

# COVID-19 and Cerebrovascular Disease

---

**Dr. Sairah Bashir**

Lead Physician

**Dr. Saqib A. Chaudhry**

Research Stroke Director

**Dr. Laith Altaweel**

Stroke Director

INOVA Neuroscience and Spine Institute  
Fairfax, Virginia

# Disclosures

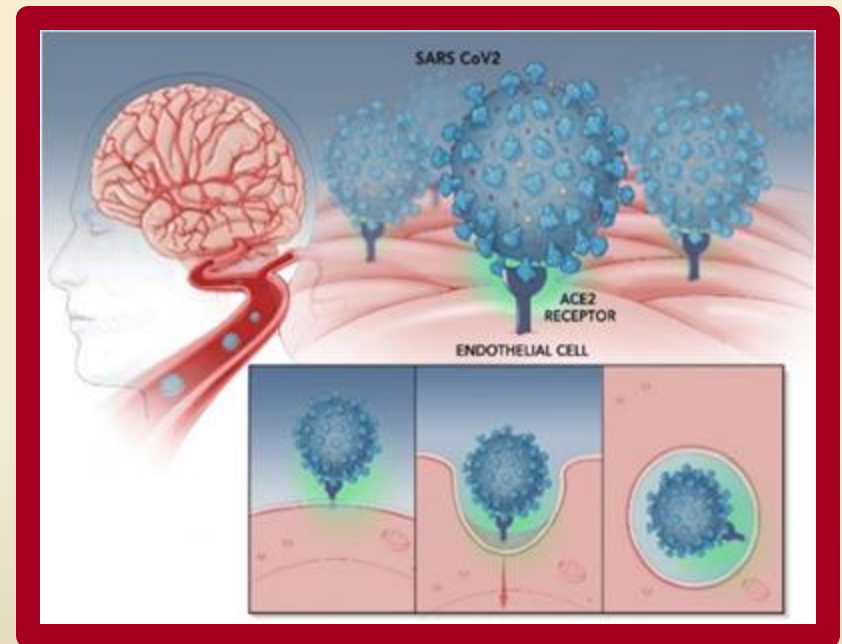
None

# Pathophysiology

COVID-19 infects the host using the angiotensin converting enzyme 2 (ACE2) receptor

-Systemic inflammatory and prothrombotic state

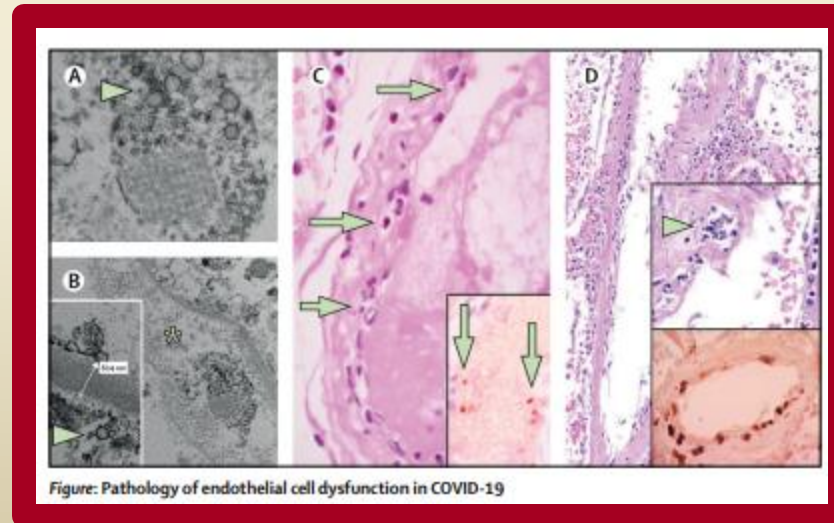
-Endothelial dysfunction related to ACE2 depletion



Klok, *Thromb Res*, 2020, Hess, *Trans Stroke Res*, 2020

# Pathophysiology

- ACE2 receptor: lung, kidneys, heart, intestine and endothelium of various organ
- Vascular endothelium : an active paracrine, endocrine, and autocrine organ that is indispensable for the regulation of vascular tone and the maintenance of vascular homeostasis



# Typical Symptoms and Severity Are Pulmonary

## Asymptomatic

- up to 90% of infected subjects are asymptomatic

## Symptomatic patients

- 81% mild (no or mild pneumonia)

- 14% severe (dyspnea, hypoxia)

- 5% critical (resp failure, shock , multiorgan failure)

Overall case fatality rate 2.3.%

Neurological manifestation are less defined

# Neurological Manifestations

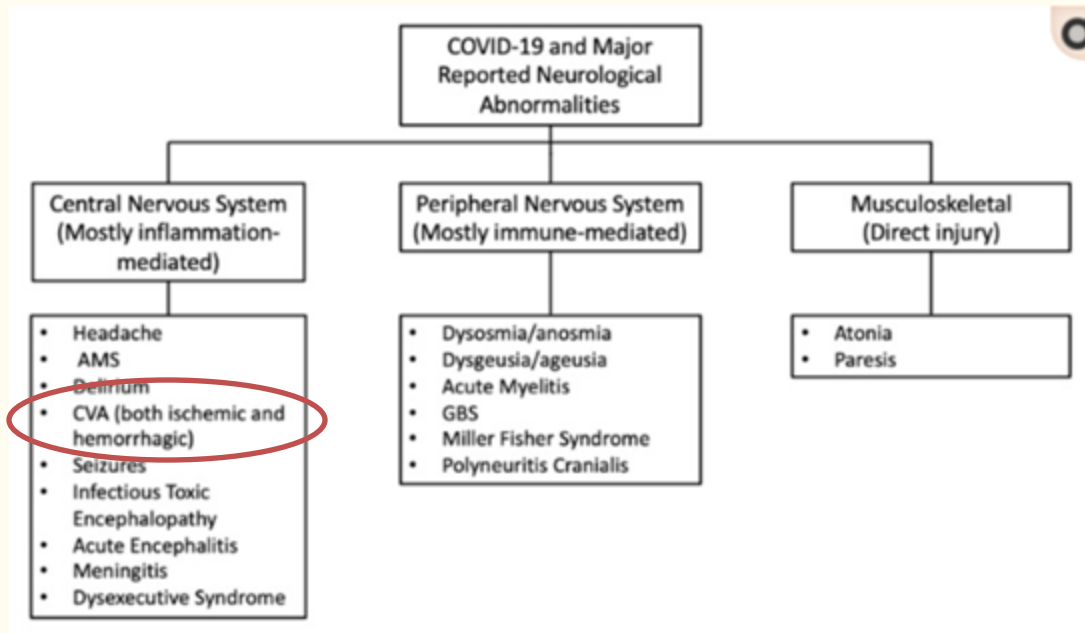


Figure 1

Summary of major neurological abnormalities in COVID-19.

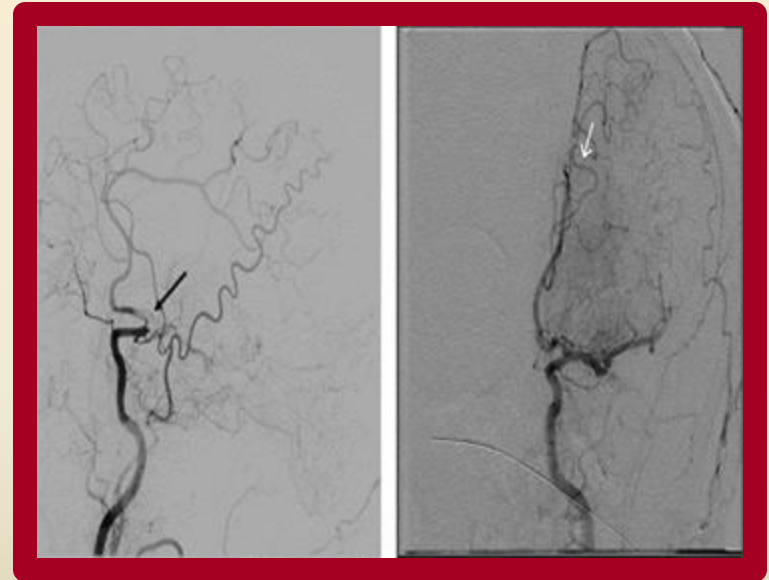
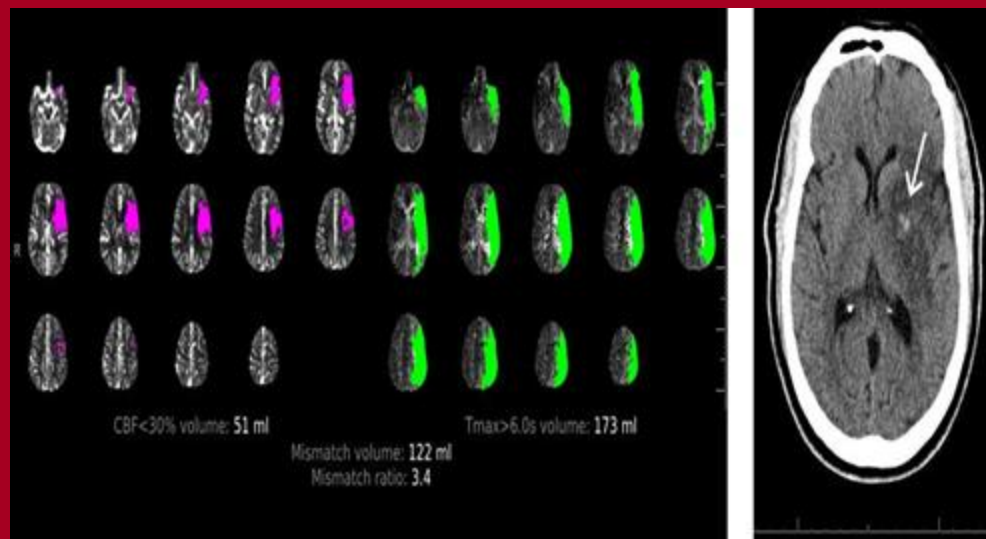
# Stroke Incidence In Hospitalized COVID-19 Patients

- Wuhan, China (n=214)
  - Severe respiratory infection in 41%
  - Ischemic stroke - non-severe(0.8%) and severe(6%) COVID-19.
  - Intracerebral hemorrhage (0.5%)
  - Cerebral venous sinus thrombosis (0.5%)
- Netherlands (n=184 ICU patients)
  - Ischemic stroke (2.7%)
- New York (n=3000+ hospitalized)
  - Ischemic stroke (0.8%, of whom 65% LVO)
  - Intracerebral hemorrhage (0.2%)
- Risk factors
  - Traditional risk factors (older age, hypertension, diabetes, prior cerebrovascular disease)
  - Elevated C-reactive protein, elevated D-dimer
  - High acuity of illness
- True incidence likely higher as neurological assessment challenging, or limited in critically ill patients

*Li Preprint in Lancet, 2020,; Aggarwal, Int J Stroke, 2020; Mao, JAMA Neurology, 2020 ; Lodigiani, Thromb Res, 2020; Klok, THrombosis Research , 2020; Yaghi Et al., Stroke 2020.*

# Acute Stroke due to LVO and COVID19

Case reports have suggested that COVID-19 infection may predispose to large-vessel occlusion strokes in young patients



*Beyrouti, J Neurol Neurosurg Psychiatry, 2020; Oxley, NEJM, 2020; González-Pinto, .*

*Eur J Neurol, 2020; Valderrama, Stroke, 2020; Viguier, J Neuroradiol, 2020*



# Mechanical Thrombectomy In Patients Infected With COVID-19 In France

- Small series of 37 Acute LVO patients who underwent mechanical thrombectomy
  - 10 were COVID-19 positive
    - 3 of 10 had stroke during hospitalization
- Compared to non-COVID LVO Controls(N=19):
  - **Younger** (median age 60 vs 72) and predominantly male (80% vs 49%)
  - Risk factors - DM(40 vs 22%) and atrial fibrillation (10 vs 30%)
  - Median COVID-19 symptoms to stroke onset 6 day(range 2-18)
    - 50% fever, respiratory symptom 70%(mostly **mild**)
    - **Higher D-Dimer** levels as compared to COVID-19 patients without stroke\*
    - **CT chest opacities 100% vs 0%**
  - Median admitting NIHSS 22 vs 15
  - Median time of onset to imaging: 119 vs 177 min
  - **ASPECTS 5 vs 7**
  - Occlusion site: Proximal (ICA/proximal MCA) and multi-territory (50 vs 7%)

# LVO In setting of COVID-19 Continued: Treatment and Outcomes

- Intravenous tissue plasminogen activator:
  - Administered to 50 vs 50%
  - Onset-to-tPA 175 vs 175 min
- Mechanical thrombectomy
  - Onset-to-recanalization 302 vs 392 min
  - Successful recanalization 90 vs 88 %

## Outcomes:

- Dramatic neurological improvement: 0 vs 22%
- Malignant cerebral edema: 20 vs 7 %
- In hospital mortality : 60 vs 11%
- **Early cerebral re-occlusion : 40 vs 0%**
- **Summary: younger, more severe neurological symptoms and larger strokes on presentation, with more proximal occlusion, and worse outcomes; similar reports from NYC and London.**

# Management of Acute Stroke in COVID-19

Acute treatment: Alteplase, Thrombectomy

-Unless contraindicated, TPA/MET should be offered all suspected patients

Secondary prevention: Antiplatelet, Anticoagulation\*\*\*

-Recommend single or DAPT based on existing clinical guidelines.

Other Therapies such : Remdesivir, steroids , Interleukin-6 Inhibitors (tocilizumab), hydroxychloroquine, ace inhibitors, interferon beta 1b, may have therapeutic efficacy in COVID19, particularly with non-neurologic manifestations.

# Should COVID-19 Associated Ischemic Strokes Patients Receive Anticoagulation?

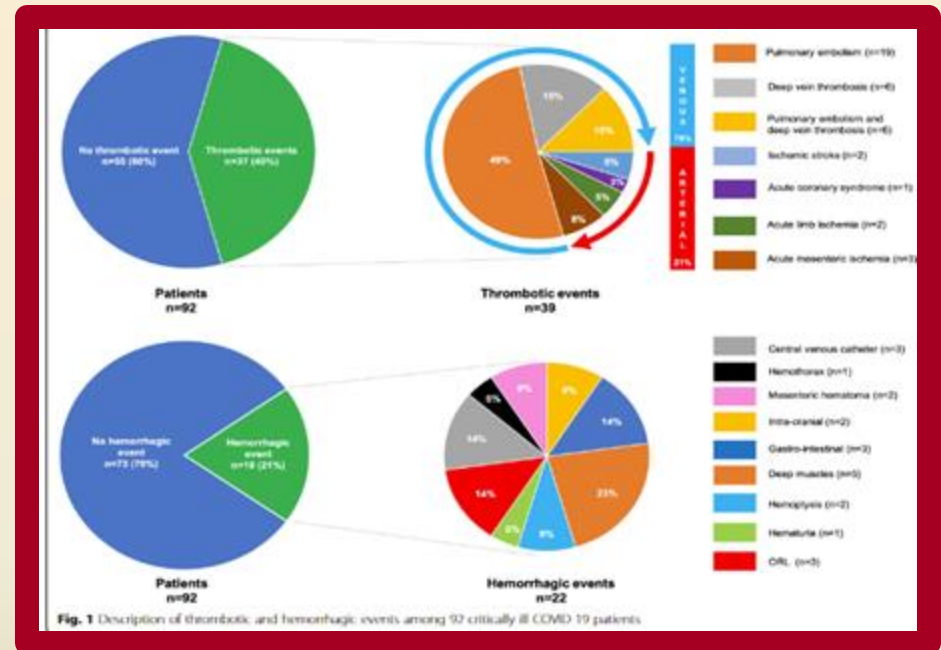
- Reasons to administer
  - COVID-19 associated with a high rate of thromboembolism, especially in sicker patient with higher D-Dimer levels
  - For LVO patients - potentially higher-reocclusion rate
- Reason not to administer
  - Efficacy in COVID-19 patients unclear
  - Potentially high risk for bleeding(see next slide).
  - AC in stroke patients typically considered risky in non-COVID-19 patients

# Thromboembolism in COVID-19

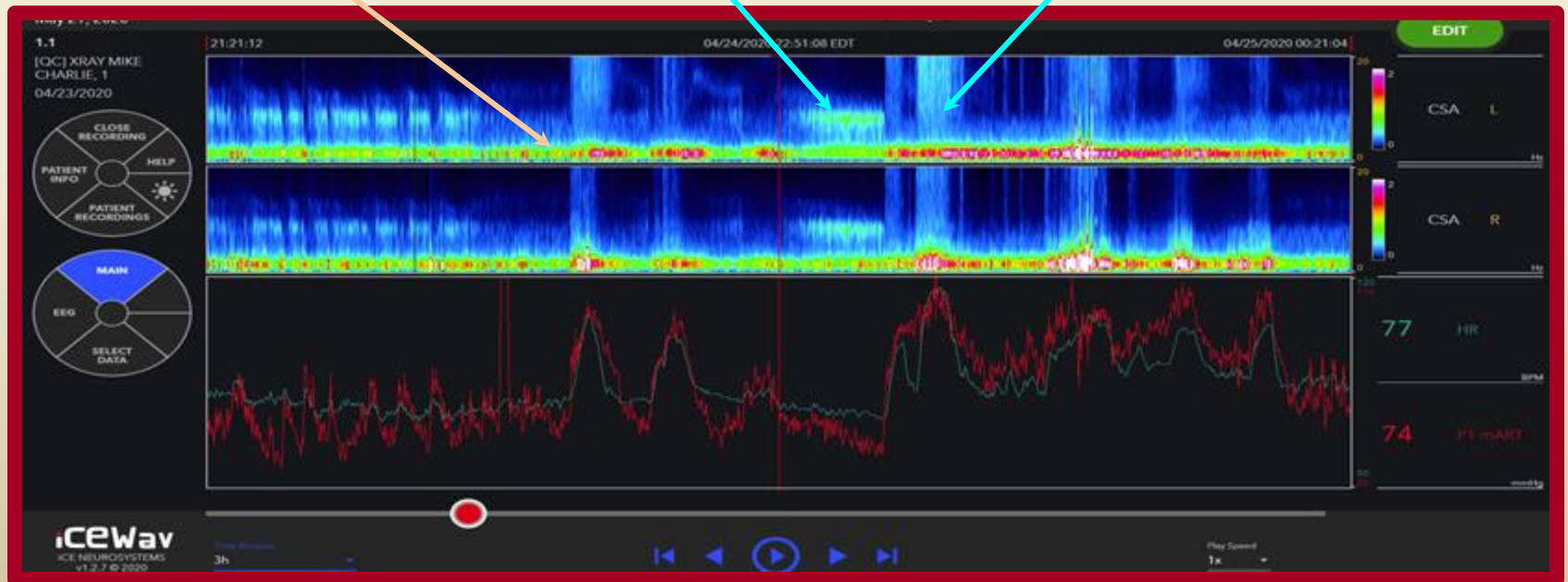
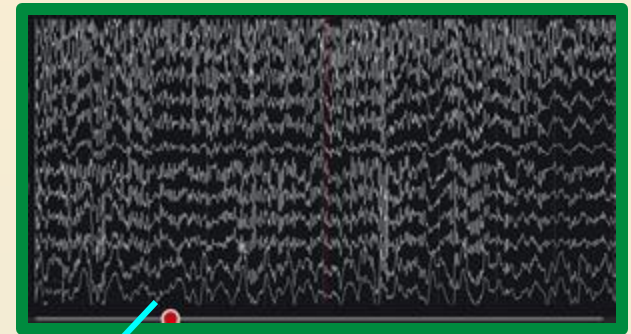
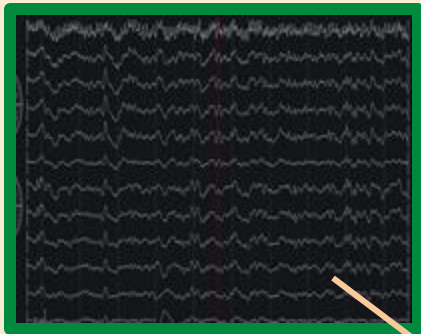
- 3 Centers in the Netherlands, 184 COVID-19 ICU patients
- All patients on at least standard dose thromboprophylaxis
  - 10% on therapeutic anticoagulation on admission to ICU
- 57% cumulative incidence of thrombotic complications
  - 87% PE
  - 4% other venous thromboembolic events
  - 7% stroke (2.7% of total ICU population)
- Thromboembolism associated with higher mortality
- True incidence of stroke is likely higher as an informative neurologic exam and brain imaging rarely done

# Thrombotic Events and Bleeding in Critically Ill Covid Patients

- Thromboembolism
  - High incidence
  - Predominantly venous
  - Higher D-dimer levels 54% were already on full dose AC
- Treatment with AC
  - 21% significant bleeding
  - Higher mortality (49 vs 36%)



# qEEG



# Impact of COVID-19 on Hospital Admissions for Stroke

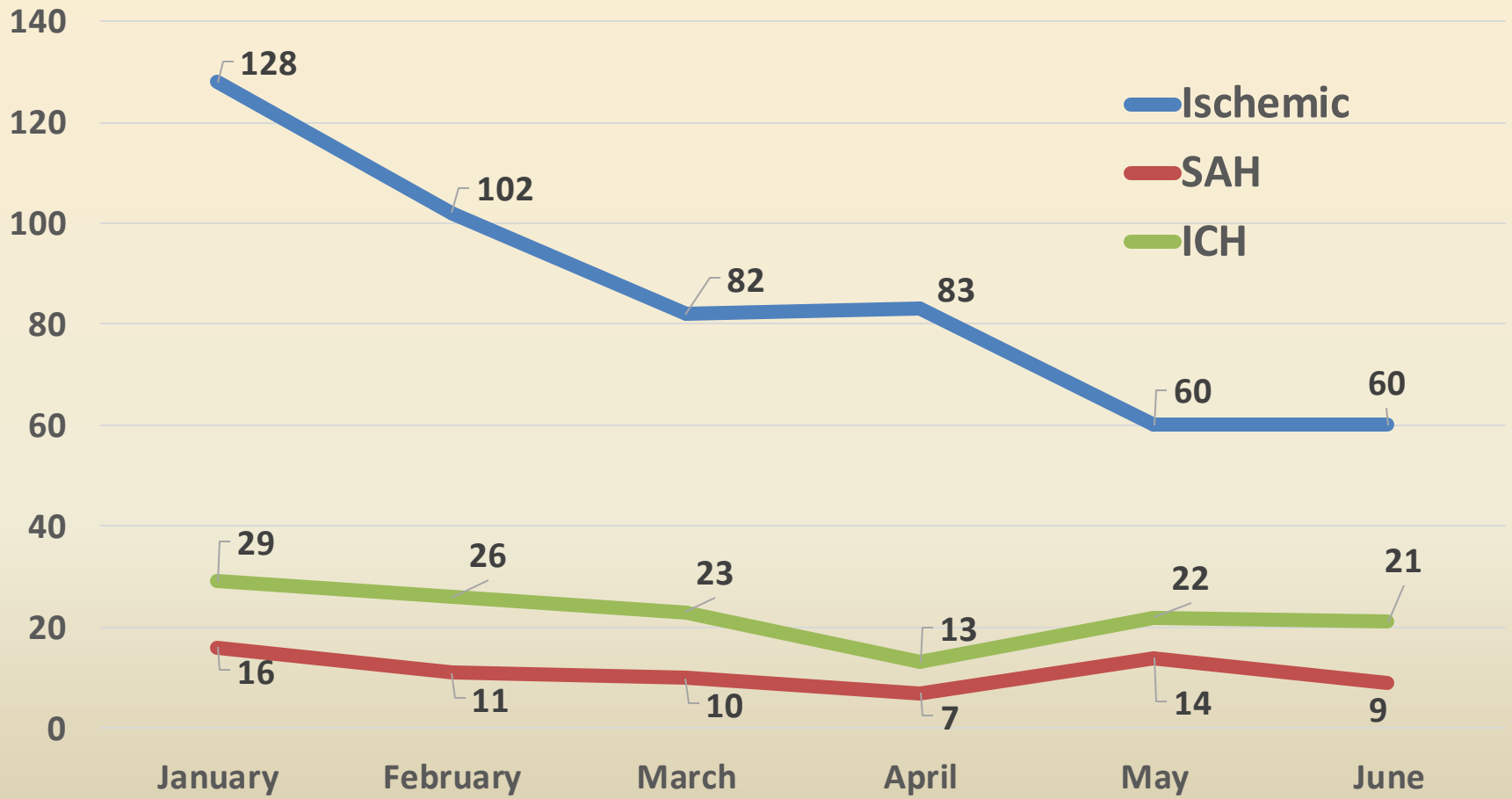
## Analysis from INOVA Hospital

	COVID testing not performed	COVID (-)	COVID (+)
	574	129	13
Age	67 ± 15	70 ± 16	<b>73 ± 15</b>
Gender (male)	55 %	54 %	<b>85 %</b>
Ischemic stroke	413 (72%)	94 (73%)	<b>8 (61%)</b>
ICH	105 (18%)	26 (20%)	3 (23%)
SAH	56 (10%)	9 (7%)	2 (15%)



# Impact of COVID-19 on Hospital Admissions for Stroke

## Analysis from INOVA Hospital



# Impact of COVID-19 on Hospital Admissions for Stroke

## Analysis from INOVA Hospital

### Ischemic stroke

	Pre-COVID era Jan - Feb	COVID era March -June	
Age	70.2 ± 14	70.3 ± 15	P=0.25
Gender (female)	47.3 %	43.5 %	P=0.37
Mean NIHSS	7.0	7.9	P=0.23
% of IV thrombolytics	6.1 %	11.3 %	<b>P=0.04</b>
% of thrombectomy	9.1 %	18.6 %	<b>P=0.0023</b>

# Impact of COVID-19 on Hospital Admissions for Stroke

## Analysis from INOVA Hospital

### ICH and SAH

	Pre-COVID era Jan - Feb	COVID era March -June
Age	64.3	63.0
Gender (female)	47 %	43%
Mean ICH Score	1.50	1.53
Mean Hunt Hess	2.30	2.27

# Impact of COVID-19 on Hospital Admissions for Stroke

## Analysis from INOVA Hospital

### Discharge disposition

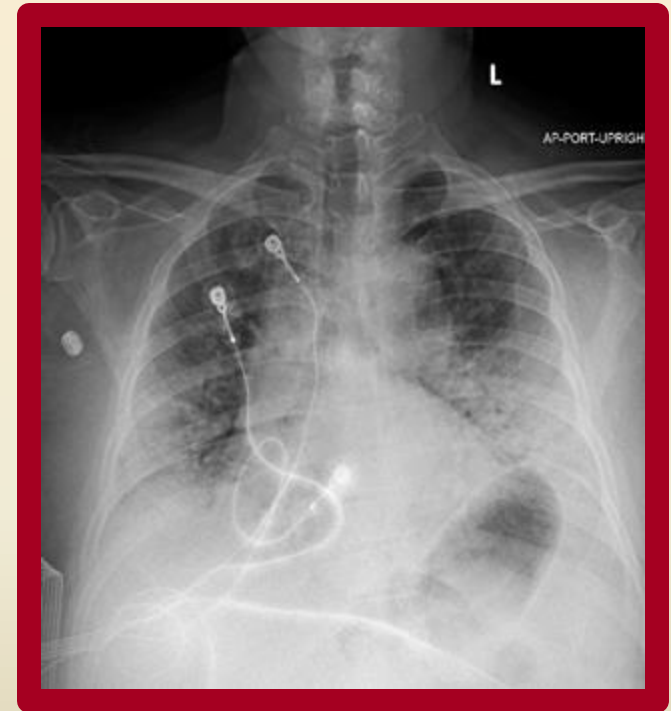
	Pre-COVID era Jan - Feb	COVID era March -June
Home discharges	45.5 %	49.7 %
Short term facility	28.2 %	29.8 %
Long term facility	14.4 %	11.1 %
In hospital mortality	11.8 %	9.2 %

# IFMC-Case

61 y.o. presented to ED with dry cough, headache, subjective fevers, chills on 5/11, tested positive for COVID 19.

Admitted to COVID unit, however as hypoxia worsened and he was transferred to the ICU on 5/19.

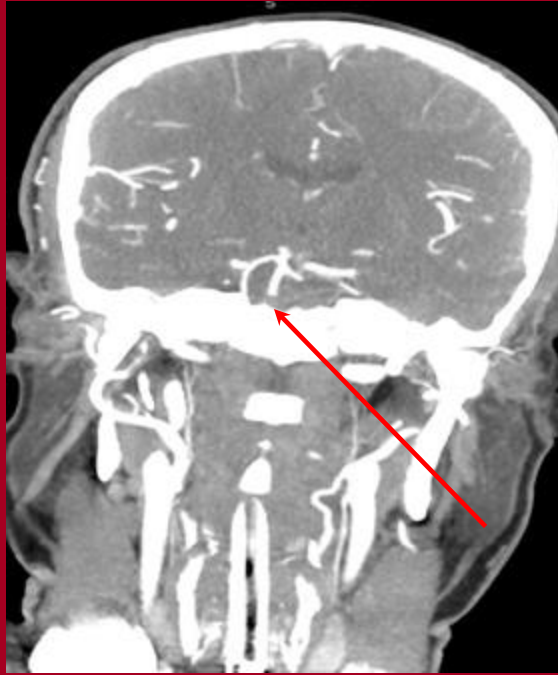
On 5/23 nurse noted he wasn't able to self prone himself experiencing sudden onset left hemiparesis, altered mental status, and left gaze deviation with NIHSS 12. Intubated as high O2 requirements and taken to CT



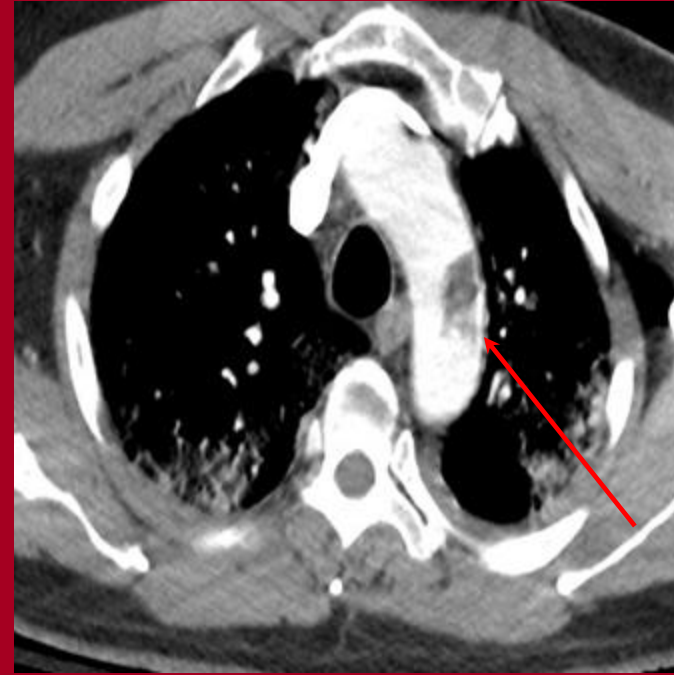
# IFMC-Case



Left Cerebellar infarct



Basilar artery occlusion with vertebral artery stenosis b/l



Large aortic arch thrombus

# IFMC-Case

Post thrombectomy placed on Heparin gtt.

Developed RLE ischemia, gangrenous right toes while on Heparin drip due to arterial embolism, transitioned to Bilvarudin gtt → lovenox with no subsequent embolic events.



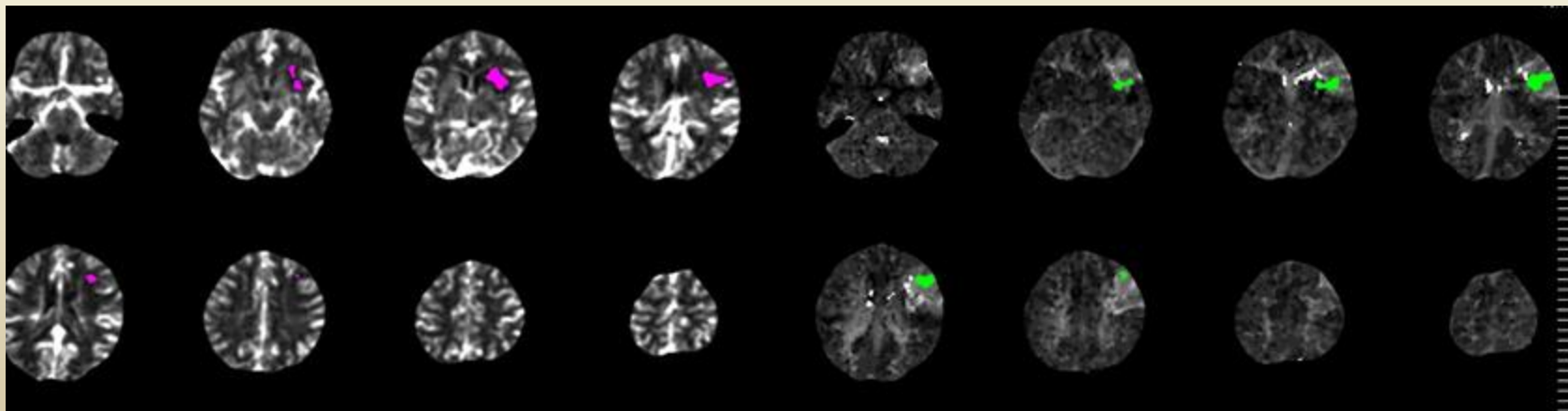
# IAH-Case

33 y.o. male with no PMHx presented with acute right hemiparesis, facial droop and aphasia, NIHSS of 12 , not a tpa candidate outside the window.

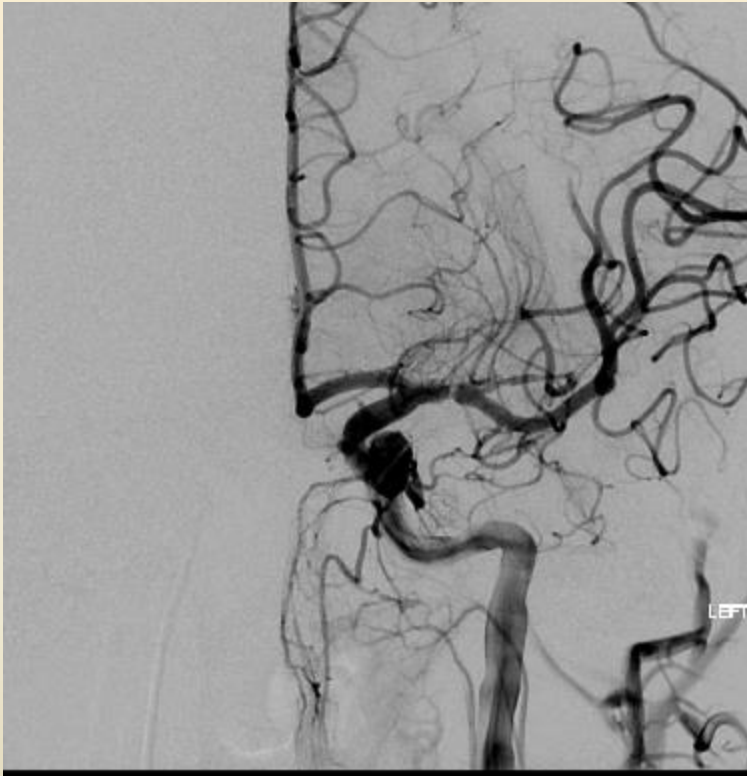




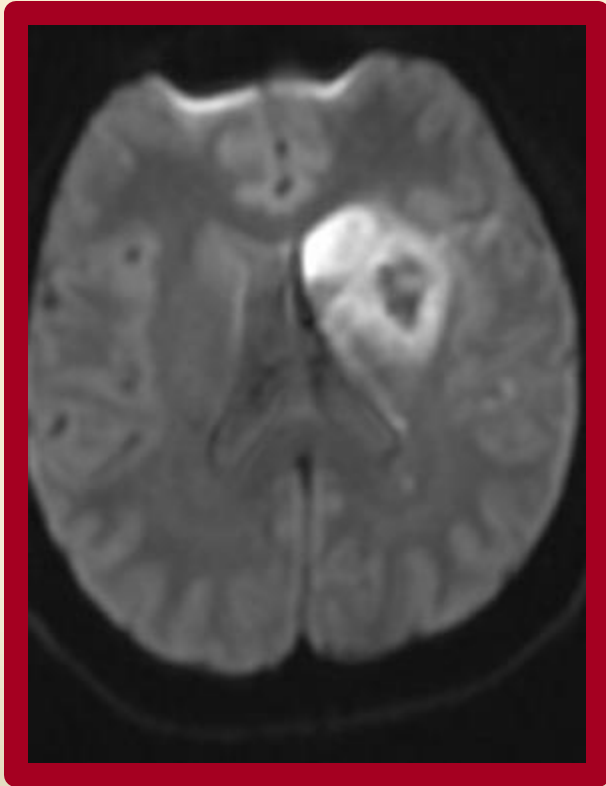
# IAH-Case



# IAH-Case



# IAH-Case



Discharged on Asa/Statin with mild aphasia and walking independently.

# Conclusion

- ❖ COVID-19 has placed an unprecedented strain on healthcare systems and resources.
- ❖ Onset of COVID-19 is correlated with a reduction in admissions for TIA and mild strokes
- ❖ The relation between stroke and COVID-19 is complex and we need long term studies for further understanding

# Thank you

