { years } \\ \mathrm{M} \end{gathered}$ | Fever, myalgia, shortness of breath, cola-coloured urine, muscle tenderness | No | Elevated CK (427,656 U/L), AST, ALT, procalcitonin, LDH, CRP | NA | NA | IV fluids/improved |

The interaction between SARS-CoV-2 and ACE2 may have consequences for skeletal muscle viral susceptibility and myopathies
${ }^{1,3}$ Peter J. Ferrandi, ${ }^{2,3}$ Stephen E. Alway, ${ }^{1,3}$ Junaith S. Mohamed*

$\rightarrow$ Skeletal muscles and other cells in the muscles like satellite cells, leukocytes, fibroblasts, and endothelial cells express ACE-2. Therefore, it is postulated that skeletal muscles are susceptible to direct muscle invasion by SARS- CoV-2.
$\rightarrow$ Other possible mechanisms suggested are immune complex deposition in muscles, release of myotoxic cytokines, damage due to homology between viral antigens and human muscle cells, and adsorption of viral protein on muscle membranes leading to expression of viral antigens on myocyte surface.
$\rightarrow$ Whether these postulated mechanisms for COVID-19- related myositis are also responsible for myalgia is also not known.
22/09/2020

Presente: esiti e bilanci


## Acute stroke management pathway during Coronavirus-19 pandemic

## Neurological Sciences (2020) 41:1003-1005

Claudio Baracchini ${ }^{1}$ • Alessio Pieroni ${ }^{1}$ © $\cdot$ Federica Viaro ${ }^{1} \cdot$ Vito Cianci $^{2}$ • Anna M. Cattelan ${ }^{3}$ • Ivo Tiberio ${ }^{4}$. Marina Munari ${ }^{5}$. Francesco Causin ${ }^{6}$

(...) "Compared with the same period in 2019, we have observed a half of minor strokes, TIAs, and transfers from spokes, along with longer onset-to-door and door-to-treatment times for major strokes. As a result, the number of patients who have undergone intravenous thrombolysis or bridging therapy (combined intravenous and thrombectomy) is decreased (- $26 \%$ and $-30 \%$ respectively), while the number of primary thrombectomies is increased by 41\% " (...)

## Sanità 24 <br> " 24 DRIR

Home Analisi Sanità risponde Scadenze fiscall Santtà in borsa

21 lug 2020
AZIENDE ERECIONI
㕇 Coronavirus: urgente un Piano nazionale di "rientro" delle liste di attesa

SECNALIBRO
FACEBOOK f TWITTER
di Tonino Acet ${ }^{*}$

Post-discharge persistent symptoms and healthrelated quality of life after hospitalization for COVID-19 J Infect. 2020 Aug 25;S0163-4453(20)30562-4.

Eve Garrigues ${ }^{1}$, Paul Janvier ${ }^{2}$, Yousra Kherabi ${ }^{1}$, Audrey Le Bot ${ }^{1}$, Antoine Hamon ${ }^{1}$ , Hélène Gouze ${ }^{1}$, Lucile Doucet ${ }^{1}$, Sabryne Berkani ${ }^{1}$, Emma Oliosi ${ }^{1}$, Elise Mallart ${ }^{1}$, Félix
Corre ${ }^{1}$, Virginie Zarrouk ${ }^{1}$, Jean-Denis Moyer ${ }^{3}$, Adrien Galy ${ }^{1}$, Vasco Honsel ${ }^{1}$, Bruno
Fantin ${ }^{1}$, Yann Nguyen ${ }^{4}$

|  | Overall | Ward patients | ICU patients | P value |
| :---: | :---: | :---: | :---: | :---: |
|  | $N=120$ | $N=96$ | $N=24$ |  |
| Age, years | 63.2 (15.7) | 64.1 (16.1) | 59.6 (13.7) | 0.208 |
| Sex, male | 75 (62.5) | 56 (58.3) | 19 (79.2) | 0.099 |
| Comorbidities |  |  |  |  |
| Diabetes | 26 (21.7) | 22 (22.9) | 4 (16.7) | 0.698 |
| Hypertension | 56 (46.7) | 45 (46.9) | 11 (45.8) | 1.000 |
| Body mass index ( $\mathrm{kg} / \mathrm{m}^{2}$ ) |  |  |  | <0.001 |
| $<25, \mathrm{n}(\%)$ | 35 (29.2) | 32 (33.3) | 3 (12.5) |  |
| $\geq 25, \mathrm{n}$ (\%) | 57 (47.5) | 37 (38.5) | 20 (83.3) |  |
| Micsing n (\%) | 28 (23.3) | 27 (28.1) | 1 (4.2) |  |
| Clinical features at admission |  |  |  |  |
| Confusion | 7 (5.8) | 6 (6.2) | 1 (4.2) | 1.000 |
| Cough | 87 (72.5) | 69 (71.9) | 18 (75.0) | 0.959 |
| Dyspnoea | 88 (73.3) | 68 (70.8) | 20 (83.3) | 0.327 |
| Myalgia | 19 (15.8) | 16 (16.7) | 3 (12.5) | 0.851 |
| Diarrhoea | 29 (24.2) | 25 (26.0) | 4 (16.7) | 0.488 |
| Admission data |  |  |  |  |
| Length of stay in hospital, days | 11.2 (13.4) | 7.4 (5.4) | 26.5 (22.3) | <0.001 |
| I ength of ctay in IClI dave | ( | - | 17.1 (15.7) | - |
| Persistent symptoms |  |  |  |  |
| Cough | 20 (16.7) | 14 (14.6) | 6 (25.0) | 0.358 |
| Chest pain | 13 (10.8) | 11 (11.5) | 2 (8.3) | 0.941 |
| Fatigue | 66 (55.0) | 52 (54.2) | 14 (58.3) | 0.891 |
| Dyspnoea | 50 (41.7) | 38 (39.6) | 12 (50.0) | 0.487 |
| Ageusia | 13 (10.8) | 9 (9.4) | 4 (16.7) | 0.509 |
| Anosmia | 16 (13.3) | 14 (14.6) | 2 (8.3) | 0.638 |
| Hair loss | 24 (20.0) | 18 (18.8) | 6 (25.0) | 0.690 |
| Attention disorder | 32 (26.7) | 28 (29.2) | 4 (16.7) | 0.327 |
| Memory ${ }^{\text {a }}$ Ss 20 | 41 (34.2) | 36 (37.5) | 5 (20.8) | 0.194 |
| Sleep disorder | 37 (30.8) | 29 (30.2) | 8 (33.3) | 0.535 |

## ESITI E BILANCI: OLFATTO

- donna, 55 anni
- Infezione da SARS-CoV2 in marzo
- 15 marzo comparsa di anosmia ed ageusia, nega altri segni e sintomi
- Tamponi nasali negativi, titolo anticorpale positivo (in agosto $\operatorname{lgG}$ index $=6.505$ )
- Permane anosmia, percezione dei gusti primari senza chiara distinzione

Acute-onset smell and taste disorders in the context of COVID-19: a pilot multicentre polymerase chain reaction based case-control study

Á. Beltrán-Corbellinia (D) J. L. Chico-Garcíaa, J. Martínez-Poles ${ }^{\text {b.c }}$, F. Rodríguez-Jorge ${ }^{\mathrm{a}}$,
E. Natera-Villalba ${ }^{\mathrm{a}}$ (D), J. Gómez-Corral ${ }^{\text {a }}$, A. Gómez-López ${ }^{\mathrm{a}}$, E. Monreala ${ }^{\text {a }}$, P. Parra-Díaz ${ }^{\text {a }}$ (D),
J. L. Cortés-Cuevas ${ }^{\text {d }}$, J. C. Galán ${ }^{\text {d }}$, C. Fragola-Arnaue ${ }^{\text {, J. Porta-Etessam }}{ }^{\text {c.t. }, ~ J . ~ M a s j u a n ~}{ }^{\text {a }}$ (D) and A. Alonso-Cánovas ${ }^{\text {a }}$

> European Journal of Neurology 2020, 0: 1-4

Table 2 Description of smell and/or taste disorder (STD) features in COVID-19 and influenza patients

| STD characteristic | COVID-19 <br> $(n=31)$ | Influenza <br> $(n=5)$ |
| :--- | :---: | :---: |
| Nasal obstruction, $N(\%)$ | $4(12.9 \%)$ | $4(80 \%)$ |
| Smell disorder pattern | $14(45.2 \%)$ | $0(0 \%)$ |
| Anosmia, $N(\%)$ | $9(29.0 \%)$ | $4(80 \%)$ |
| Hyposmia, $N(\%)$ | $2(6.5 \%)$ | $0(0 \%)$ |
| Dysosmia, $N(\%)$ | $14(45.2 \%)$ | $4(80 \%)$ |
| Taste disorder pattern | $7(22.6 \%)$ | $1(20 \%)$ |
| Ageusia, $N(\%)$ | $8(25.8 \%)$ | $2(40 \%)$ |
| Hypogeusia, $N(\%)$ | $21(67.7 \%)$ | $5(100 \%)$ |
| Dysgeusia, $N(\%)$ |  |  |
| Capable of distinguishing sweetness/ |  |  |
| $\quad$ saltiness/bitterness, $N(\%)$ | $21(67.7 \%)$ | $2(40 \%)$ |
| Pattern of onset of STD | $10(32.3 \%)$ | $3(60 \%)$ |
| Acute, $N(\%)$ | $7.1(3.1)$ | $9.8(4.8)$ |
| Subacute, $N(\%)$ |  |  |
| Duration of taste/smell disorder, mean |  |  |
| (SD), days |  |  |

Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study

Jerome R. Lechien ${ }^{1,2,3,4}$. Carlos M. Chiesa-Estomba ${ }^{1,5}$. Daniele R. De Siati ${ }^{1,6} \cdot$ Mihaela Horoi ${ }^{4}$.
Serge D. Le Bon ${ }^{4}$. Alexandra Rodriguez ${ }^{4}$. Didier Dequanter ${ }^{4}$. Serge Blecic $^{7}$. Fahd El Afia ${ }^{1,3}$. Lea Distinguin ${ }^{1,3}$. Younes Chekkoury-Idrissi ${ }^{1,3}$. Stéphane Hans ${ }^{3}$. Irene Lopez Delgado ${ }^{1,8}$. Christian Calvo-Henriquez ${ }^{1,9}$.
Philippe Lavigne ${ }^{1,10}$. Chiara Falanga ${ }^{1,11}$. Maria Rosaria Barillari ${ }^{1,11}$. Giovanni Cammaroto ${ }^{1,12}$. Mohamad Khalife ${ }^{13}$. Pierre Leich ${ }^{14}$. Christel Souchay ${ }^{14}$. Camelia Rossi ${ }^{15}$. Fabrice Journe ${ }^{2}$. Julien Hsieh ${ }^{1,16}$. Myriam Edjlali ${ }^{17,18}$. Robert Carlier ${ }^{18}$. Laurence Ris ${ }^{19}$. Andrea Lovato ${ }^{20}$. Cosimo De Filippis ${ }^{20}$. Frederique Coppee ${ }^{21}$. Nicolas Fakhry ${ }^{1,22}$. Tareck Ayad ${ }^{1,10} \cdot$ Sven Saussez ${ }^{1,2,4,13}$

Eur Arch Otorhinolaryngol 2020 Aug;277(8):2251-2261


367 cases of Covid
$\rightarrow 86 \%$ olfactory dysfunction
$\rightarrow 80 \%$ anosmya, $20 \%$ hyposmia
67-73\% recovered within 8 days

## ESITI E BILANCI: MIALGIE

# Autoimmune and rheumatic musculoskeletal diseases as a consequence of SARS-CoV-2 infection and its treatment 

Rheumatol Int 2020 Oct;40(10):1539-1554.
 Vir Singh Negi ${ }^{1}$ ©

Reported with SARS-CoV-2
Clinical characteristics
Refs.
Musculoskeletal manifestations
Arthralgia-Myalgia
in 14.4-44\% of the cases
Early and transient features
[21]

Acute Myositis
Case report
Symptom of myalgia and proximal muscle

Elevate Creatine kinase (CK) level (25,384 IU/L)
MRI showed muscle edema
Negative MSA and MAAs

Estimating the impact of
ACTA MYOLOGICA 2020; XXXIX: p. 57-66
COVID-19 pandemic on
services provided by Italian
Neuromuscular Centers:
an Italian Association of
Myology survey of the acute
phase

|  |  | Outpatient visit and exams | Therapy |  |  |  | Services |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | Total | DH | Chronic home therapy | Clinical trials | Total | FKT | Psychological support | Home nursing service | Prenatal diagnosis |
| Italy | Yes |  | 16.7\% | 64\% | 39\% | 93.3\% | 63\% | 43\% | 7\% | 66.7\% | 33\% | 87.5\% |
|  | No | 40.\% | 22\% | 7\% | 3.4\% | 37\% | 57\% | 93\% | 33.3\% | 67\% | 12.5\% |
|  | Partial | $\begin{gathered} 43.3 \% \\ \begin{array}{c} \text { (urgencies } \\ \text { only) } \end{array} \\ \hline \end{gathered}$ | 14\% | $\begin{gathered} 54 \% \\ \text { (some) } \end{gathered}$ | $\begin{gathered} \hline 3.3 \% \\ \text { (some) } \end{gathered}$ |  |  |  |  |  |  |
| North | Yes | 11\% | 63.6\% | 41\% | 89\% | 63\% | 34\% | 0\% | 84\% | 20\% | 77.5\% |
|  | No | 44.5\% | 23.4\% | 12\% | 5.5\% | 37\% | 66\% | 100\% | 16\% | 80\% | 22.5\% |
|  | Partial | $\begin{gathered} 44.5 \% \\ \text { (urgencies } \\ \text { only) } \end{gathered}$ | 13\% | $\begin{gathered} 47 \% \\ \text { (some) } \end{gathered}$ | $\begin{gathered} \hline 5.5 \% \\ \text { (some) } \end{gathered}$ |  |  |  |  |  |  |
| Center | Yes | 0\% | 73\% | 43\% | 100\% | 76\% | 57\% | 12.5\% | 50\% | 87.5\% | 100\% |
|  | No | 25\% | 13\% | 0\% | 0\% | 24\% | 43\% | 87.5\% | 50\% | 12.5\% | 0\% |
|  | Partial | $75 \%$ <br> $\left(\begin{array}{c}\text { (urgencies } \\ \text { only) }\end{array}\right.$ | 13\% | $\begin{gathered} 57 \% \\ \text { (some) } \end{gathered}$ |  |  |  |  |  |  |  |
| South | Yes | 0\% | 60\% | 25\% | 100\% | 62\% | 56\% | 20\% | 50\% | 75\% | 100\% |
|  | No | 50\% | 20\% | 0\% | 0\% | 38\% | 44\% | 80\% | 50\% | 25\% | 0\% |
|  | Partial | $\begin{gathered} 50 \% \\ \text { (urgencies } \\ \text { onlv) } \end{gathered}$ | 20\% | $\begin{gathered} 75 \% \\ \text { (some) } \end{gathered}$ |  |  |  |  |  |  |  |

Futuro: telemedicina



Diagnostic Improvements
Medical Association Diagnostic Guidelines



Natul
Disease Course

Tests and Exome Sequencing Longitudinal Clinical Data to Understand

## Estimates of Progress from Diagnosis and Care Management Changes and Their Expected Impact in the Next Five Years

Care Management Improvements
Digital Monitoring Tools (e.g., Telemedicine)


## Telemedicine in care

| Modality | Role |
| :--- | :--- |
| Felehealth | Replace in-person visits, reduce travel efforts and costs, maintain connection with <br> people who have lost ability to travel to clinic |
| Mobile health <br> Allow for real-time access to clinic staff using relatively low-cost technology, <br> dedicated apps can provide patients with information or monitor function in the <br> patient's environment |  |
| Remote monitoring <br> platforms | Remote monitoring of well-being based on information from treatment devices (e.g., <br> data collected by non-invasive or invasive ventilation machines, data collected from <br> eye-gaze or communication platforms, or other connected devices) |
| Patient support groups | Loaner closets, peer-to-peer support groups, funding for research and clinical care |
| Advocacy groups | Raise awareness about the disease, fundraising, advocate for policy changes |
| Philanthrophy (foundations, | Provide or help raise funding for research and clinical care |
| private donors) | Raise awareness about the disease and treatment and research options |
| Newsletters/websites | Online access to one's own clinical and research information |
| Patient portal | $22 / 09 / 2020$ |

## COVID-19 in people with multiple sclerosis: A global data sharing initiative

Liesbet M Peeters (D), Tina Parciak, Clare Walton, Lotte Geys, Yves Moreau,
Edward De Brouwer, Daniele Raimondi, Ashkan Pirmani (D), Tomas Kalincik, Gilles Edan,
Steve Simpson-Yap(D), Luc De Raedt, Yann Dauxais, Clément Gautrais (D), Paulo R Rodrigues, Landon McKenna, Nikola Lazovski, Jan Hillert, Lars Forsberg, Tim Spelman (D,
Robert McBurney, Hollie Schmidt, Arnfin Bergmann, Stefan Braune, Alexander Stahmann,
Rodden Middleton (D) Amber Salter (D), Bruce F Bebo, Juan I Rojas, Anneke van der Walt
Helmut Butzkueven, Ingrid van der Mei, Rumen Ivanov, Kerstin Hellwig,
Guilherme Sciascia do Olival, Jeffrey A Cohen (D) Wim Van Hecke, Ruth Dobson (D),
Melinda Magyari, Doralina Guimarães Brum, Ricardo Alonso, Richard Nicholas, Johana Bauer,
Anibal Chertcoff, Jérôme de Sèze, Céline Louapre, Giancarlo Comi and Nick Rijke


PublMed.gov


High utilityl
appropriateness Moderate utility/appropriateness Low utility/appropriateness

| NMD follow-up | New or unstable NMD | All patients with discrepancy beween reported symptoms and abnormal |
| :---: | :---: | :---: |
| PN followup: stable or | New or unstable PN | examination findings |
| management of | New MG: well established diagnosicor unstable | Ald diorders second opinions for patients where nuances of physial |
| nuropathic pain | new/follow-up | examination will highly infuencemedical dection-making and diagnosic. |
| MG follow-up. stable | All patients with worsening symptoms to tridge | evaluation |
| Myosits followtye titabe | need and timeframe for further or more urgent | Primary management of unstable patients |

A mobile app for patients with Pompe disease and its possible clinical applications
Giulia Ricci ${ }^{\text {a }}$, Sigrid Baldanzi ${ }^{\text {a }}$, Fabrizio Seidita ${ }^{\text {b }}$, Chiara Proietti ${ }^{\text {c }}$, Francesca Carlini ${ }^{\text {c }}$,
Silvia Peviani ${ }^{\text {c }}$, Giovanni Antonini ${ }^{\text {d }}$, Andrea Vianello ${ }^{\text {c }}$, Gabriele Siciliano ${ }^{\text {a,* }}$,
Italian GSD II group

WLANCGL PAPERWORK that is structured as a clary in which the pentient can sehedile heothis therapeutic infussoms by settivg the fist infiuton applint the followint oner) mportantly, collect veveral datareileted to her/his health status in real-wortid tramework

Interactive section

moten trannas yas
That h thougtt to be waflu for patiema to creativ traing vections mishs dithert esertion.
 personplez the motor traning progam, sact patient can set ip protocols of thusse easose if akteemens with ner/his physicians ans
prasbetherapists.


# Telemedicine for neuromuscular disorders during the COVID-19 outbreak 

Matteo Garibaldi ${ }^{1}$ © Gabriele Siciliano $^{2}$. Giovanni Antonini ${ }^{1}$

Valorizzazione delle scale cliniche!


#### Abstract

"... Validated scales for myopathies and neuropathies are quite disease-specific and difficult to use in remote consultation due to a number of predominantly examinerdependent items. We conceived the Myo-FRS and the N-FRS, two functional scales, which, rather than explore too much disease-specific tasks, are aimed to capture, basically through a functional ques- tionnaire, the overall characteristics of neuromuscular performance, both in myopathies and in neuropathies MYO-FRS and N-FRS have never been used before, however, they provide a practical and useful tool to assign a functional score, which reflects the overall neuromuscular impairment along the disease course"


$\rightarrow$ The COVID-19 pandemic has forced a rapid and unprecedented reorganization of clinical care delivery worldwide, according to local geopolitic realty, local COVID-19 prevalence, practice or institutional structures.
$\rightarrow$ Most diagnostic studies may be postponed unless in case of urgent need and the results would change management (e.g., new ALS, MG, immune-mediated neuropathy or myopathy).




[^0]:    $\rightarrow$ Acute paralytic disease-like GBS, encephalomyelitis or myositis, even without systemic symptoms, may represent the first manifestation of COVID-19.
    $\rightarrow$ Anosmia, ageusia, other cranial neuropathies and lymphocytopenia are red-flags enhancing early diagnostic suspicion.
    $\rightarrow$ In Miller-Fisher Syndrome,ganglioside antibodies against GD1b, instead of QG1b, were found; because the COVID-19 spike protein also binds to sialic acid-containing glycoproteins for cell-entry and anti-GD1b antibodies typically cause ataxic neuropathy, cross-reactivity between COVID-19-bearing gangliosides and peripheral nerve glycolipids was addressed.
    $\rightarrow$ Elevated Creatine Kinase (>10,000) is reported in10\% of COVID-19-infected patients; two such patients presented with painful muscle weakness responding to IVIg indicating that COVID-19-triggered NAM is an overlooked entity.

