STROKE IN THE TIME OF COVID-19 SPECIAL CONSIDERATIONS

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HOST: DR MICHAEL FRANKEL

Since 1992, **Dr. Michael Frankel** has served as Chief of Neurology at Grady Memorial Hospital. He became the Director of the Marcus Stroke and Neuroscience Center at Grady when it opened in 2010. He is also a Professor of Neurology and Division Director of Vascular Neurology at Emory University School of Medicine.

Photo: The Wall Street Journal

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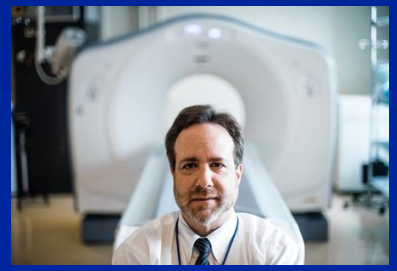
Stroke in the Time of COVID-19

Special Considerations



Host: Michael Frankel, MD
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MARCUS STROKE & NEUROSCIENCE CENTER

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Disclosures (Frankel)

- Grant support
  - Industry
    - Nico Corporation: (ENRICH clinical trial)
  - NIH/CDC

The opinions expressed during this webinar are those of the speaker and do not necessarily reflect the opinions, recommendations or guidance of American Heart Association. For more information about AHA, visit heart.org.

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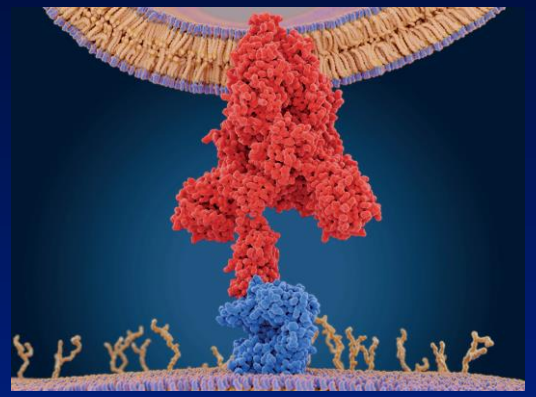
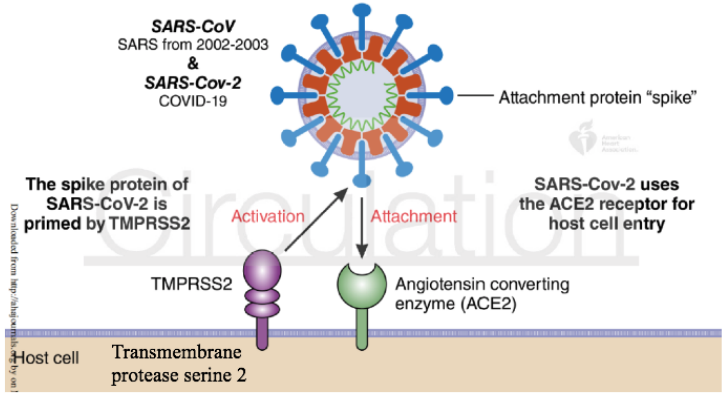
COVID-19 Data 5/7/2020

- Global Cases: 3,775,667
- Global Deaths: 264,406
- US Cases: 1,228,609
- US Deaths: 73,431

https://coronavirus.jhu.edu/map.html



Fang L et al. Lancet Resp Med April 2020.



Clerkin KJ et al. Circulation 2020.

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NEUROSCIENCE CENTER
Grady

Heart Attacks and Strokes Don't Stop During Pandemics.

Call 911 right away if you have symptoms.
Even while fighting the coronavirus,
emergency systems stand ready to help.

heart.org

Lyden P, on behalf of the AHA/ASA Stroke Council Leadership. Temporary Emergency Guidance to US Stroke Centers During the COVID-19 Pandemic. April 2020. https://www-ahajournals-org.proxy.library.emory.edu/doi/pdf/10.1161/STROKEAHA.120.030023

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The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

COVID-19 CASES

To rapidly communicate information on the global clinical effort against Covid-19, the Journal has initiated a series of case reports that offer important teaching points or novel findings. The case reports should be viewed as observations rather than as recommendations for evaluation or treatment. In the interest of timeliness, these reports are evaluated by in-house editors, with peer review reserved for key points as needed.

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

NEJM. April 2020

Presentation

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

Stanley Tuhrim, MD

Dr. Tuhrim is the Director of the Division of Vascular Neurology and Vice-Chair for Clinical Affairs in the Department of Neurology. He is a Professor of Neurology and Geriatrics and Palliative Medicine in the Icahn School of Medicine at Mount Sinai.

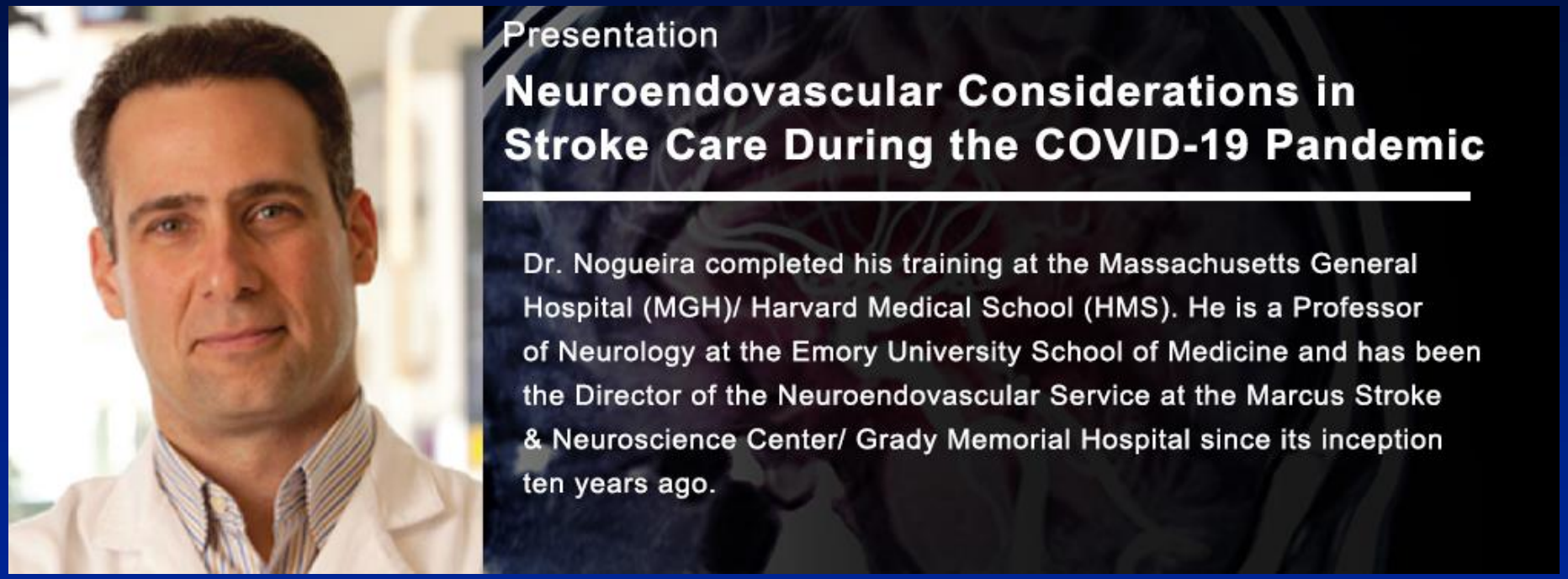
Special Report

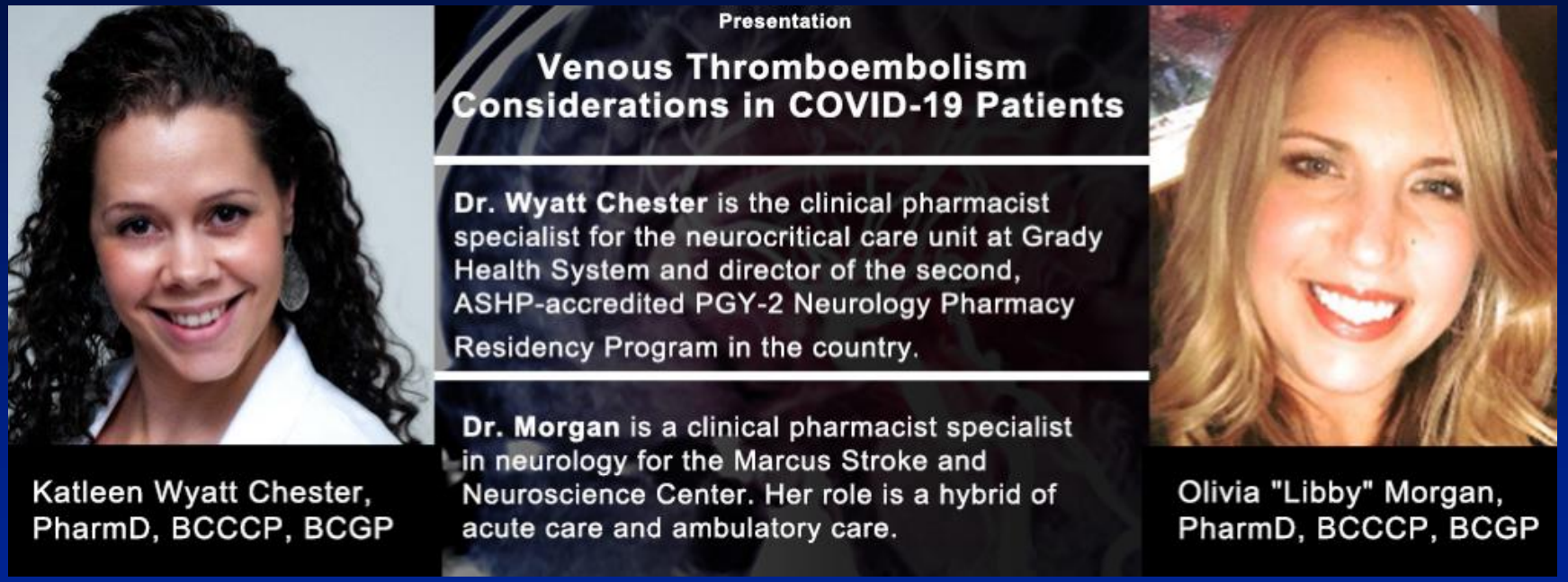
Mechanical Thrombectomy in the Era of the COVID-19 Pandemic: Emergency Preparedness for Neuroscience Teams

A Guidance Statement From the Society of Vascular and Interventional Neurology

Thanh N. Nguyen, MD, FRCPc; Mohamad Abdalkader, MD; Tudor G. Jovin, MD; Raul G. Nogueira, MD; Ashutosh P. Jadhav, MD; Diogo C. Haussen, MD; Ameer E. Hassan, DO; Roberta Novakovic, MD; Sunil A. Sheth, MD; Santiago Ortega-Gutierrez, MD, MSc; Peter D. Panagos, MD; Steve M. Cordina, MD; Italo Linfante, MD; Ossama Yassin Mansour, MD, PhD; Amer M. Malik, MD, MBA; Sandra Narayanan, MD; Hesham E. Masoud, MD; Sherry Hsiang-Yi Chou, MD; Rakesh Khatri, MD; Vallabh Janardhan, MD; Dileep R. Yavagal, MD; Osama O. Zaidat, MD; David M. Greer, MD; David S. Liebeskind, MD

Stroke. April 2020





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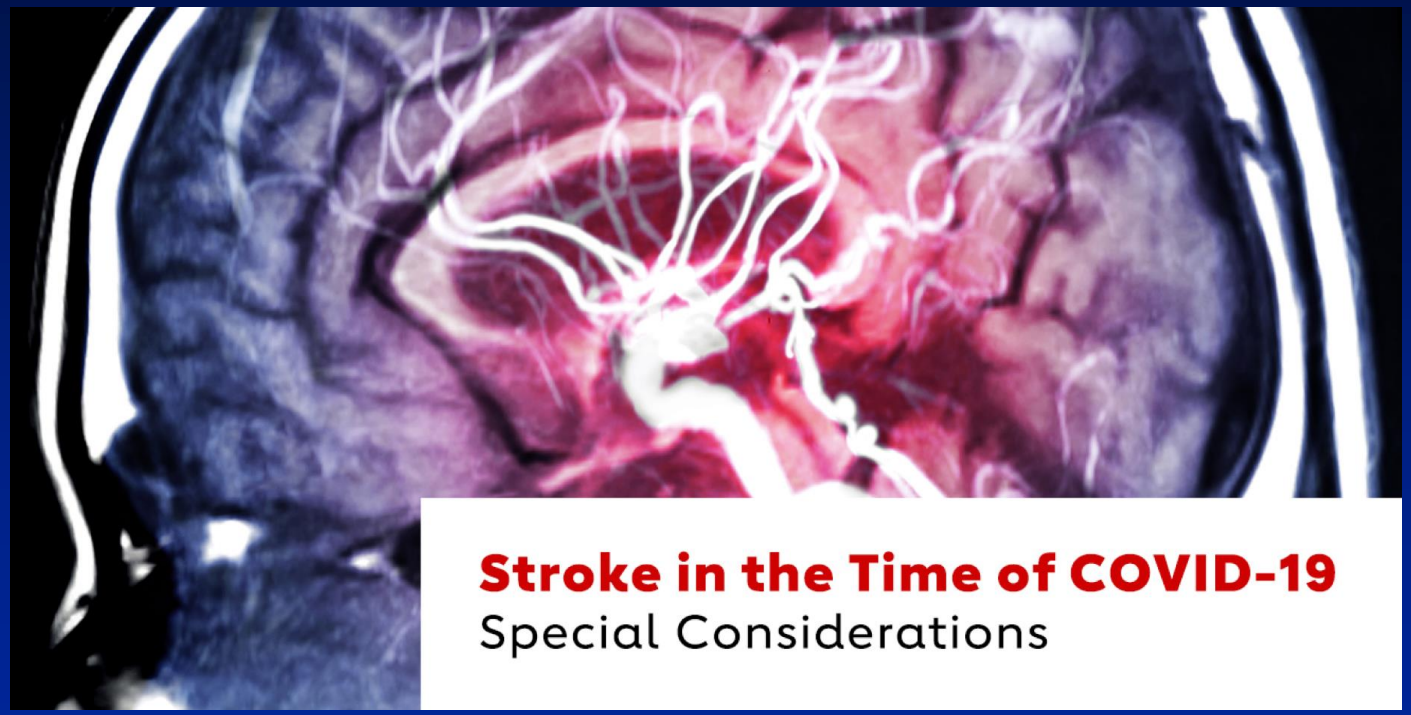
Questions & Answers at the end of all the presentations
Use the chat function to submit questions



- **Large Vessel Stroke as a Presenting Feature of COVID-19 in the Young**
- **Neuroendovascular Considerations in Stroke Care During the COVID-19 Pandemic**
- **Venous Thromboembolism Considerations in Stroke Care During the COVID-19 Pandemic**

Stroke in the Time of Covid-19:

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

Stanley Tuhrim, M.D.

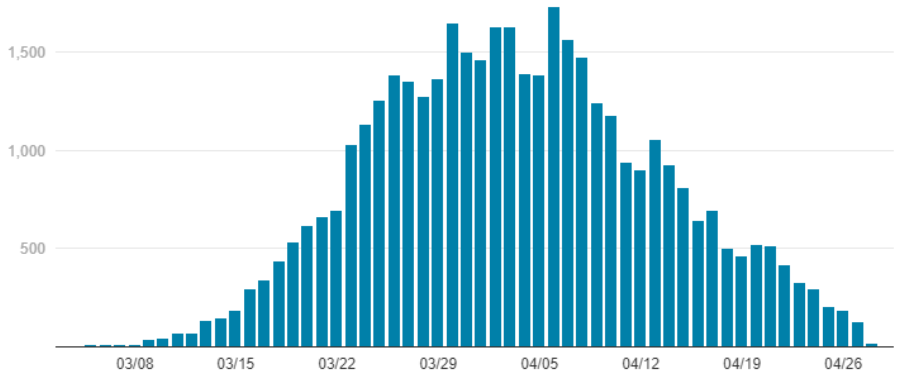
Daily Counts

This chart shows the number of positive cases by diagnosis date, hospitalizations by admission date and deaths by date of death from COVID-19 on a daily basis since March 3.

Hover over bars to see exact values.

Due to delays in reporting, recent data are incomplete.

Cases | **Hospitalizations** | Deaths



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Rates by Borough

This chart shows the number of positive cases per 100,000 people in each borough. It indicates the spread of COVID-19 relative to each borough's population.

	Rate per 100,000 people	Count
The Bronx	2,513	36,969
Staten Island	2,339	11,752
Queens	2,011	50,304
Brooklyn	1,585	42,996
Manhattan	1,069	20,121
Citywide		162,212

Get the data • Created with Datawrapper

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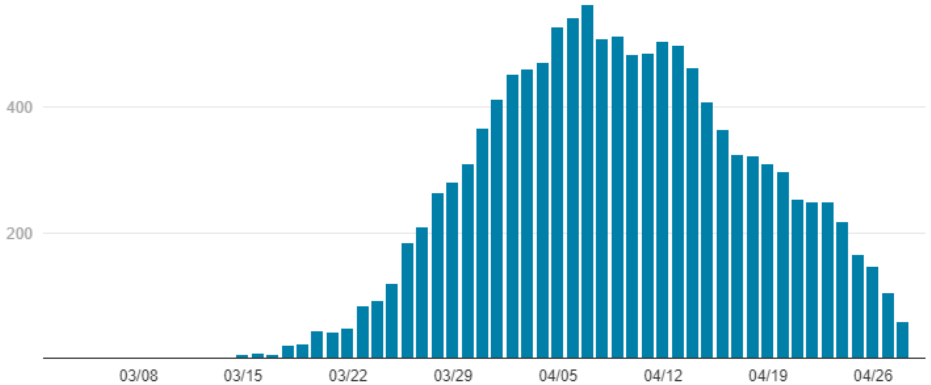

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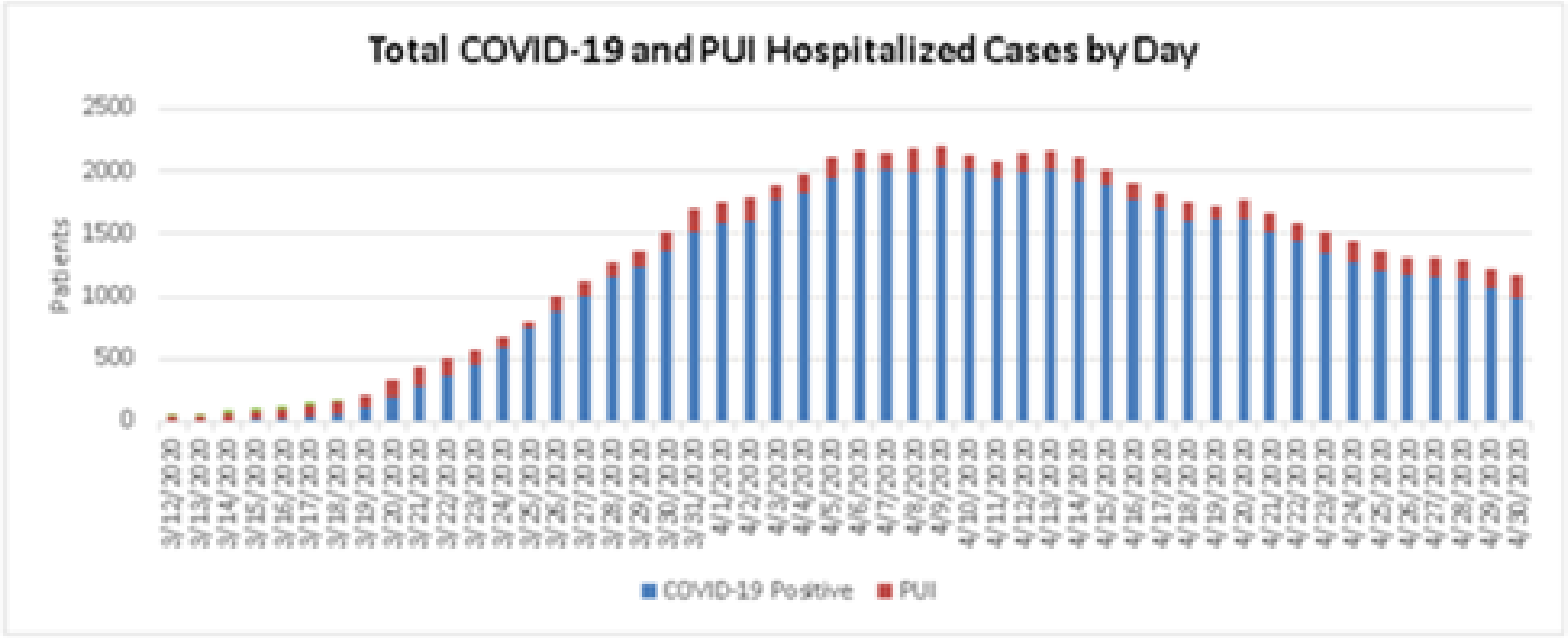
Total COVID-19 and PUI Hospitalized Cases by Day
Patients
2500
2000
1500
1000
500
0
3/12/2020
3/13/2020
3/14/2020
3/15/2020
3/16/2020
3/17/2020
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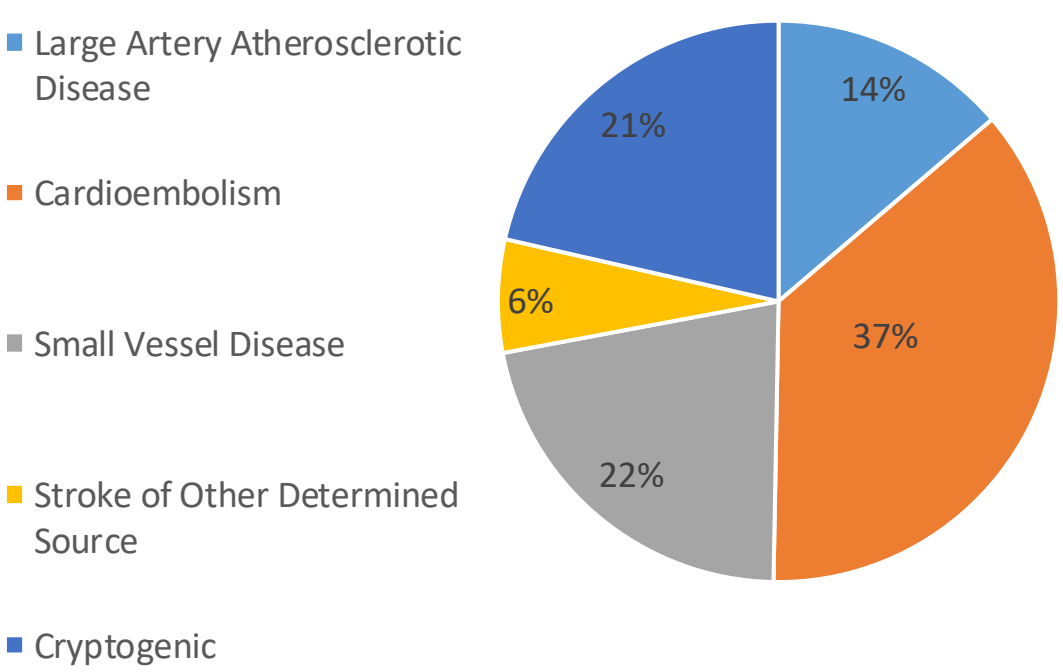
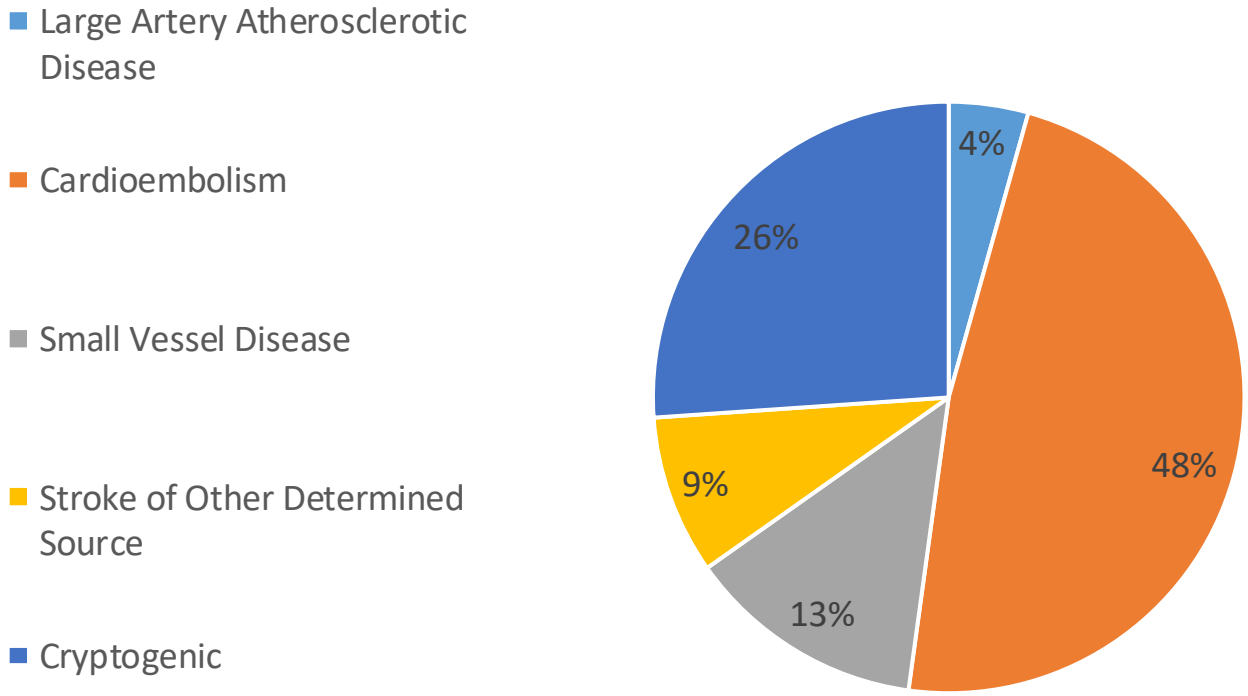
COVID-19 Positive
PUI

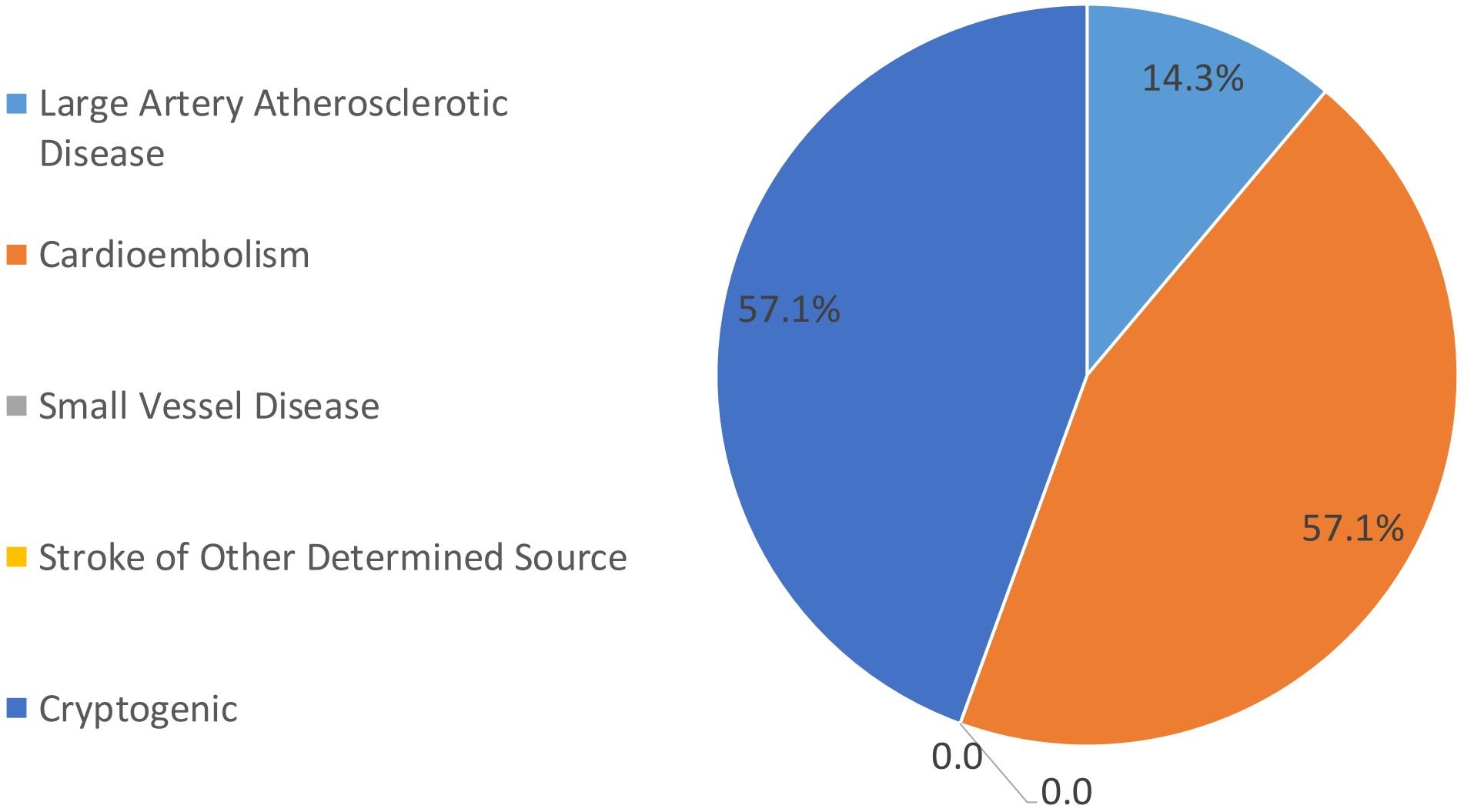
2019 Mount Sinai Health System Stroke Mechanisms



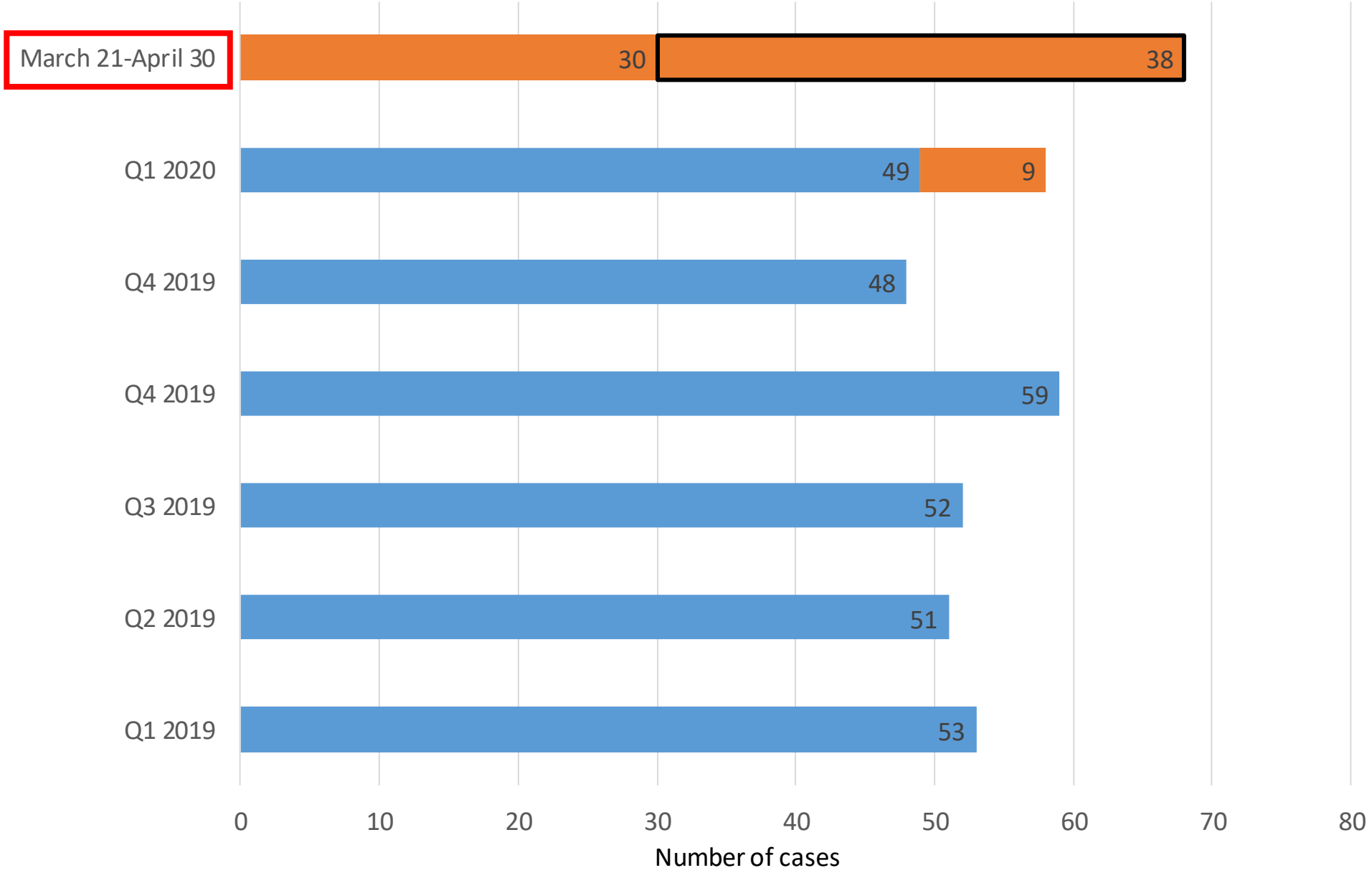
March 21-April 14 2020 Mount Sinai Hospital Stroke Mechanisms



Mechanism of Large Vessel Occlusion Covid Cohort (March 21-April14)



Mount Sinai Health System Endovascular Case Volumes



Clinical Characteristics of Five Young Patients Presenting with Large-Vessel Stroke.*

Table 1. Clinical Characteristics of Five Young Patients Presenting with Large-Vessel Stroke.*

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†	None	None	Hyperlipidemia, hypertension	Undiagnosed diabetes	Mild stroke, diabetes
Medications	None	None	None	None	Aspirin (81 mg), atorvastatin (80 mg)
NIHSS score‡					
On admission	19	13	16	23	13
At 24 hr	17	11	4	19	11
At last follow-up	13 (on day 14)	5 (on day 10)	NA; intubated and sedated, with multiorgan failure	19 (on day 12)	7 (on day 4)
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	Cough, headache, chills	No symptoms; recently exposed to family member with PCR-positive Covid-19	None	Lethargy	Fever, cough, lethargy
White-cell count — per mm^3	7800	9900	5500	9000	4900
Platelet count — per mm^3	427,000	299,000	135,000	372,000	255,000
Prothrombin time — sec	13.3	13.4	14.4	12.8	15.2
Activated partial-thromboplastin time — sec	25.0	42.7	27.7	26.9	37.0
Fibrinogen — mg/dl	501	370	739	443	531
D-dimer — ng/ml	460	52	2230	13,800	1750
Ferritin — ng/ml	7	136	1564	987	596

* Reference ranges are as follows: platelet count, 150,000 to 450,000 per cubic millimeter; prothrombin time, 12.3 to 14.9 seconds; activated partial-thromboplastin time, 25.4 to 34.9 seconds; fibrinogen, 175 to 450 mg per deciliter; D-dimer, 0 to 500 ng per milliliter; and ferritin, 30 to 400 ng per milliliter. CT denotes computed tomography, CTA CT angiography, CTP CT perfusion, MRI magnetic resonance imaging, NA not applicable, PCR polymerase chain reaction, and t-PA tissue plasminogen activator.
† The patients were screened for smoking, hypertension, hyperlipidemia, diabetes, atrial fibrillation, congestive heart failure, illicit drug use, and neck trauma.
‡ Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher numbers indicating more severe stroke.

TJ Oxley et al. N Engl J Med 2020. DOI: 10.1056/NEJMc2009787

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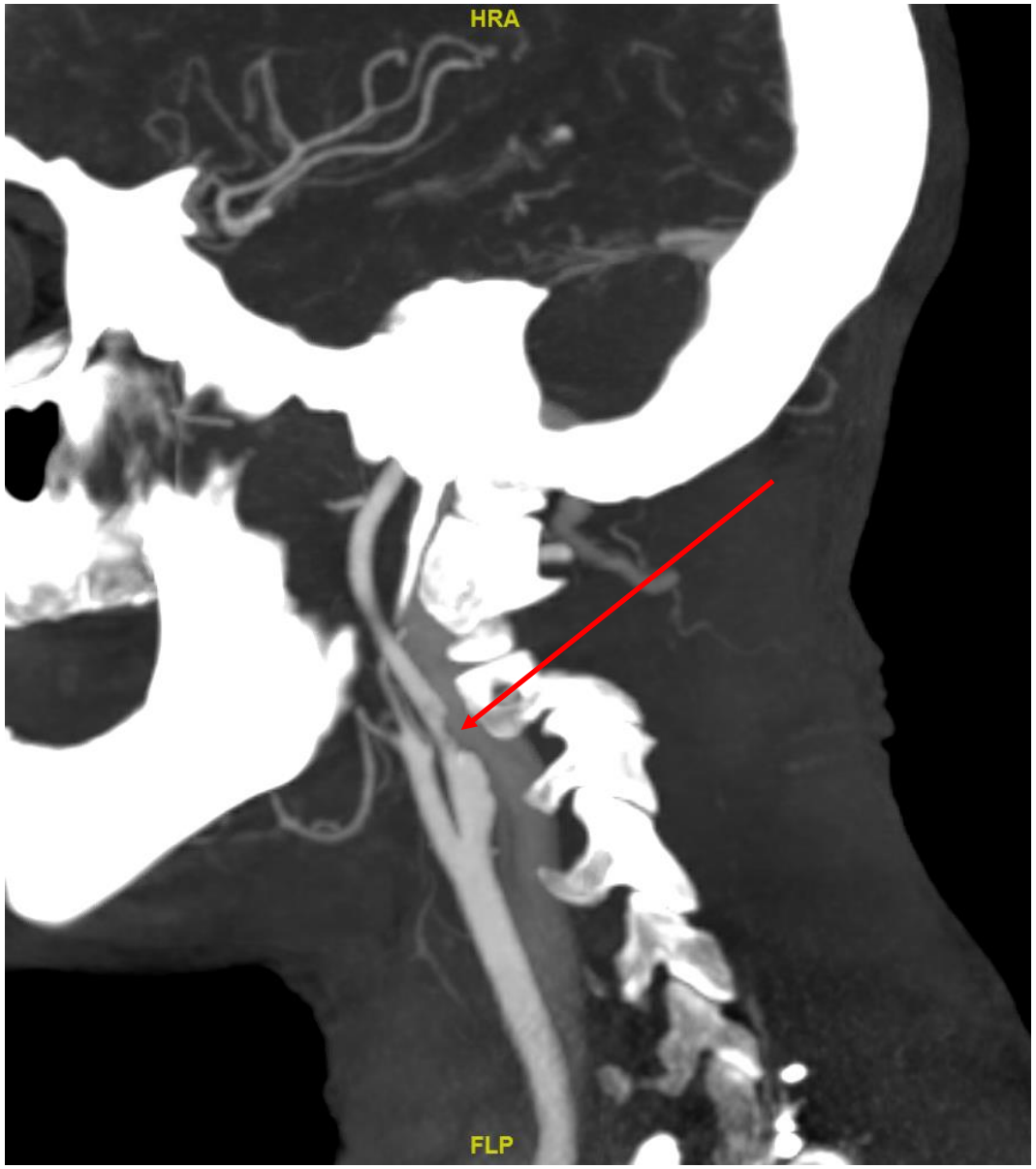
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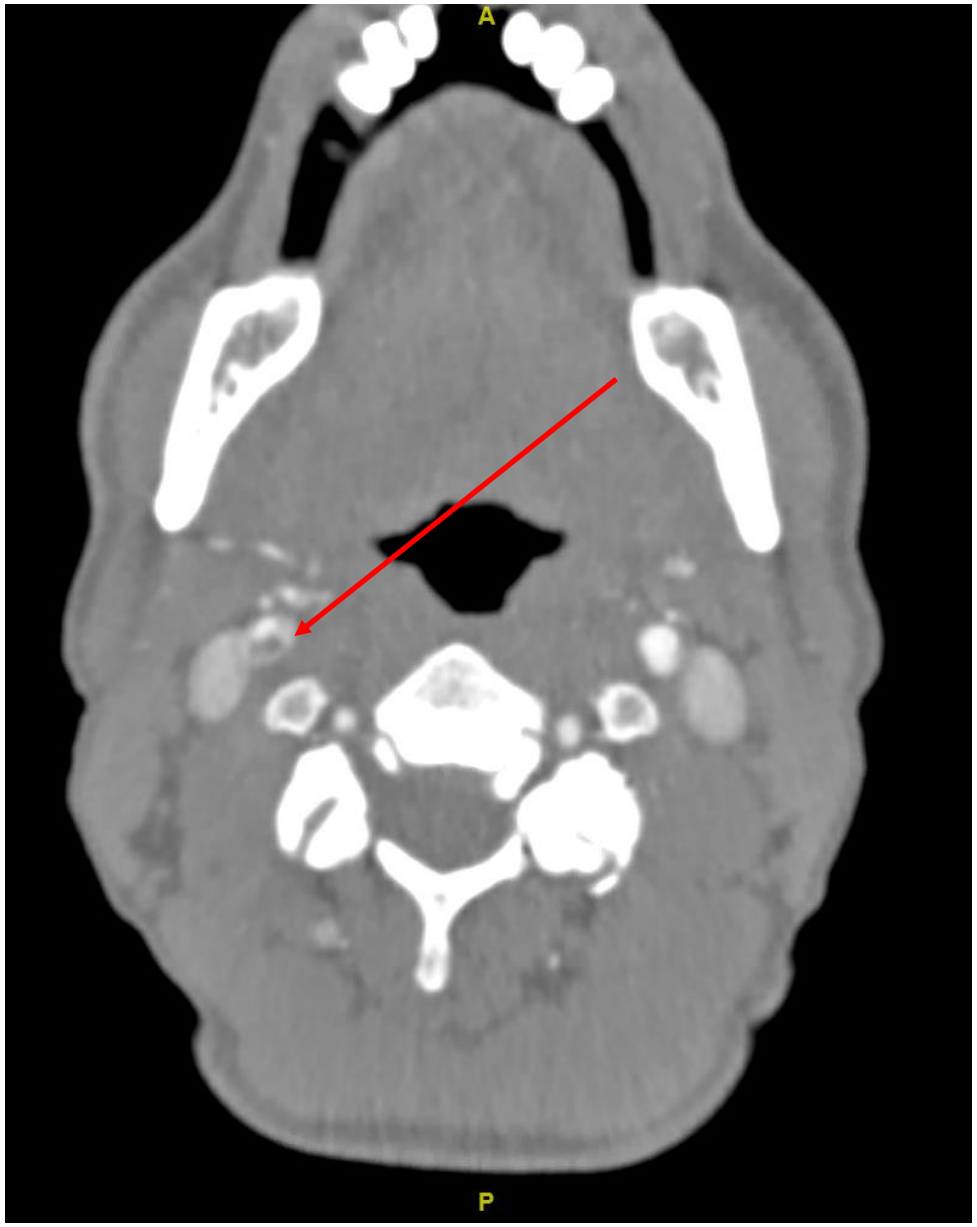
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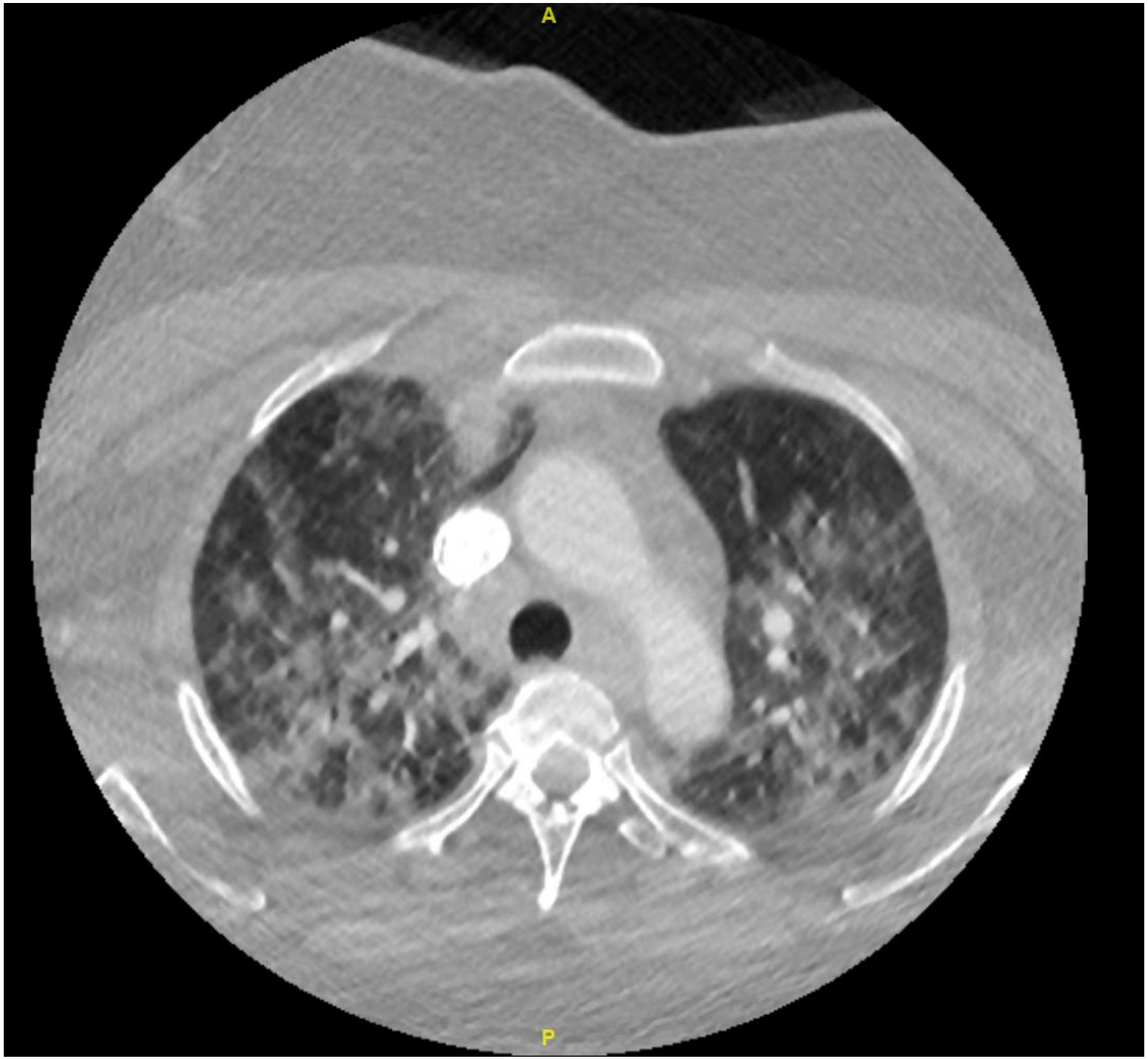
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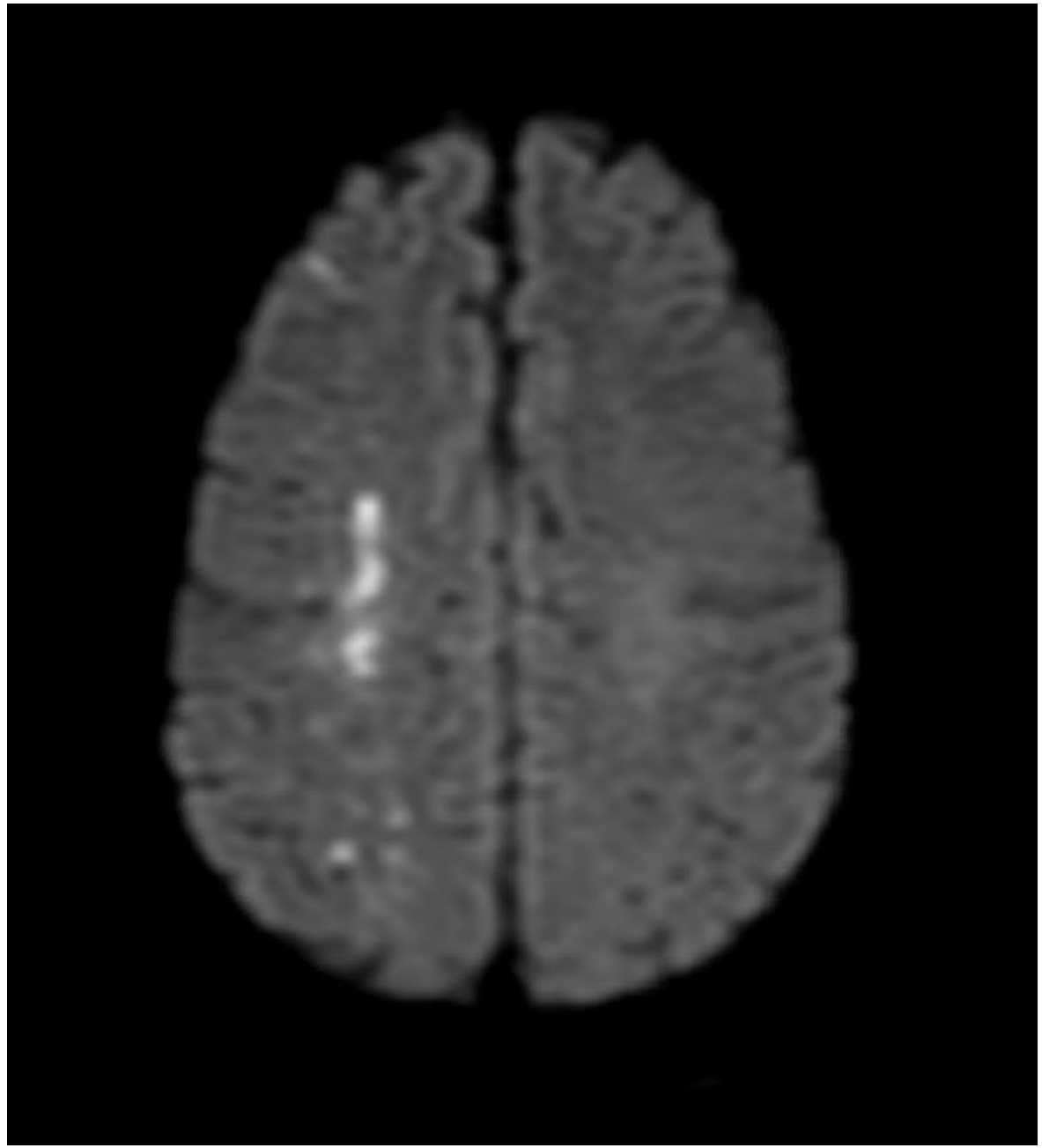
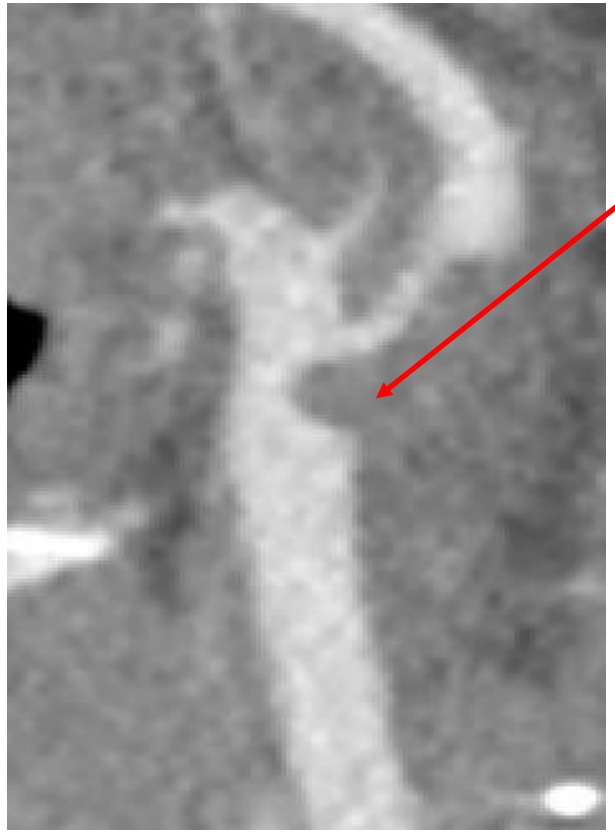
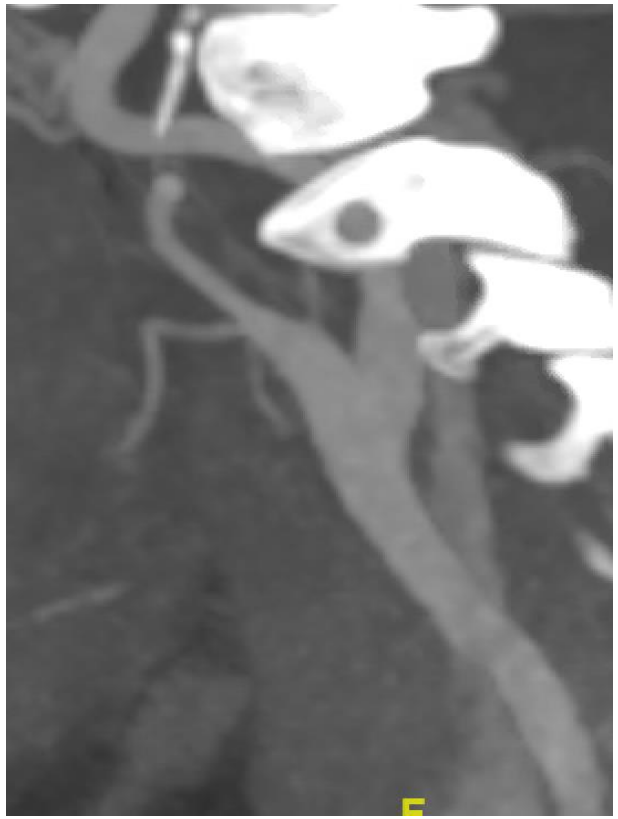
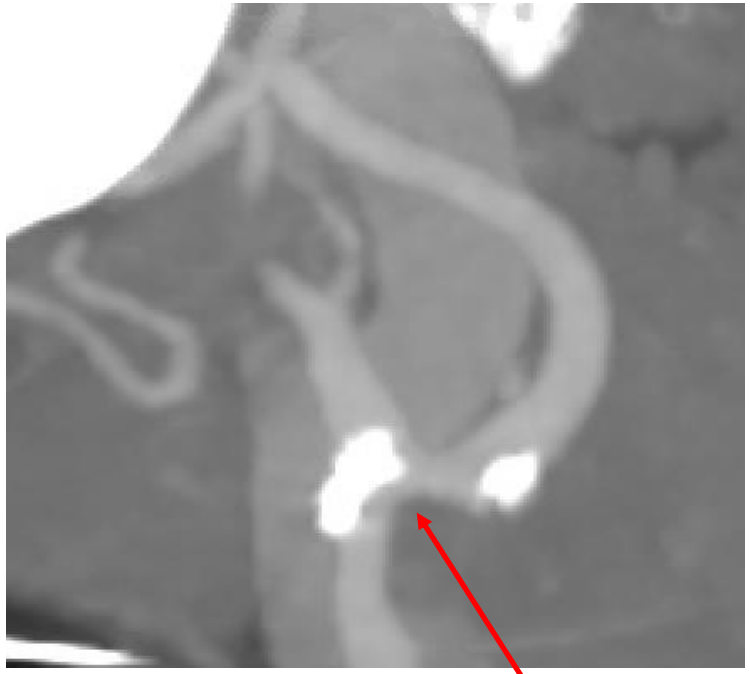
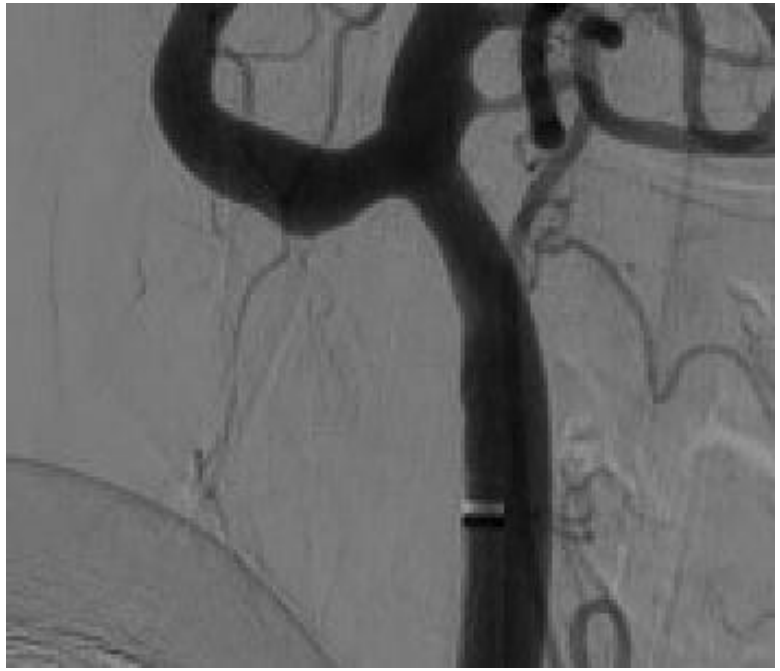










Hypothesized Mechanisms of LVO in COVID-19

- Coagulopathy now well-recognized in COVID-19 disease state
- Extent seems to correlate with severity of respiratory disease
- Virally mediated disruption of endothelium (endotheliitus) leading to thrombus formation may also play a role in LVO
- SARS-CoV-2 virus may infect host cells via ACE2 receptors expressed in multiple organs and on vascular endothelial cells
- Viral particles and accumulations of inflammatory cells have been identified in multiple organs

Endothelial cell infection and endotheliitis in COVID-19

Cardiovascular complications are rapidly emerging as a key threat in coronavirus disease 2019 (COVID-19) in addition to respiratory disease. The mechanisms underlying the disproportionate effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on patients with cardiovascular comorbidities, however, remain incompletely understood.[1,2]

SARS-CoV-2 infects the host using the angiotensin converting enzyme 2 (ACE2) receptor, which is expressed in several organs, including the lung, heart, kidney, and intestine. ACE2 receptors are also expressed by endothelial cells.[3] Whether vascular derangements in COVID-19 are due to endothelial cell involvement by the virus is currently

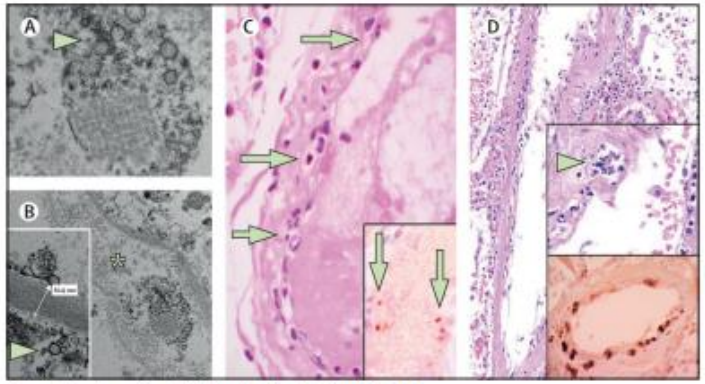


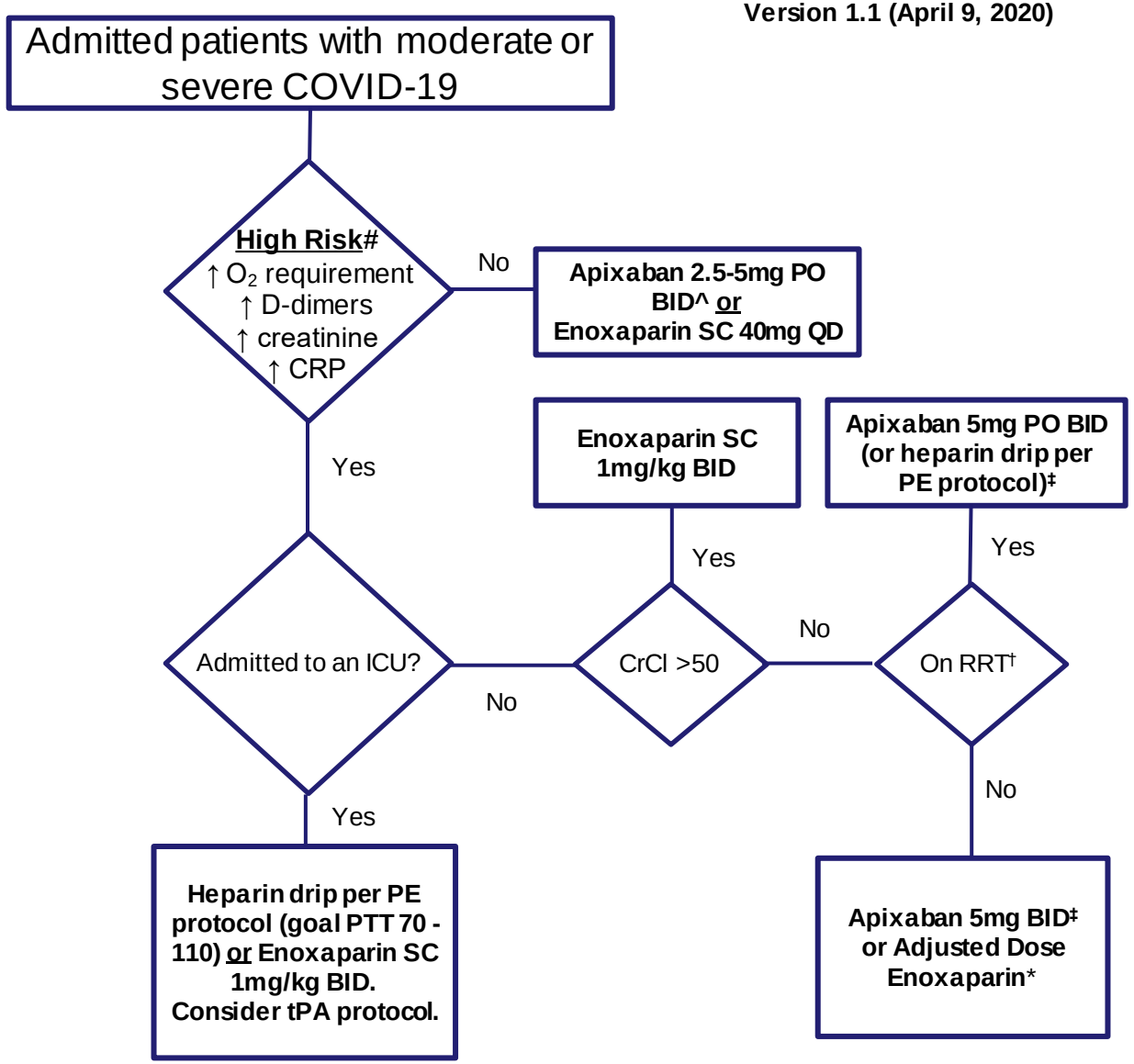
Figure: **Pathology of endothelial cell dysfunction in COVID-19**
(A, B) Electron microscopy of kidney tissue shows viral inclusion bodies in a peritubular space and viral particles in endothelial cells of the glomerular capillary loops. Aggregates of viral particles (arrow) appear with dense circular surface and lucid centre. The asterisk in panel B marks peritubular space consistent with capillary containing viral particles. The inset in panel B shows the glomerular basement membrane with endothelial cell and a viral particle (arrow; about 150 nm in diameter). (C) Small bowel resection specimen of patient 3, stained with haematoxylin and eosin. Arrows point to dominant mononuclear cell infiltrates within the intima along the lumen of many vessels. The inset of panel C shows an immunohistochemical staining of caspase 3 in small bowel specimens from serial section of tissue described in panel D. Staining patterns were consistent with apoptosis of endothelial cells and mononuclear cells observed in the haematoxylin-eosin-stained sections, indicating that apoptosis is induced in a substantial proportion of these cells. (D) Post-mortem lung specimen stained with haematoxylin and eosin showed thickened lung septa, including a large arterial vessel with mononuclear and neutrophilic infiltration (arrow in upper inset). The lower inset shows an immunohistochemical staining of caspase 3 on the same lung specimen; these staining patterns were consistent with apoptosis of endothelial cells and mononuclear cells observed in the haematoxylin-eosin-stained sections. COVID-19=coronavirus disease 2019.

Published Online
April 17, 2020
https://doi.org/10.1016/
S0140-6736(20)30937-5

Varga, Z., et al. (2020). "Endothelial cell infection and endotheliitis in COVID-19." The Lancet **395**(10234): 1417-1418.

Mount Sinai COVID-19 Anticoagulation Algorithm

Version 1.1 (April 9, 2020)



Inclusion: All admitted patients with moderate or severe COVID-19
Exclusion: High risk of bleeding as judged by treating physician

Obtain at baseline and daily:
- CBC, PT/PTT, D-dimer

Hold anticoagulation if:
- Platelet count <50,000; INR>1.5
- Evidence of current or recent bleeding

If patients take AC at home:
- May switch to therapeutic enoxaparin or heparin (as per algorithm) for the duration of hospitalization, unless contraindicated

Rivaroxaban may be used in place of Apixaban at any indication

Discharged COVID-19 patient on therapeutic anticoagulation while hospitalized

Consider Prophylactic AC for 2 weeks post discharge (Apixaban 5mg PO BID for 2 wks)

#High Risk: No precise metrics exist. Consider exam (eg O_2 sat<90%, RR >24), ↑O_2 requirement (eg, ≥4L NC), labs (eg, ↑d-dimers, C-reactive protein)
^Efficacy and dose not established; prophylactic or treatment doses acceptable

†RRT – Renal Replacement Therapy
‡ If ≥80 years of age or weight ≤60 kg, reduce apixaban to 2.5 mg BID
* If CrCl <30: enoxaparin 0.5mg/kg BID with anti-Xa level after 3rd dose

Mount Sinai COVID-19 Anticoagulation Algorithm

Definition of high risk for progression to ICU

- There is insufficient evidence to precisely define "high-risk" or provide specific cut-off values for individual factors
- Clinicians should consider a combination of exam findings (e.g, labored breathing, RR >24, decreased O_2 sat<90%), increased O_2 requirement (eg, ≥4L NC), and lab biomarkers (eg, elevated CRP, elevated creatinine, rising d-dimer >1.0).

Rationale for early anticoagulation

- Pathophysiology of COVID-19 associated respiratory disease is consistent with pulmonary vascular thromboemboli with increased dead space ventilation
- Autopsy studies have demonstrated venous thromboembolism in deceased coronavirus patients[1]
- Early anticoagulation is necessary to prevent propagation of microthrombi at disease presentation
- Anticoagulation may be associated with decreased mortality[2]

Rationale for choice of anticoagulant

- Heparins bind tightly to COVID-19 spike proteins[3,4]
- Heparins also downregulate IL-6 and directly dampen immune activation[5]
- DOACs do not appear to have these anti-inflammatory properties
- Rivaroxaban can be used in place of Apixaban in this algorithm

References

1. Xiang-Hua et al. Am J Respir Crit Care Med, 182 (3), 436-7. PMID: 20675682
2. Tang et al. J Thromb Haemost 2020 Mar 27. PMID: 32220112
3. Belouzard et al. Proc Natl Acad Sci, 2009 106 (14), 5871-6. PMID: 19321428
4. de Haan et al. J Virol. 2005 Nov; 79(22): 14451–14456. PMID: 16254381
5. Mummery et al. J Immunol, 2000. 165 (10), 5671-9. PMID: 1106792

Version 1.1 (April 9, 2020)

Journal Pre-proof

Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19

Ishan Paranjpe, BS, Valentin Fuster, MD, PhD, Anuradha Lala, MD, Adam Russak, MD, Benjamin S. Glicksberg, PhD, Matthew A. Levin, MD, Alexander W. Charney, MD, PhD, Jagat Narula, MD, PhD, Zahi A. Fayad, PhD, Emilia Bagiella, PhD, Shan Zhao, MD, PhD, Girish N. Nadkarni, MD, MPH

PII: S0735-1097(20)35218-9

DOI: https://doi.org/10.1016/j.jacc.2020.05.001

Reference: JAC 27327

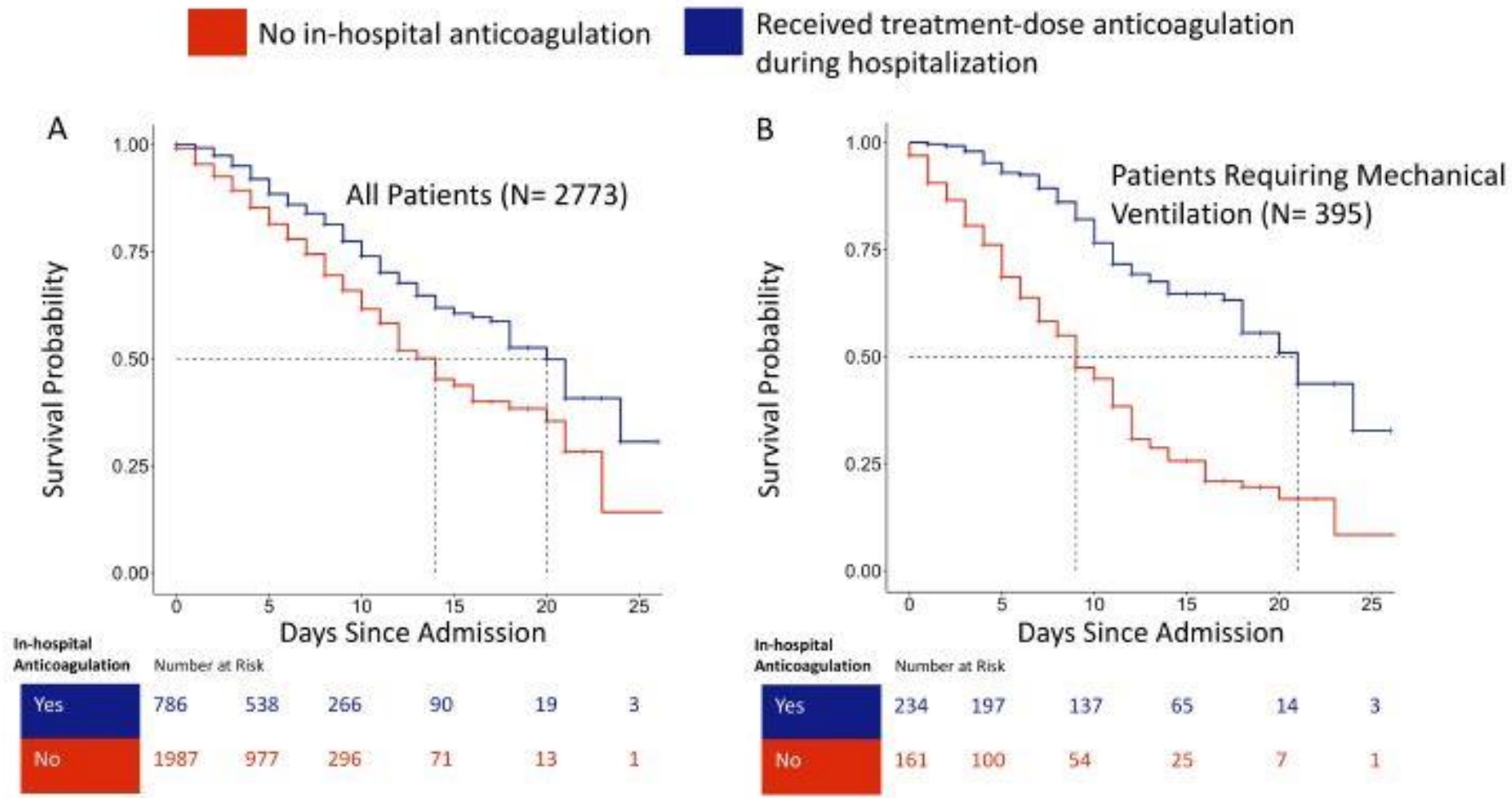
To appear in: *Journal of the American College of Cardiology*

Paranjpe I, Fuster V, Lala A, Russak A, Glicksberg BS, Levin MA, Charney AW, Narula J, Fayad ZA, Bagiella E, Zhao S, Nadkarni GN, Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19, *Journal of the American College of Cardiology* (2020), doi: https://doi.org/10.1016/j.jacc.2020.05.001.

Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19

- Between March 14 and April 11, 2020, 2773 patients with laboratory-confirmed COVID-19 were admitted to the MSHS
- 786 received systemic anticoagulation during their hospital course
- Median time from admission to anticoagulation was 2 days
- Serious bleeding events occurred in 3% of AC and 1.9% non-AC but 1/3 of AC group's bleeds occurred before anticoagulation
- AC group was more likely to require mech ventilation (30% vs 8%)
- In-hospital mortality for the 2 groups was similar, 22.5% in AC, 22.8 % non-AC, but median survival was increased 21 vs 14 days
- Multivariate proportional hazard model longer duration of AC was associated with a reduced risk of mortality (HR .86/day, p<.001)

Paranjpe I, Fuster V, Lala A, Russak A, Glicksberg BS, Levin MA, Charney AW, Narula J, Fayad ZA, Bagiella E, Zhao S, Nadkarni GN, Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19, Journal of the American College of Cardiology (2020), doi: https://doi.org/10.1016/j.jacc.2020.05.001.


No in-hospital anticoagulation
Received treatment-dose anticoagulation during hospitalization
A
All Patients (N= 2773)
Survival Probability
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
25
Days Since Admission
In-hospital Anticoagulation
Number at Risk
Yes 786 538 266 90 19 3
No 1987 977 296 71 13 1
B
Patients Requiring Mechanical Ventilation (N= 395)
Survival Probability
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
25
Days Since Admission
In-hospital Anticoagulation
Number at Risk
Yes 234 197 137 65 14 3
No 161 100 54 25 7 1

Large Vessel Stroke in the COVID ERA Summary

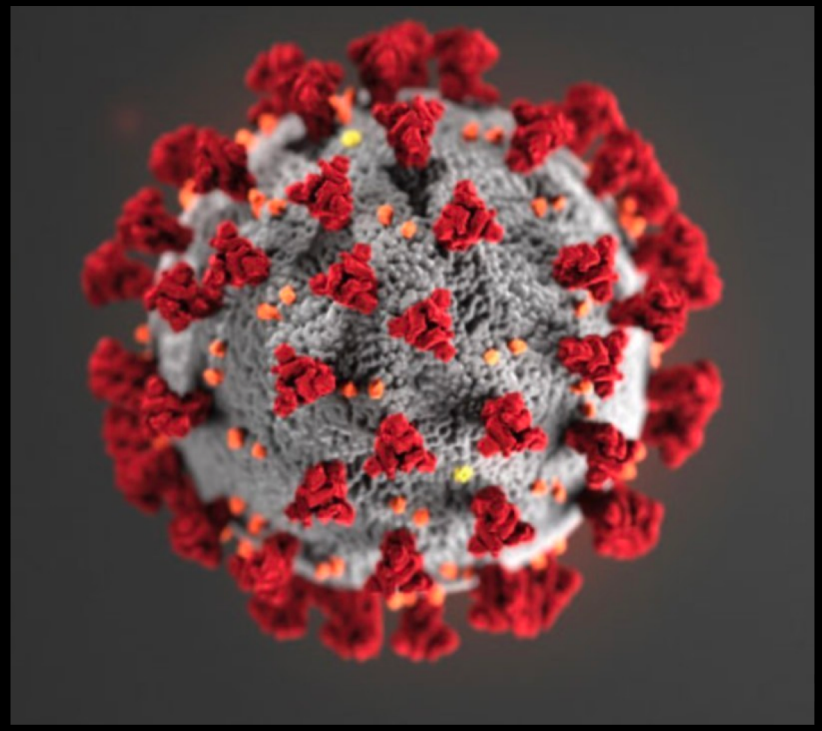
- Stroke involving LVO seems to occur in patients with mild COVID-19 symptoms
- Stroke mechanism is not yet known but may be independent of hypercoagulable markers, or relate to a combination of a hypercoagulable state and direct endothelial damage (endotheliitis)
- Anticoagulation of hospitalized patients may improve outcome
- Other interventions, including those targeting the endothelium (ACEI?, statins?), may prove helpful

Neuroendovascular Considerations In Stroke Care During the COVID-19 Pandemic

Raul G Nogueira, MD

Professor in Neurology,
Neurosurgery, and Radiology
Emory University

Director, Neuroendovascular Service
Grady Memorial Hospital
Atlanta, GA



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The opinions expressed during this webinar are those of the speaker and do not necessarily reflect the opinions, recommendations or guidance of American Heart Association. For more information about AHA, visit heart.org.

Disclosures:

Stryker's Neurovascular Division

- DAWN Trial PI (unpaid)
- Trevo Registry Steering Committee
- Trevo-2 Trial PI
- Consultant

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- STAR Trial Core Lab

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Phenox, Anaconda, Corindus Robotics, Biogen, Genentech, Prolong Pharmaceuticals

Allm Inc - JOIN (unpaid)

- Free Consultant and Beta-Site
- FAST-ED App (Freeware)
- RESILIENT Trial Collaboration

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- CRISP, SWIFT-PRIME, & DAWN Trials (unpaid)
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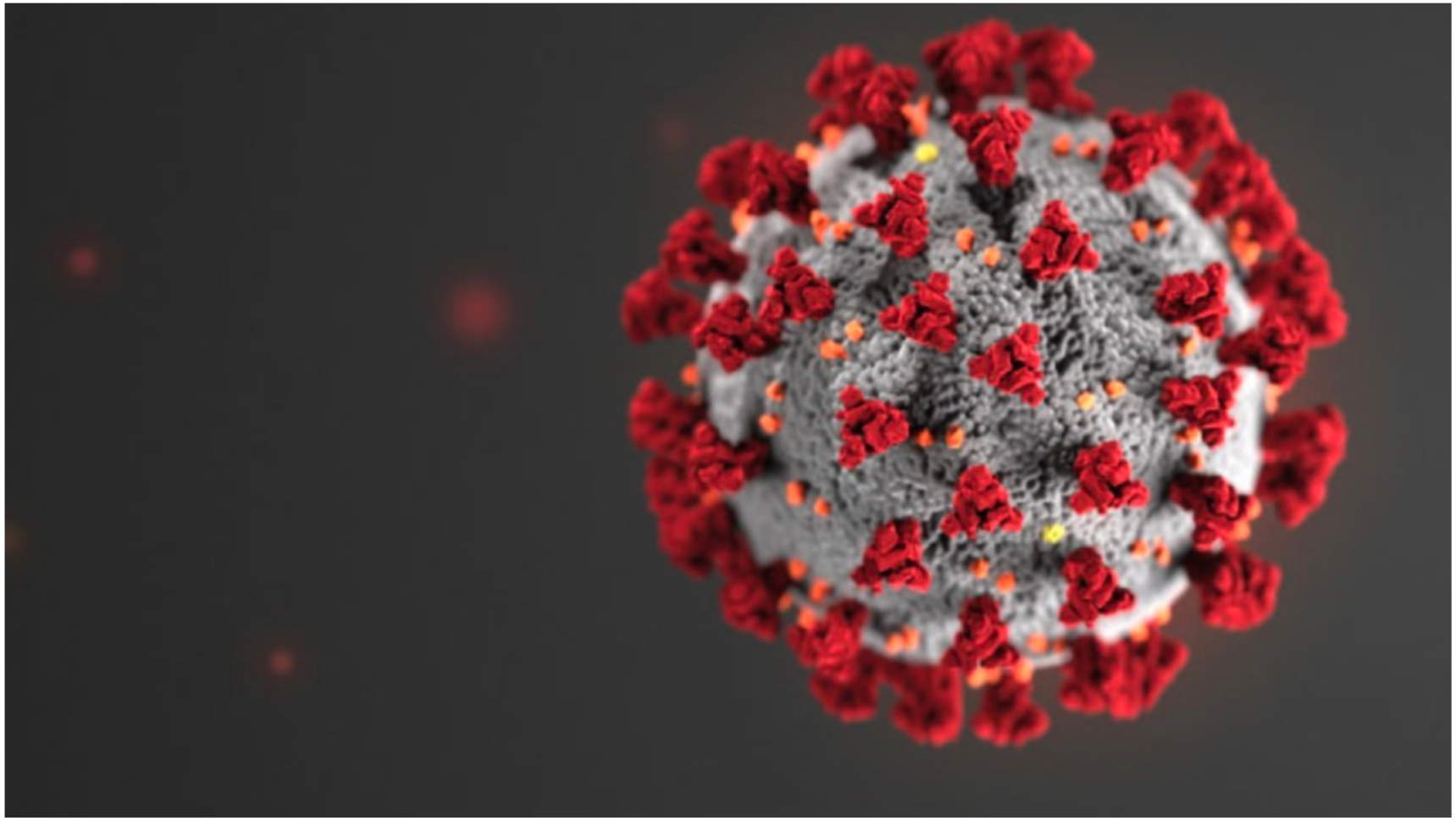
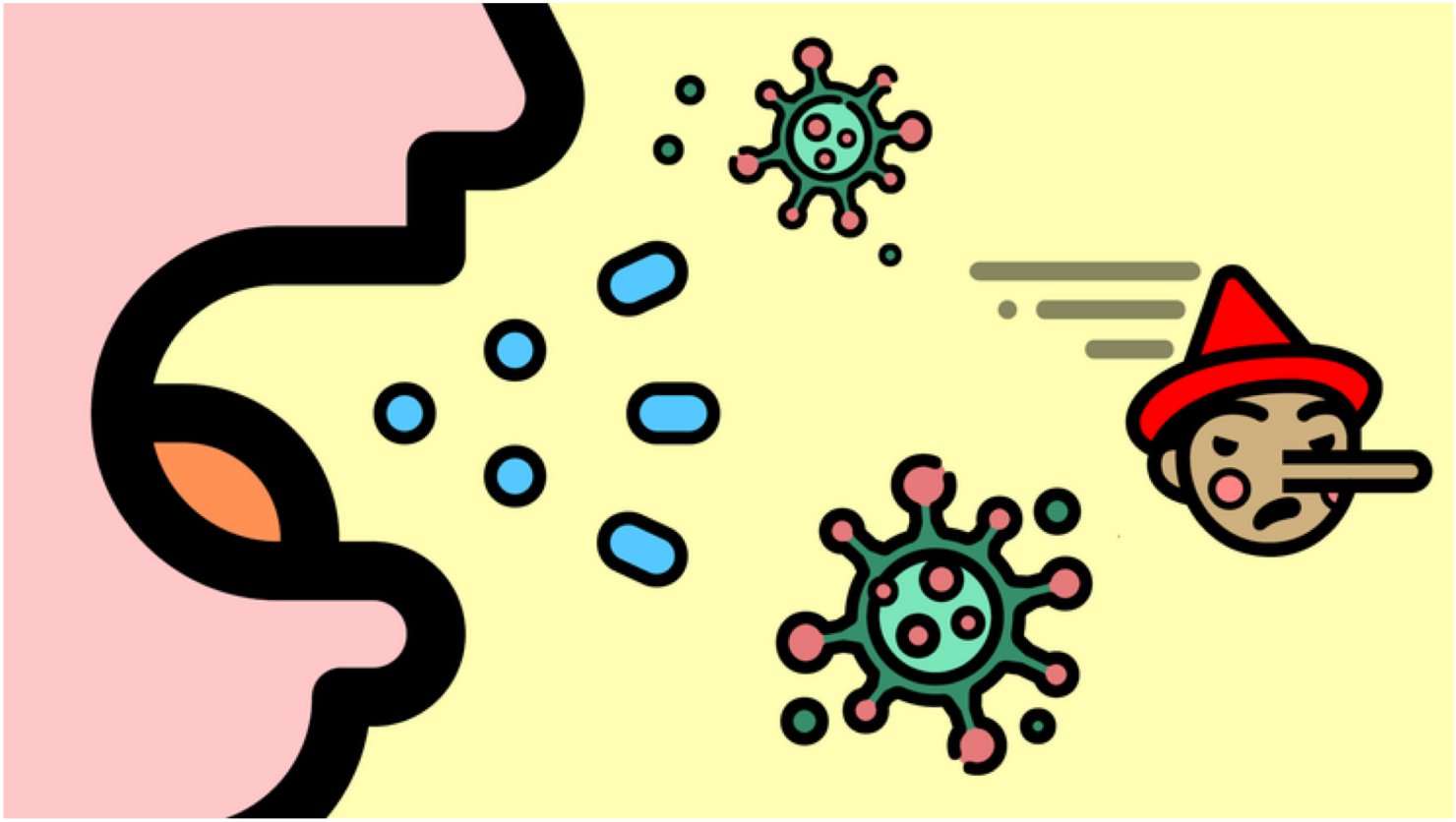
Before We Start….

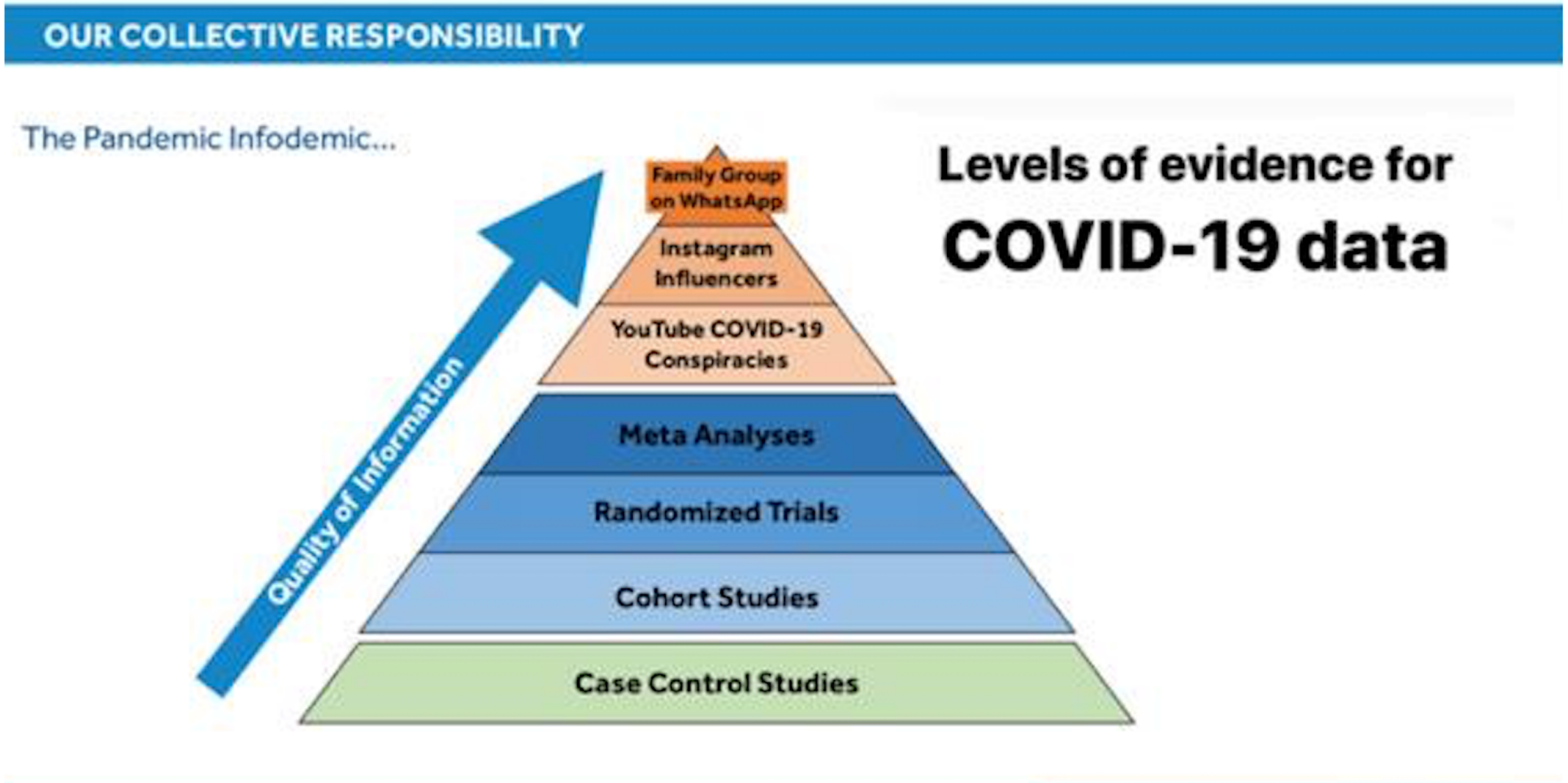


INFODEMIC: A Strong Ally to COVID-19



Opinions are not FACTS!

INFODEMIC: A Strong Ally to COVID-19



Courtesy: Pedro Magalhaes, MD

INFODEMIC: A Strong Ally to COVID-19

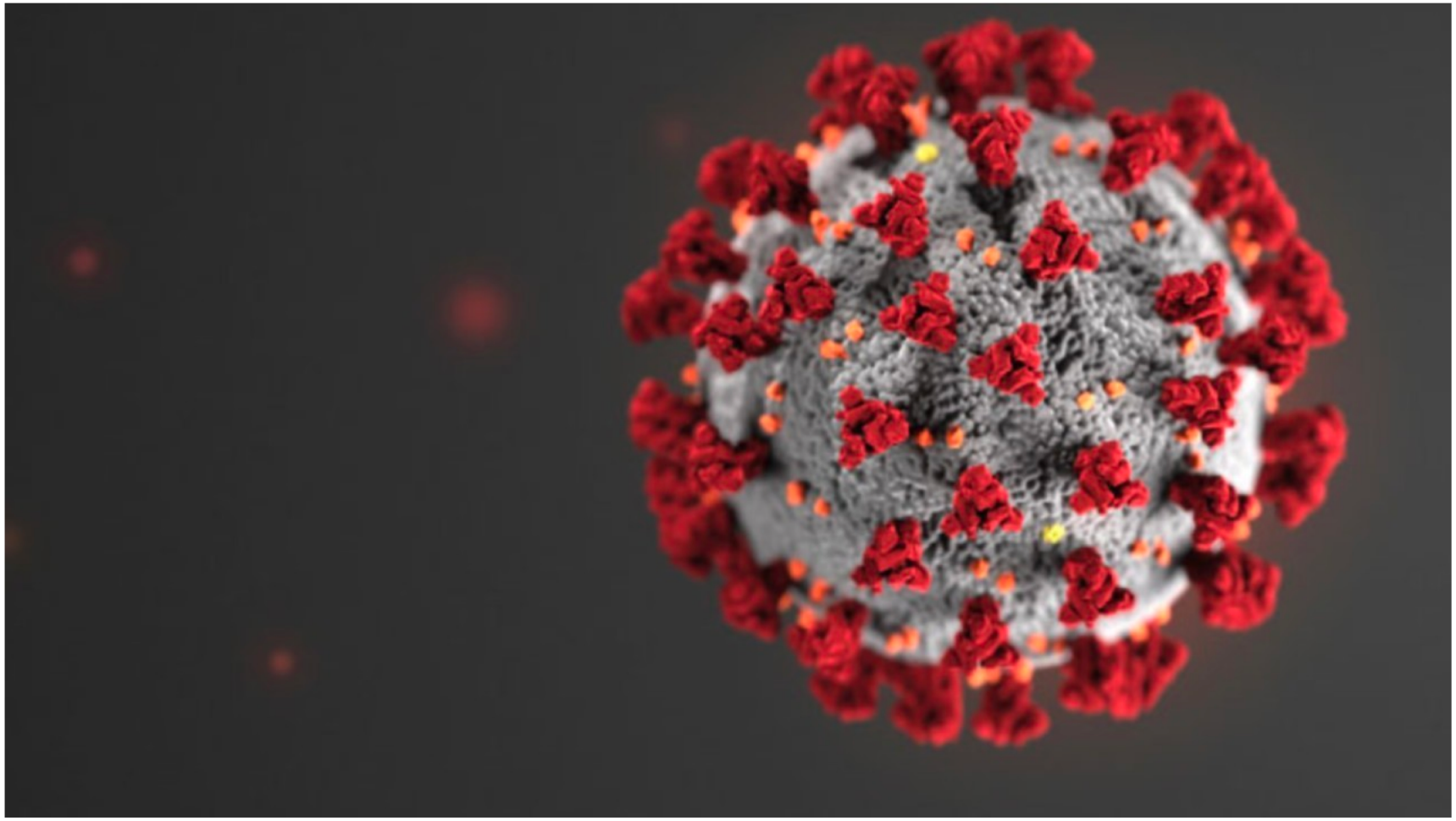
The NEW ENGLAND JOURNAL of MEDICINE

Covid-19 — A Reminder to Reason

Ivry Zagury-Orly, B.Sc., and Richard M. Schwartzstein, M.D.

Thus far in the Covid-19 pandemic, we've observed that therapeutic management has often been initiated and altered on the basis of individual case reports and physician opinion, rather than of randomized trials. In these uncertain times, physicians fall prey to cognitive error and unconsciously rely on limited experiences, whether their own or others', instead of scientific inquiry. We believe that physicians should be acting in concert with clinical equipoise. We should be skeptical of any purported therapeutic strategy until enough statistical evidence is gathered that would convince any "open-minded clinician informed of the results" that one treatment is superior to another

COVID-19: Neurological Manifestations and Stroke

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Young and middle-aged people, barely sick with covid-19, are dying of strokes
Doctors sound alarm about patients in their 30s and 40s left debilitated or dead. Some didn't even know they were infected.


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NJ cardiologist suffers stroke likely due to COVID-19
Dr. Troy Randle discusses his experience with recovering from COVID-19.
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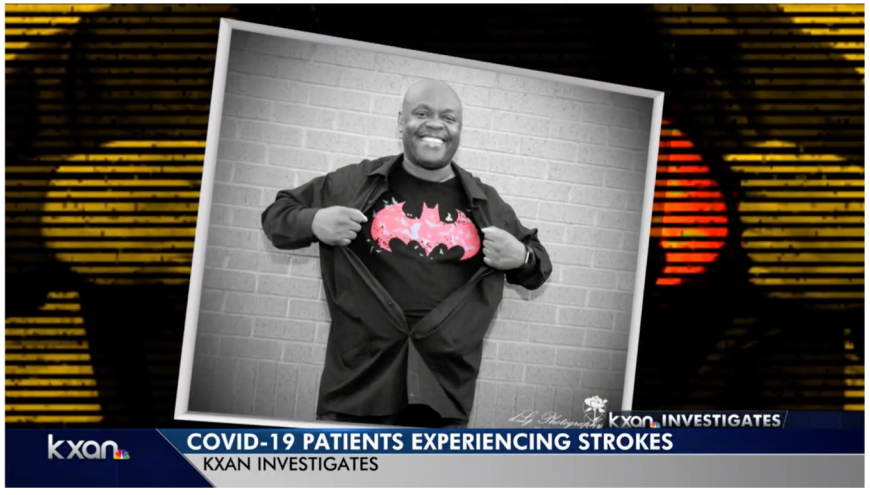
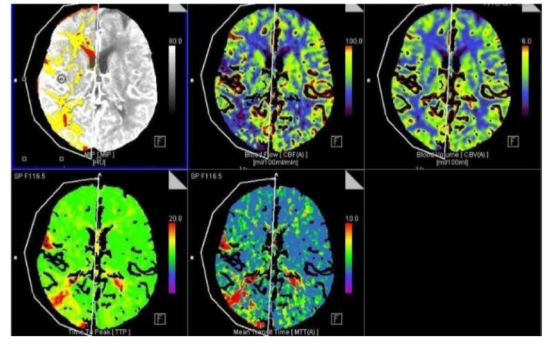
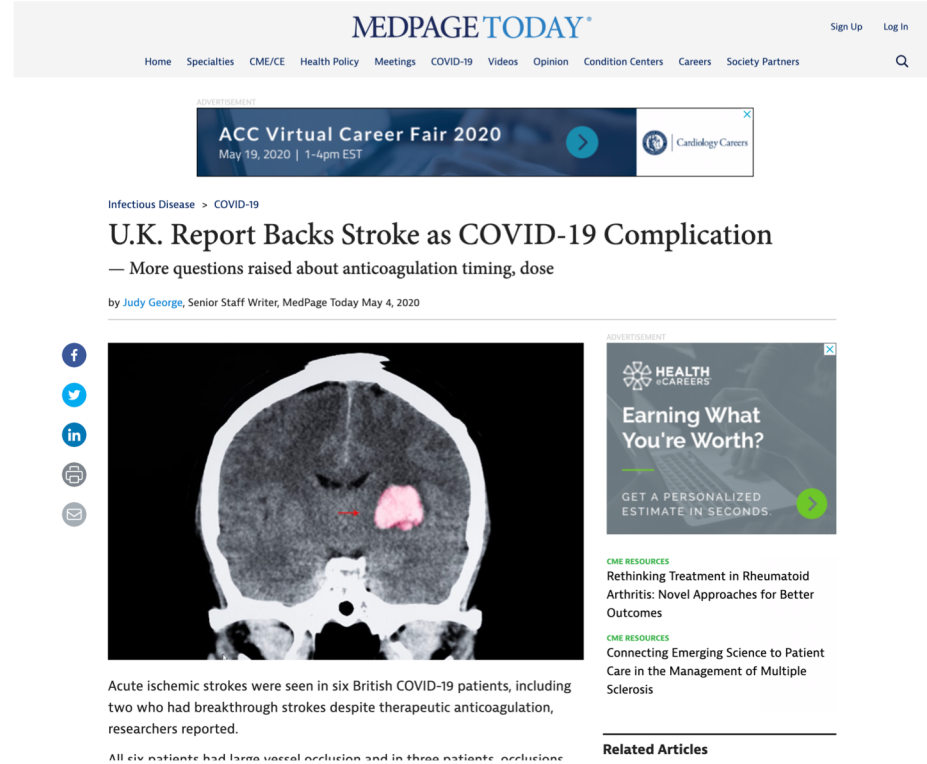

INVESTIGATIONS
Research shows COVID-19 is causing strokes in patients, including a Texas correctional officer
kxan INVESTIGATES
COVID-19 PATIENTS EXPERIENCING STROKES
KXAN INVESTIGATES


MAY 6, 2020
COVID-19 may increase blood clotting and blockage of brain blood vessels
by Henry Killworth, University College London
CT brain images highlighting acuate ischaemic stroke. Credit: Jacob F ...
Clinical observations of COVID-19 patients, who went on to have a stroke, suggest coronavirus may cause clots within blood vessels (arteries) in the brain, finds a team of neurologists from UCL and UCLH (the National Hospital for Neurology and Neurosurgery), London.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Infectious Disease > COVID-19
U.K. Report Backs Stroke as COVID-19 Complication
— More questions raised about anticoagulation timing, dose
by Judy George, Senior Staff Writer, MedPage Today May 4, 2020
Acute ischemic strokes were seen in six British COVID-19 patients, including two who had breakthrough strokes despite therapeutic anticoagulation, researchers reported.
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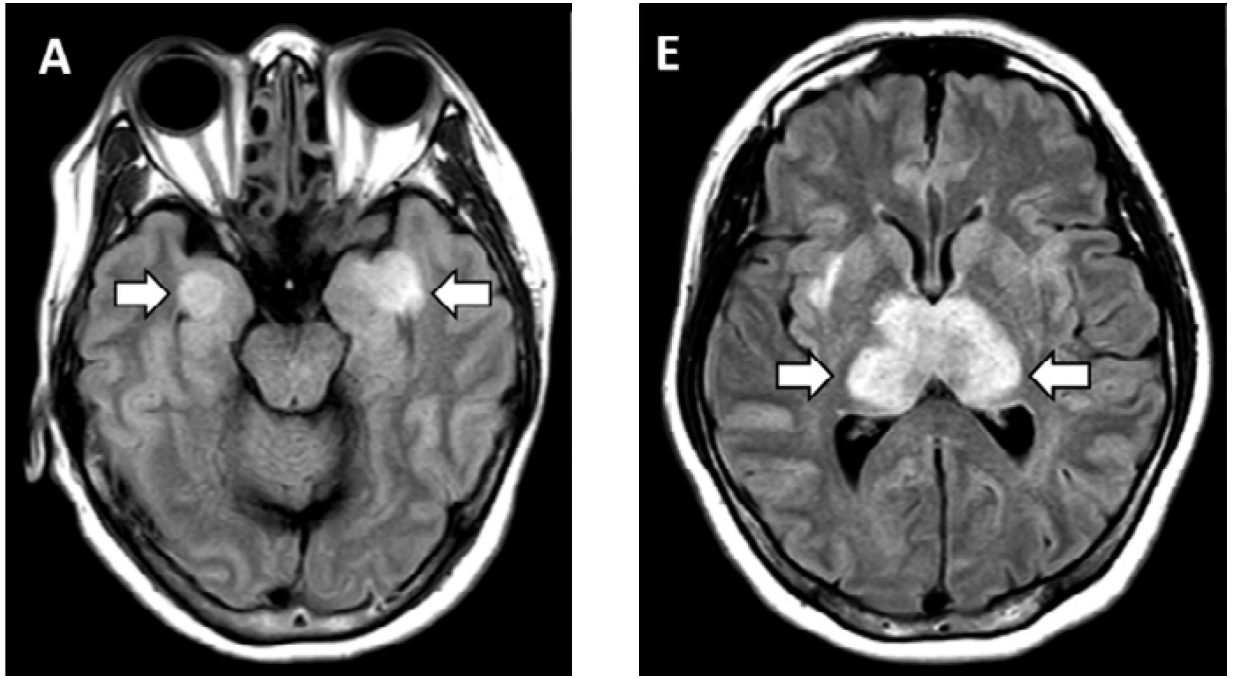
Encephalitis in COVID 19

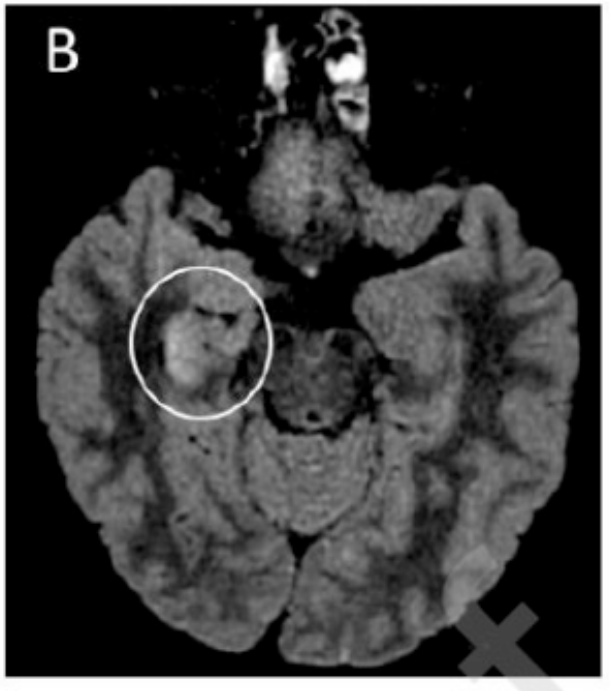


58 year old woman (airline worker) with 3-day history of cough, fever, and altered mental status.

Nasal swab PCR positive for SARS-CoV-2

Diagnosed with acute hemorrhagic necrotizing encephalopathy

Poyiadji N et al. Radiology 2020.



26 year old with seizures; nasal swab negative;
CSF positive for SARS-CoV-2
Diagnosed with meningitis/encephalitis

Moriguchi T et al. Int J Infect Dis. 2020.

CORRESPONDENCE

Guillain–Barré Syndrome Associated with SARS-CoV-2

Table 1. Characteristics of Five Patients with Guillain–Barré Syndrome after the Onset of Covid-19.*

Patient No.	Onset of Neurologic Syndrome	Neurologic Signs and Symptoms	CSF Findings†	Antiganglioside Antibodies‡	MRI Results	Treatment and Outcomes at Week 4
1	7 Days after fever, cough, and ageusia	Flaccid areflexic tetraplegia evolving to facial weakness, upper-limb paresthesia (36 hr), and respiratory failure (day 6)	Day 2 (first lumbar puncture): normal protein level; no cells; negative PCR assay for SARS-CoV-2 Day 10 (second lumbar puncture): protein level, 101 mg/dl; white-cell count, 4 per mm^3; negative PCR assay for SARS-CoV-2	Negative	Head: normal Spine: enhancement of caudal nerve roots	Received 2 cycles of IVIG; had poor outcomes, including persistence of severe upper-limb weakness, dysphagia, and lower-limb paraplegia
2	10 Days after fever and pharyngitis	Facial diplegia and generalized areflexia evolving to lower-limb paresthesia with ataxia (day 2)	Day 3: protein level, 123 mg/dl; no cells; negative PCR assay for SARS-CoV-2	Not tested	Head: enhancement of facial nerve bilaterally Spine: normal	Received IVIG; had improvements, including decrease in ataxia and mild decrease in facial weakness
3	10 Days after fever and cough	Flaccid tetraparesis and facial weakness evolving to areflexia (day 2) and respiratory failure (day 5)	Day 3: protein level, 193 mg/dl; no cells; negative PCR assay for SARS-CoV-2	Negative	Head: normal Spine: enhancement of caudal nerve roots	Received 2 cycles of IVIG; had poor outcomes, including ICU admission owing to neuromuscular respiratory failure and flaccid tetraplegia
4	5 Days after cough and hyposmia	Flaccid areflexic tetraparesis and ataxia (day 4)	Day 5: normal protein level; no cells; negative PCR assay for SARS-CoV-2	Not tested	Head: normal Spine: normal	Received IVIG; had mild improvement but unable to stand 1 mo after onset
5	7 Days after cough, ageusia, and anosmia	Facial weakness, flaccid areflexic paraplegia (days 2–3), and respiratory failure (day 4)	Day 3: protein level, 40 mg/dl; white-cell count, 3 per mm^3; CSF:serum albumin ratio, 1.2%; negative PCR assay for SARS-CoV-2	Negative	Head: not performed Spine: normal	Received IVIG and plasma exchange; had bacterial pneumonia during IVIG treatment, which delayed plasma exchange

* Covid-19 denotes coronavirus disease 2019, CSF cerebrospinal fluid, ICU intensive care unit, IVIG intravenous immune globulin, MRI magnetic resonance imaging, PCR polymerase chain reaction, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.

† On CSF analysis, all the patients had a normal glucose level and IgG index and a polyclonal pattern on electrophoresis. The normal range for the protein level is 15 to 45 mg per deciliter.

‡ An enzyme-linked immunosorbent assay was used to test for antibodies to GM1, GQ1b, and GD1b.

Research

JAMA Neurology | Original Investigation

Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China

Ling Mao; Huijuan Jin; Mengdie Wang; Yu Hu; Shengcai Chen; Quanwei He; Jiang Chang; Candong Hong; Yifan Zhou; David Wang; Xiaoping Miao; Yanan Li, MD, PhD; Bo Hu, MD, PhD

- Patients **severe infection** (n=88/214; 41.1%) (as per the international guidelines for community-acquired pneumonia were older and more often had other underlying disorders but had **less typical symptoms such as fever** (40 [45.5%] vs 92 [73%], P<0.001) **and dry cough** (30 [34.1%] vs 77 [61.1%], P<0.001).

- **Neurological symptoms** were significantly **more common in severe cases** as compared with non-severe cases (40 [45.5%] vs. 38 [30.2%], P<0.05).

- **Neurological symptoms** included **stroke** in **5.7%** (n=5; 4 ischemic; 1 hemorrhagic), impaired consciousness in14.8% and muscle injury in 19.3% of the 88 patients with **severe disease**.

- Patients with CNS symptoms had lower lymphocyte and platelet counts and higher blood urea nitrogen levels.

- There is a neuroinvasive potential of SARS-CoV2. Notably, infection of SARS-CoV has been reported in the brains from both patients and experimental animals, where the brainstem was heavily infected (J Med Virol. 2020 Feb 27. doi: 10.1002/jmv.25728. [Epub ahead of print]

Clinical neurological findings in COVID-19

- Chinese autopsy reports of endovasculitis, endothelial damage, cerebral edema, hyperemia, and neurodegeneration in SARS-CoV-2

  Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Version 7). *March 3, 2020.*

- Other neurological complications of critical illness, such as critical illness myopathy, increased thrombotic risk, and cerebral hypoperfusion, may result from the extended intensive care stays.

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CORRESPONDENCE

COVID-19 CASES

To rapidly communicate information on the global clinical effort against Covid-19, the Journal has initiated a series of case reports that offer important teaching points or novel findings. The case reports should be viewed as observations rather than as recommendations for evaluation or treatment. In the interest of timeliness, these reports are evaluated by in-house editors, with peer review reserved for key points as needed.

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

Table 1. Clinical Characteristics of Five Young Patients Presenting with Large-Vessel Stroke.*

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†	None	None	Hyperlipidemia, hypertension	Undiagnosed diabetes	Mild stroke, diabetes
Medications	None	None	None	None	Aspirin (81 mg), atorvastatin (80 mg)
NIHSS score‡					
On admission	19	13	16	23	13
At 24 hr	17	11	4	19	11
At last follow-up	13 (on day 14)	5 (on day 10)	NA; intubated and sedated, with multiorgan failure	19 (on day 12)	7 (on day 4)
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	Cough, headache, chills	No symptoms; recently exposed to family member with PCR-positive Covid-19	None	Lethargy	Fever, cough, lethargy
White-cell count — per mm^3	7800	9900	5500	9000	4900
Platelet count — per mm^3	427,000	299,000	135,000	372,000	255,000
Prothrombin time — sec	13.3	13.4	14.4	12.8	15.2
Activated partial-thromboplastin time — sec	25.0	42.7	27.7	26.9	37.0
Fibrinogen — mg/dl	501	370	739	443	531
D-dimer — ng/ml	460	52	2230	13,800	1750
Ferritin — ng/ml	7	136	1564	987	596

* Reference ranges are as follows: platelet count, 150,000 to 450,000 per cubic millimeter; prothrombin time, 12.3 to 14.9 seconds; activated partial-thromboplastin time, 25.4 to 34.9 seconds; fibrinogen, 175 to 450 mg per deciliter; D-dimer, 0 to 500 ng per milliliter; and ferritin, 30 to 400 ng per milliliter. CT denotes computed tomography, CTA CT angiography, CTP CT perfusion, MRI magnetic resonance imaging, NA not applicable, PCR polymerase chain reaction, and t-PA tissue plasminogen activator.

† The patients were screened for smoking, hypertension, hyperlipidemia, diabetes, atrial fibrillation, congestive heart failure, illicit drug use, and neck trauma.

‡ Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher numbers indicating more severe stroke.

Stroke in COVID-19

Table 1. Baseline characteristics of COVID-19 patients with new onset of CVD during infection

	Type of CVD	Subtype of AIS	Age, y	Sex	Smoking History	Drinking History	Blood pressure (mm Hg)	Fasting Blood-glucose (mmol/L)	Type of COVID-19 Patients (Severe/Non-Severe)	Onset Time of SARS-CoV-2 Infection	Onset Time of CVD	Treatment of CVD	Outcome Event
1	AIS	Small vessel	70	M	No	No	110/70	5·44	Severe	01/26/20	02/23/20	Antiplatelet	Survival
2	AIS	Large vessel stenosis	75	F	No	No	110/67	6·03	Severe	01/24/20	02/15/20	Antiplatelet	Survival
3	AIS	Cardioembolic	89	F	No	No	97/64	6·77	Non-severe	02/19/20	02/19/20	Anticoagulant	Survival
4	AIS	Large vessel stenosis	91	F	No	No	192/97	6·7	Severe	02/01/20	02/10/20	Anticoagulant	Survival
5	AIS	Large vessel stenosis	72	F	No	No	155/89	7·93	Severe	02/01/20	02/12/20	Anticoagulant	Survival
6	AIS	Cardioembolic	71	M	Yes	No	142/67	16·25	Severe	01/31/20	02/07/20	Anticoagulant	Death
7	AIS	Cardioembolic	86	M	Yes	No	110/72	13·81	Severe	01/24/20	02/11/20	Antiplatelet	Death
8	AIS	Large vessel stenosis	82	F	No	No	140/83	24·2	Severe	02/02/20	02/16/20	Antiplatelet	Death
9	AIS	Small vessel	78	M	Yes	No	156/82	11·0	Severe	01/17/20	01/17/20	Antiplatelet	Death
10	AIS	Large vessel stenosis	57	M	No	No	127/83	13·24	Non-severe	02/06/20	02/07/20	Antiplatelet	Survival
11	AIS	Small vessel	66	F	No	No	98/62	8·67	Severe	02/11/20	02/17/20	Anticoagulant	Survival
12	CVST		32	M	Yes	Yes	130/80	8·23	Severe	02/09/20	02/23/20	Anticoagulant	Survival
13	CH		62	M	Yes	Yes	150/80	5·81	Severe	01/23/20	02/01/20		Death

* The patients of COVID-19 were confirmed by SARS-CoV-2 RT-PCR positive in throat swab and viral-like pneumonia in chest CT.

Abbreviations: COVID-19, Coronavirus disease 2019; CVD, Cerebrovascular disease; AIS, Acute ischemia stroke; CH, Cerebral hemorrhage; CVST, Cerebral Venous Sinus Thrombosis; F, Female; M, Male

Li Y, et.al. Lancet. Mar 13 2020.

BMJ Journals

Journal of
Neurology, Neurosurgery
& Psychiatry

Characteristics of ischaemic stroke associated with COVID-19

Rahma Beyrouti[1], Matthew E Adams[2], Laura Benjamin[3, 4], Hannah Cohen[5], Simon F Farmer[6], Yee Yen Goh[6], Fiona Humphries[1], Hans Rolf Jäger[2, 7], Nicholas A Losseff[1, 8], Richard J Perry[1, 4], Sachit Shah[2], Robert J Simister[1, 4], David Turner[1], Arvind Chandratheva[1, 4], David J Werring[1, 4]

Six consecutive AIS pts b/w 04/6-16/20 at the Queen Square, London, UK

COVID-19 confirmed by RT-PCR; Age 53-85 years; 5/6 males

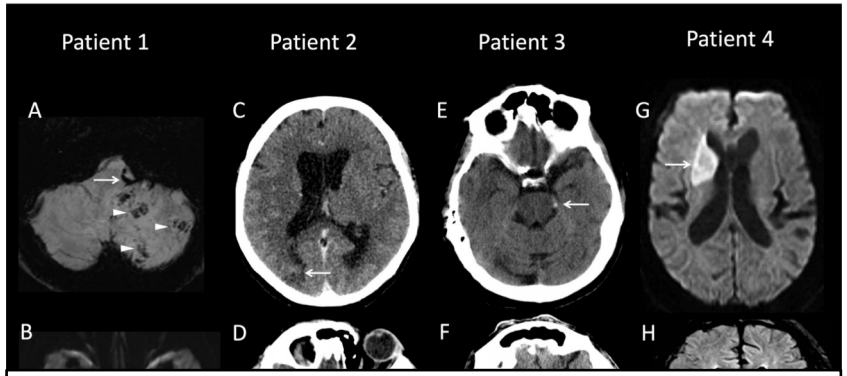
Time COVID Sx to Stroke Sx: 8-24 days but preceded by 2 days in 1 case

All six pts had LVO with D-dimer levels ≥1000 (range, 1,080->80,000)
All six pts had elevated ferritin and LDH levels
Lupus anticoagulant positive in 5/6 pts but Anticardiolipin and Anti-β2-glycoprotein-1 negative in 5/6

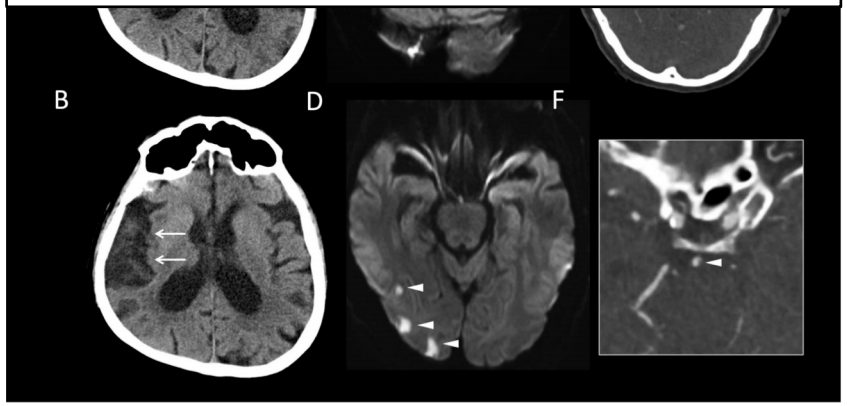
Three pts had multi-territory infarcts

Two had concurrent venous thrombosis

In two ischemic strokes occurred despite therapeutic anticoagulation



Our data cannot confirm a causal relationship
between SARS-CoV-2 and ischaemic stroke, since competing vascular risk factors and mechanisms were present in most patients; four of six had hypertension, and two had AF.



Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy

Corrado Lodigiani[a,b,*], Giacomo Iapichino[c], Luca Carenzo[c], Maurizio Cecconi[b,c], Paola Ferrazzi[a], Tim Sebastian[d], Nils Kucher[d], Jan-Dirk Studt[e], Clara Sacco[a], Bertuzzi Alexia[f], Maria Teresa Sandri[g], Stefano Barco[d,h], on behalf of the Humanitas COVID-19 Task Force

388 patients (median age 66 years, 68% men, 16% ICU) consecutive symptomatic pts with laboratory-proven COVID-19 admitted to a university hospital in Milan, Italy

Table 3
Venous and arterial thromboembolic events in hospitalized COVID-19 patients.

	Intensive care unit			General ward			Total		
Thromboembolic events	n	% of closed cases (n = 48)	% of imaging tests performed*	n	% of closed cases (n = 314)	% of imaging tests performed*	n	% of closed cases (n = 362)	% of imaging tests performed
At least one thromboembolic event	8	16.7% (95%CI 8.7%–29.6%)	–	20	6.4% (95%CI 4.2%–9.6%)	–	28	7.7% (95%CI 5.4%–11.0%)	–
VTE	4	8.3%	22%	12	3.8%	46%	16	4.4%	36%
PE (± 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 DVT	1	2.1%	50%	0	–	–	1	0.3%	50%
Ischemic stroke	3	6.3%	–	6	1.9%	–	9	2.5%	–
ACS/MI	1	2.1%	–	3	1.0%	–	4	1.1%	–

ACS, acute coronary syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; pDVT, proximal deep vein thrombosis; dDVT, distal DVT; PE, pulmonary embolism; VTE, venous thromboembolism.

Overall: 9/362 (2.5%)

ICU: 3/48 (6.3%)

Thrombosis Research 191 (2020) 9–14

Incidence of thrombotic complications in critically ill ICU patients with COVID-19

F.A. Klok[a,*], M.J.H.A. Kruip[b], N.J.M. van der Meer[c], M.S. Arbous[d], D.A.M.P.J. Gommers[e], K.M. Kant[f], F.H.J. Kaptein[a], J. van Paassen[d], M.A.M. Stals[a], M.V. Huisman[a,1], H. Endeman[e,1]

184 consecutive ICU patients (mean age 64 years, 76% men, median duration 7 days [IQR 1-13]) with laboratory-proven COVID-19 pneumonia in 3 Dutch Hospitals.

Table 3
Description of thrombotic complications.

Type of event	Number of cases	Relevant details
Pulmonary embolism	25	– 18 cases with at least PE in segmental arteries, 7 cases PE limited to subsegmental arteries
Other venous thromboembolic events	3	– 1 proximal deep-vein thrombosis of the leg – 2 catheter related upper extremity thrombosis
Arterial thrombotic events	3	– All ischemic strokes

Note: acute pulmonary embolism was diagnosed with CT-pulmonary angiography, deep vein thrombosis/upper extremity vein thrombosis was diagnosed with ultrasonography, strokes were diagnosed with CT.

ICU: 3/184 (1.6%)

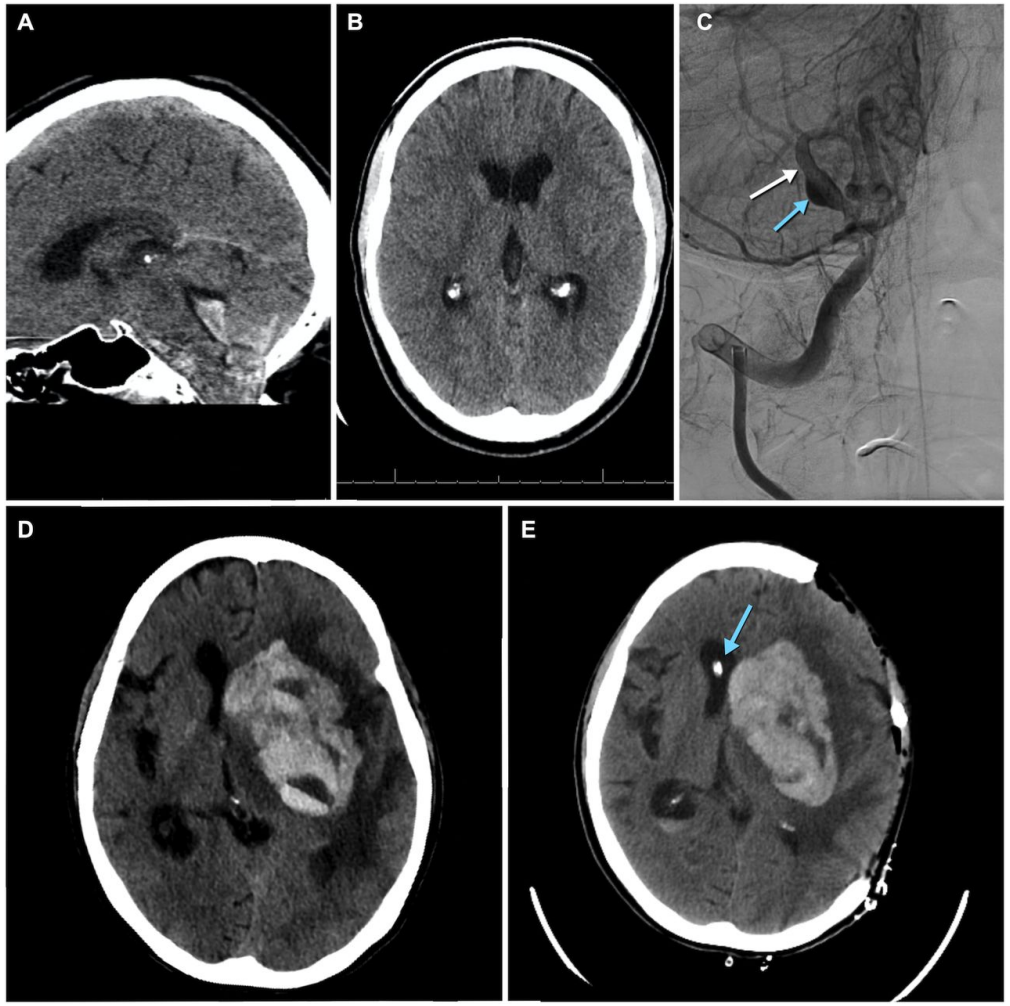
Thrombosis Research

BMJ Journals

Journal of
Neurology, Neurosurgery
& Psychiatry

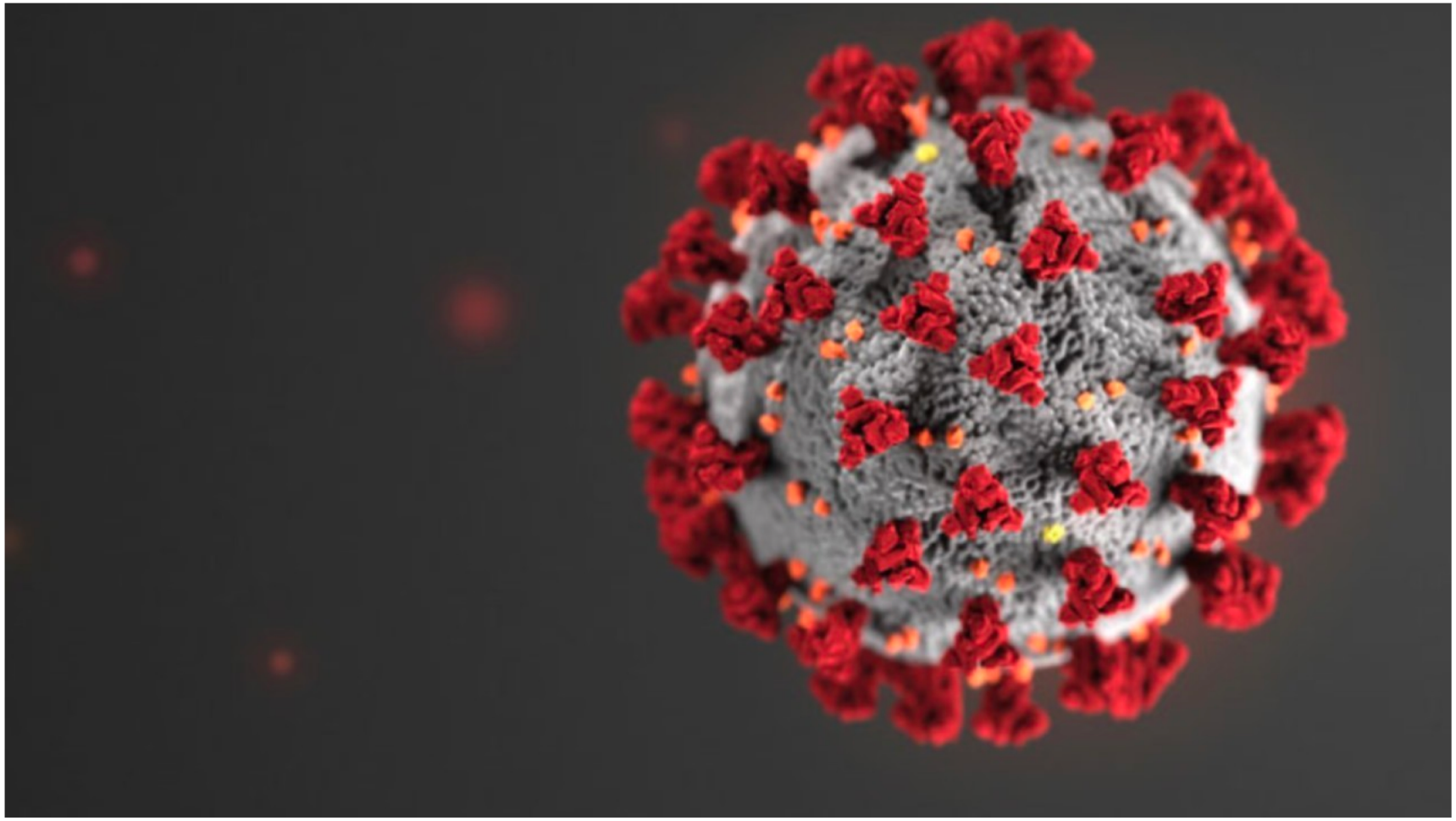
Status of SARS-CoV-2 in cerebrospinal fluid of patients with COVID-19 and stroke

Fadi Al Saiegh[1], Ritam Ghosh[1], Adam Leibold[1], Michael B Avery[1], Richard F Schmidt[1], Thana Theofanis[1], Nikolaos Mouchtouris[1], Lucas Philipp[1], Stephen C Peiper[2], Zi-Xuan Wang[3], Fred Rincon[1], Stavropoula I Tjoumakaris[1], Pascal Jabbour[1], Robert H Rosenwasser[1], M. Reid Gooch[1]



- 31 y/o man flu-like sx: later SAH from a ruptured PICA aneurysm
- 62 y/o woman no COVID sx: AIS due to LMCA occlusion s/p MT with massive hemorrhagic conversion requiring a decompressive hemicraniectomy 10 days later
- Both patients' **CSF repeatedly negative** on real-time PCR analysis despite concurrent neurological disease
- ? Underlying inflammatory and hypercoagulable state may incite cerebrovascular disease without disruption of the blood–brain barrier

COVID-19: Stroke as a Disease Modifier



Review

International Journal of Stroke
0(0) 1–5

DOI: 10.1177/1747493020921664
journals.sagepub.com/home/wso
SAGE

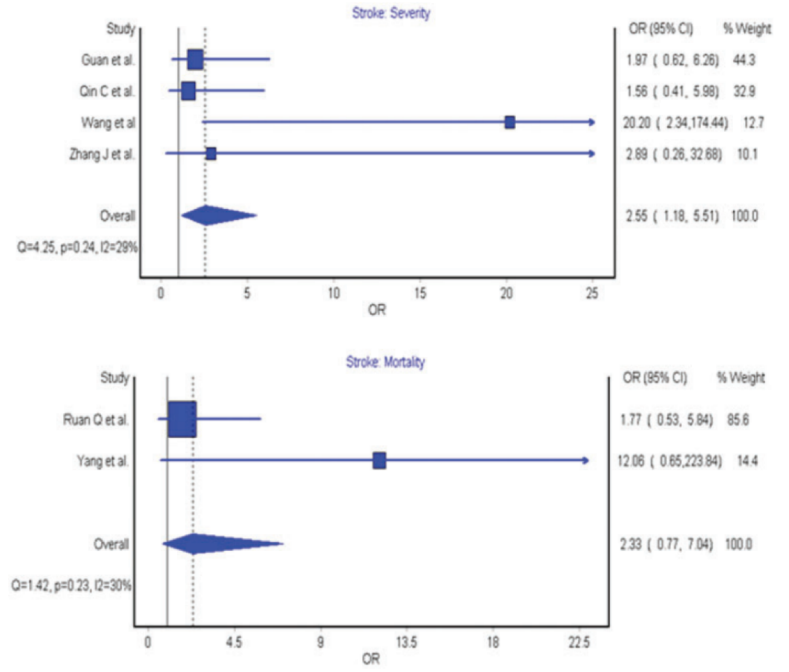
Cerebrovascular disease is associated with an increased disease severity in patients with Coronavirus Disease 2019 (COVID-19): A pooled analysis of published literature

Gaurav Aggarwal[1], Giuseppe Lippi[2,*] and Brandon Michael Henry[3,*]

Study	Sample size	Outcomes	Severe patients/non-survivors				Non-severe patients/survivors			
			n (%)	Age (yrs)[a]	Women (%)	Cerebrovascular disease n (%)	n (%)	Age (yrs)[a]	Women (%)	Cerebrovascular disease n (%)
Guan et al.[5]	1099	Admission to ICU, MV, Death	173 (15.7%)	52 (40–65)	42%	4 (2.3%)	926 (84.3%)	45 (34–57)	42%	11 (1.2%)
Qin et al.[6]	452	Respiratory distress/ insufficiency	286 (63.3%)	61 (51–69)	45.8%	8 (2.8%)	166 (36.7%)	53 (41.25–62)	51.8%	3 (1.8%)
Ruan et al.[7]	150	Death	68 (45.3%)	67 (15–81)	28%	7 (10%)	82 (54.6%)	50 (44–81)	35%	5 (6%)
Wang et al.[8]	138	Clinical variables, MV, death	36 (26.1%)	66 (57–78)	39%	6 (16.7%)	102 (73.9%)	51 (37–62)	48%	1 (1%)
Yang et al.[9]	52	Death	32 (61.5%)	64.6 (11.2)	34%	7 (22%)	20 (38.5%)	51.9 (12.9)	30%	0 (0%)
Zhang et al.[10]	140	Respiratory distress/ insufficiency	58 (41.4%)	64 (25–87)	43%	2 (3.4%)	82 (58.6%)	52 (26–78)	54%	1 (1.2%)

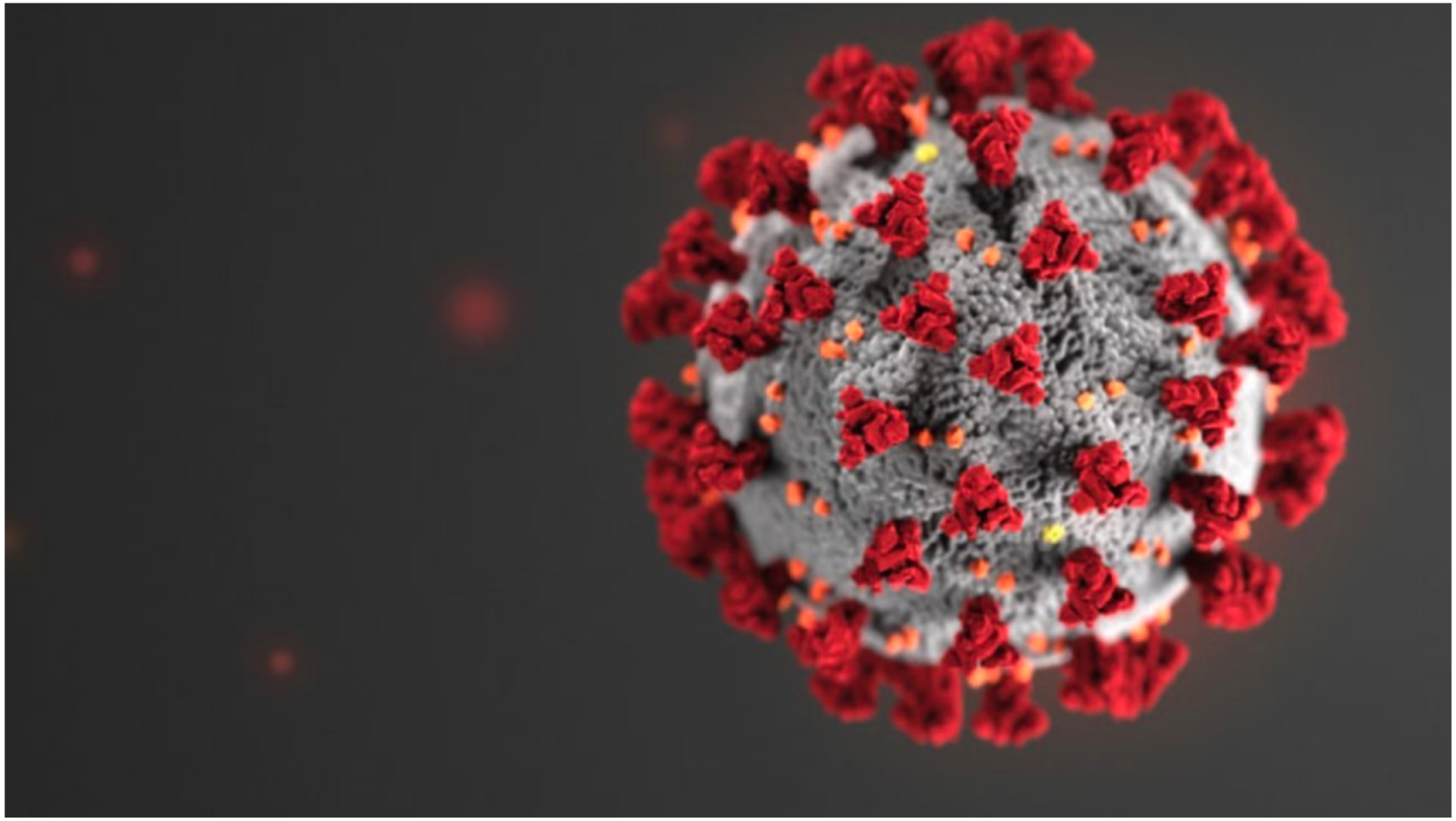
[a]Age data presented as median (IQR) or mean (SD). MV: mechanical ventilation; ICU: intensive care unit; NR: not reported.

Figure 1. Results of meta-analysis showing association of cerebrovascular disease with severity of disease and mortality in patients with COVID-1.

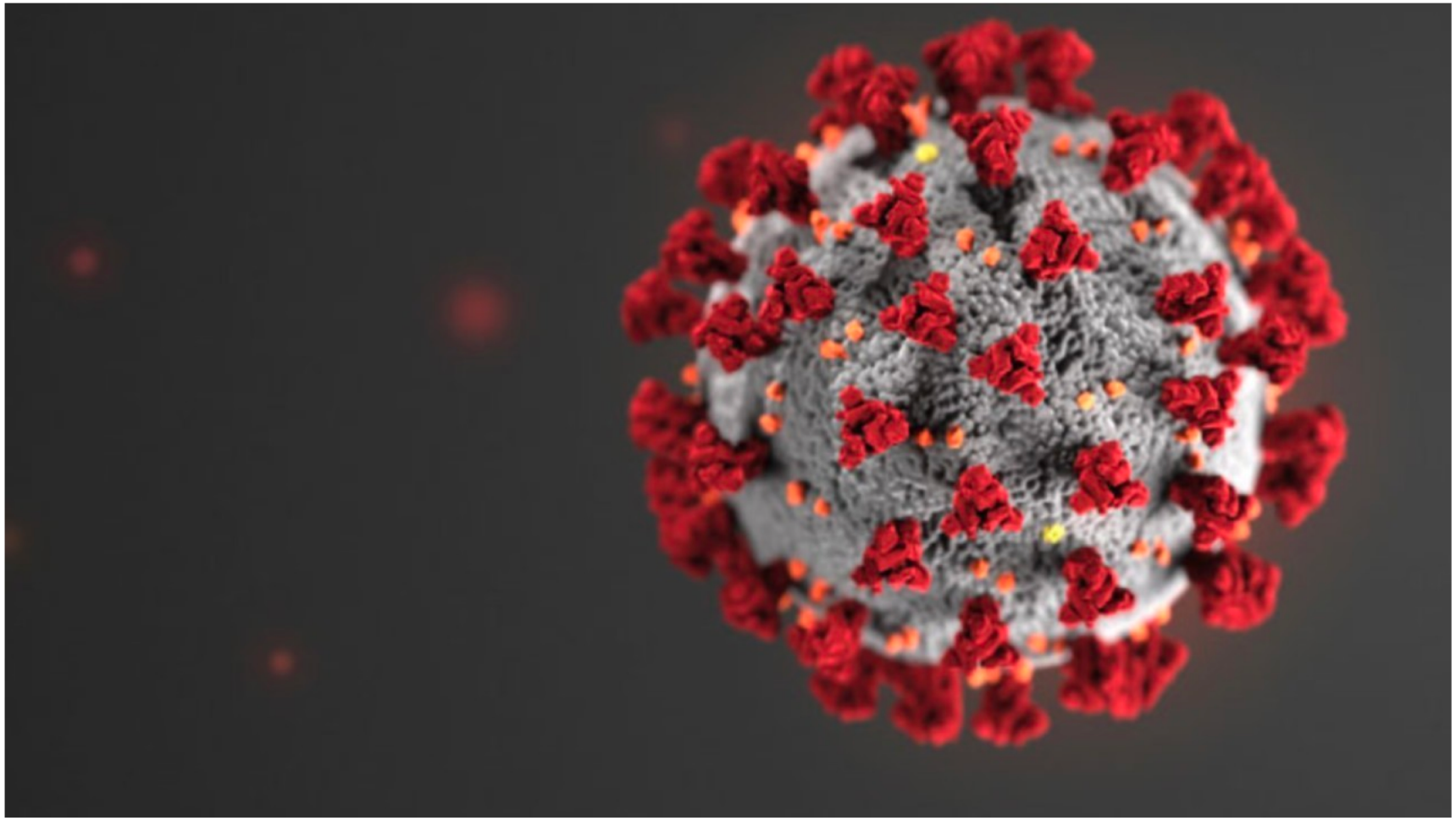


Conclusion: There is a ~2.5-fold increase in odds of severe COVID-19 illness with a history of cerebrovascular disease.

A More Definite Problem: The COVID-19 Collateral Damage on the Non-COVID-19 Stroke Care…



COVID-19 in Stroke Care: USA



MARCH 17, 2020

Artificial intelligence recruited to find clues about COVID-19

by Gopal Ratnam

Credit: CC0 Public Domain

COVID-19 in Stroke Care: USA

Viz.ai
ANALYTICS

Methodology

Data downloaded from Viz Analytics™, a dynamic, live clinical intelligence software package, were analyzed from suspected stroke patients from 38 US hospitals. Number of patients, scans, age, and LVO alerts were analyzed over a period of 25 weeks, between November 4, 2019 - April 26, 2020. CT Perfusion core was measured by rCBF < 30%.

The weekly mean number of CTAs, LVOs and core volume, and median age, were plotted versus time, relative to the incidence of COVID cases. The collection period was divided into pre and post Covid period, defined as before March 1st 2020, and after March 1st, 2020.

P values were calculated to compare means of pre and post Covid period, with significance demonstrated at <0.05.

COVID-19 in Stroke Care: USA

Viz.ai
ANALYTICS

Summary Statistics

Study period: November 4th, 2019 - April 26, 2020

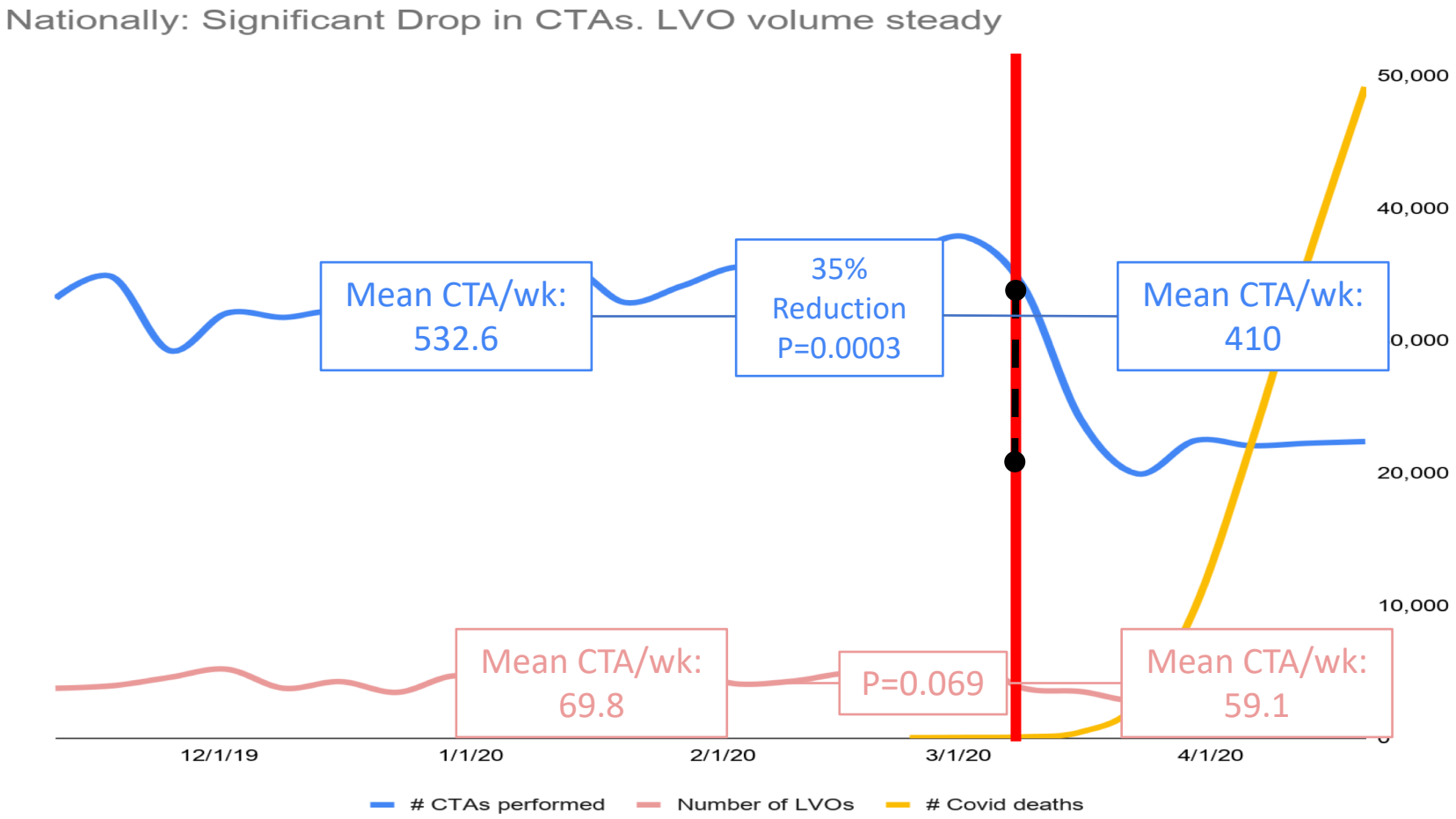
Total Number of Patients: 75,079

Total number CTAs in study: 11,801
Total Number of CTPs in study: 3,616
Total Number and % of LVOs: 1,594, 13%

Median Age for the Total Population: 63 +/- 18
Median Age for the LVO Population: 67 +/- 16
Average Core Volume for the Total Population: 9 +/- 28
Average Core for the LVO Population: 22 +/- 40

National CTA v LVO

Viz.ai
ANALYTICS



National Median Age of LVO

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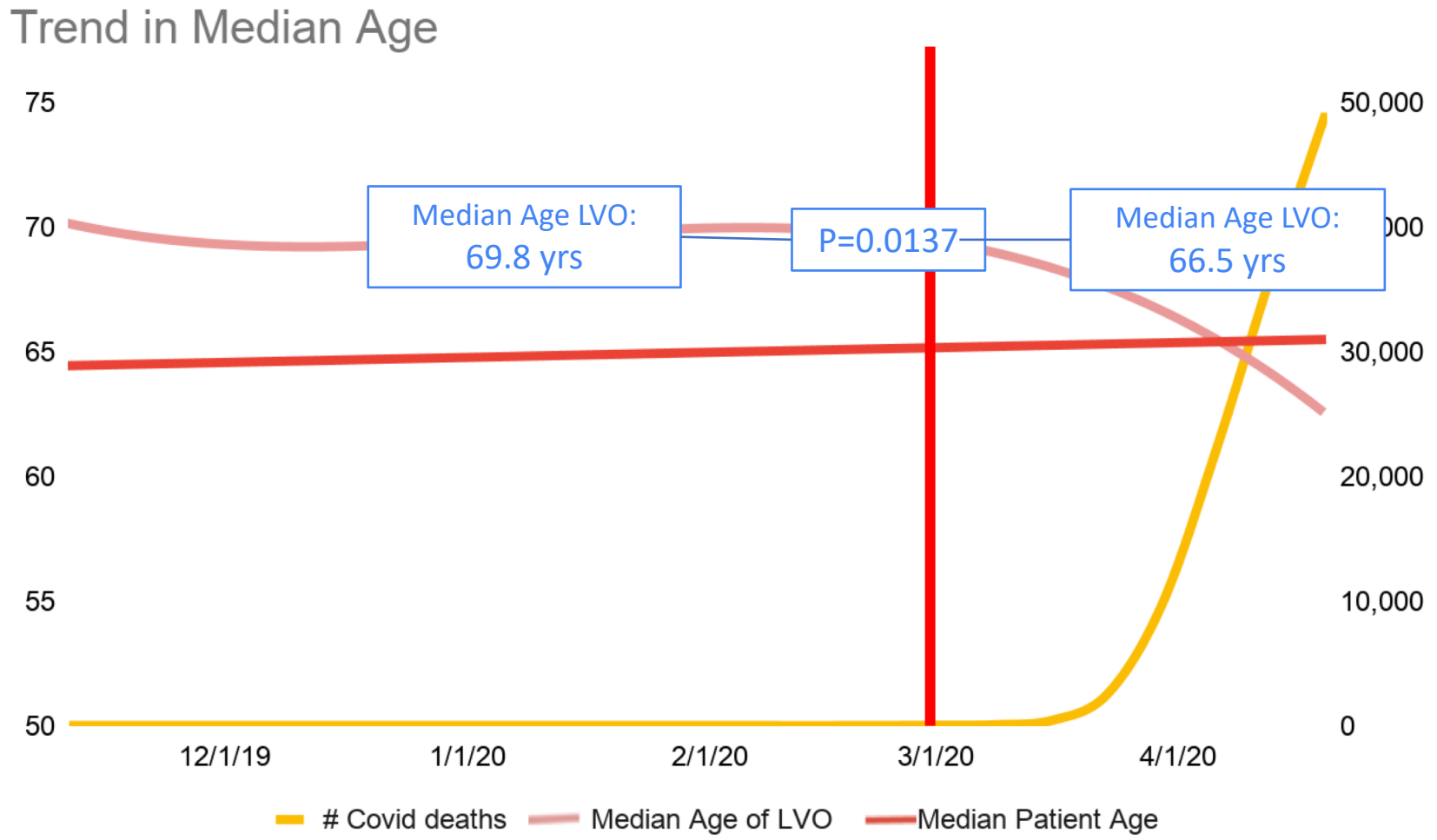
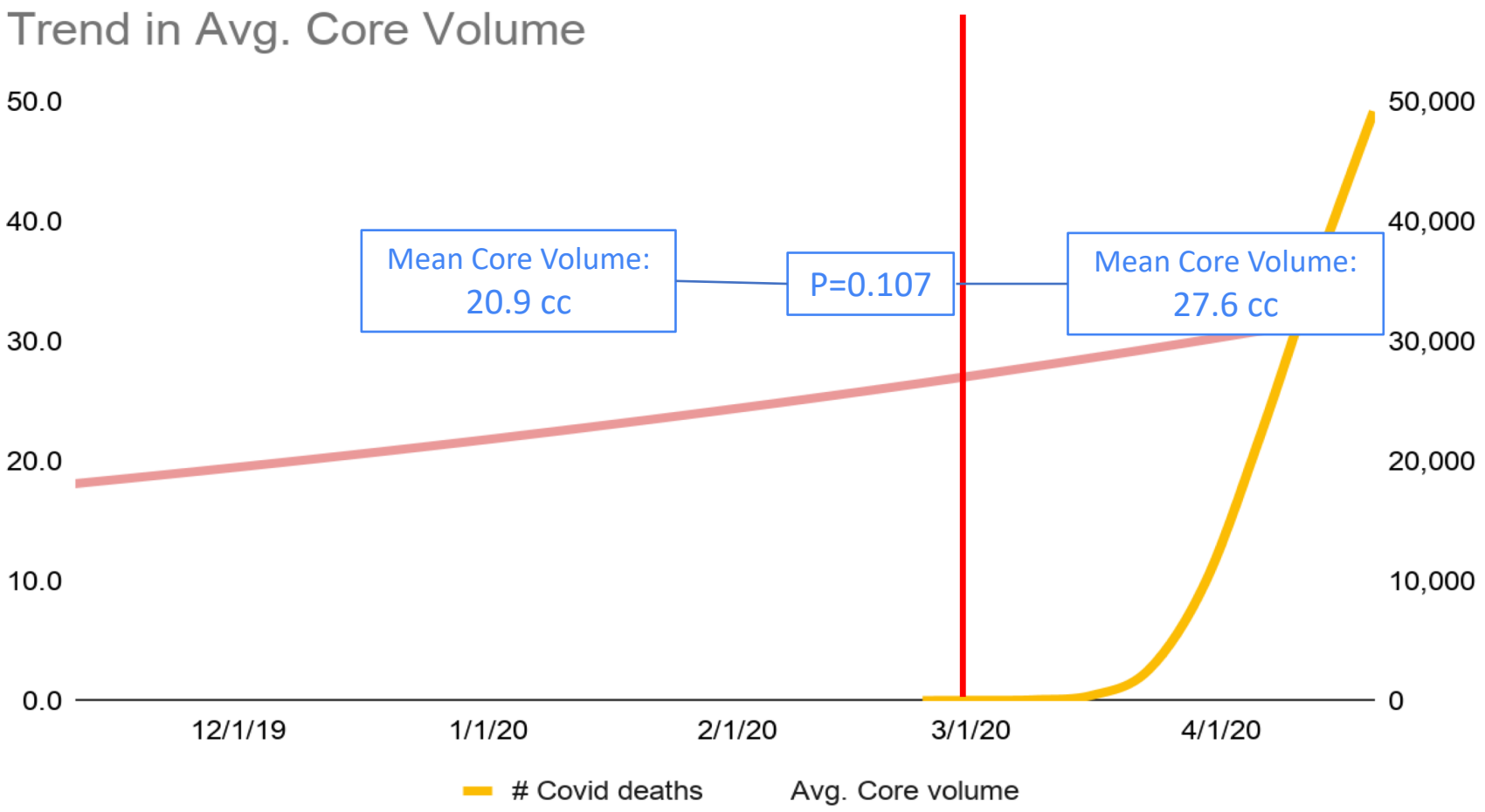
ANALYTICS

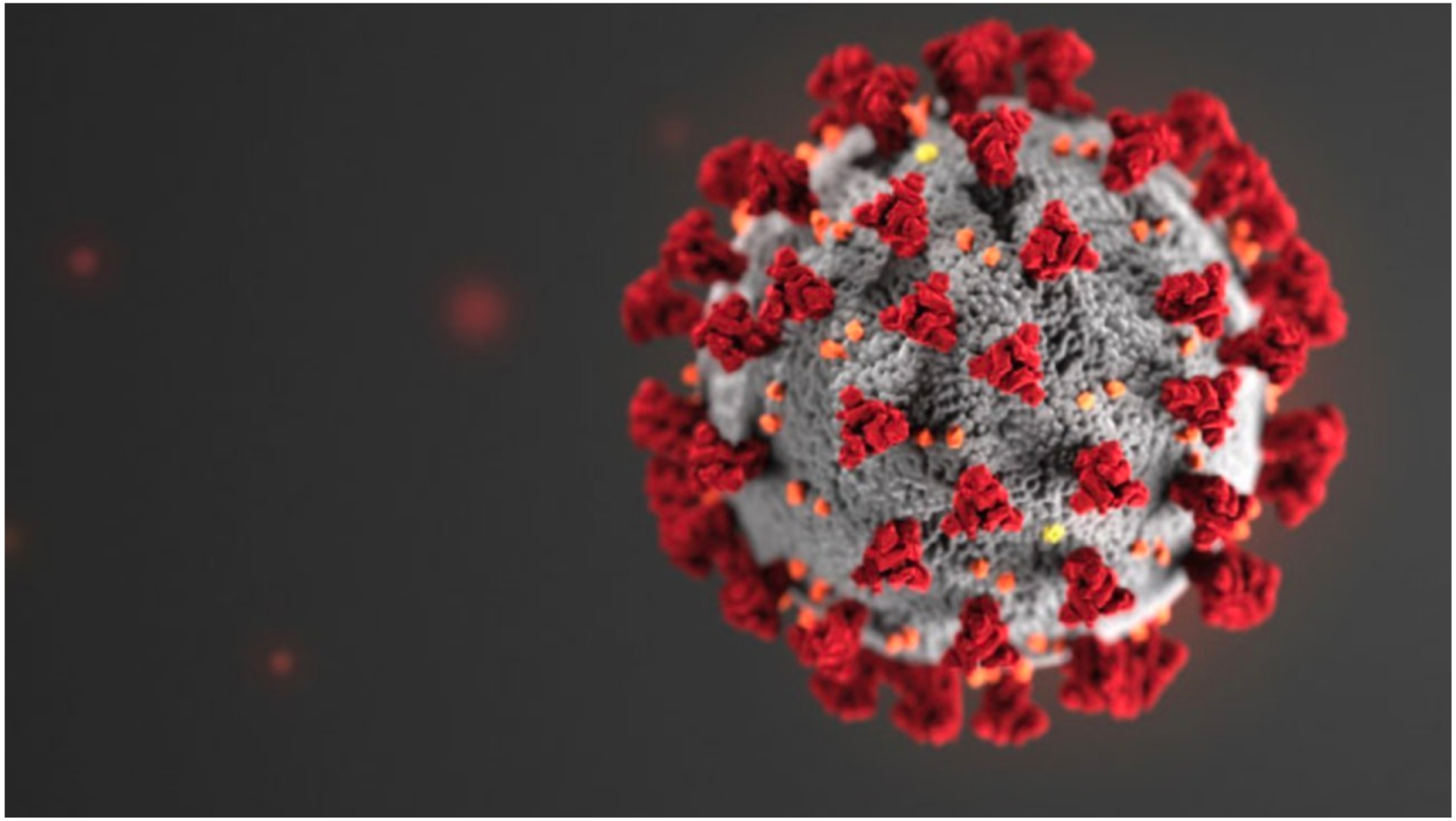


National Av Core Volume

Viz.ai
ANALYTICS



COVID-19 in Stroke Care: Italy



Neurological Sciences (2020) 41:1003–1005
https://doi.org/10.1007/s10072-020-04375-9

COVID-19

Acute stroke management pathway during Coronavirus-19 pandemic

Claudio Baracchini[1] · Alessio Pieroni[1] · Federica Viaro[1] · 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**.

- Intravenous thrombolysis: decreased by 26%
- Bridging therapy (combined IVT and MT): decreased by 30%
- Primary MT: increased by 41% - “most of these patients had very serious strokes arriving late, sometimes too late”

The Baffling Case of Ischemic Stroke Disappearance from the Casualty Department in the COVID-19 Era

Nicola Morelli[a] Eugenia Rota[b] Chiara Terracciano[a] Paolo Immovilli[a] Marco Spallazzi[a] Davide Colombi[c] Domenica Zaino[a] Emanuele Michieletti[c] Donata Guidetti[a]

[a]Neurology Unit, Guglielmo da Saliceto Hospital, Piacenza, Italy; [b]Neurology Unit, San Giacomo Hospital, Alessandria, Italy; [c]Radiology Unit, Guglielmo da Saliceto Hospital, Piacenza, Italy

Clinical Neurology: Editorial

Eur Neurol
DOI: 10.1159/000507666

Received: March 27, 2020
Accepted: March 31, 2020
Published online: April 14, 2020

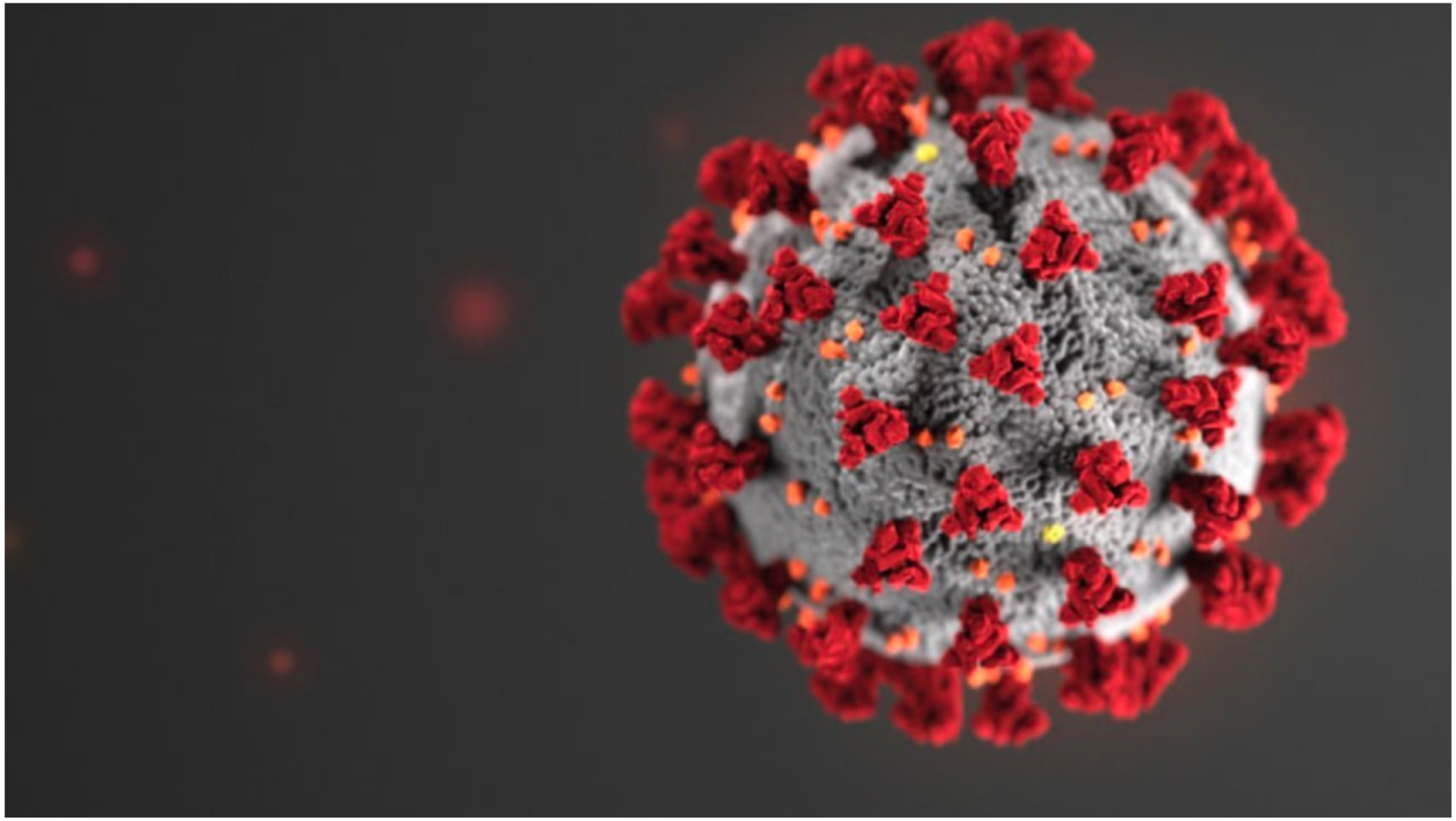
The question is: what can we say about the remaining non-COVID-19 pathologies?

Piacenza province (about 280,000 inhabitants) - one of the epicenters of the Italian epidemic, listing 2,276 cases at the time of writing.

Over the past 5 years (2015–2019): annual average of 612 new cases of ischemic stroke, with a **monthly average of 51 cases**, 21% LVOS.

Between February 21, 2020 (first SARS-CoV-2 patient recorded in Italy – in Codogno, a nearby city), and March 25, 2020, there were **only 6 admissions** from the Casualty Department for ischemic stroke (2 transient ischemic attacks, 1 cardioembolic LVO, and 3 lacunar stroke).

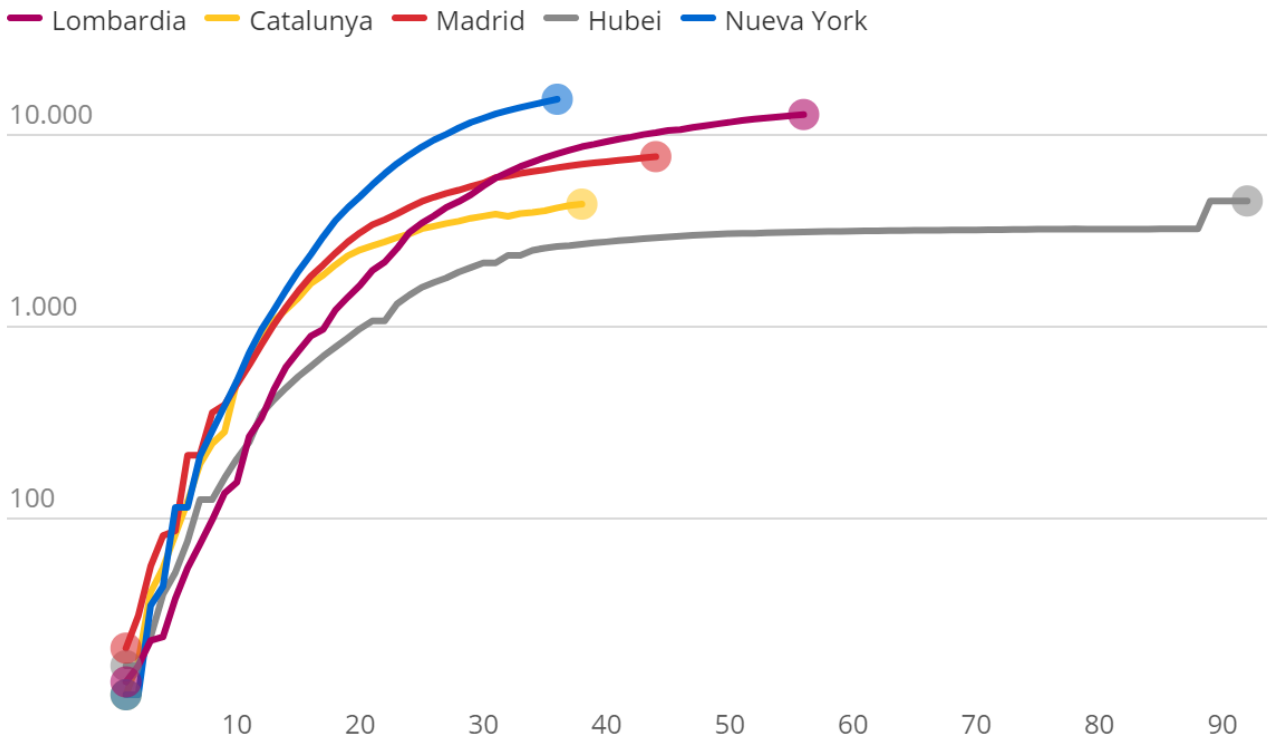
COVID-19 in Stroke Care: Barcelona



Courtesy of Marc Ribo, MD

Comparación de la letalidad del Covid-19 en las diferentes regiones más afectadas

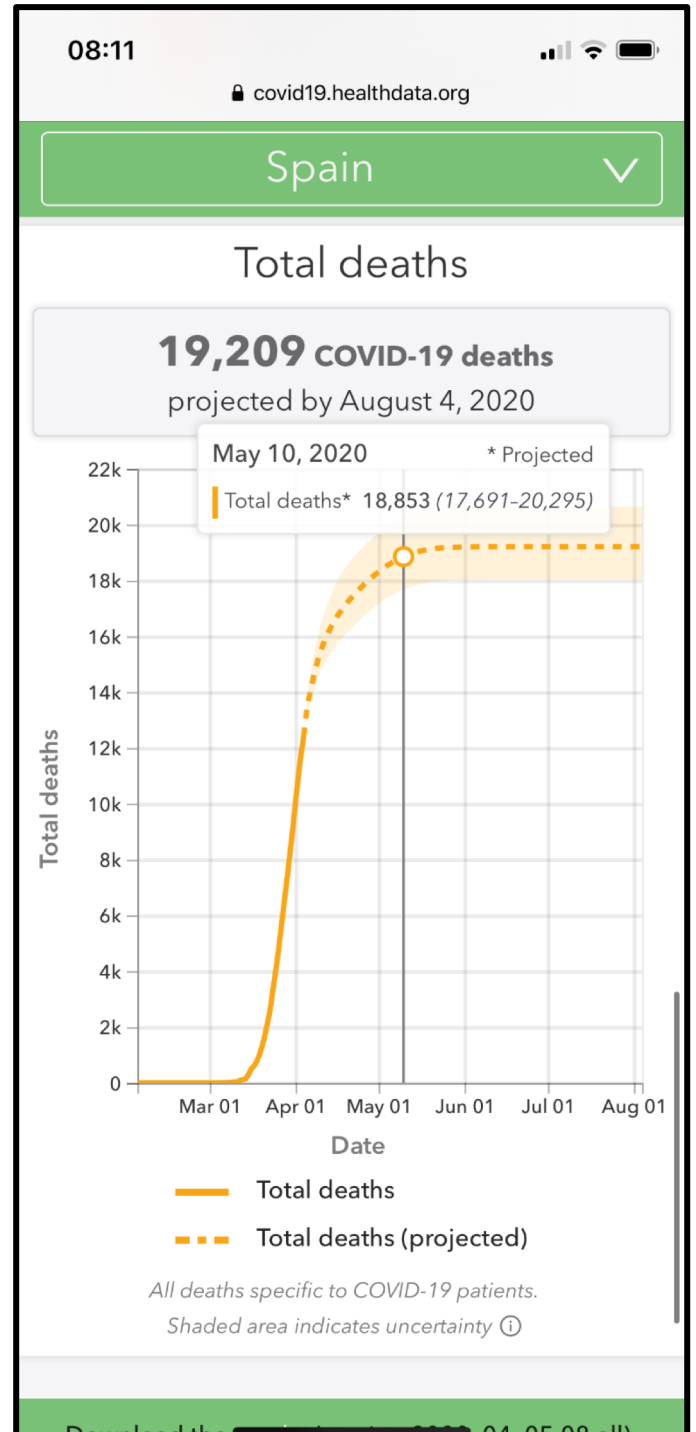
El número de fallecidos por Covid-19 desde el primer día en que se registraron 10 muertes



El salto final de la curva de Hubei se debe a un cambio en el recuento de fallecidos en China

Fuente: John Hopkins, Ministerio de Sanidad, Dipartimento della Protezione Civile

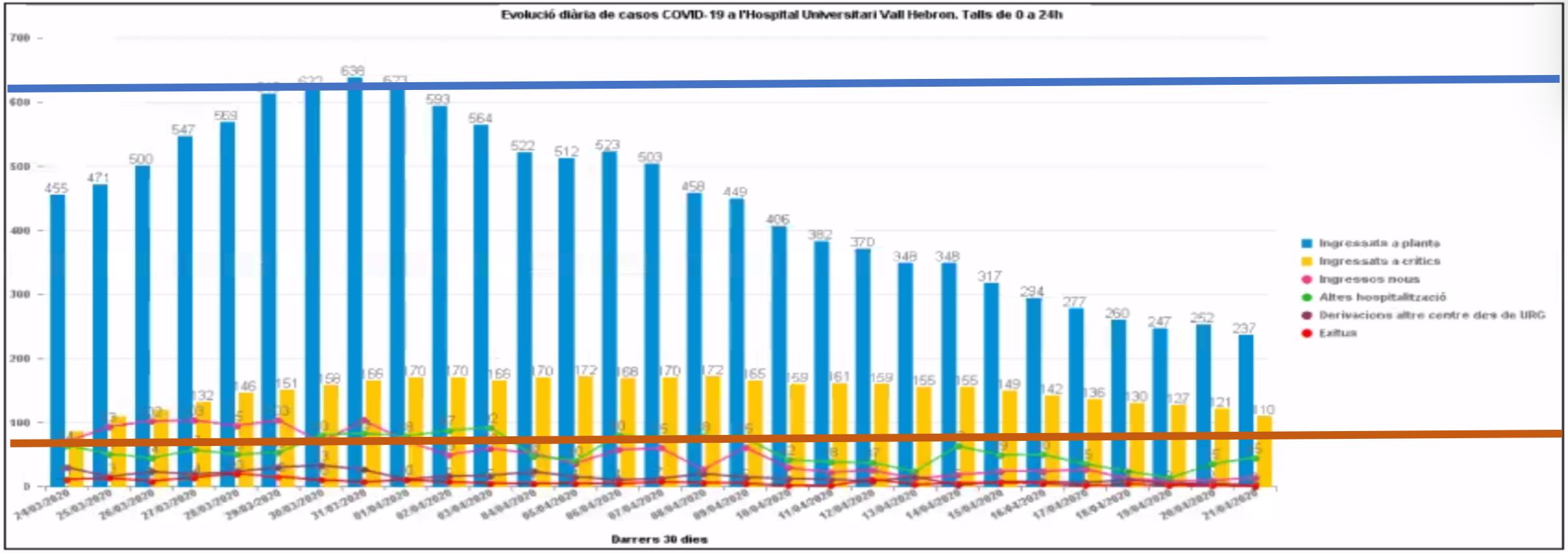
LA VANGUARDIA



Vall d'Hebron
Barcelona Campus Hospitalari

Evolució de pacients COVID-19

Direcció de Sistemes de la Informació i Suport a la Decisió
sistemes.informacio@vhebron.net



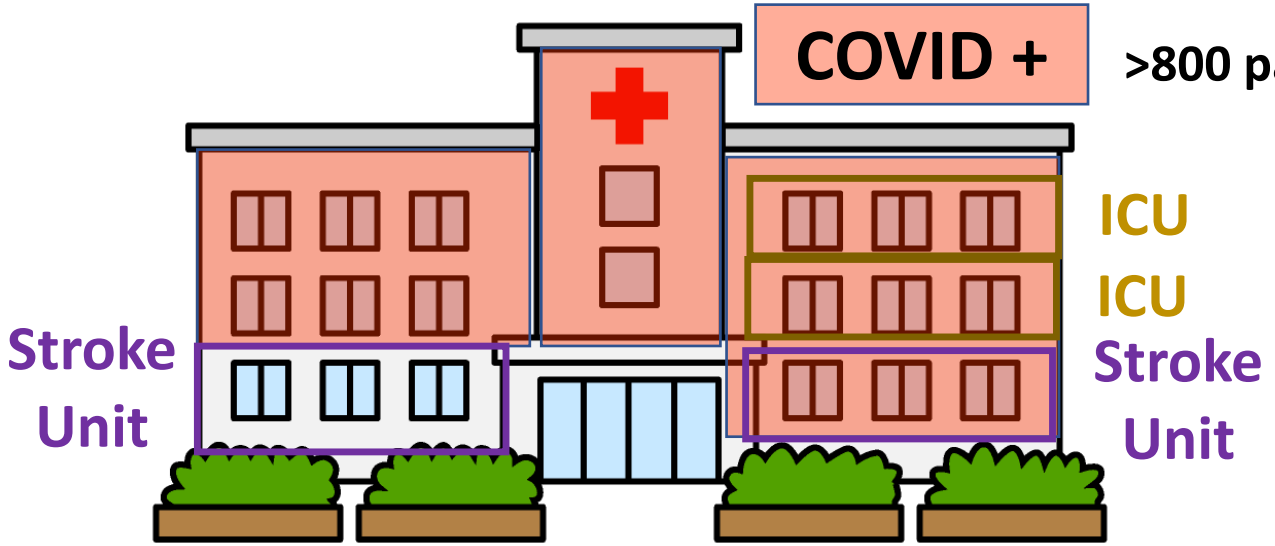
Data	24/03	25/03	26/03	27/03	28/03	29/03	30/03	31/03	01/04	02/04	03/04	04/04	05/04	06/04	07/04	08/04	09/04	10/04	11/04	12/04	13/04	14/04	15/04	16/04	17/04	18/04	19/04	20/04	21/04
Ingressats a planta	455	471	500	547	589	613	622	638	623	593	564	522	512	523	503	458	449	406	382	370	348	348	317	294	277	260	247	252	237
Ingressats a crítics	86	109	120	132	146	151	158	166	170	170	166	170	172	168	170	172	165	159	161	159	155	155	149	142	136	130	127	121	110
Ingressos nous	69	93	102	103	95	103	69	103	71	49	59	51	36	57	60	26	61	29	22	25	12	18	23	23	27	12	8	9	14
Altes hospitalització	64	51	44	57	50	53	80	83	78	87	92	48	40	80	75	78	75	42	38	37	23	63	49	50	35	24	13	35	45
Derivacions altres centres URG	30	15	23	19	23	30	33	26	11	16	17	23	15	10	12	20	14	12	11	8	15	2	7	7	6	10	5	4	3
Exitus	11	13	8	14	20	15	10	7	10	7	5	4	4	4	7	6	5	1	1	11	3	5	6	5	1	4	2	2	0

En cas que un pacient, en un mateix dia, hagi sigut traslladat entre diferents UTs (Planta / UCIs) pot comptabilitzar-se per duplicat. Talls de dia de 0 a 24h

Home

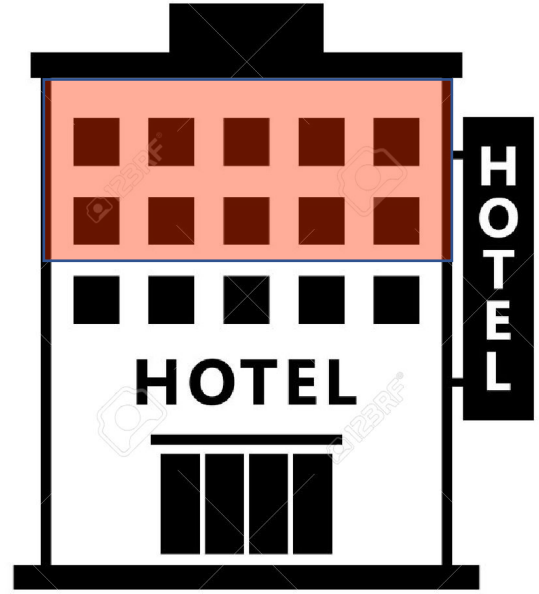
NRL
On call

INR
On call



Neurologist

Neurologist



2019 García-Tornel 2020 (submited)

March

S	M	T	W	T	F	S
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

April

S	M	T	W	T	F	S
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30				

2020

First admited case

Lockdown

March

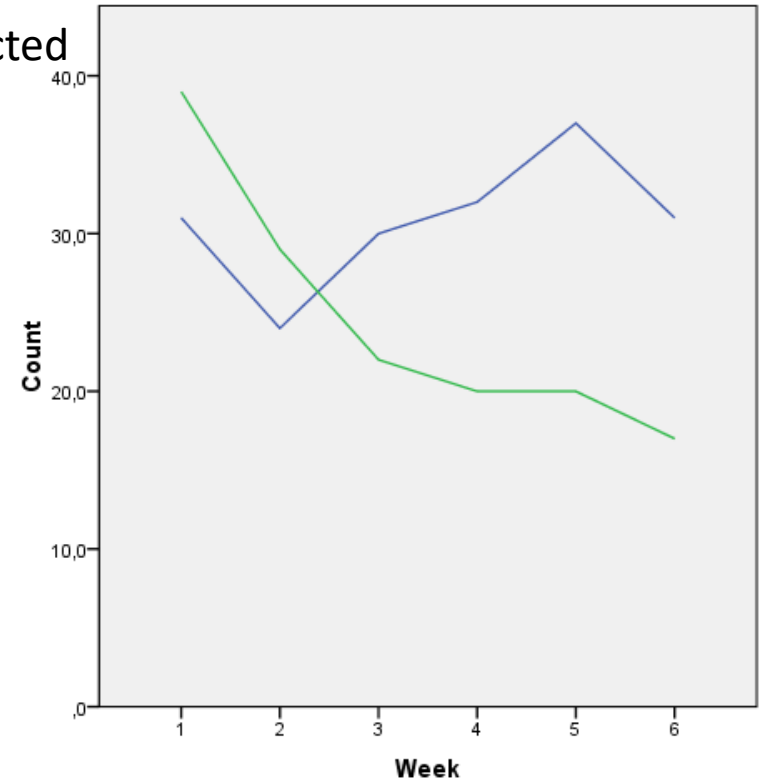
S	M	T	W	T	F	S
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

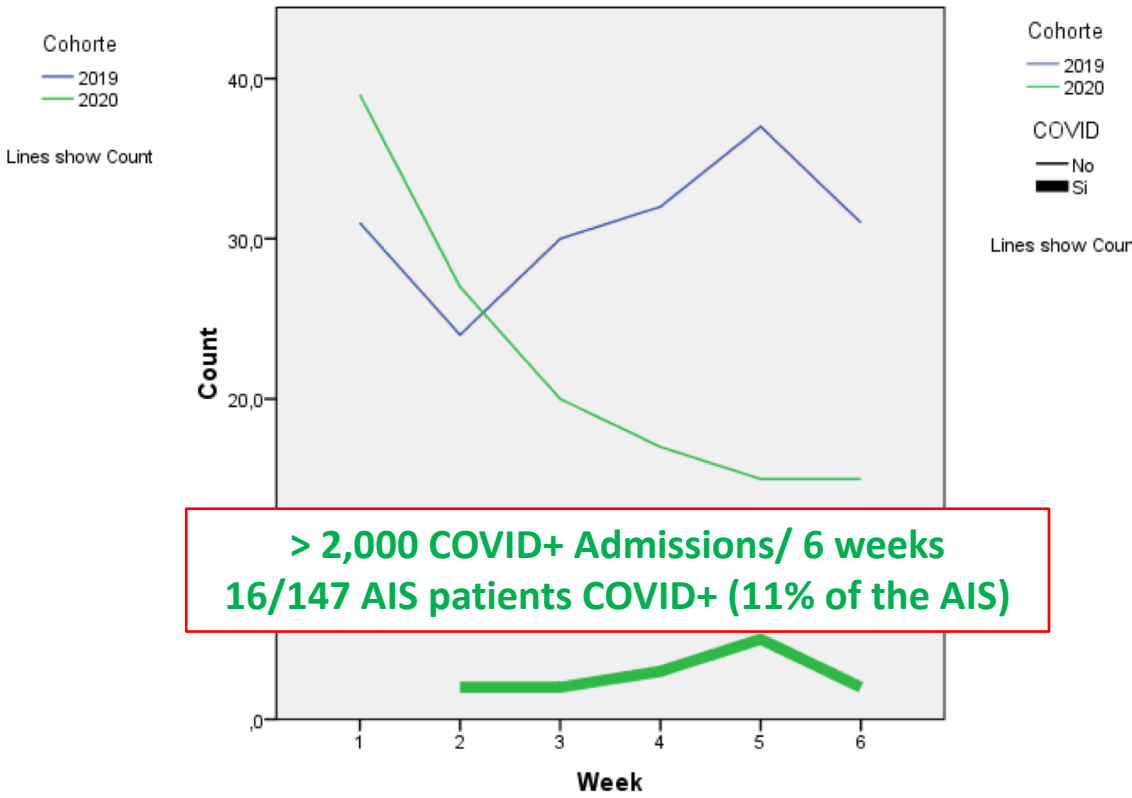
April

S	M	T	W	T	F	S
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

Patients admitted for a suspected stroke in **2020: 147 (44%)**

Vs **2019: 185 (56%)**

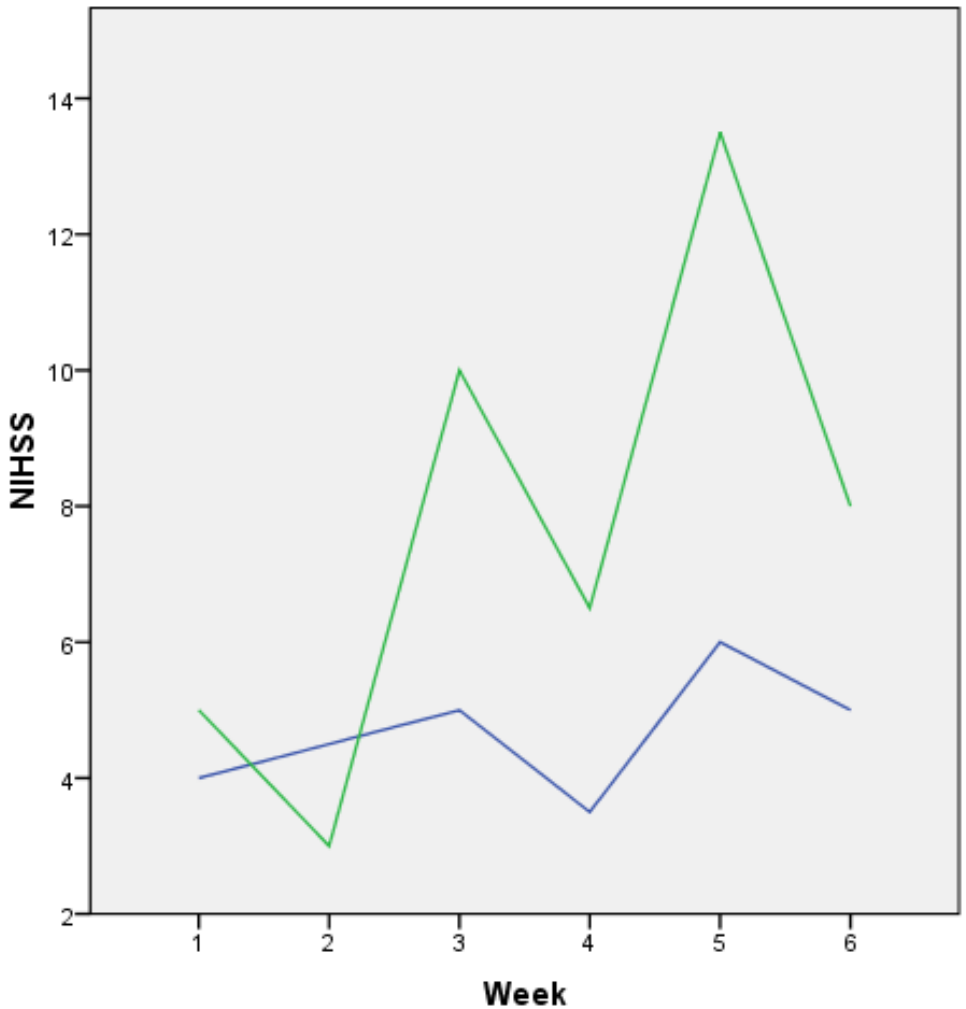


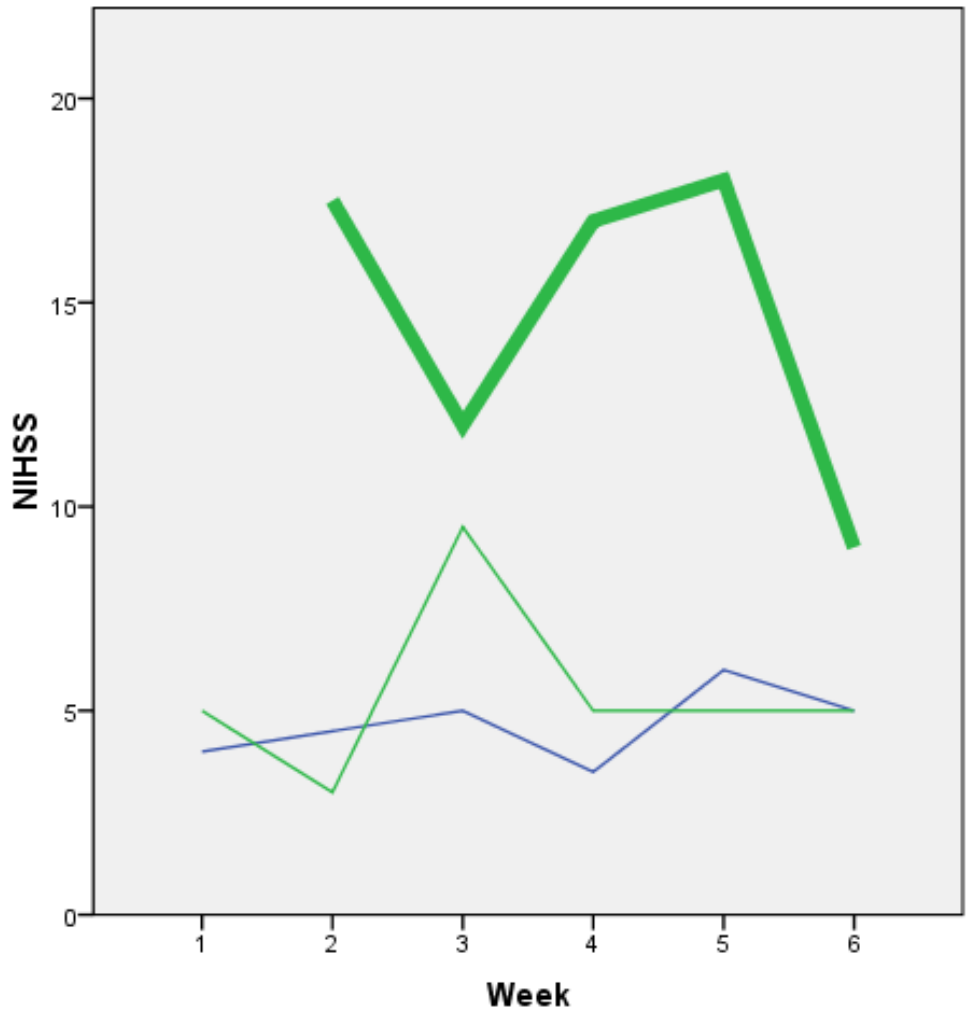


> 2,000 COVID+ Admissions/ 6 weeks

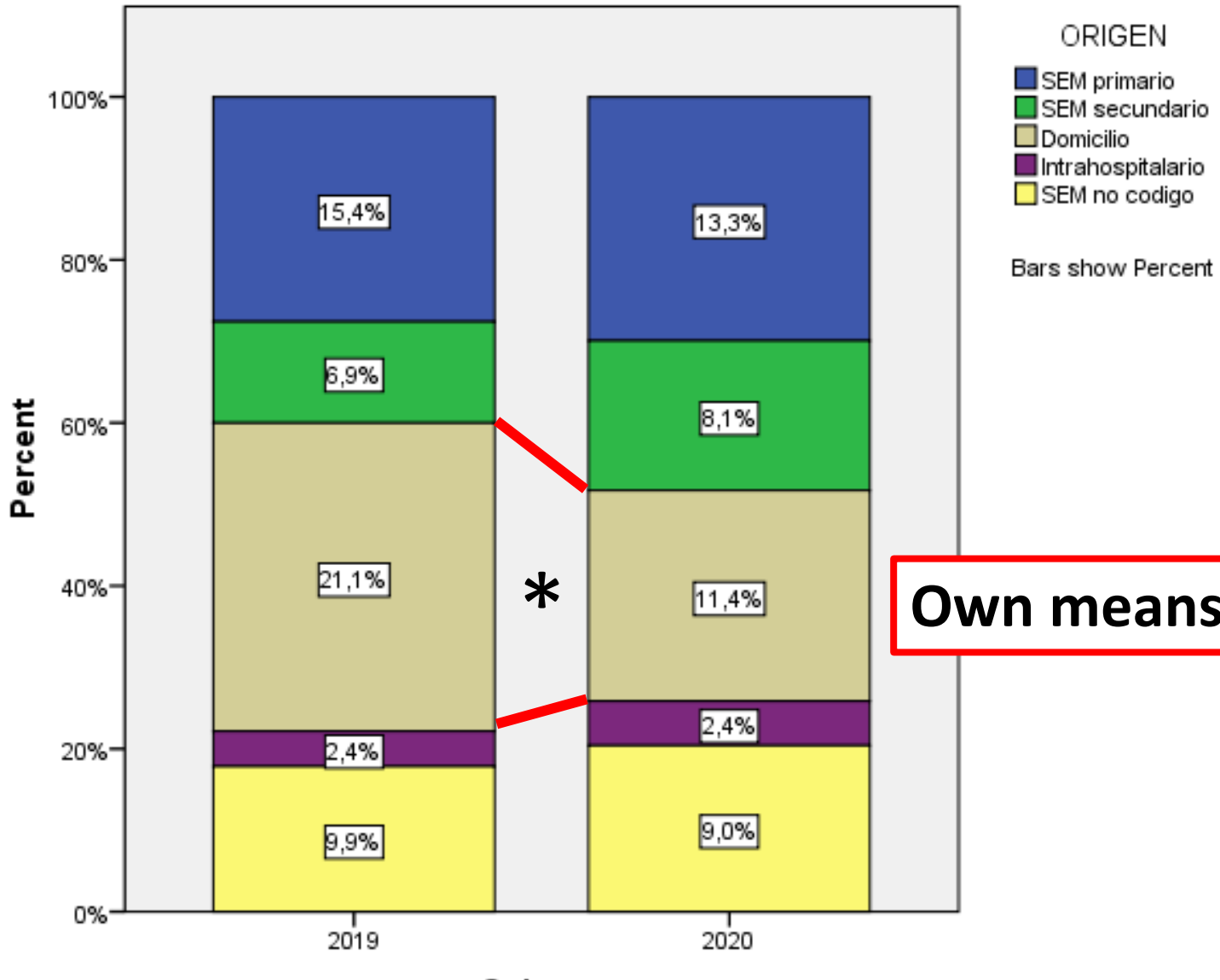
16/147 AIS patients COVID+ (11% of the AIS)

NIHSS on admission



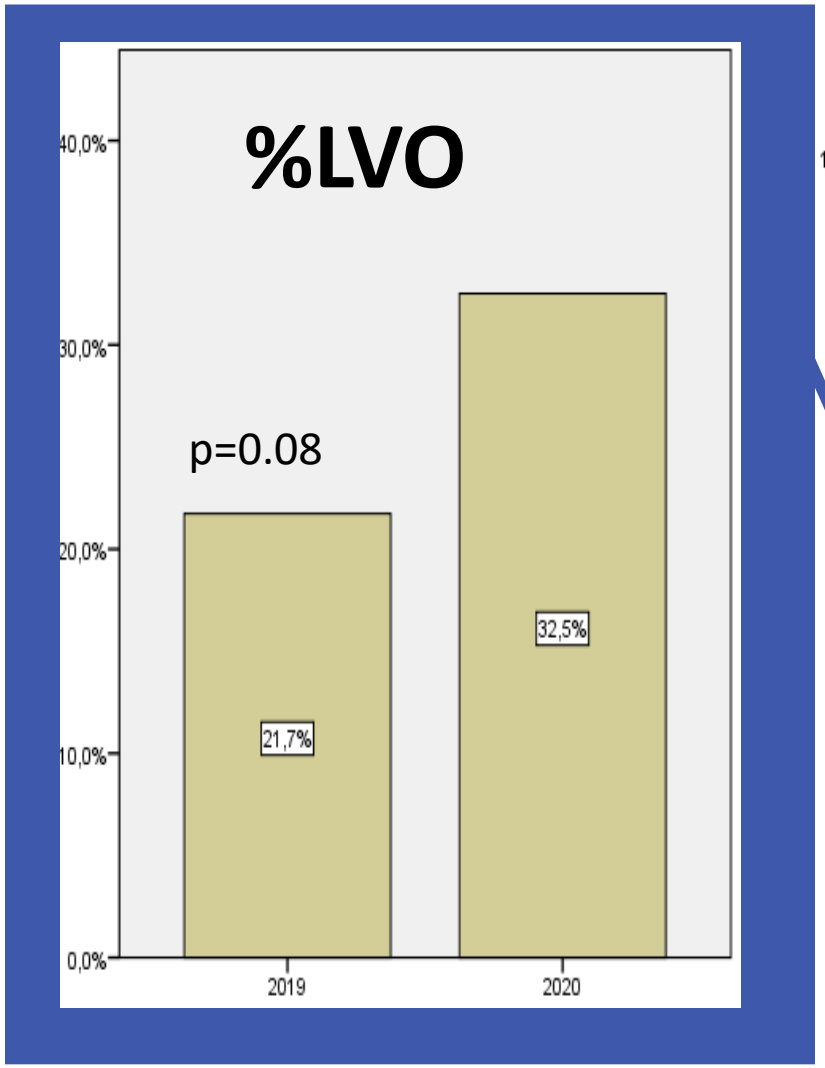


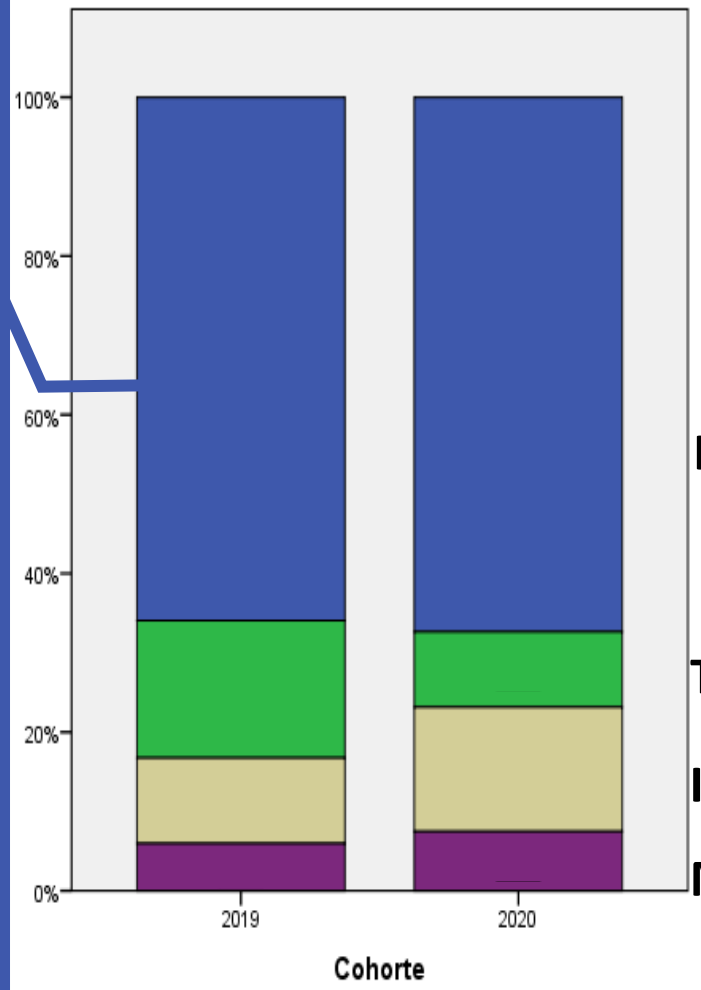
Arrival to the Hospital



Own means (p=0.025)

Stroke type



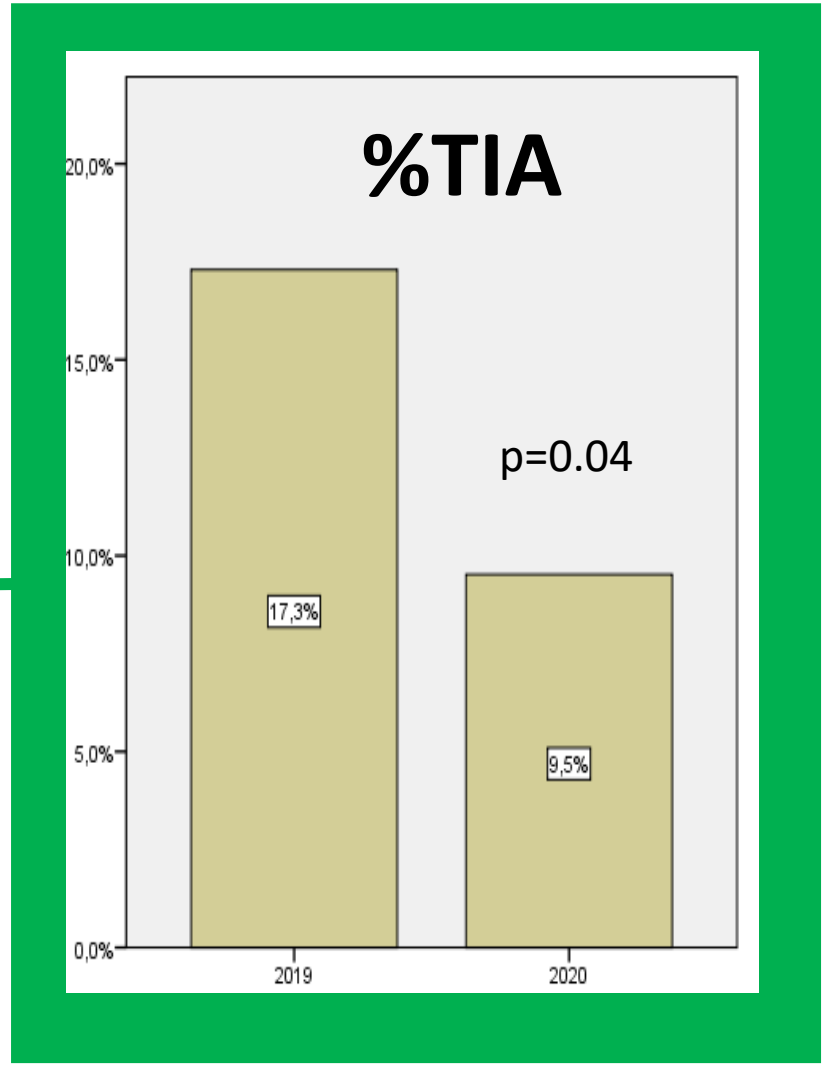


Ischemic

TIA

ICH

Mimic



03:30

Vida

EMERGENCIA SANITARIA

Los infartados están llegando tarde por miedo a ir al hospital

• Cardiólogos de diez centros catalanes piden a sus enfermos que no esperen

Ambulancias de Emergències Mèdiques en la entrada de Urgencias del hospital Vall d'Hebron (Àlex Garcia)

ANA MACPHERSON, BARCELONA

30/03/2020 01:51 | Actualizado a 30/03/2020 02:44

"¡La gente está pasando sus infartos en casa por miedo al coronavirus!", alerta **Antoni Bayés**, responsable de

14:12

◀ WhatsApp

4G

ccma.cat

Dades morts coronavirus Catalunya

alacarta

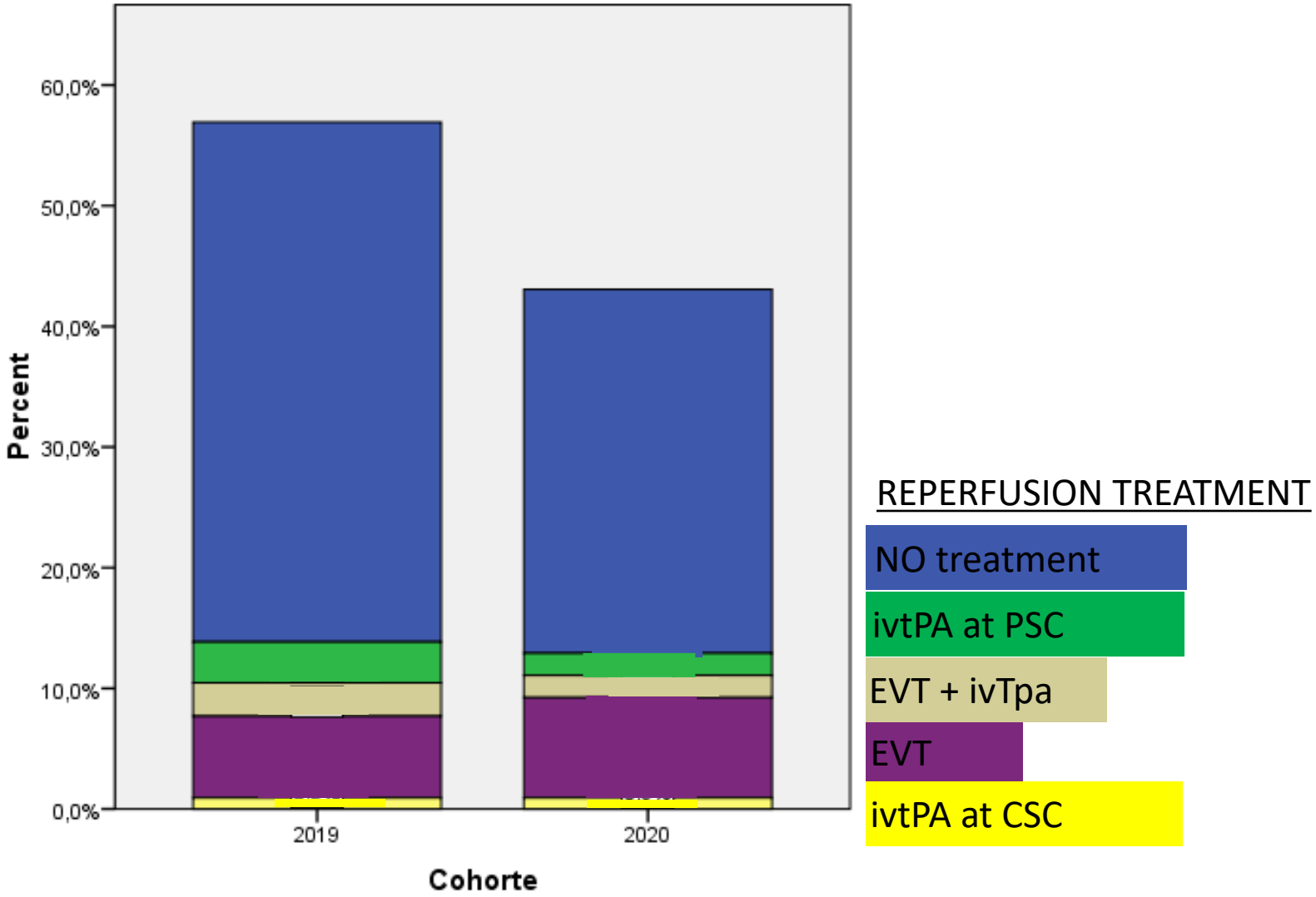
Busca vídeos

PLANTA BAIXA

Natàlia Pérez de la Ossa: "Gran part de la població amb símptomes lleus de malalties que no són el coronavirus s'està quedant a casa. Això ens preocupa"

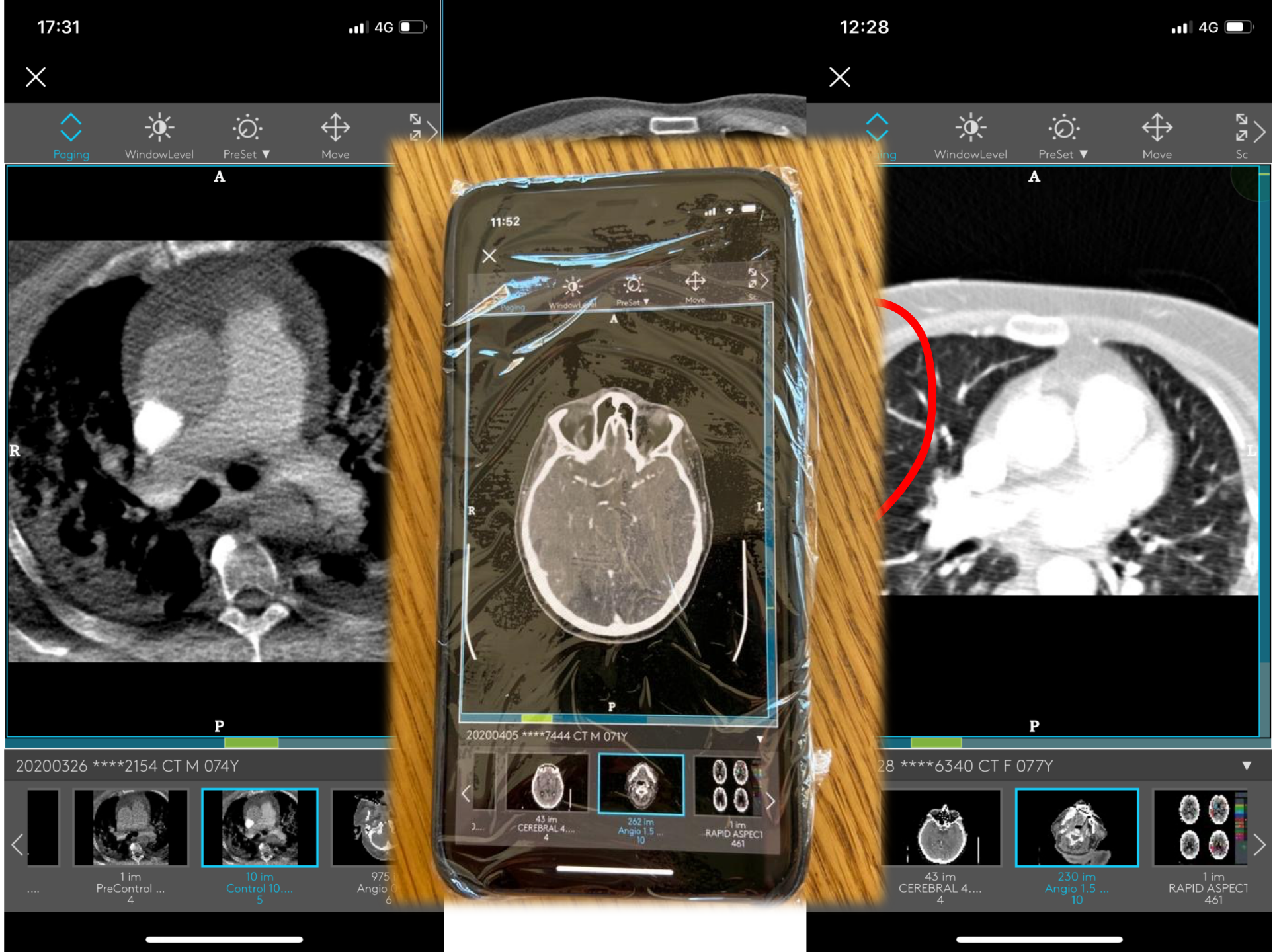
06/04/2020 | Planta baixa ha avançat que les

LOWER NUMBER OF ADMISSIONS
BUT
SIMILAR NUMBER OF REPERFUSION TREATMENTS

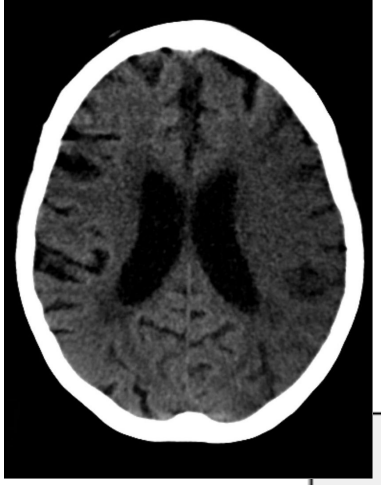


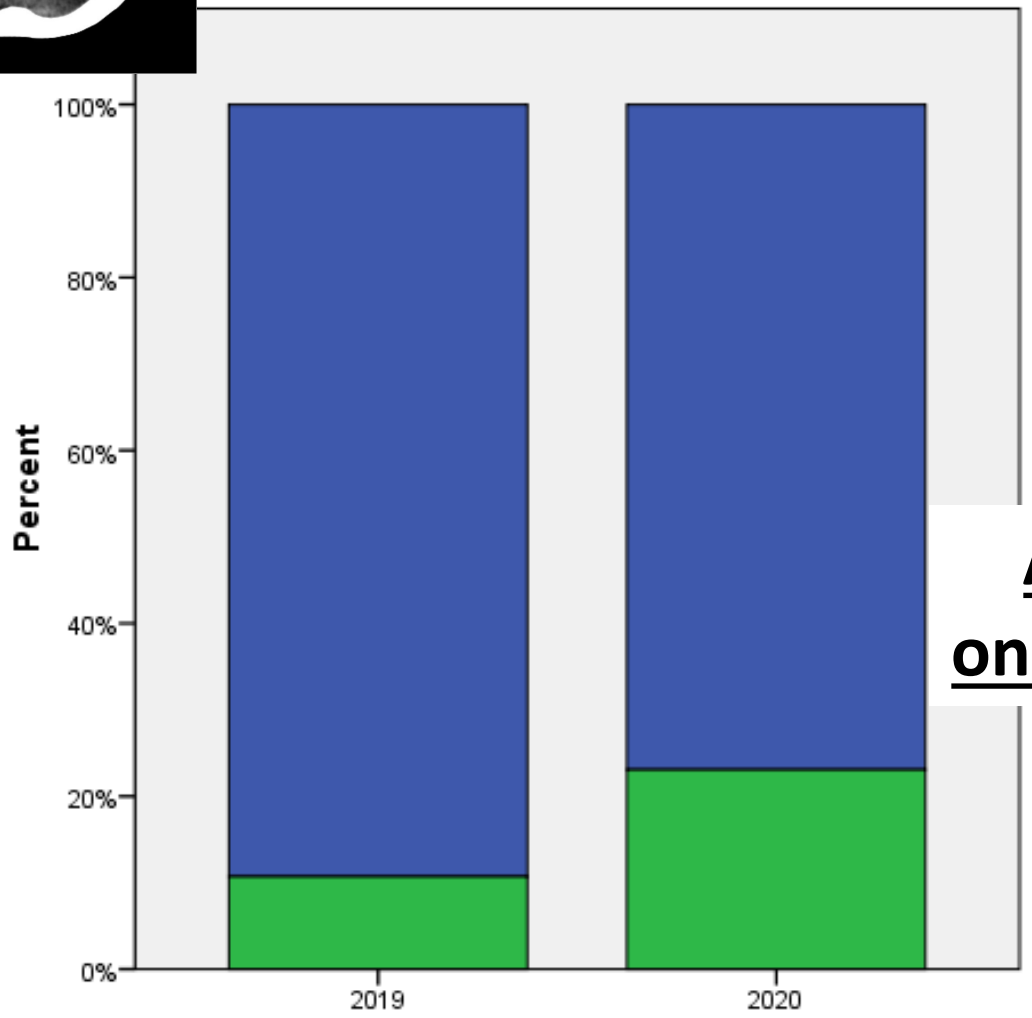
REPERFUSION TREATMENT

- NO treatment
- ivtPA at PSC
- EVT + ivTpa
- EVT
- ivtPA at CSC


17:31
4G
Paging
WindowLevel
PreSet
Move
A
R
P
20200326 ****2154 CT M 074Y
1 im
PreControl ...
4
10 im
Control 10....
5
11:52
20200405 ****7444 CT M 071Y
43 im
CEREBRAL 4....
4
262 im
Angio 1.5 ...
10
1 im
RAPID ASPECT
461
12:28
4G
WindowLevel
PreSet
Move
A
L
P
43 im
CEREBRAL 4....
4
230 im
Angio 1.5 ...
10
1 im
RAPID ASPECT
461

ASPECTS on admission

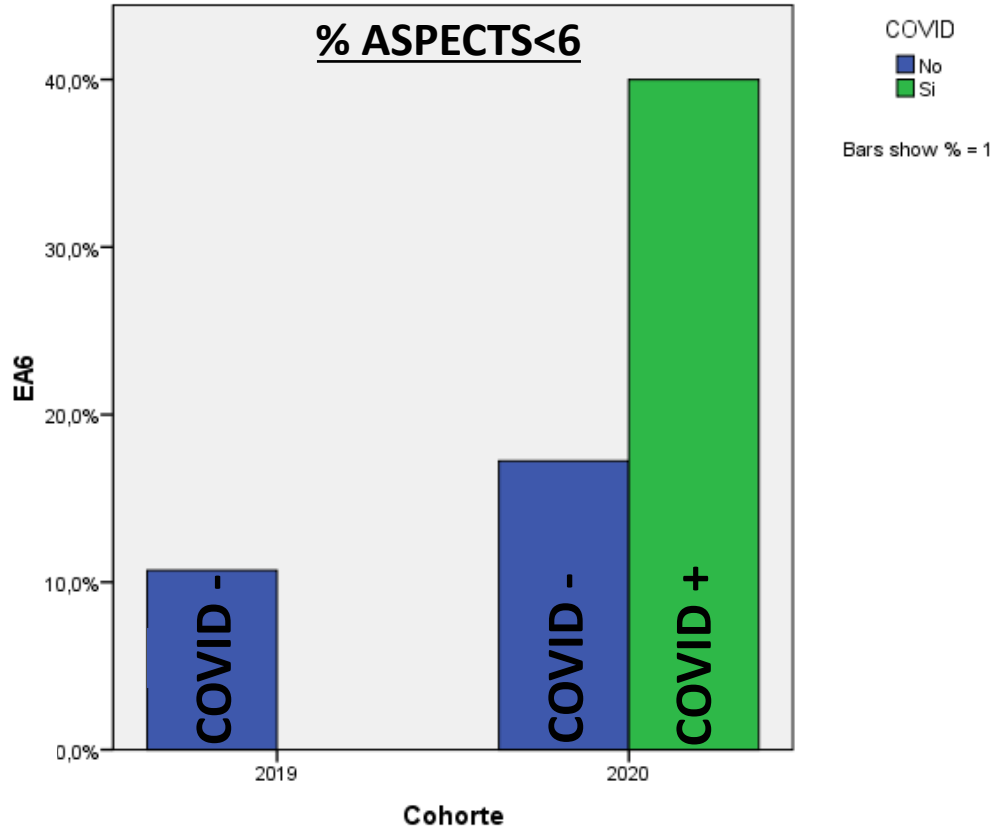




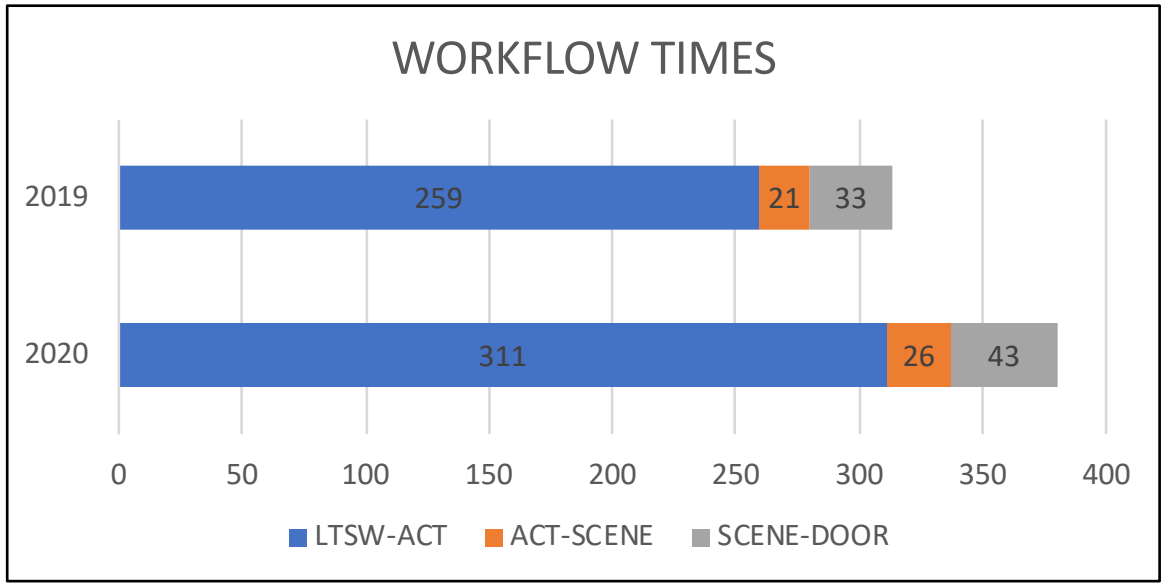
ASPECTS on admission

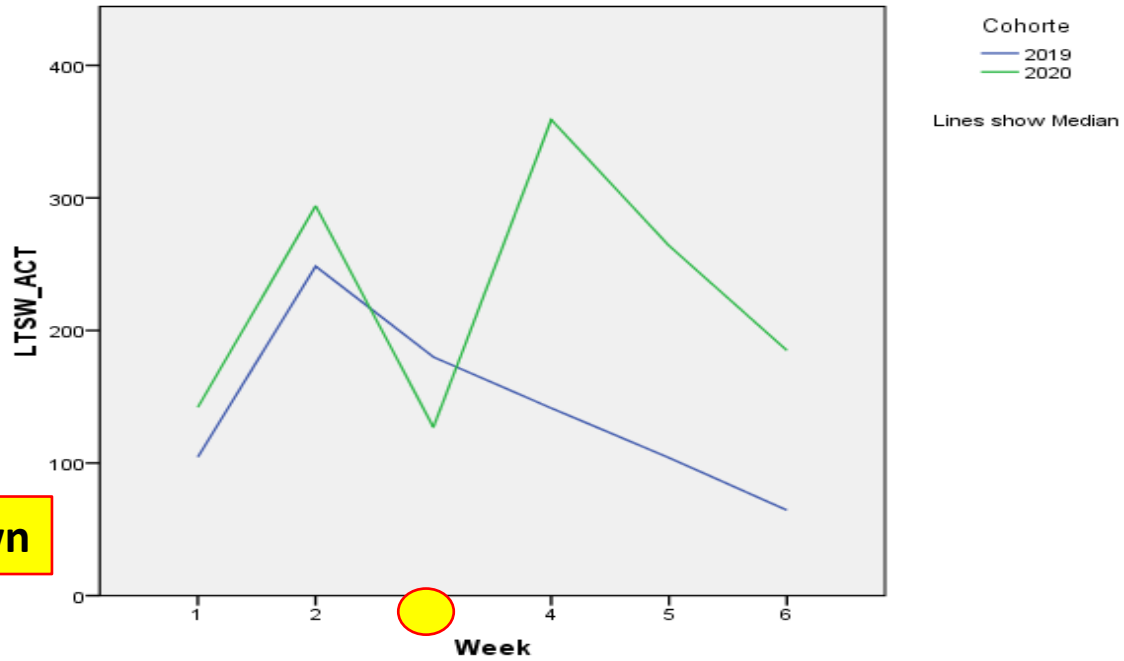
6-10

<6



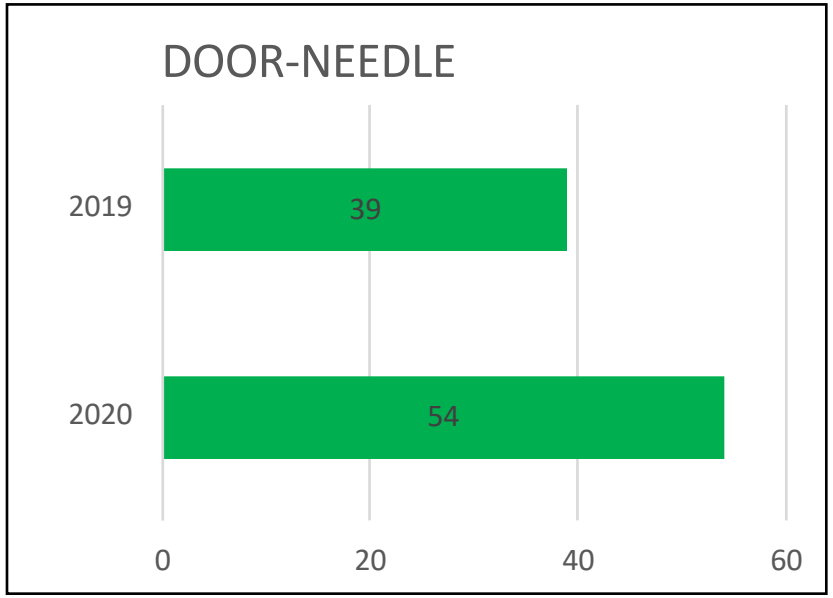
PRE-HOSPITAL

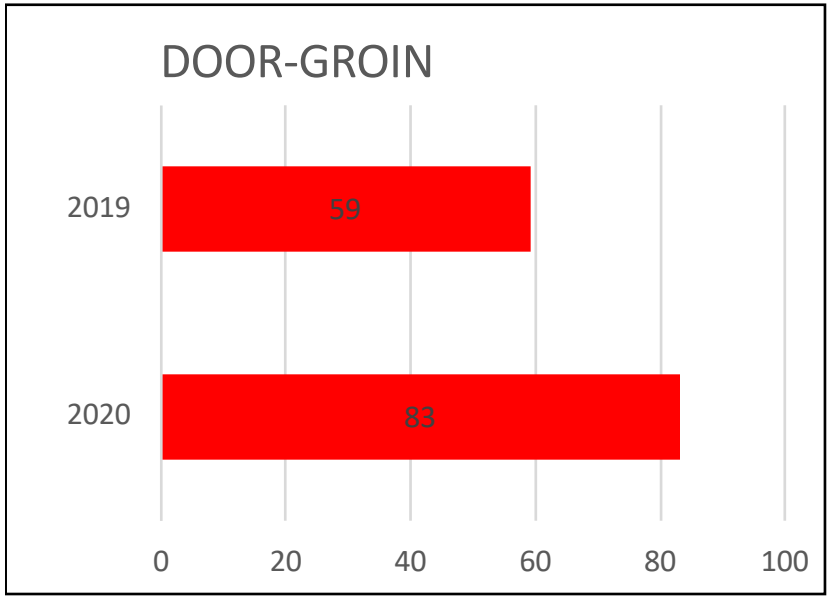




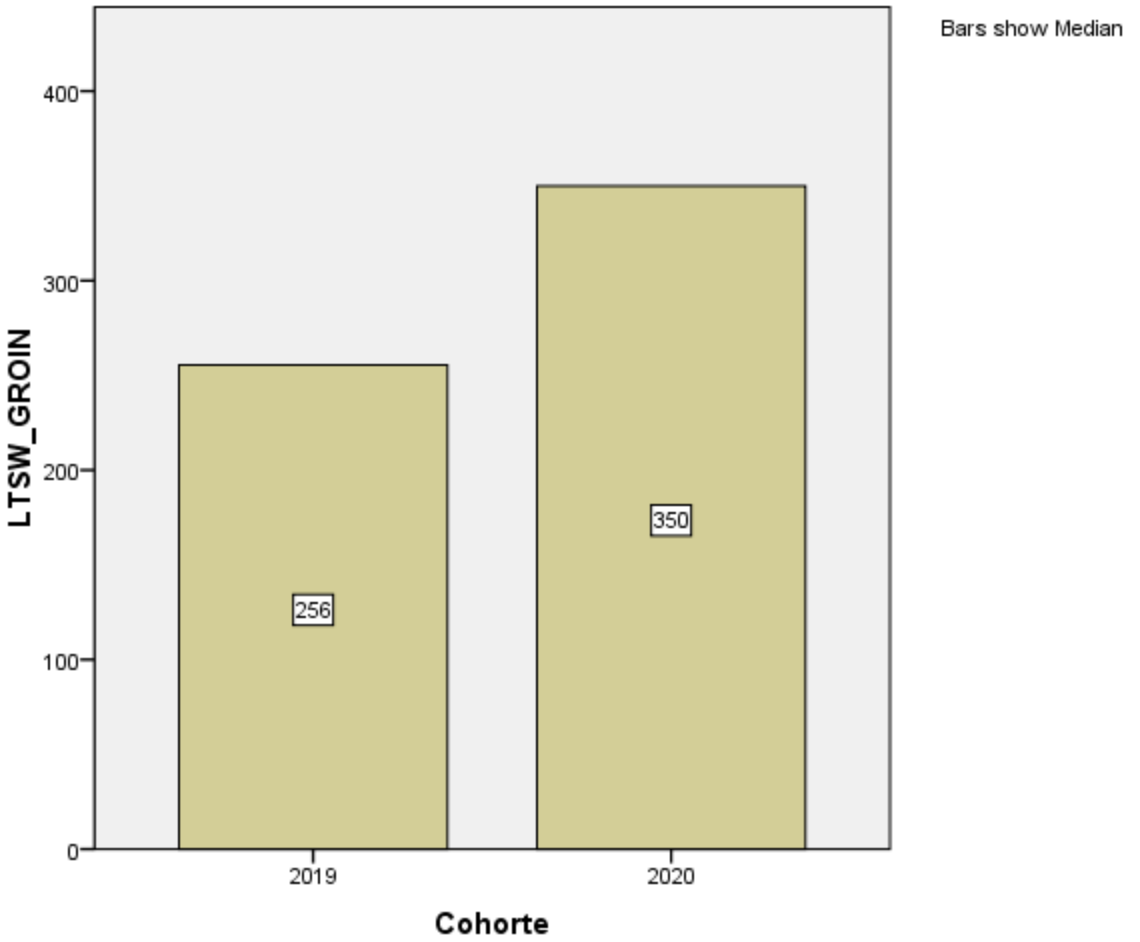
Lockdown

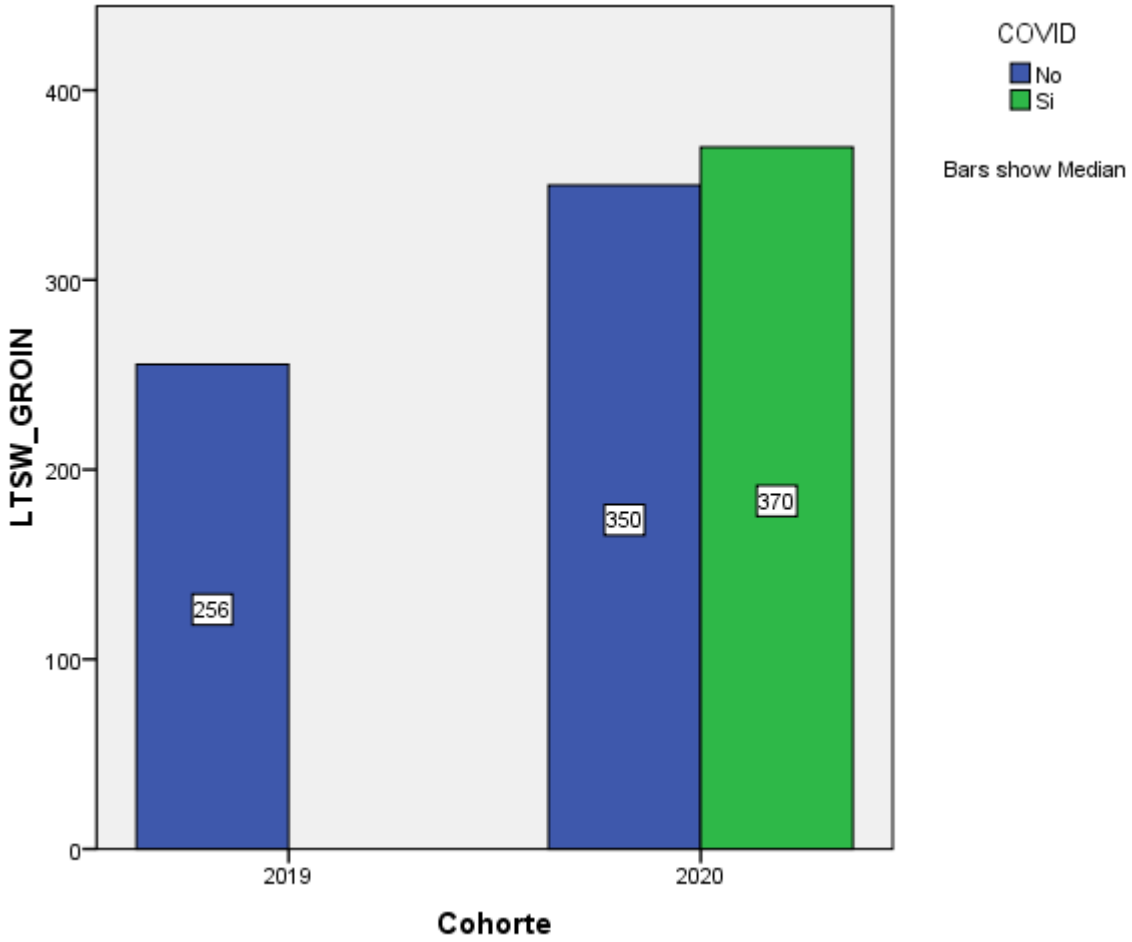
IN-HOSPITAL





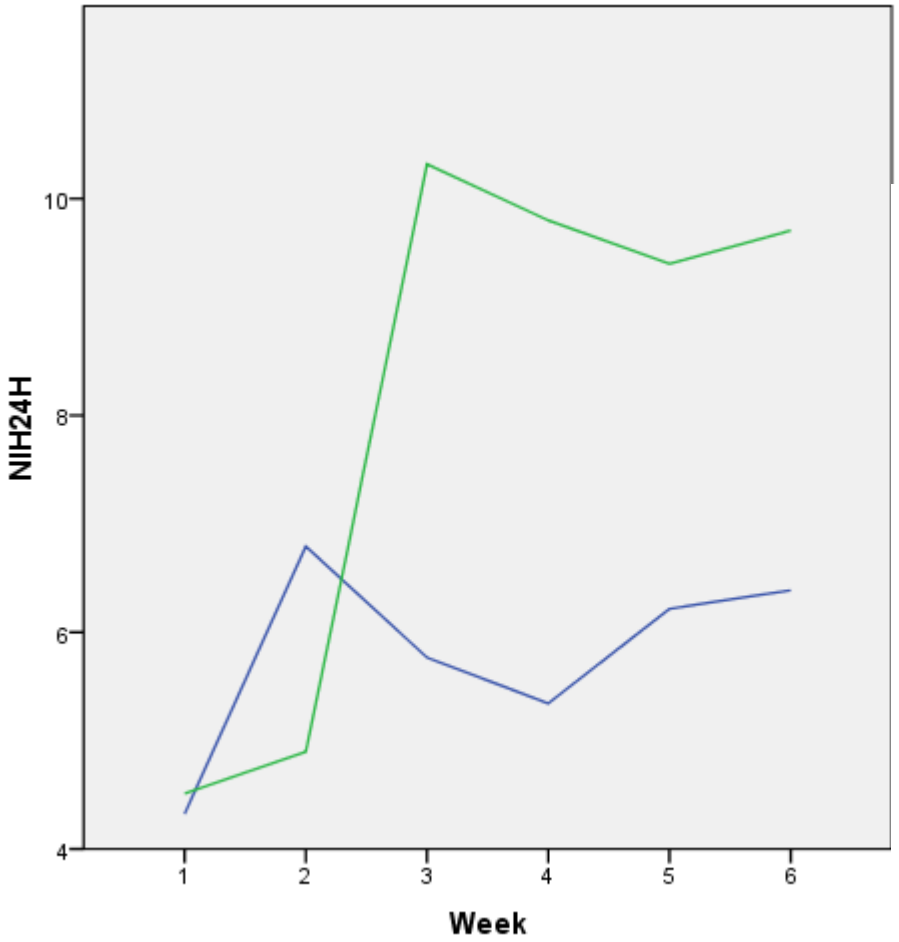
EVT: LTSW TO GROIN

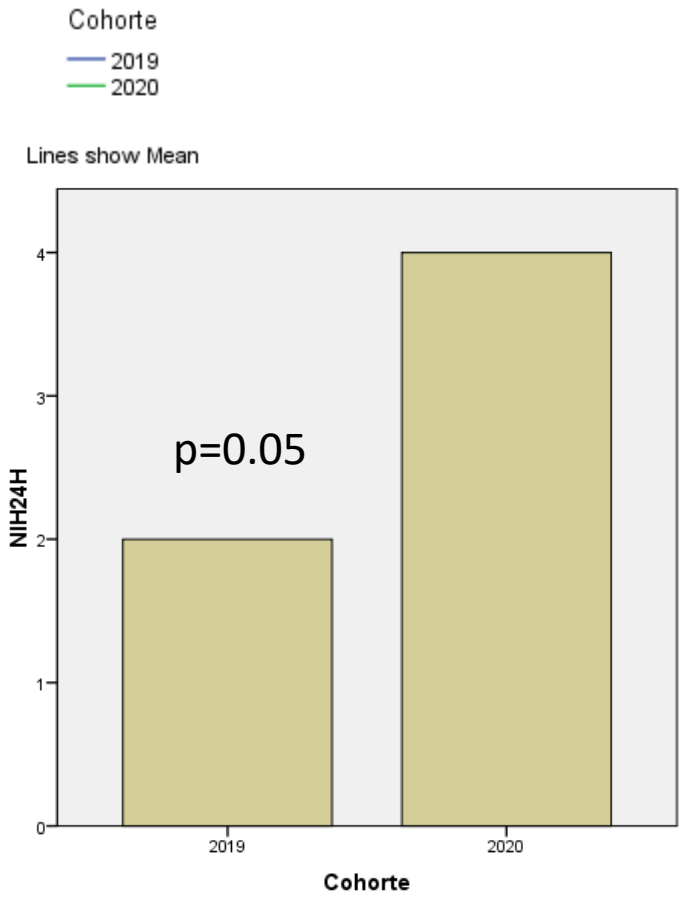


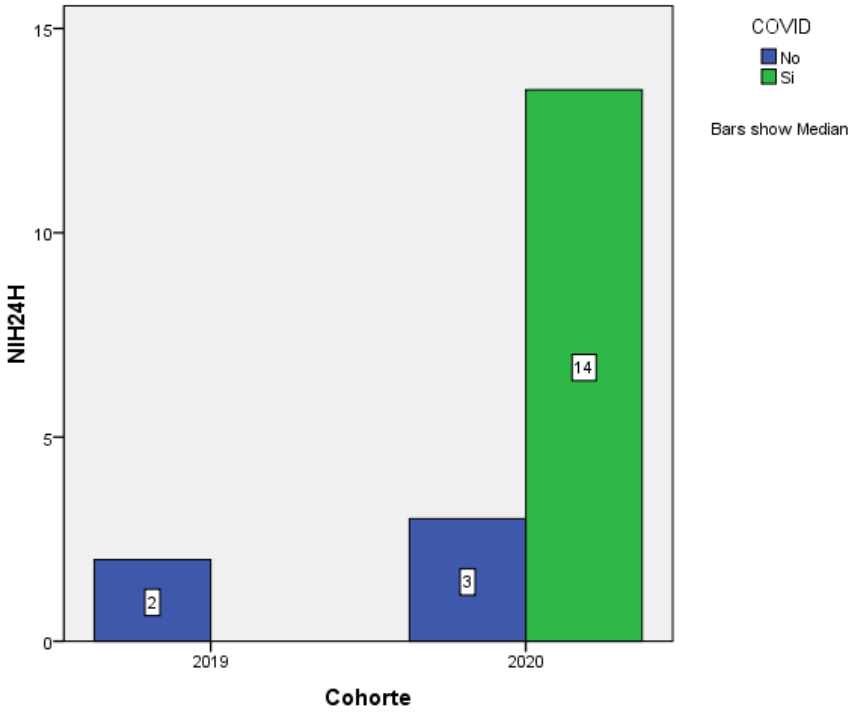


OUTCOME

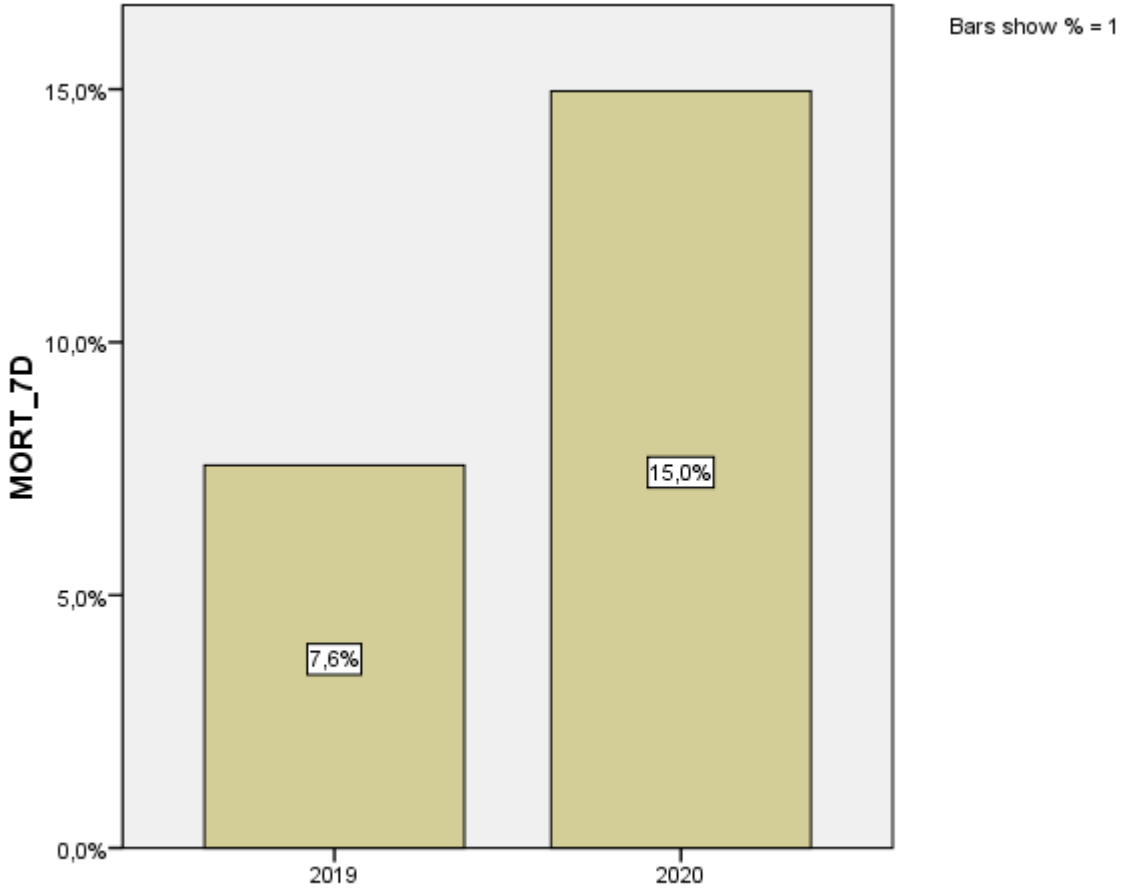
24 NIHSS

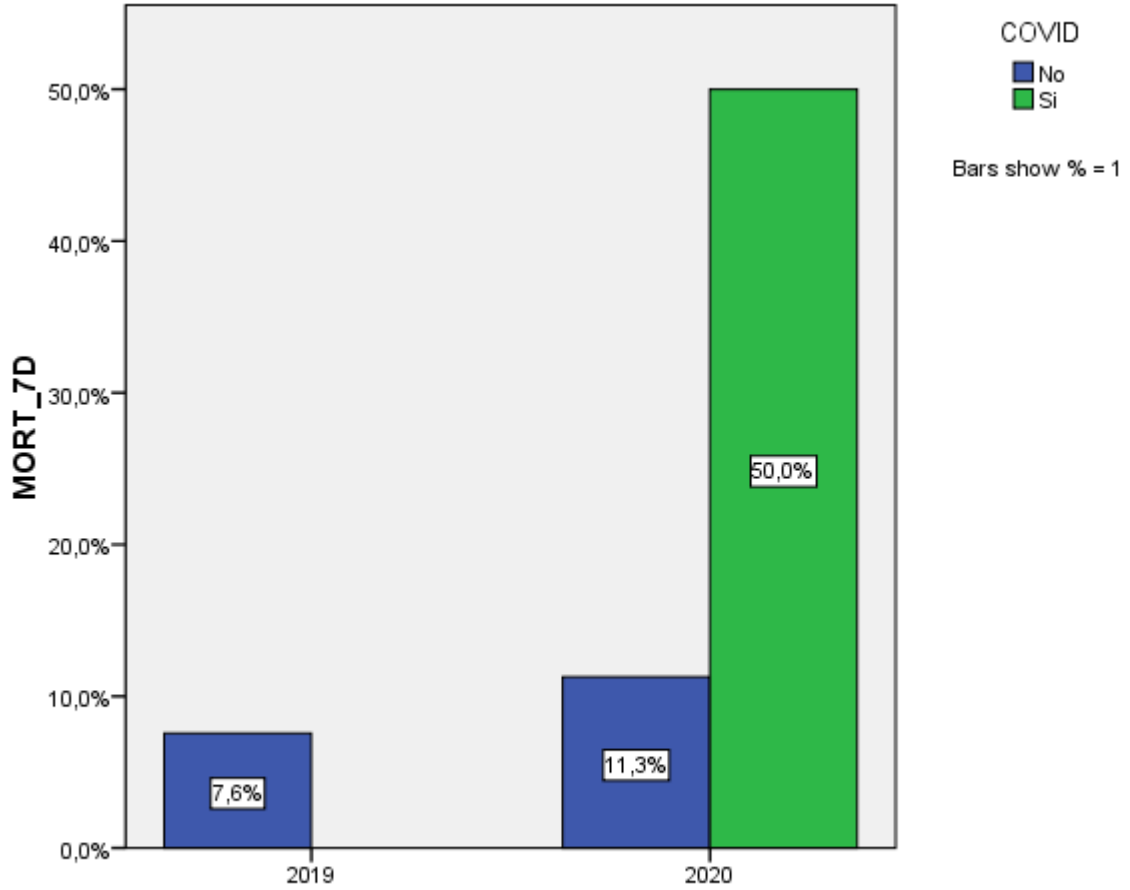






MORTALITY AT 7 DAYS

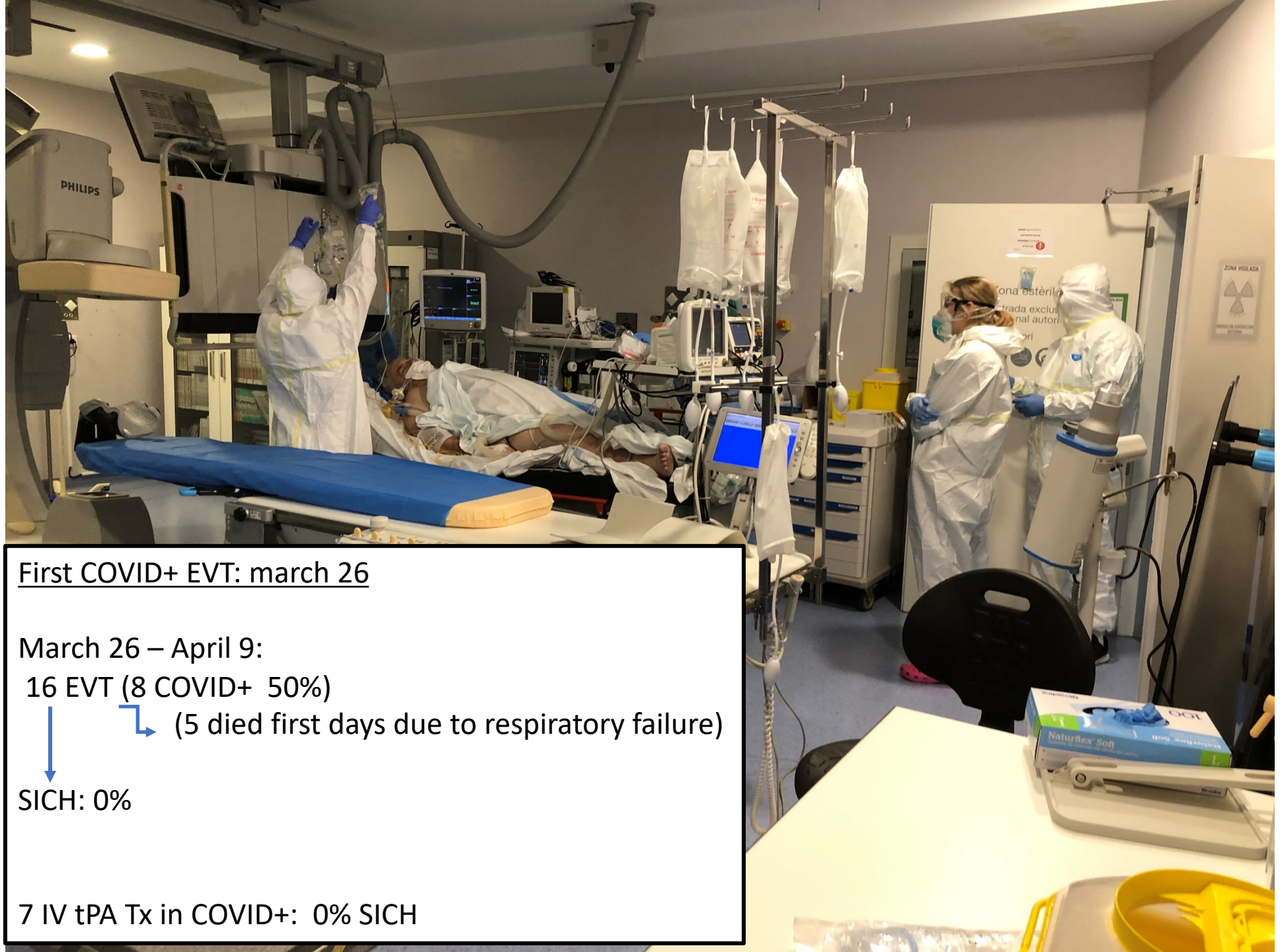




A binary logistic regression analysis adjusted by age and NIHSS score showed 2 **independent predictors of early mortality**:

Patients in 2020-C (OR 3.1 CI 1.1-8.8 p=0.03)

SARS-CoV-2 infection (OR 7.1 CI 1.8-29, p<0.01)



First COVID+ EVT: march 26

March 26 – April 9:

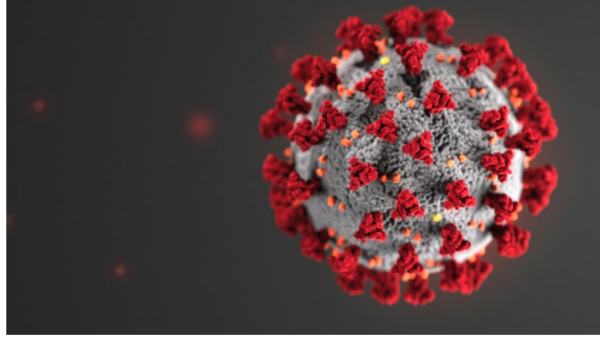
16 EVT (8 COVID+ 50%)

(5 died first days due to respiratory failure)

SICH: 0%

7 IV tPA Tx in COVID+: 0% SICH

The COVID-19 Collateral Damage to Stroke Care:



- The pandemic is a major healthcare disaster with significant impact on stroke care (and likely other cardiovascular emergencies)
- High complexity:
  - home confinement and the fear of hospital consultation
  - Impact of Pre- and Intra-Hospital Work-Flow
  - Potential greater severity of stroke in COVID+ patients

We Must Also Focus on the COVID-19 Impact on Non-COVID Diseases…

Editorial

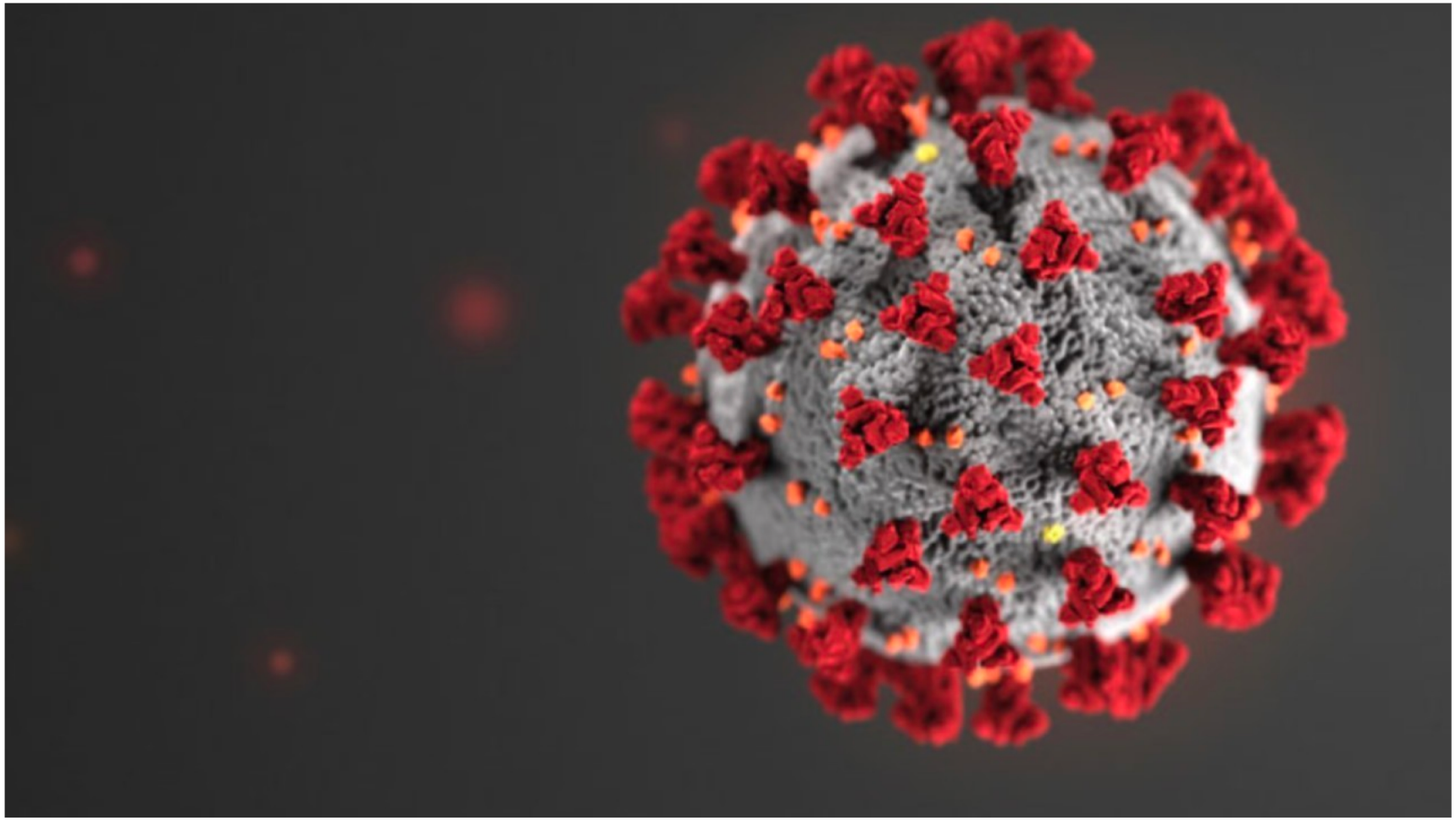
Challenges and Potential Solutions of Stroke Care During the Coronavirus Disease 2019 (COVID-19) Outbreak

Jing Zhao, MD, PhD; Anthony Rudd, FRCP (Lond); Renyu Liu, MD, PhD

3. Inform the emergency medical system and the public that these centers will be protected and will remain fully operational even during crises.
4. Improve education of health professionals and the public, especially those who are at high risk of stroke, to recognize stroke and call emergency medical services immediately to be taken to one of the designated stroke centers so as to avoid significant delay in transferring patient from one hospital to the other.

Stroke. 2020;51:1356-1357

Procedural Aspects: How Much PPE?



The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Universal Screening for SARS-CoV-2 in Women Admitted for Delivery

215 pregnant women on delivery unit

Four women (1.9%) had fever or other symptoms of Covid-19 on admission, and all 4 women tested positive for SARS-CoV-2

Nasopharyngeal swabs were obtained from 210 women with no Covid-19 symptoms, 29 (13.7%) were positive for SARS-CoV-2. One (3.4%) positive patient developed COVID-19 fever.

88% of SARS-CoV-2 positive patients on admission had no symptoms at presentation!

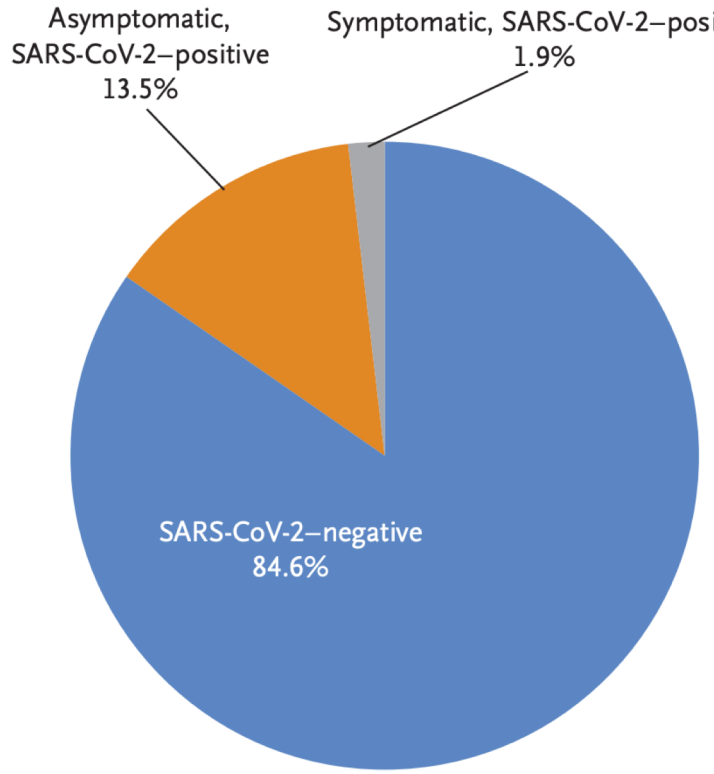


Figure 1. Symptom Status and SARS-CoV-2 Test Results among 215 Obstetrical Patients Presenting for Delivery.

April 13, 2020
DOI: 10.1056/NEJMc2009316

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility

M.M. Arons, K.M. Hatfield, S.C. Reddy, A. Kimball, A. James, J.R. Jacobs, J. Taylor, K. Spicer, A.C. Bardossy, L.P. Oakley, S. Tanwar, J.W. Dyal, J. Harney, Z. Chisty, J.M. Bell, M. Methner, P. Paul, C.M. Carlson, H.P. McLaughlin, N. Thornburg, S. Tong, A. Tamin, Y. Tao, A. Uehara, J. Harcourt, S. Clark, C. Brostrom-Smith, L.C. Page, M. Kay, J. Lewis, P. Montgomery, N.D. Stone, T.A. Clark, M.A. Honein, J.S. Duchin, and J.A. Jernigan, for the Public Health–Seattle and King County and CDC COVID-19 Investigation Team*

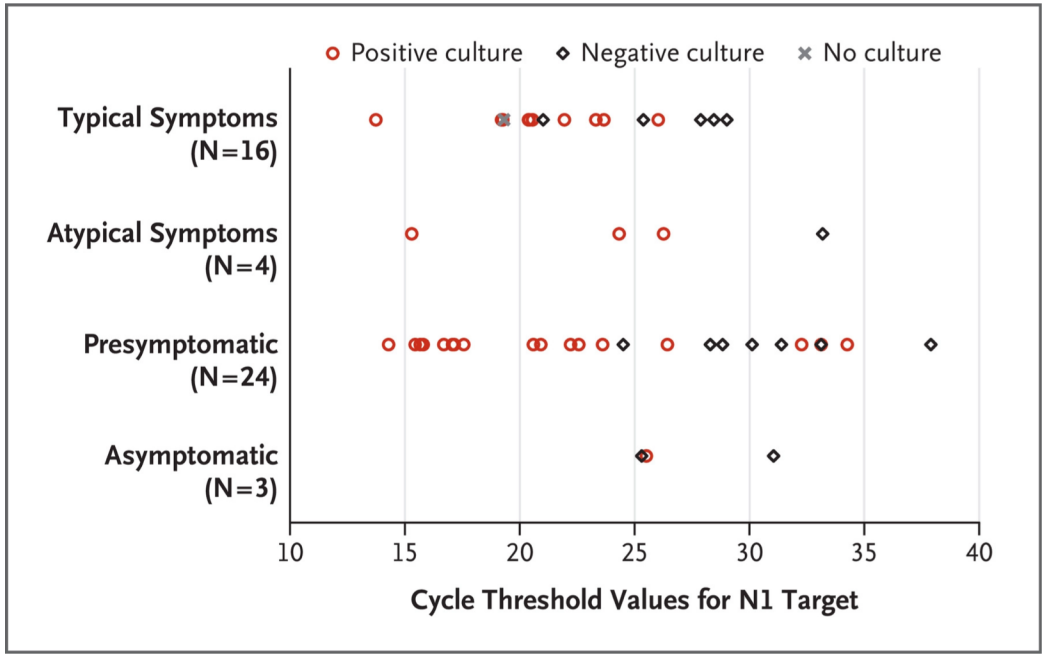
- 89 SNF Residents
- 64% (n=57, age, 78.6±9.5y) tested positive for SARS-CoV-2 either during the point-prevalence surveys, clinical evaluation, or postmortem examination
- 76 residents participated in the first point-prevalence survey:
  - 35% (17): typical symptoms
  - 8% (4): only atypical symptoms
  - 56% (27): no new symptoms
    - 89% (24) new symptoms within 7 (median, 4 [IQR, 3-5]) days

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

Asymptomatic Transmission, the Achilles' Heel of Current Strategies to Control Covid-19

Monica Gandhi, M.D., M.P.H., Deborah S. Yokoe, M.D., M.P.H., and Diane V. Havlir, M.D.



56% of SARS-CoV-2 positive patients on first survey had no symptoms at that time!

nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-020-0869-5

Check for updates

Temporal dynamics in viral shedding and transmissibility of COVID-19

Xi He[1,3], Eric H. Y. Lau[2,3] ✉, Peng Wu[2], Xilong Deng[1], Jian Wang[1], Xinxin Hao[2], Yiu Chung Lau[2], Jessica Y. Wong[2], Yujuan Guan[1], Xinghua Tan[1], Xiaoneng Mo[1], Yanqing Chen[1], Baolin Liao[1], Weilie Chen[1], Fengyu Hu[1], Qing Zhang[1], Mingqiu Zhong[1], Yanrong Wu[1], Lingzhai Zhao[1], Fuchun Zhang[1], Benjamin J. Cowling[2,4], Fang Li[1,4] and Gabriel M. Leung[2,4]

We report temporal patterns of viral shedding in 94 patients with laboratory-confirmed COVID-19 and modeled COVID-19 infectiousness profiles from a separate sample of 77 infector–infectee transmission pairs. We observed the highest viral load in throat swabs at the time of symptom onset, and inferred that infectiousness peaked on or before symptom onset. We estimated that 44% (95% confidence interval, 25–69%) of secondary cases were infected during the index cases' presymptomatic stage, in settings with substantial household clustering, active case finding and quarantine outside the home. Disease control measures should be adjusted to account for probable substantial presymptomatic transmission.

In conclusion, we have estimated that **viral shedding of patients with laboratory-confirmed COVID-19 peaked on or before symptom onset**, and a substantial proportion of transmission probably occurred before first symptoms in the index case.

RESEARCH ARTICLE

CORONAVIRUS

Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2)

Ruiyun Li[1]*, Sen Pei[2]*†, Bin Chen[3]*, Yimeng Song[4], Tao Zhang[5], Wan Yang[6], Jeffrey Shaman[2]†

Estimation of the prevalence and contagiousness of undocumented novel coronavirus [severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2)] infections is critical for understanding the overall prevalence and pandemic potential of this disease. Here, we use observations of reported infection within China, in conjunction with mobility data, a networked dynamic metapopulation model, and Bayesian inference, to infer critical epidemiological characteristics associated with SARS-CoV-2, including the fraction of undocumented infections and their contagiousness. We estimate that 86% of all infections were undocumented [95% credible interval (CI): 82–90%] before the 23 January 2020 travel restrictions. The transmission rate of undocumented infections per person was 55% the transmission rate of documented infections (95% CI: 46–62%), yet, because of their greater numbers, undocumented infections were the source of 79% of the documented cases. These findings explain the rapid geographic spread of SARS-CoV-2 and indicate that containment of this virus will be particularly challenging.

Nature. 2020 Apr 1. doi: 10.1038/s41586-020-2196-x. [Epub ahead of print]

Virological assessment of hospitalized patients with COVID-2019.

Wölfel R[1], Corman VM[2], Guggemos W[3], Seilmaier M[3], Zange S[1], Müller MA[2], Niemeyer D[2], Jones TC[2,4], Vollmar P[1], Rothe C[5], Hoelscher M[5], Bleicker T[2], Brünink S[2], Schneider J[2], Ehmann R[1], Zwirglmaier K[1], Drosten C[6], Wendtner C[7].

Author information

Abstract

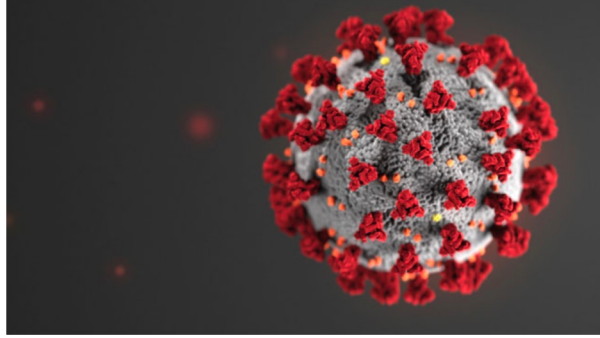
Coronavirus disease 2019 (COVID-19) is an acute infection of the respiratory tract that emerged in late 2019[1,2]. Initial outbreaks in China involved 13.8% of cases with severe courses, and 6.1% of cases with critical courses[3]. This severe presentation may result from the virus using a virus receptor that is expressed predominantly in the lung[2,4]; the same receptor tropism is thought to have determined the pathogenicity-but also aided in the control-of severe acute respiratory syndrome (SARS) in 2003[5]. However, there are reports of cases of COVID-19 in which the patient shows mild upper respiratory tract symptoms, which suggests the potential for pre- or oligosymptomatic transmission[6-8]. There is an urgent need for information on virus replication, immunity and infectivity in specific sites of the body. Here we report a detailed virological analysis of nine cases of COVID-19 that provides proof of active virus replication in tissues of the upper respiratory tract. Pharyngeal virus shedding was very high during the first week of symptoms, with a peak at 7.11×10^8 RNA copies per throat swab on day 4. Infectious virus was readily isolated from samples derived from the throat or lung, but not from stool samples-in spite of high concentrations of virus RNA. Blood and urine samples never yielded virus. Active replication in the throat was confirmed by the presence of viral replicative RNA intermediates in the throat samples. We consistently detected sequence-distinct virus populations in throat and lung samples from one patient, proving independent replication. The shedding of viral RNA from sputum outlasted the end of symptoms. Seroconversion occurred after 7 days in 50% of patients (and by day 14 in all patients), but was not followed by a rapid decline in viral load. COVID-19 can present as a mild illness of the upper respiratory tract. The confirmation of active virus replication in the upper respiratory tract has implications for the containment of COVID-19.

Vall d'Hebron
Barcelona Campus Hospitalari

Infection Among Hospital Staff in Barcelona

	MD	Nurse	Nurse Aid	Transport	Residents	Technician	Administration	Others	Total
Total Staff	1348	1745	1042	417	579	649	622	119	6731
# COVID+	71	261	143	34	30	33	30	17	619
% COVID+	5.3%	14.9%	13.7%	8.2%	5.2%	5.1%	4.8%	14.2%	9.2%

Procedural Aspects: How Much PPE?



- History is limited in the setting of Acute Stroke
- High Rates of Asymptomatic and Atypical Patients (? ~55-90%)
- Higher viral shedding in the upper (vs. lower) respiratory tract vs. SARS and Influenza
- Early and Pre-Symptomatic Spread (? ~45-55%)

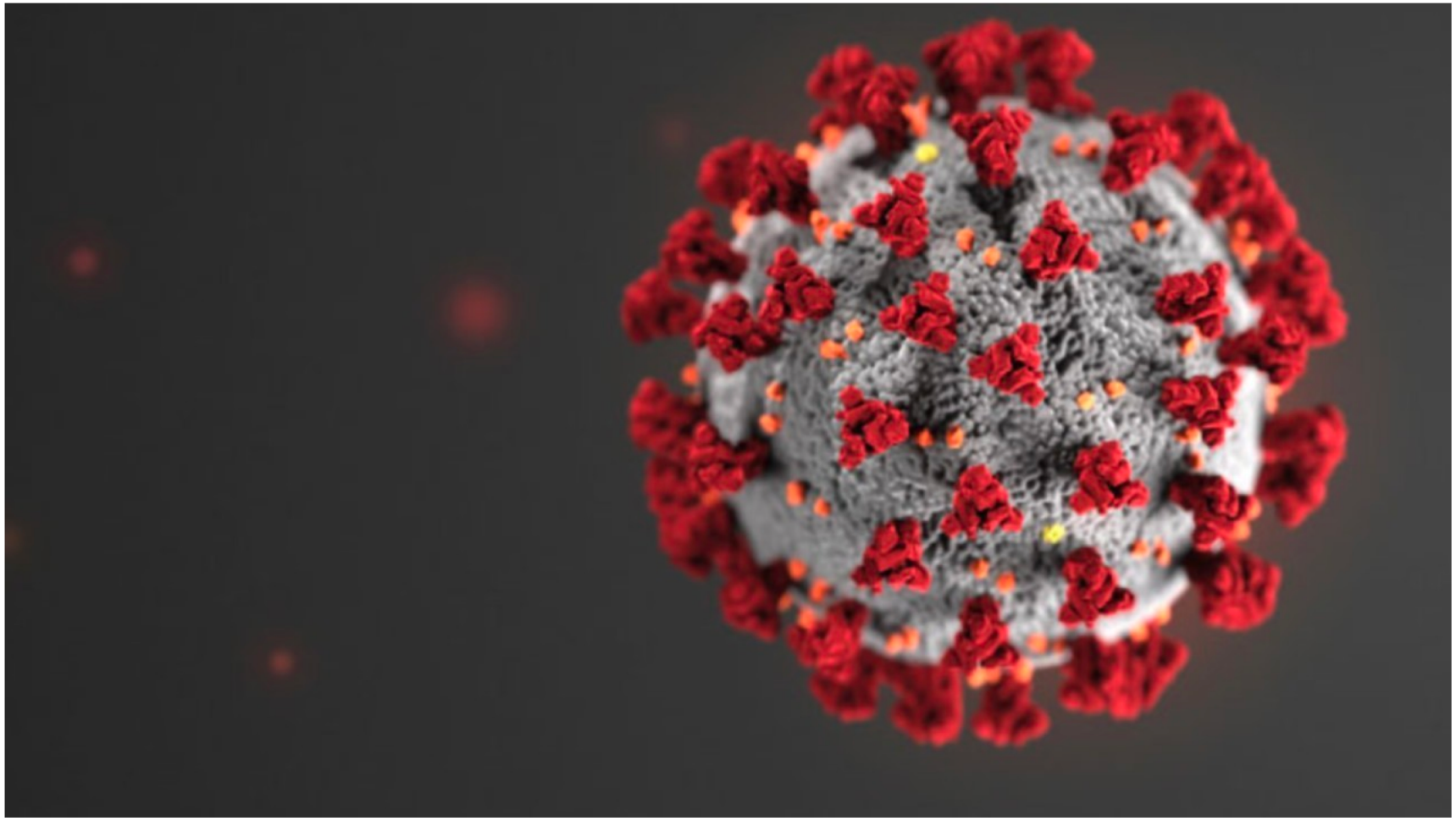
Do Not Trust COVID-19 Screening to Make Intra-Procedural Decisions Regarding PPE!

We are the Gladiators in this Battle – A Gladiator would never go to a fight without a strong shield….

Grady Memorial Hospital, Atlanta, USA

Vall ‘Hebron Hospital, Barcelona, Spain

Anesthesia Management: A Change is just Different not Necessary Better …



American Heart Association | American Stroke Association

Stroke

Mechanical thrombectomy in the era of the COVID-19 pandemic.

Emergency preparedness for neuroscience teams.

A guidance statement from the Society of Vascular & Interventional Neurology

Cover Title: Mechanical thrombectomy in the era of the COVID-19

Thanh N. Nguyen, MD FRCPc,[1] Mohamad Abdalkader, MD,[2] Tudor G. Jovin, MD,[3] Raul G. Nogueira, MD,[4] Ashutosh P. Jadhav, MD,[5] Diogo C. Haussen, MD,[4] Ameer E. Hassan, DO,[6] Roberta Novakovic, MD,[7] Sunil A. Sheth, MD,[8] Santiago Ortega-Gutierrez, MD,[9] MSc, Peter D. Panagos, MD,[10] Steve M. Cordina, MD,[11] Italo Linfante, MD,[12] Ossama Yassin Mansour, MD PhD,[13] Amer M. Malik, MD, MBA[14] Sandra Narayanan, MD,[5] Hesham E. Masoud, MD,[15] Sherry Hsiang-Yi Chou,[5, 16] MD, Rakesh Khatri, MD,[17] Vallabh Janardhan, MD,[18] Dileep R. Yavagal, MD,[14] Osama O. Zaidat, MD,[19] David M. Greer, MD,[1] David S. Liebeskind, MD.[20]

Pre-hospital and Emergency Department care of acute LVO

- Every acute stroke patient (direct presenting to ED or in transfer) should be triaged for symptoms and signs of COVID-19, including potential contact.
- If there is positive screening for COVID-19, this patient should wear a surgical mask and immediately be placed in a negative pressure room in the ED.
- If unknown assume it is a possible case!
- Downsize stroke team and minimize exposure
- PPE including full sleeved gown, surgical mask, eye protection (face shield or equivalent) and gloves.

Pre-hospital and Emergency Department care of acute LVO

- Personal protection should be escalated to N95 mask, hair cap, double gloves, shoe covers in the setting of contact with confirmed COVID-19 patient and/or aerosolizing events such as coughing, sneezing, nebulizer treatment, suctioning, nasogastric tube placement, bag mask ventilation, CPR, and intubation.
- A dedicated CT scan room for COVID-19 patients should be established if multiple CT rooms are available.
- As it would minimize exposure to emergency department and CT suite personnel a “direct to the angiography suite” approach should be considered for stable transferred patients with stroke symptoms onset within 24 hours, particularly if the time from the outside hospital imaging to arrival is less than two hours and CT ASPECTS is $\geq$ 7.

Airway Management for MT

- The anesthesiologist should be alerted early of a COVID-19 or suspect patient.
- Local policies for intubation and general anesthesia versus conscious sedation differ at different centers – **not the best time for changes!**
- **If appropriate, consider conscious sedation as first-line:**
  - to protect anesthesiologists from exposure
  - to protect our patients from unnecessary intubation
  - conserving mechanical ventilator and ICU resources.
- Converting a patient from conscious sedation to general anesthesia in the middle of the procedure in the angiography suite should be avoided due to high risk of aerosolization in a positive pressure room.

General Endotracheal Anesthesia

- **Converting** a patient from conscious sedation to general anesthesia in the middle of the procedure in the angiography suite **should be avoided** due to high risk of aerosolization in a positive pressure room.

- Early and controlled intubation is preferred if:
  - Acute respiratory distress/ hypoxemia/ high oxygen requirement
  - Unable to protect their airway/ low GCS (<9)
  - Agitation, uncooperative
  - Active vomiting
  - Active cough

- **These are not isolated reasons to intubate on our opinion:**
  - **Dominant cerebral hemisphere occlusions**
  - **Aphasic patients**
  - **High NIHSS (>15)**

General Endotracheal Anesthesia

- Only essential personnel
- Avoid high flow pre-oxygenation
- Rapid sequence induction using video-laryngoscopy (most experienced person available to intubate)
- Vasopressors immediately available.
- Maintain SBP >140mmHg, SpO_2 >94%, normocarbia
- HEPA (High Efficiency Particulate Air) filter on ETT and CO_2 sampling line
- Avoid circuit disconnections
- Extubate preferably in a negative pressure location avoiding coughing

General Endotracheal Anesthesia

- An “aerosol box” can be used as a cover as an additional measure of PPE protection during intubation.

Monitored Anesthesia Care

- Patient should wear surgical mask
- Avoid high flow nasal cannula oxygen
- Careful titration of sedation to avoid oro- or nasopharyngeal airway insertion or chin lift/jaw thrust.
- Consider use of expiratory viral filter on oxygen masks.

TAVISH® OXYGEN MASK

SNACC Consensus Statement:

Anesthetic Management of Endovascular Treatment of Acute Ischemic Stroke During COVID-19 Pandemic: Consensus Statement from Society for Neuroscience in Anesthesiology & Critical Care (SNACC)

Endorsed by Society of Vascular & Interventional Neurology (SVIN), Society for NeuroInterventional Surgery (SNIS), Neurocritical Care Society (NCS), and European Society of Minimally Invasive Neurological Therapy (ESMINT) and American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) Cerebrovascular Section

Deepak Sharma, MD, DM[1] Mads Rasmussen, MD, PhD[2] Ruquan Han, MD, PhD[3]
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Andrew Kofke, MD MBA FCCM FNCS[6] Lakshmikumar Venkatraghvan MD[7]
Radoslav Raychev MD, FAHA[8] Justin F. Fraser, MD, FAANS, FAHA[9]

Standards

Society of NeuroInterventional Surgery recommendations for the care of emergent neurointerventional patients in the setting of covid-19

Justin F Fraser ,[1] Adam S Arthur ,[2,3] Michael Chen,[4] Michael Levitt,[5] J Mocco,[6] Felipe C Albuquerque,[7] Sameer A Ansari,[8] Guilherme Dabus,[9] Mahesh V Jayaraman,[10] William J Mack,[11] James Milburn,[12] Maxim Mokin ,[13] Sandra Narayanan,[14] Ajit S Puri,[15] Adnan H Siddiqui ,[16,17] Jenny P Tsai,[18] Richard P Klucznik[19]

Society of NeuroInterventional Surgery recommendations for the care of emergent neurointerventional patients in the setting of covid-19

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UNDOCUMENTED COVID STATUS

Screening for fever and respiratory symptoms should be part of the screening of all potential neurointerventional patients. Intubation of these patients prior to transportation to the angiography suite should be considered, especially in patients with risk factors for intraprocedural intubation as noted above. Given that thrombectomy is such a time-sensitive procedure, that family members are often not available to provide a complete medical history, and that a neurologically impaired patient may not be able to answer screening questions, it is recommended that patients of unknown COVID status be treated as high risk for COVID-positive (see above), provided institutional resources are available.

DOCUMENTED COVID-POSITIVE STATUS

Patients with COVID-positive documentation (or those presumed positive; see below) should be treated with maximum safety precautions. Intubation, extubation, suction, and active CPR may result in aerosolization of respiratory secretions, increasing the risk of exposure to personnel. Intubated patients pose less of a transmission risk to neurointerventional staff given that their ventilation is managed through a closed circuit. Nonetheless, disruption of the circuit (such as for a cuff leak, suctioning, endotracheal tube manipulation) can release additional aerosolized secretions. Therefore, we recommend standard institutional protocols with a low threshold for intubation of stroke thrombectomy COVID-19-positive patients prior to transport to the angiography suite, ideally in a negative pressure environment. For instance, patients with dominant hemisphere occlusions, very high National Institutes of Health Stroke Scale score or a low Glasgow Coma Scale score, or posterior circulation occlusions (as well as any patient with significant symptomatic respiratory difficulty) should be considered for prophylactic intubation as

Fraser JF, *et al*. *J NeuroIntervent Surg* 2020;**0**:1–3. doi:10.1136/neurintsurg-2020-016098

SNACC Consensus Statement:

Anesthetic Management of Endovascular Treatment of Acute Ischemic Stroke During COVID-19 Pandemic: Consensus Statement from Society for Neuroscience in Anesthesiology & Critical Care (SNACC)

Endorsed by Society of Vascular & Interventional Neurology (SVIN), Society for NeuroInterventional Surgery (SNIS), Neurocritical Care Society (NCS), and European Society of Minimally Invasive Neurological Therapy (ESMINT) and American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) Cerebrovascular Section

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The threshold for tracheal intubation will need to be altered by the situation presented and is likely to be impacted by availability of equipment and personnel. In general, the threshold for the use of GA for EVT may be reduced during COVID-19 pandemic. If the anesthesiologist has any concerns for possible urgent conversion from MAC to GA during EVT, it is advisable to start with GA. However, not all patients undergoing EVT need to be intubated solely for the purpose of reducing the risk to healthcare personnel. In fact, intubation may increase the risk of aerosolization and hence, the exposure.

My Suggestions:

Do any of the following apply?

- Acute respiratory distress / hypoxemia / requiring high flow oxygen
- Active cough
- Inability to protect airway
- Active vomiting
- ~~Posterior circulation / dominant cerebral hemisphere occlusions~~
- ~~High NIHSS (>15) or~~ low GCS (<9)
- Agitated / uncooperative ~~/ aphasic patients~~

SNACC
SOCIETY FOR NEUROSCIENCE IN ANESTHESIOLOGY AND CRITICAL CARE

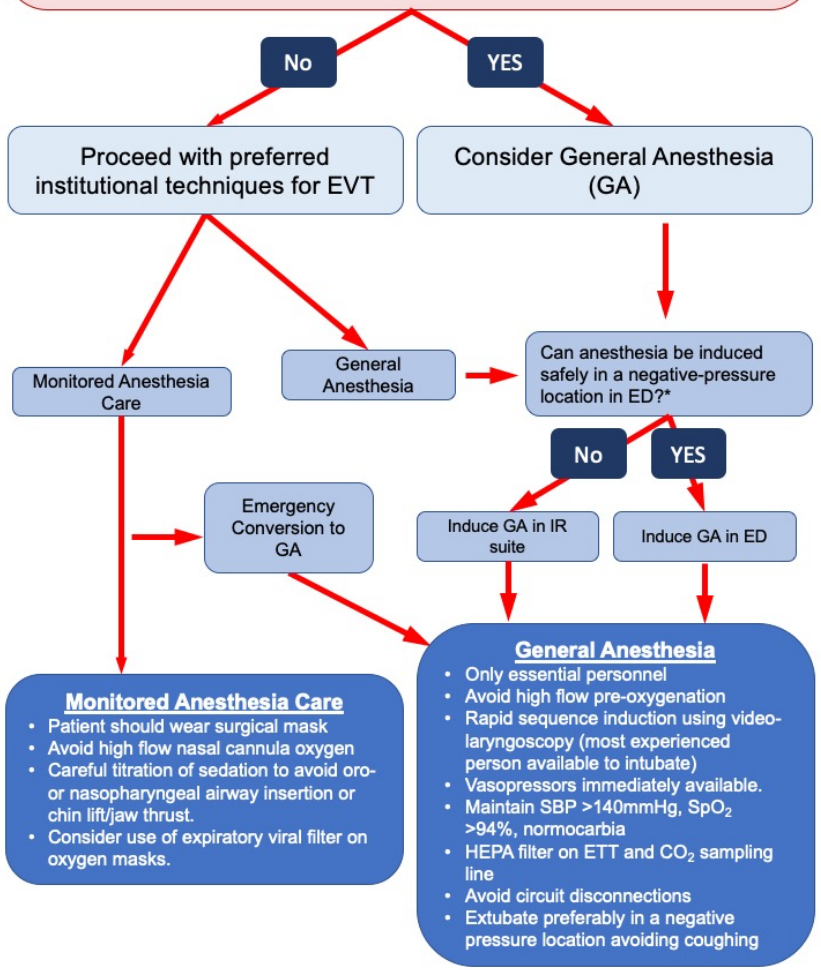
Endovascular Therapy for Acute Ischemic Stroke

(All EVTs Should Proceed With Airborne Precautions)

Discussion between anesthesiologist and interventionalist regarding optimal anesthetic technique to occur prior to the patient entering IR suite (ideally in the ED)

Do any of the following apply?

- ❑ Acute respiratory distress / hypoxemia / requiring high flow oxygen
- ❑ Active cough
- ❑ Inability to protect airway
- ❑ Active vomiting
- ❑ Posterior circulation / dominant cerebral hemisphere occlusions
- ❑ High NIHSS (>15) or low GCS (<9)
- ❑ Agitated / uncooperative / aphasic patients



*It is recognized that patients in acute respiratory distress / hypoxemia may require emergent intubation in ED. Patients suffering from AIS while already in hospital and requiring GA for EVT should be intubated safely is a suitable negative pressure location while minimizing delays in reperfusion.

Should Ischemic Stroke Patients with Aphasia or High National Institutes of Health Stroke Scale Score Undergo Preprocedural Intubation and Endovascular Treatment?

Ameer E. Hassan, DO,*† Malik M. Adil, MD,* Haralabos Zacharatos, DO,* Basit Rahim, MD,* Saqib A. Chaudhry, MD,* Wondwossen G. Tekle, MD,*† and Adnan I. Qureshi, MD*

Abstract

BACKGROUND: Presence of aphasia or severe neurologic deficits is considered an indication for preprocedural intubation (PPI) for endovascular treatment (ET) in acute ischemic stroke patients. We determined the feasibility, technical success rates, and outcomes of ET without PPI in 2 groups of patients: those with aphasia and those with an admission NIHSS score of 20 or more.

METHODS: The rates of intraprocedural intubation (IPI), good functional outcome at discharge (modified Rankin Scale score of 0-2), mortality, and intracerebral hemorrhage (ICH) were compared between those who did or did not undergo PPI in the above-mentioned patient groups.

RESULTS: A total of 60 (50%) of 120 patients with aphasia underwent ET without PPI; 6 of 60 patients required IPI. The odds of any ICH (odds ratio [OR] 6.3) and in-hospital mortality (OR 9.3) were significantly higher in those undergoing PPI. In the second analysis, 36 (39%) of 93 patients with an NIHSS score of 20 or more underwent ET without PPI; 6 of 57 patients required IPI. The risk of any ICH (OR 7.6) and in-hospital mortality (OR 5.0) was higher among patients who underwent PPI. The rates of good outcome at discharge were significantly lower among patients with aphasia (OR .1, 95% confidence interval [CI] .04-.2) or those with an NIHSS score of 20 or more (OR .07, 95% CI .005-.9) with PPI compared with those without PPI.

CONCLUSIONS: Despite the risk of IPI, patients with aphasia or an admission NIHSS score of 20 or more who underwent ET with PPI had lower rates of good outcomes and higher rates of ICH and death.

Aphasia (n=60): 10% (n=6) Conversions to GA
NIHSS ≥20 (n=36): ? Conversions Rate
Good outcomes at discharge lower with GA (OR .07, P=0.04)
Good outcome at discharge only 1 of 6 patients who converted

J Stroke Cerebrovasc Dis. 2014 May-Jun;23(5):e299-304.

Agitated Confusional States in Patients With Right Hemisphere Infarctions

JAMES W. SCHMIDLEY, M.D., AND ROBERT O. MESSING, M.D.

SUMMARY **Patients with infarctions in the territory of the right middle cerebral artery (RMCA) sometimes present with an agitated confusional state. We reviewed clinical data on 46 patients with RMCA infarcts and compared neurologic findings in patients with and without agitated confusion. Neither of the two patients presenting with agitated confusion showed obvious localizing neurologic signs; subtle motor, visual field and sensory deficits referable to the infarcted regions were present, but difficult to elicit because of the mental state. In contrast, all but one of the patients without agitated confusion had prominent motor and sensory signs. Infarction of the RMCA territory may cause agitated confusion in patients without prominent localizing signs; the initial neurologic findings may suggest a metabolic encephalopathy. However, the possibility of a cerebrovascular cause should not be dismissed in confused and agitated patients who have no definite lateralizing signs.**

Stroke Oct 15, No 5, 1984

PATIENTS WITH INFARCTIONS in the territory of the right middle cerebral artery (RMCA) may present with an agitated confusional state and a paucity of lateralized deficits.[1] We have encountered two such patients in three years. A detailed description of this syndrome has been published only once,[1] and we were unable to find any information concerning the frequency of this presentation among patients with RMCA infarctions. We therefore undertook this study to ascertain how common this presentation was, and to determine whether there were any clinical features distinguishing those patients presenting with agitated confusion from other patients with RMCA territory infarctions.

Methods

We reviewed the records of patients with RMCA strokes who were seen by the Neurology Services of San Francisco General and University of California, Moffitt Hospitals, between July 1, 1979 and June 30, 1982. Patients with coma, metabolic derangement, septicemia, preexisting dementia, or other conditions capable of causing an abormal mental state were excluded from consideration, as were those with frank intracerebral hemorrhage on computed tomographic (CT) scan, and those whose CT scan and examination indicated lacunar infarction.[2] During the period of the study, a CT scan was a standard part of the investigation of all patients with unexplained confusion.

Forty-six patients fulfilled these criteria. Orientation and level of consciousness were recorded in all cases. An agitated confusional state was defined by the presence of disorientation, distractibility, agitation, impaired cognition and perceptual errors (illusions, delusions or hallucinations). CT scans confirmed the presence of cerebral cortical infarction in 35 patients. Of the remaining 11 patients, four had only deep cerebral infarctions on CT scan and seven showed no lesion on CT scan (in six of these seven, CT scans were done within 24 hours of onset of neurologic symptoms). All 11, however, had sensory deficits suggesting parietal cortical infarction, such as agraphesthesia, astereognosis, extinction to double simultaneous stimulation, impaired sensory localization, unilateral neglect, and anosagnosia. They were therefore included in the study. Two patients with infarctions in the right internal carotid artery (RICA) distribution were grouped with RMCA stroke patients.

Results

The two patients who presented with an agitated confusional state are described briefly. Both were seen

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Received November 21, 1983: accepted February 22, 1984.

Grady Memorial Hospital 2010 to 2/18/2020

ALL patients: 2127

- **MAC: 1651**
- GA: 476
- **Converted: 26 (1.22%)**

Anterior circulation: 1849

- MAC: 1499
- GA:350
- Converted: 22

Posterior circulation 278

- MAC: 152
- GA: 126
- Converted: 4

Anterior Circulation stroke

- Left sided lesion: 1003
- MAC: 788
- GA: 215
- Converted: 10

All NIHSS > 6 and anterior circulation : 1728

- MAC 1393
- GA: 335
- Converted: 19 (1.36%)

Left side lesion and NIHSS > 6: 935

- MAC: 734
- GA:201
- Converted: 7 (0.95%)

Anterior circulation with NIHSS > 15: 1058

- MAC: 801
- GA: 257
- Converted: 10 (1.24%)

Left sided with NIHSS > 15 :669

- MAC: 498
- GA:171
- Converted: 4 (0.80%)

Grady Memorial Hospital 2010 to 2/18/2020

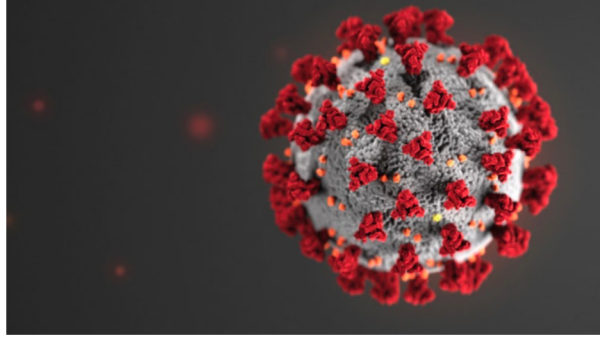
Predictor	Odds Ratio	95% CI	p	AUC	95% CI
Age	0.99	0.97 – 1.02	0.56	0.46	0.34 – 0.57
BMI (continuous)	0.99	0.94 – 1.06	0.93	0.48	0.35 – 0.61
BMI (>30)	1.10	0.46 – 2.64	0.84	-	-
NIHSS (continuous)	0.96	0.90 – 1.02	0.18	0.42	0.29 – 0.55
NIHSS (>15)	0.62	0.28 – 1.36	0.23	-	-
Echo EF	1.004	0.98 – 1.03	0.77	0.53	0.42 – 0.64
Location					
Right vs Left	1.48	0.62 – 3.53	0.38	-	-
Basilar vs Left	2.73	0.90 – 8.27	0.08	-	-

The summary is that only 19 of 1,393 patients (1.36%) with anterior circulation strokes and NIHSS >=6 were converted from MAC to GA.

Neither left-sided occlusion or NIHSS >15 seem to be reasonable predictors for conversion.

In fact, not even their combination seems to mean much.

Anesthesia Management for MT:



- Patient-Centric: Workflow, Times, Drop in Blood Pressure

- Consider that intubation will often be expected to be done at the a negative pressure room in the ED which will increase the risks to the ED personnel and overload them even more.... Similarly, for extubation will expose ICU personnel and take ICU resources.

Do you best to avoid conversions but stick with what you know best…

Angiography Room Post Treatment Care

EPA United States Environmental Protection Agency

Environmental Topics | Laws & Regulations | About EPA | Search EPA.gov

CONTACT US SHARE

Pesticide Registration

List N: Disinfectants for Use Against SARS-CoV-2

All products on this list meet EPA's criteria for use against SARS-CoV-2, the virus that causes COVID-19.

Other COVID-19 Resources

- EPA's Coronavirus Site
- CDC's Coronavirus Disease 2019 Site
- CDC's Cleaning and Disinfection Recommendations for COVID-19
- NPIC 's COVID-19 Virus Factsheet

Finding a Product

The easiest way to find a product on this list is to enter **the first two sets** of its **EPA registration number** into the search bar below.

For example, if EPA Reg. No. 12345-12 is on List N, you can buy EPA Reg. No. 12345-12-2567 and know you're getting an equivalent product. You can find this number by looking for the EPA Reg. No. on the product label.

Using Other Products

If you can't find a product on this list to use against SARS-CoV-2, look at a different product's label to confirm it has an EPA registration number and that human coronavirus is listed as a target pathogen.

Follow the Label

When using an EPA-registered disinfectant, **follow the label directions** for safe, effective use. Make sure to follow the contact time, which is the amount of time the surface should be visibly wet, listed in the table below.

These products are for use on surfaces, not humans.

Additional Resources

- Still have questions? See our FAQs about this list.
- My company has a product it would like included on this list.

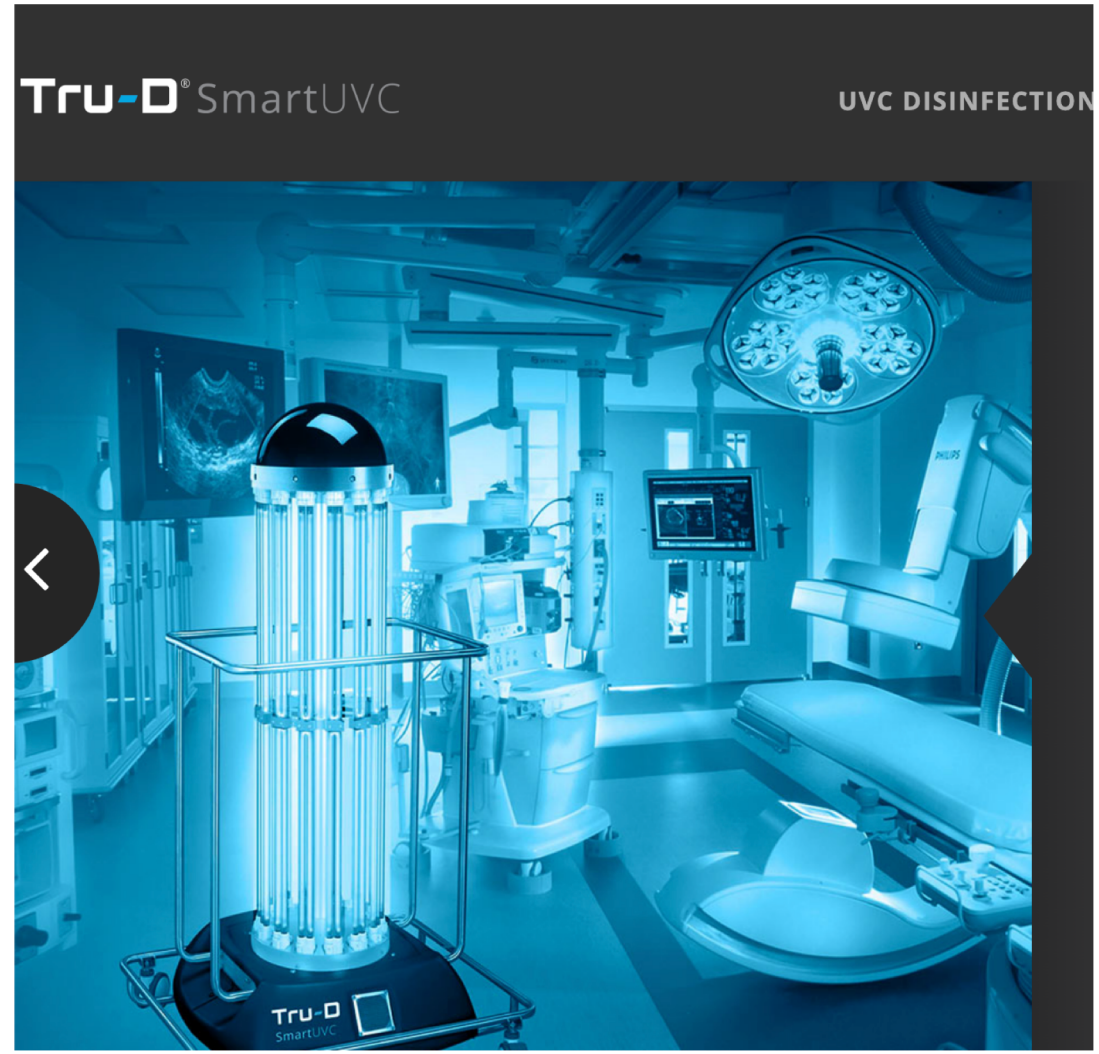
Note: Inclusion on this list does not constitute an endorsement by EPA. Additional disinfectants may meet the criteria for use against SARS-CoV-2. EPA will update this list with additional products as needed.

List N was last updated on April 16, 2020.

Search the Table | Show 25 entries | Export to PDF | Export to CSV

List N: Products with Emerging Viral Pathogens AND Human Coronavirus claims for use against SARS-CoV-2

EPA Registration Number	Active Ingredient(s)	Product Name	Company	Follow the disinfection directions and preparation for the following virus	Contact Time (in minutes	Formulation Type	Surface Types for Use	Use Site	Emerging Viral Pathogen Claim?	Date Added to List N
Search	Search	super s	Search	Search	Search	Search	Search	Search	Search	Search
9480-4	Quaternary ammonium; Isopropanol	Super Sani-Cloth Germicidal Disposable Wipe	Professional Disposables International Inc	Rhinovirus 39; Adenovirus	2	Wipe	Hard nonporous	Healthcare; Institutional	Yes	03/19/2020



IUVA Fact Sheet on COVID-19

POSTED BY TRU-D SMARTUVC 03.27.20

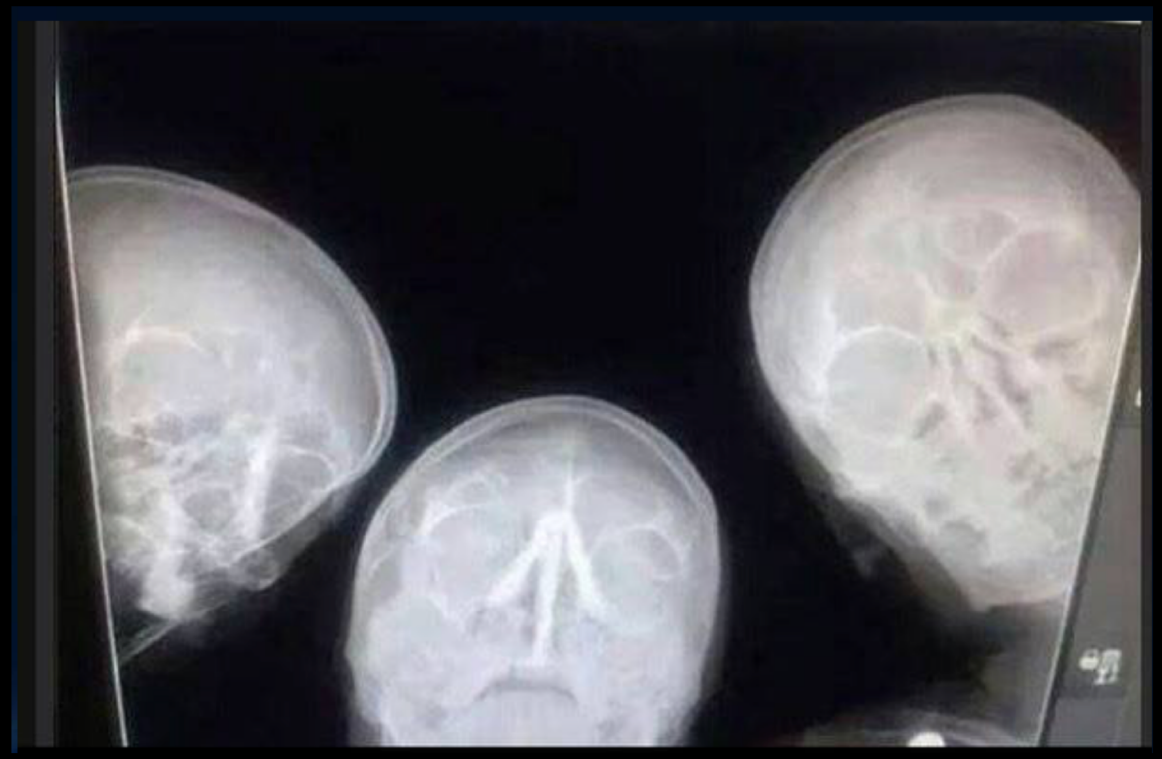
Today, the International Ultraviolet Association (IUVA) released an important document regarding UV Disinfection for COVID-19.

Currently, there is no published literature on this particular strain of the coronavirus and UVC efficacy.

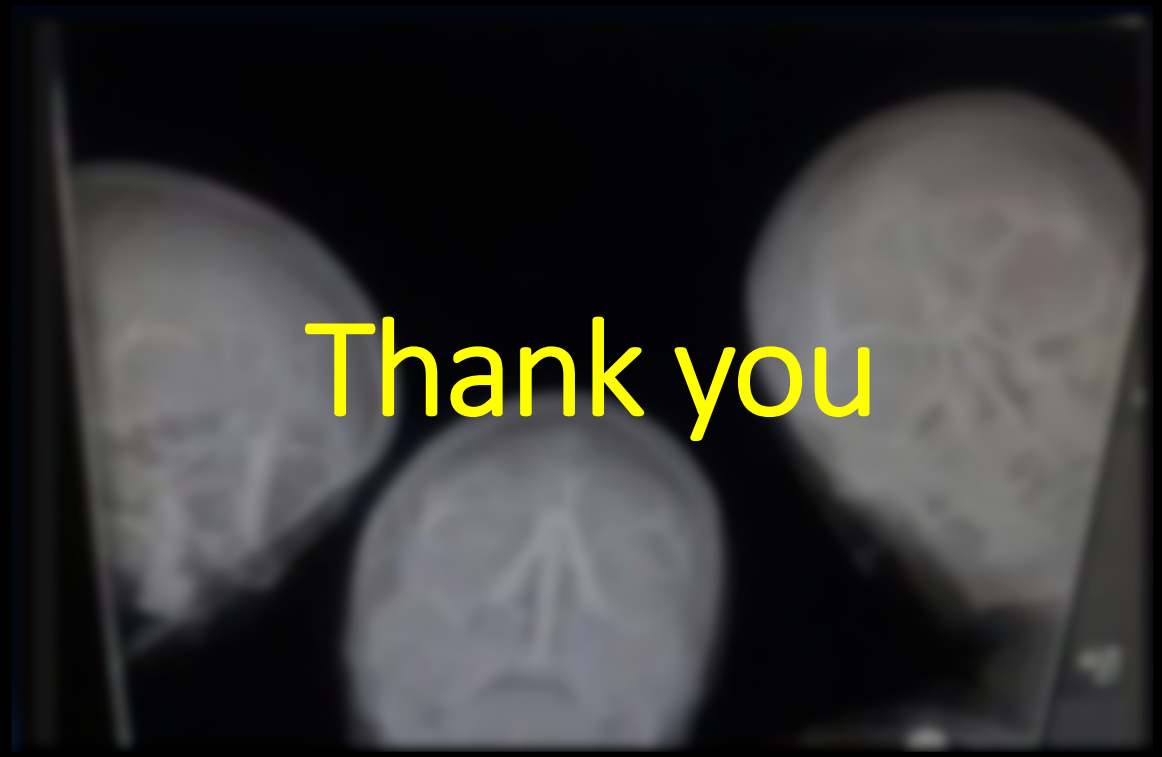
Reviewing Our Objectives

- COVID-19: Neurological Manifestations and Stroke
  - WHO Concept of Infodemic's
  - Data on Neurological Diseases and Stroke
  - Potential Mechanisms for Stroke
    - Neurotropism
    - Clotting Disorder
- A More Definite Problem: The COVID-19 Collateral Damage on the Non-COVID-19 Stroke Care
- Rationale for Standard Protection
  - Asymptomatic Patients
  - Pre-symptomatic Spread
- Anesthesia: A Change is just Different not Necessary Better…
  - Understanding the Pre-COVID data: Multicentric Non-Anesthesia Trials vs Monocentric Anesthesia Trials – Stick with what you do well…
  - ? Predictors of MAC to GA Conversion
  - Best practices
- Post-treatment Care – Now :)

When neurointerventionists take a selfie…



When neurointerventionists take a selfie…



COVID-19 Associated Coagulation Disorders

Katleen W. Chester, PharmD, BCCCP, BCGP
Olivia J. Morgan, PharmD, BCCCP, BCGP
Marcus Stroke & Neuroscience Center
Grady Health System

Disclosure Statement

The following individuals have nothing to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation:

- Katleen W. Chester, PharmD, BCCCP,BCGP
- Olivia J. Morgan, PharmD, BCCCP, BCGP

COVID-19 Associated Coagulopathy (CAC) Presentation Outline

- Epidemiology and pathogenesis
- Clinical/Laboratory presentation
- Prophylaxis
- Treatment

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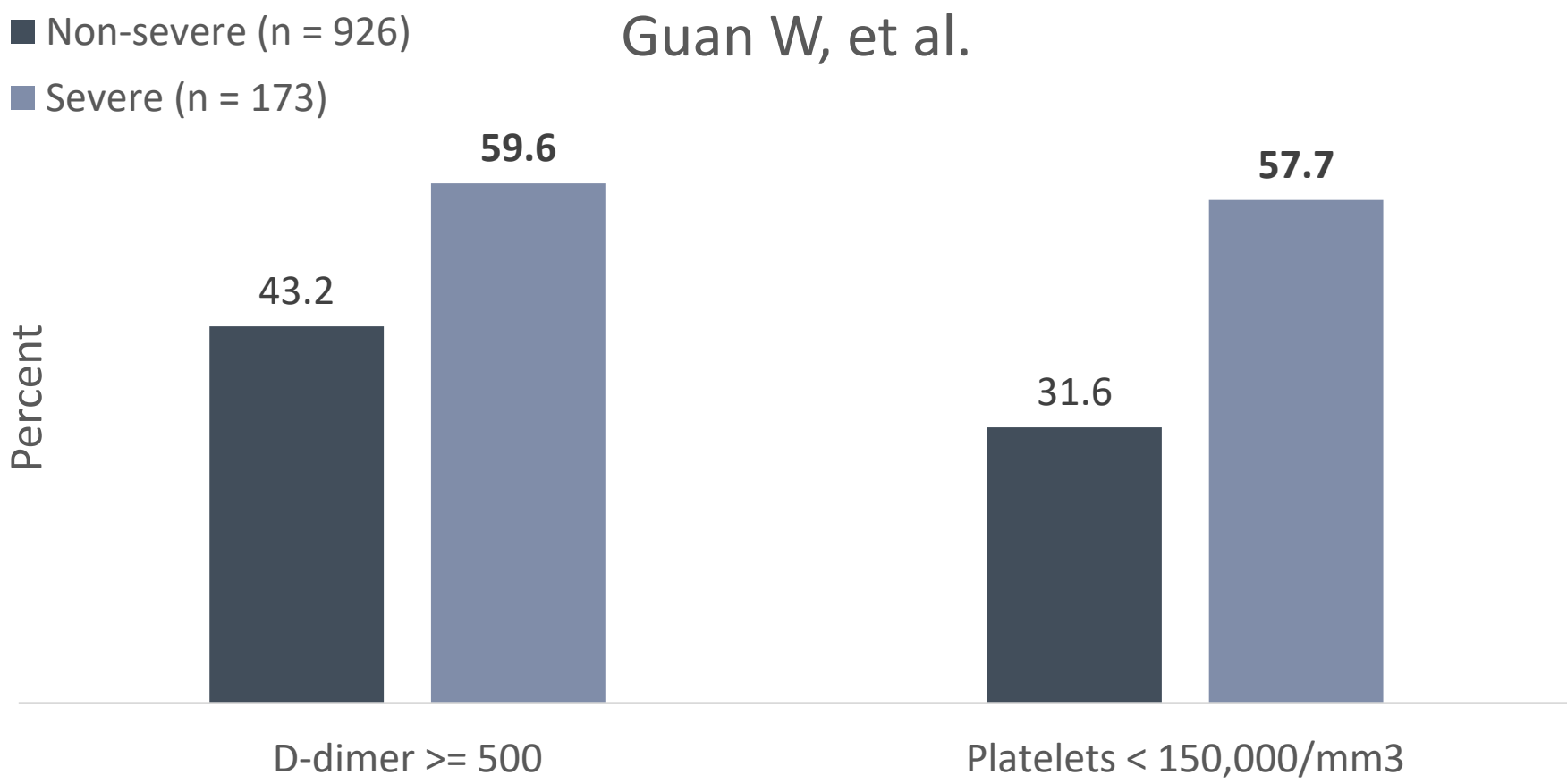
CACD = COVID-19 Associated Coagulation Disorder

Earliest Report of Coagulopathy



Elevations in D-Dimer and reductions in platelet count in majority with severe infection

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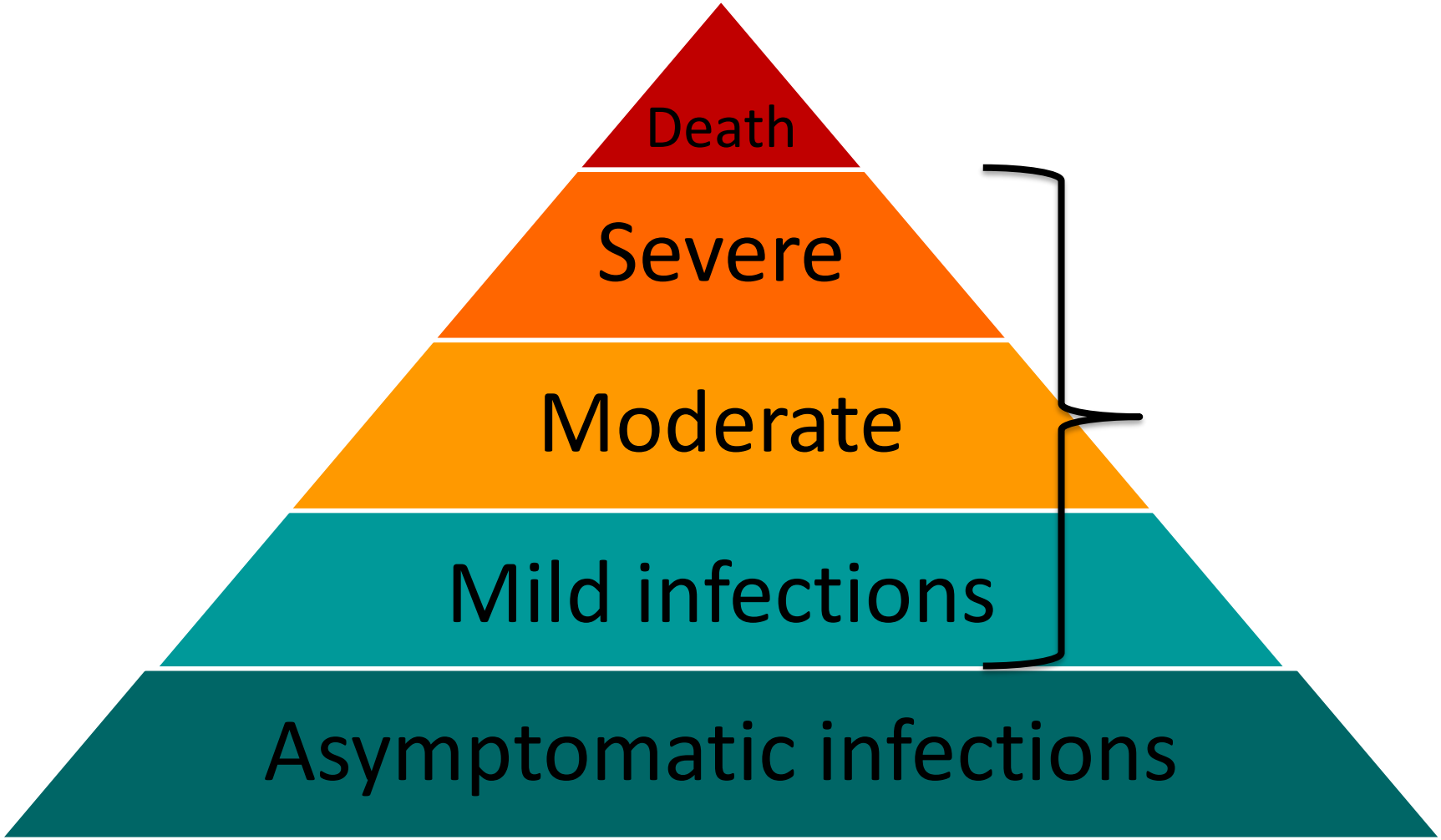
Guan W, et al. NEJM. 2020. DOI: 10.1056/NEJMoa2002032
Kollias A, et al. Br J Haematol. 2020. DOI: 10.1111/bjh.16727

Severity of COVID-19 Infection



Severe COVID-19 and VTE

China
N = 81

20 (25 %)
DVT only

- No baseline chemoprophylaxis
- PE incidence unreported
- Routine VTE screening

Netherlands
N = 184

50 (27 %)
VTE

- Prophylactic doses lower than standard in some patients
- Evaluated on clinical suspicion
- PE (n= 25, 13.5%)

France
N = 26

18 (69 %)
VTE

- Admission prophylaxis or anticoagulation
- Routine VTE screening
- PE (n= 6, 23%)

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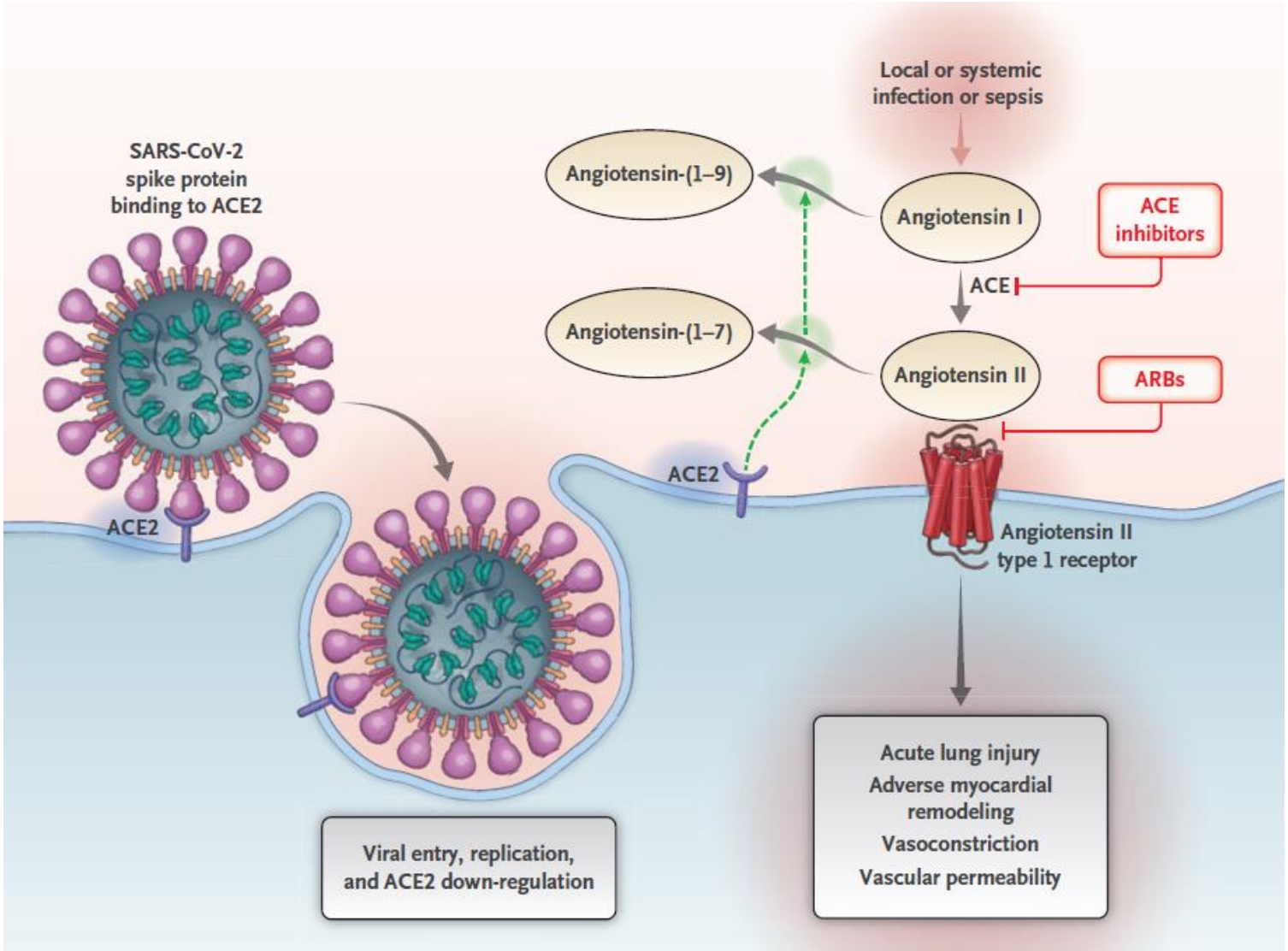
Cui et al. 2020. doi: 10.1111/JTH.14830
F.A. Klok, et al., Thrombosis Research, https://doi.org/10.1016/j.thromres.2020.04.013

Pathogenesis



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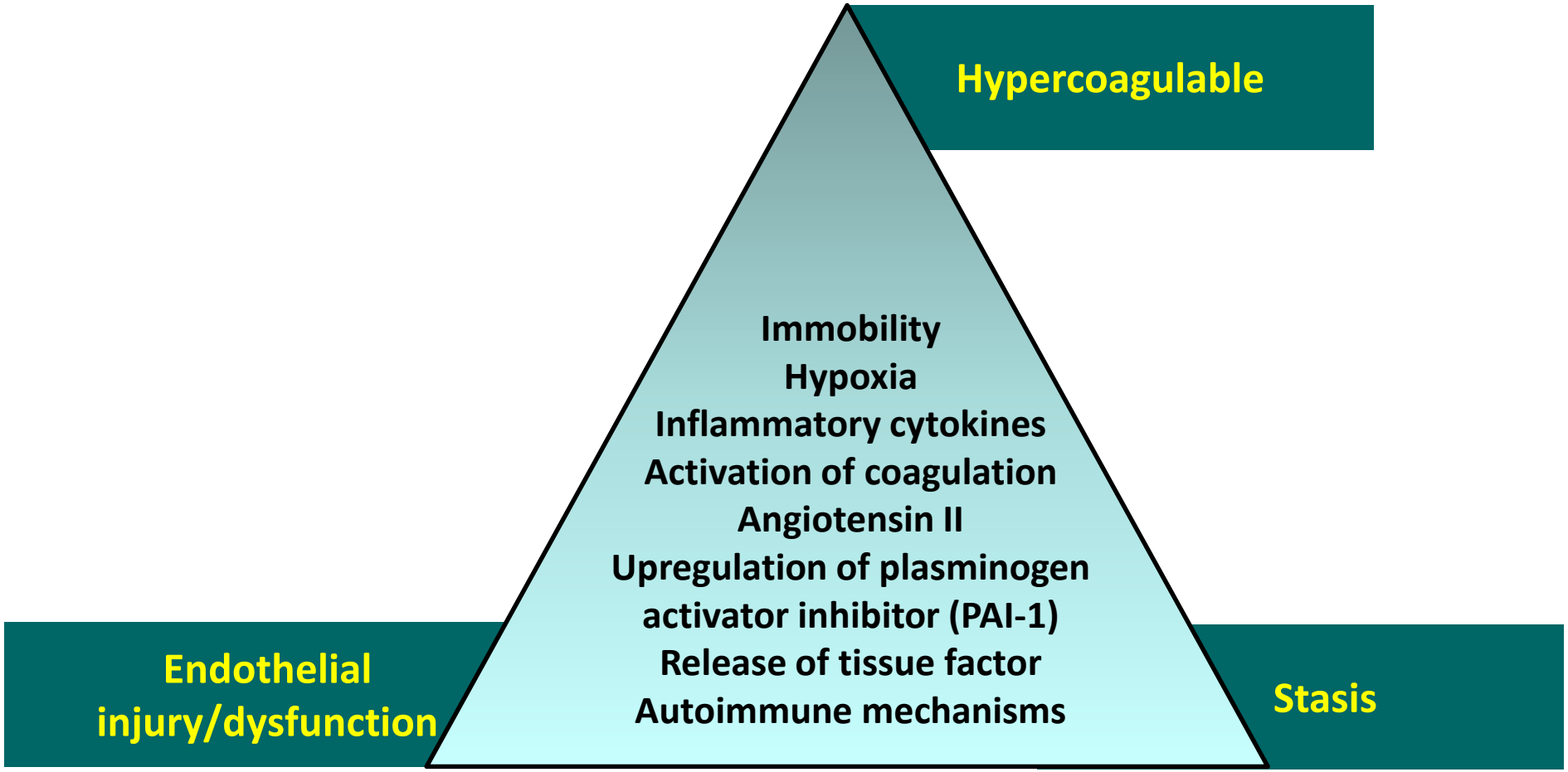
Vaduganathan M, et al. NEJM. 2020. DOI: 10.1056/NEJMsr2005760
Physiol Rev 98: 505–553. 2018

Mechanisms of Thrombosis



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Bikdeli B, et al. 2020. https://doi.org/10.1016/j.jacc.2020.04.031

Laboratory Findings

Abnormalities	Disease Severity	Mortality
• Lymphopenia • ↑ CRP • ↑ Ferritin • ↑ FDP • ↑ aPTT • Fibrinogen • **Thrombocytopenia** • **↑ D-dimer** • **↑ PT** • **↑ IL-6**	• D-Dimer* • Thrombocytopenia • PT • IL-6	• D-Dimer* • Thrombocytopenia • PT

D- dimer most strongly and consistently associated with disease severity and mortality.

Grady

Ciu et al. 2020. doi: 10.1111/JTH.14830
Bikdeli B, et al. 2020. https://doi.org/10.1016/j.jacc.2020.04.031; Cohoon et al. 2020. doi: 10.1002/rth2.12358.

Laboratory Findings

	Non-survivor (n = 54)	Survivor (n = 137)	*P* value
Prothrombin Time (PT) > 16s	7 (13%)	4/128 (3 %)	< 0.0001
D-Dimer > 1000 ng/mL	**44 (81 %)**	28/118 (24 %)	< 0.0001

	Non-survivor (n = 54)	Survivor (n = 137)	*P* value
Platelets < 100 x 10^9/L	11 (20%)	2 (1 %)	< 0.0001
Platelets count, x 10^9/L	**165.5 (107 – 229)**	220 (168 – 271)	< 0.0001

Zhou F, et al. Lancet. 2020. DOI:https://doi.org/10.1016/S0140-6736(20)30566-3
Tang N, et al. J Thromb Haemost. 2020. 18:844-847

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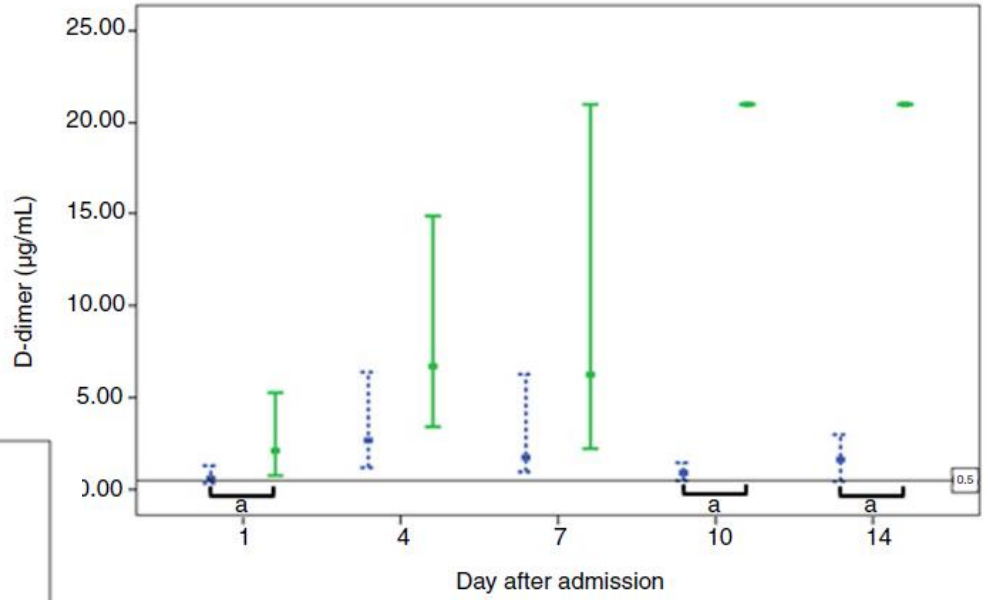
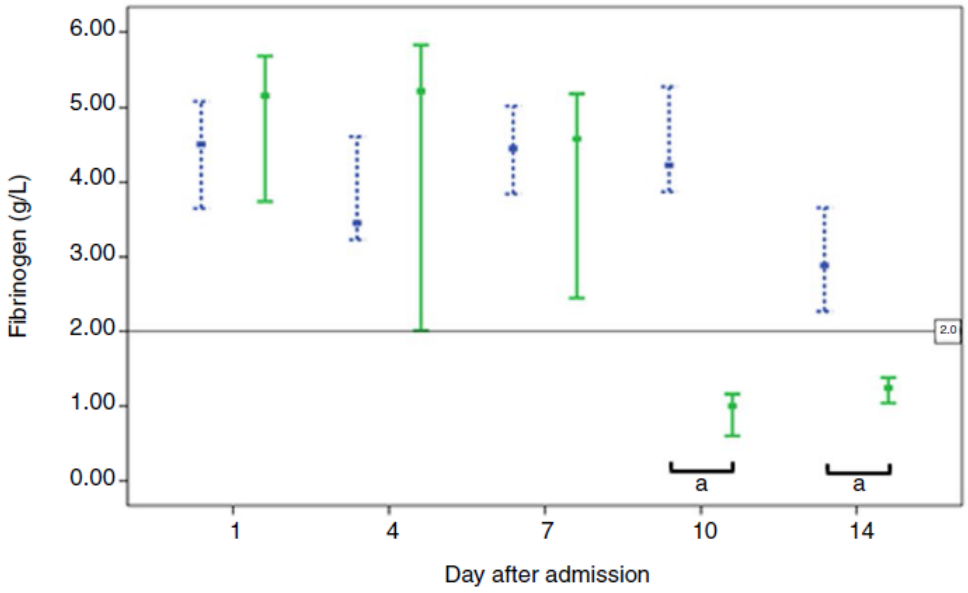
Laboratory Findings

D-Dimer and Fibrinogen





Tang N, et al. J Thromb Haemost. 2020. 18:844-847

Comparison of CAC with SIC and DIC

Item	Score	SIC Range	DIC Range
Platelet count (-10^9/L)	2 1	< 100 100 to < 150	< 50 50 - 99
FDP / D-Dimer	3 2	- -	Strong increase Moderate increase
PT Prolongation (INR for SIC)	2 1	> 1.4 > 1.2 to 1.4	≥ 6 s 3 to 6 s
Fibrinogen (g/mL)	1	-	< 100
SOFA score	2 1	≥ 2 1	- -
Total score for DIC or SIC		**≥ 4**	**≥ 5**

CAC = COVID associated coagulopathy
FDP = fibrin degradation products
DIC = disseminated intravascular coagulopathy
SIC = sepsis induced coagulopathy

Zhou F, et al. Lancet. 2020. DOI:https://doi.org/10.1016/S0140-6736(20)30566-3
Tang N, et al. J Thromb Haemost. 2020. 18:844-847
Connors JM, Levy JH. [published online ahead of print, 2020 Apr 27]. *Blood*. 2020;blood.2020006000. doi:10.1182/blood.2020006000

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Comparison of CAC with SIC and DIC

Item	Score	SIC Range	DIC Range	CAC Findings
Platelet count (-10^9/L)	2	< 100	< 50	**100 - 200**
	1	100 to < 150	50 - 99	
FDP / D-Dimer	3	-	Strong increase	**D-dimer elevated (>2000-3000)**
	2	-	Moderate increase	
PT prolongation (INR for SIC)	2	> 1.4	≥ 6 s	**Prolonged 3 - 6 s days 10, 14**
	1	> 1.2 to 1.4	3 to 6 s	
Fibrinogen (g/mL)	1	-	< 100	**Normal-elevated: typically > 100**
SOFA score	2	≥ 2	-	
	1	1	-	
Total score for DIC or SIC		**≥ 4**	**≥ 5**	

CAC may mimic DIC, but atypical of SIC

- Less prominent thrombocytopenia
- Less consumption of coagulation factors
- Normal or increased fibrinogen

CAC = COVID associated coagulopathy
FDP = fibrin degradation products
DIC = disseminated intravascular coagulopathy
SIC = sepsis induced coagulopathy

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Zhou F, et al. Lancet. 2020. DOI:https://doi.org/10.1016/S0140-6736(20)30566-3
Tang N, et al. J Thromb Haemost. 2020. 18:844-847
Connors JM, Levy JH. [published online ahead of print, 2020 Apr 27]. *Blood*. 2020;blood.2020006000. doi:10.1182/blood.2020006000

CACD Laboratory Monitoring

Non-critically ill patients

- Daily CBC
- D-dimer

Critically-ill patients

- Daily CBC
- DIC panel
- [Bi-weekly MOCHA panel and PAI-1]

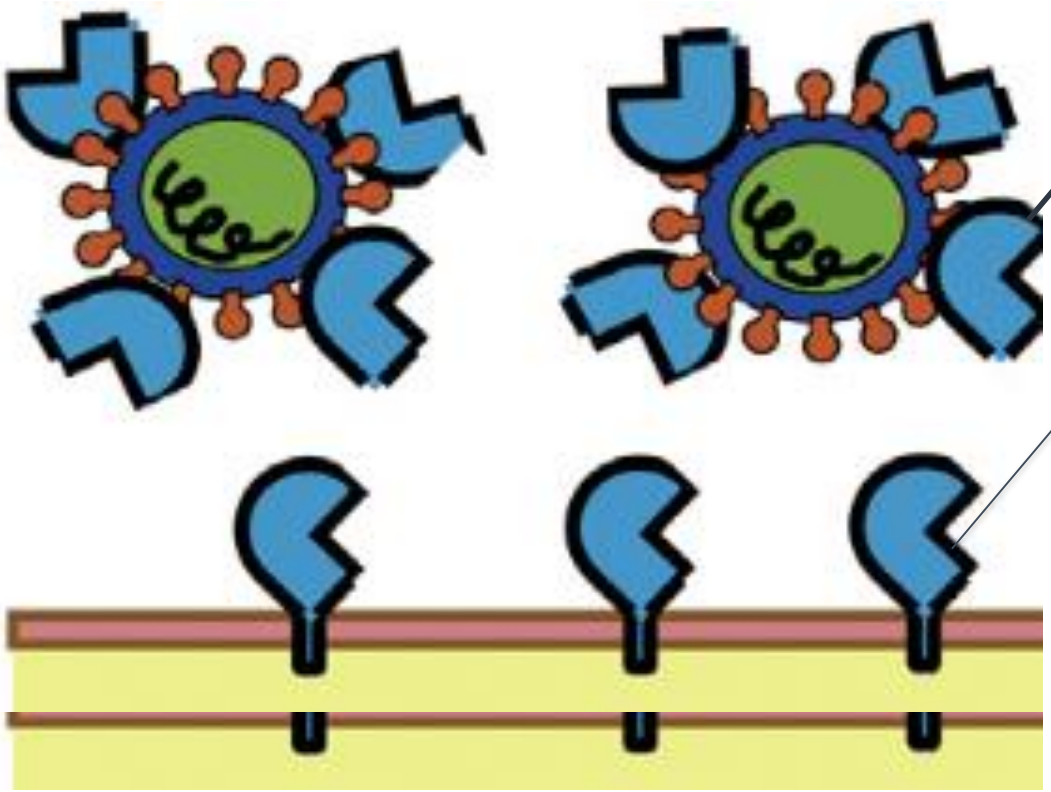
Markers of inflammation

- Consider IL-6 if significant change in clinical condition

DIC panel: PT, aPTT, fibrinogen, d-dimer; PAI-1: Plasminogen activator inhibitor-1
MOCHA: Markers of Coagulation and Hemostasis Activation Panel (Fibrinogen Activity, Prothrombin Fragment 1+2, Thrombin/Antithrombin Complex)

https://www.hematology.org/covid-19/covid-19-and-coagulopathy. Accessed may 4, 2020.
Thachil J. J Thromb Haemost. 2020.

Heparin and SARS-CoV 2



Heparin molecule bound to spike protein

ACE2 surface receptor/enzyme

Heparin reduces proinflammatory proteins such as IL-6

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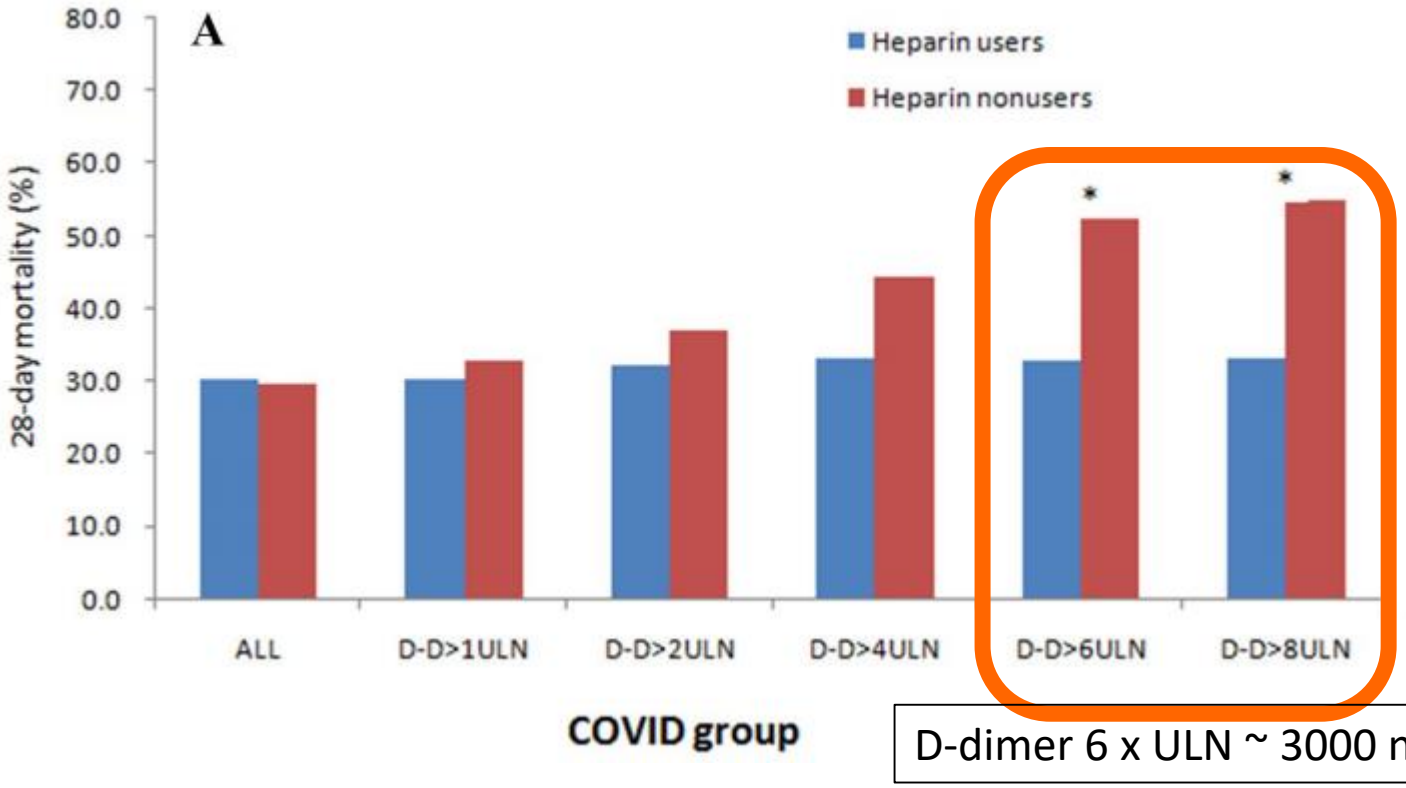
Image adapted from: Monteil et al. Cell.2020. https://doi.org/10.1016/j.cell.2020.04.004
Mycroft-West et al. 2020. https://doi.org/10.1101/2020.02.29.971093; Cohoon et al. 2020. doi: 10.1002/rth2.12358.

Heparin and Mortality



D-dimer 6 x ULN ~ 3000 ng/mL

Heparin or LMWH mostly in prophylactic doses

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Yin, S et al. J Thromb Thrombolyisis. 2020. doi: 10.1007/s11239-020-02105-8.

Management Strategies for CACD

- Quick identification of patients at increased risk for thromboembolism
- Prompt initiation of VTE prophylaxis and frequent laboratory monitoring
- Escalation of prophylactic intensity in patients with more severe coagulopathy
- Escalation of anticoagulation in patients with suspected VTE

CACD Patient Stratification

All patients should receive anticoagulation unless contraindicated

LOW RISK	MEDIUM RISK	HIGH RISK
Group A	**Group B**	**Group C**
Patients who do not have a clear indication for full dose anticoagulation	Patients at increased risk for VTE	High suspicion or confirmed VTE
D-Dimer < 6 times ULN (< 3,000 ng/mL)	D-Dimer > 6 times ULN (> 3,000 ng/mL)	

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Thachil J. J Thromb Haemost. 2020.

Group A: Prophylactic Anticoagulation

LMWH should be considered as first line agents in the absence of contraindications:

- Active bleeding
- Platelet count < 25 x 10^{9}/L
- Severe renal impairment
- Invasive procedures within 12 hours

Enoxaparin doses up to 0.5 mg/kg SQ day may be considered

- On average, patients will requires enoxaparin doses between 30 – 50 mg SQ daily
- Patients who cannot receive LMWH may get UFH 5000 units SQ 8 - 12 hours or SCDs

Routine VTE prophylaxis guidance in stroke patients should be observed

LMWH: Low Molecular Weight Heparin, UFH: Unfractionated Heparin, SCD: Sequential Compression Device

Thachil J. J Thromb Haemost. 2020.
GHS Hematology; Bikdeli B. J Am Coll Cardiol. 2020

Grady

Group B: Intermediate Anticoagulation

Elevation in d-dimer levels is a common finding in patients with COVID-19, and may correlate with detection of VTE

- Does not currently warrant routine investigation for acute VTE in absence of clinical manifestations or other supporting information

Clinicians are considering intermediate-dose anticoagulation in patients with d-dimer > 6 times ULN (> 3,000 ng/L)

Enoxaparin 1 mg/kg/day SQ to target Anti-Xa levels 0.3 - 0.5

- Anti-Xa levels should be checked 4 hrs after 3rd dose; recheck after 3rd dose with every dose change, or with significant change in clinical status
- Low intensity UFH infusions targeting similar anti-xa levels should be considered in patients unable to receive LMWH

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Thachil J. J Thromb Haemost. 2020.
GHS Hematology; Bikdeli B. J Am Coll Cardiol. 2020

Group C: Therapeutic Anticoagulation

Patients with confirmed or suspected VTE

Enoxaparin 1 mg/kg SQ Q12 hours should be considered first line to achieve Anti-Xa goal of 0.6 - 1

- High intensity UFH infusions targeting similar anti-xa levels should be considered in patients unable to receive LMWH

Heparin resistance has been reported due to reduced anti-thrombin levels and other procoagulant factors

- Failure to achieve goal Anti-Xa levels despite adequate doses (UFH > 35,000 units/ 24 hrs or LMWH > 300-500units/kg/ day) should prompt ordering an anti-thrombin level and hematology consult
- May warrant use of direct thrombin inhibitor (DTI) while inpatient and DOAC upon discharge

Patients with COVID-19 and an alternative indication for anticoagulation (atrial fibrillation, mechanical heart valve) should be converted to LMWH or UFH in the acute setting

LMWH: Low Molecular Weight Heparin, UFH: Unfractionated Heparin
DOAC: Direct Oral Anticoagulant

Thachil J. J Thromb Haemost. 2020.
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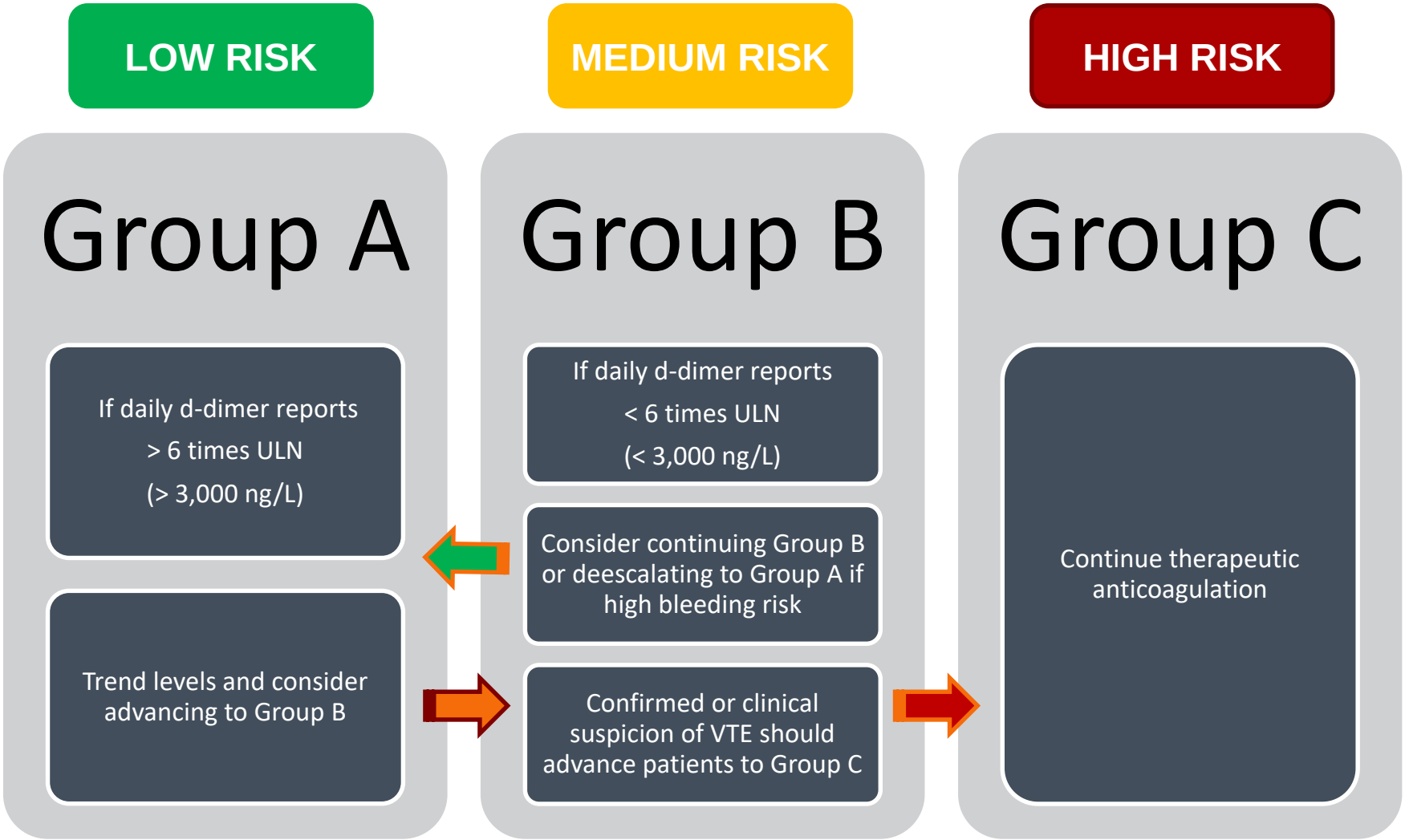
Transitioning Between Treatment Groups



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COVID-19 Associated Coagulopathy (CAC)

LMWH prophylaxis may decrease thrombin generation

- Long acting antiplatelet therapies should be discontinued unless benefit outweighs risk

There is no evidence that correction of laboratory parameters with blood products will improve outcomes

In a patient with CAC who is *actively* bleeding:

- Transfuse platelets if the platelet count is less than 50 x 10^9/L
- Fresh frozen plasma if the INR is above 1.8
- Order fibrinogen concentrate or cryoprecipitate if the fibrinogen level is less than 1.5 g/L

The hemostatic effectiveness of tranexamic acid (TXA) is unknown in this setting and is not recommended

LMWH: Low Molecular Weight Heparin

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Anticoagulant Dosing Considerations

Obesity

- Group A
  - Enoxaparin 0.5 mg/kg SQ daily (Max: 80 mg SQ daily)
  - UFH SQ every 8 hours should be considered
- Group B and C
  - Consider enoxaparin 0.8 mg/kg/day to avoid supratherapeutic anti-xa levels

Pregnancy

- Concomitant hypercoagulable state
- Can contribute to elevated d-dimers
- Utilize clinical judgment when escalating anticoagulation
- LMWH is the drug of choice
- DOAC therapy has not been formally evaluated

Heparin Induced Thrombocytopenia (HIT)

- Consider fondaparinux for prophylactic and full anticoagulation
  - Requires adjustments for weight and renal impairment
- Alternatively, direct thrombin inhibitors can be considered
- Consider hematology consult

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Tissue Plasminogen Activator (t-PA)

Proposed as a salvage treatment for COVID-19 patients with decompensating respiratory function when mechanical ventilation or extracorporeal membrane oxygenation (ECMO) is not available

Currently, there is limited clinical experience and no clinical trial data to promote routine use in COVID patients with acute respiratory distress syndrome (ARDS)

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Discharge Considerations

Extended prophylaxis with LMWH or direct oral anticoagulants (DOACs) can reduce the risk of VTE

- Limited data supports use of anticoagulation at discharge in all patients admitted for COVID-19, but optimal duration is unknown

Patients with confirmed VTE should receive a minimum of 3 months of therapeutic anticoagulation

Decision to use thromboprophylaxis at discharge should consider the individual patient's VTE risk factors

- Financial feasibility, compliance, laboratory monitoring, drug interactions, bleeding risk, immobility
- VKA or aspirin therapy can be considered in patients not appropriate for LMWH or DOAC therapy

LMWH: Low Molecular Weight Heparin, VTE: Venous Thromboembolism
VKA: Vitamin K Antagonist

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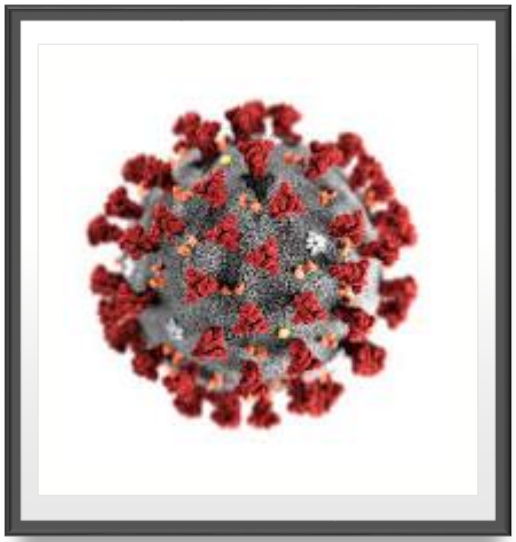

With COVID-19, what we do today may be history tomorrow. We must continuously learn as we treat patients with this disease

Select Resources

- American Heart Association/American Stroke Association
- International Society of Thrombosis and Hemostasis
- American Society of Hematology
- Journal of the American College of Cardiology
- National Blood Clot Alliance
- American Society of Health-System Pharmacists

QUESTIONS?

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On behalf of the American Heart Association/American Stroke Association, thank you.

The views expressed in this webinar do not necessarily reflect the official policy or position of the American Heart Association, American Stroke Association, or the Institutions of the Speakers. For more information about COVID-19 please visit https://professional.heart.org/COVID-19 or engage with us via social media using the hashtag #AHACovid19