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# COVID-19 and Acute Kidney Injury

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# Outline

- Pathophysiology of Acute Kidney Injury (AKI) in COVID-19 infection
- Clinical Presentation of kidney injury in COVID-19 infection
- Management of AKI in COVID-19 infection

# Pathophysiology of Acute Kidney Injury

# Pathophysiology of AKI

- SARS- CoV-2 → COVID-19
- AKI found in 1-7% cases and 3-23% of ICU patients
- Volume depletion → ischemia → acute tubular necrosis
- Virus induced cytokines- hypoxia, shock, rhabdomyolysis
- Coagulopathy – Macro/Microthrombi

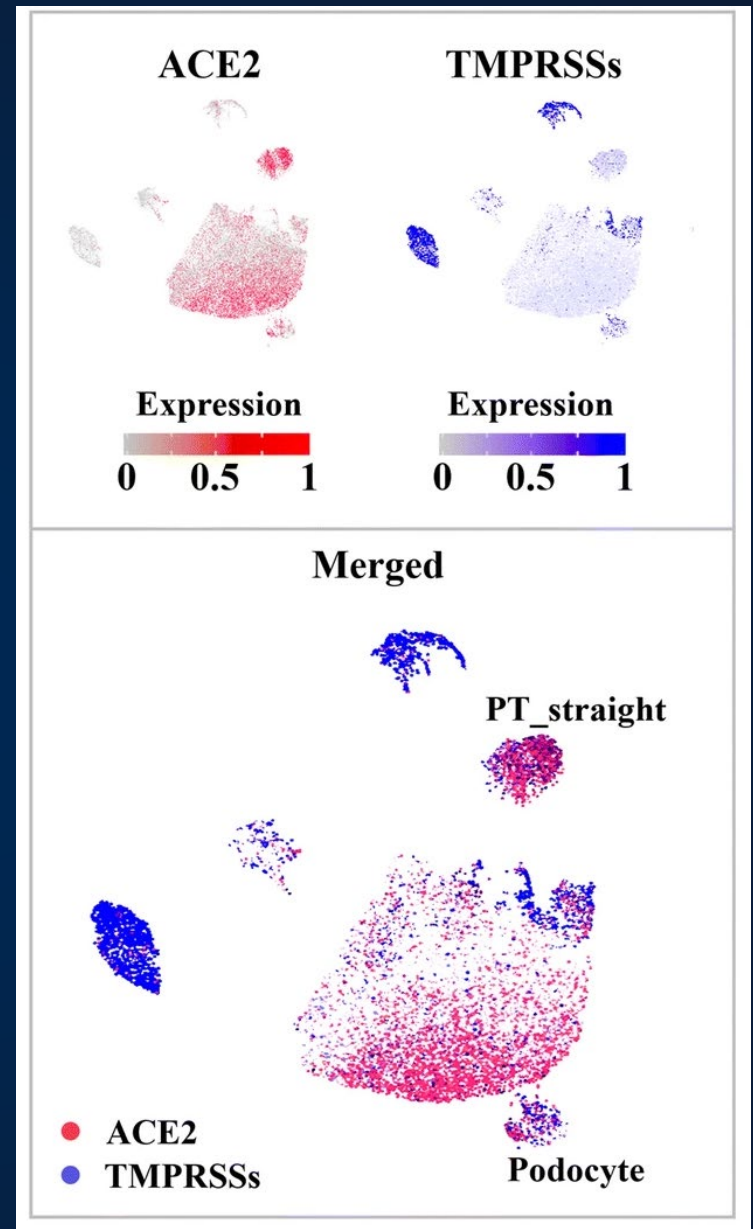
# Pathophysiology

- Angiotensin converting enzyme 2 (ACE2) as a receptor to gain cellular entry
- ACE2 is expressed on the brush border apical membrane of the proximal tubule, and is also present at lower levels in podocytes
- RNA sequencing of this ACE2 receptor expression noted to be 100 fold higher in kidneys than lung tissue
- SARS-CoV-2 has been isolated from the urine of an infected patient (Zhong et al. *Ghouangzhou Daily*)

single-cell RNA sequencing (scRNA-seq) analysis

Colocalization analysis of ACE2 and TMPRSS2 genes: high coexpression in podocytes and proximal straight tubule

Expression more pronounced in “occidental” donors vs Chinese



# RAAS and COVID-19

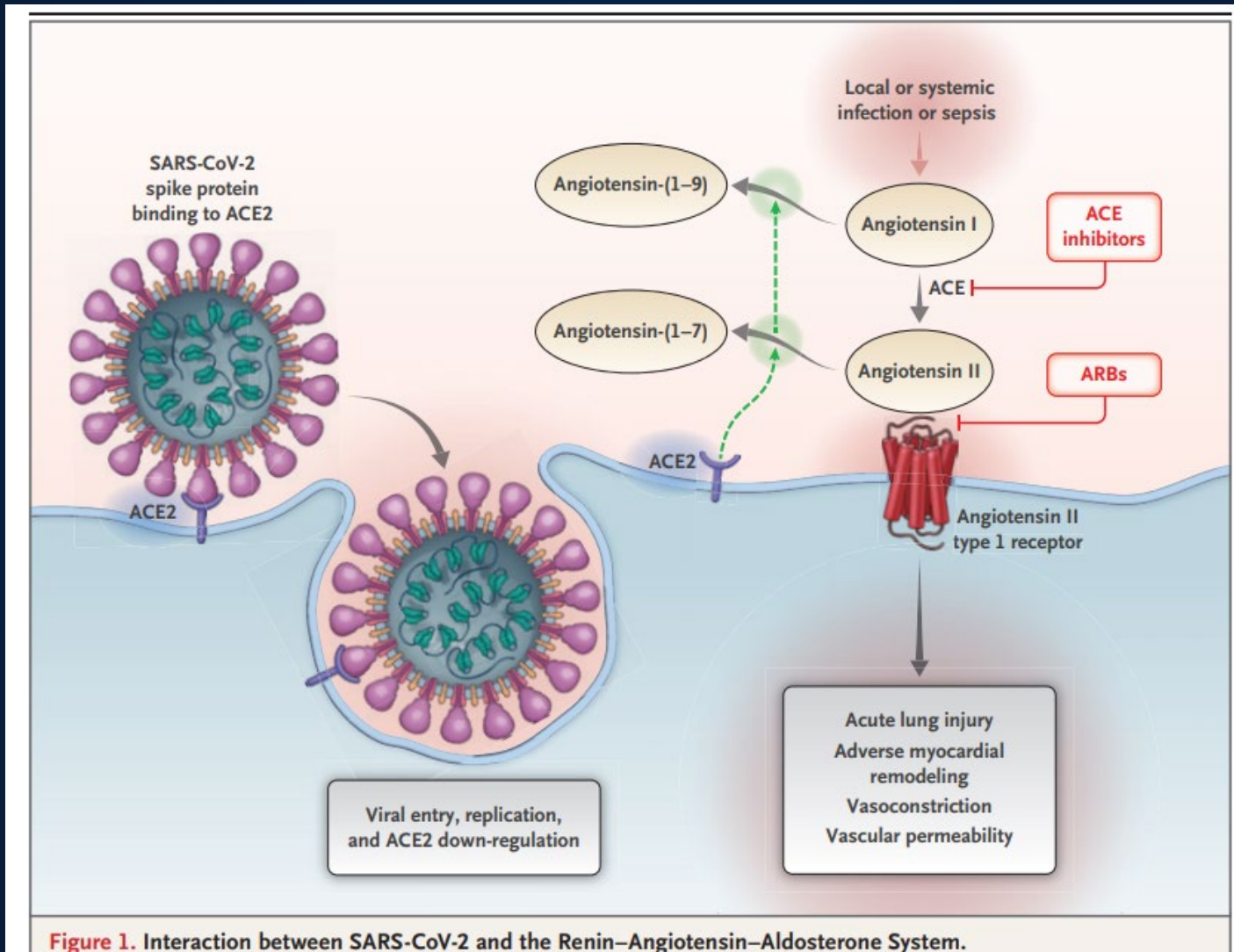


Figure 1. Interaction between SARS-CoV-2 and the Renin–Angiotensin–Aldosterone System.

# Should RAAS medications be Discontinued?

- American Heart Association
- Heart Failure Society of America
- American College of Cardiology
- European Society of Hypertension
- International Society of Hypertension
- ESC Council on Hypertension

**NO** evidence at this time to recommend discontinuation



# ACE inhib/ARB and clinical outcomes

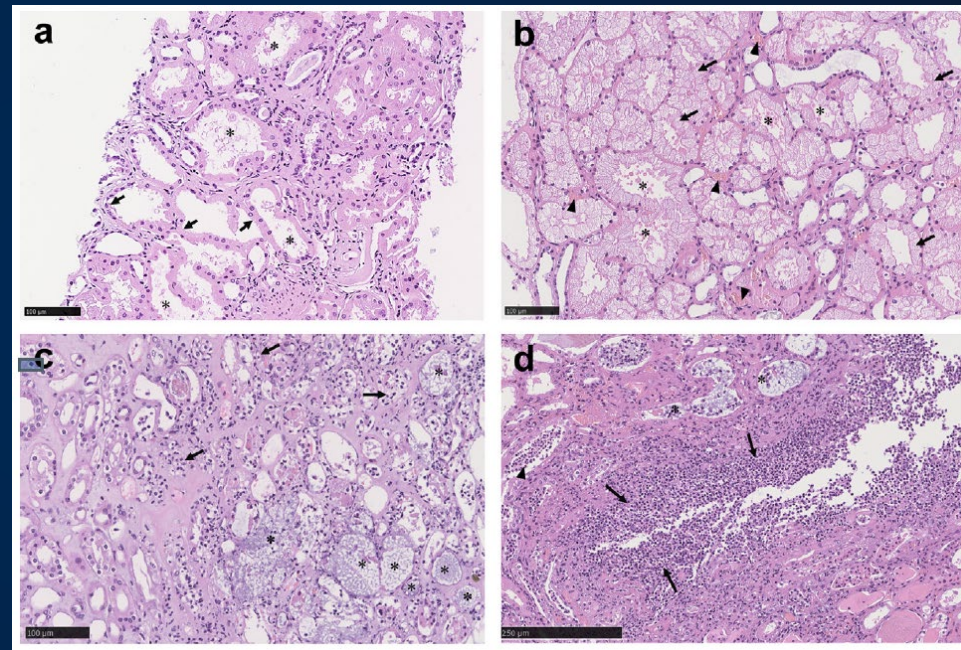
- RCT of 659 patients in Brazil
- Mild to moderate COVID-19 infection
- All were on ACE inhib/ARB prior to the study
- No significant difference in number of days alive and out of the hospital whether the drugs were continued or discontinued

# ACE inhib/ARB Meta-analysis

- 52 studies from around the world
- 101K patients with 26K on ACE inhib or ARB
- In adjusted model use of these drugs associated with lower risk of death in the overall cohort (OR 0.57; 95% CI 0.43-0.76)
- May specifically be protective effects in patients with hypertension

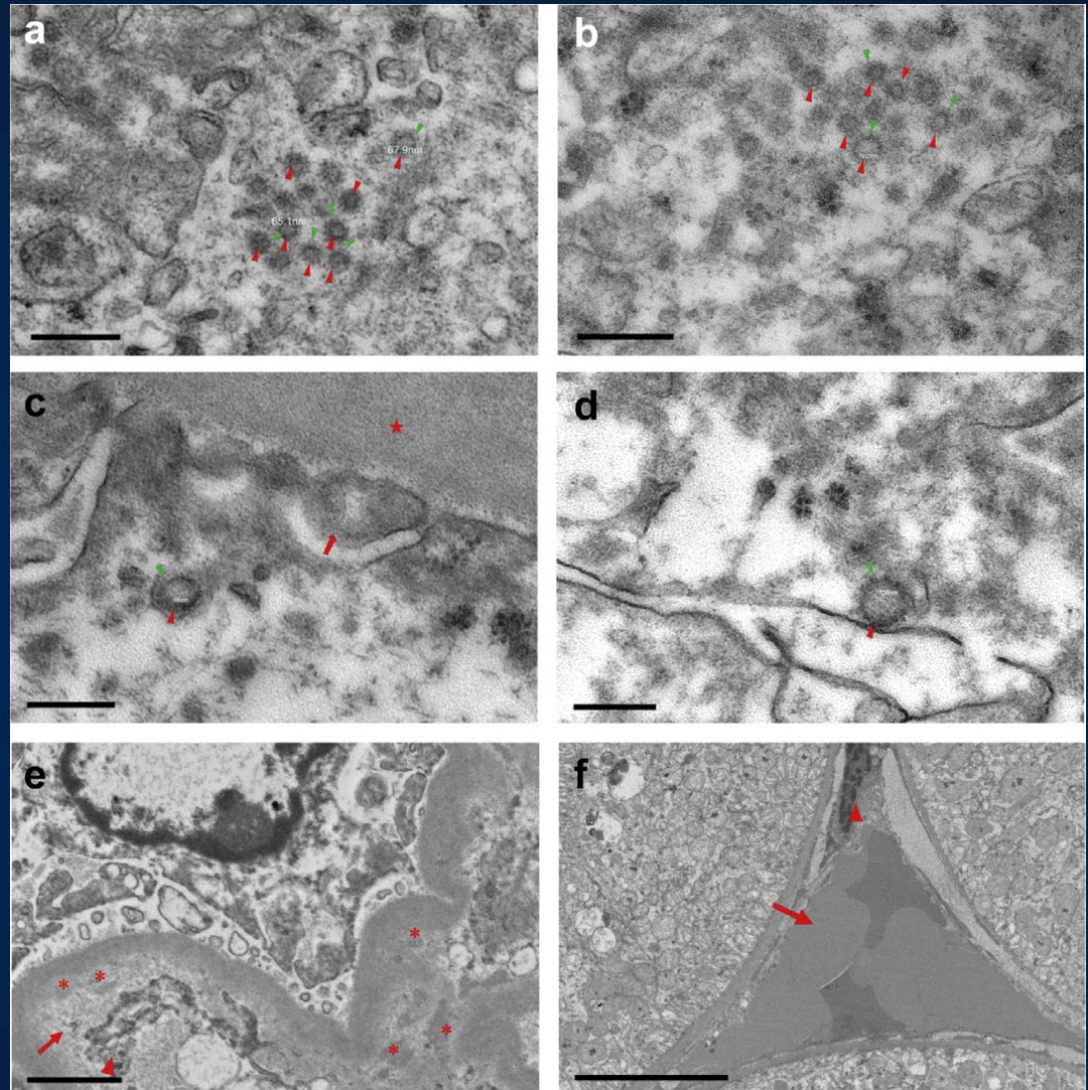
# Pathology

- 26 postmortem biopsies
  - diffuse proximal tubule injury with the loss of brush border
  - vacuolar degeneration
  - Necrosis
  - Occasional pigment casts
  - Capillary erythrocyte aggregation without platelets



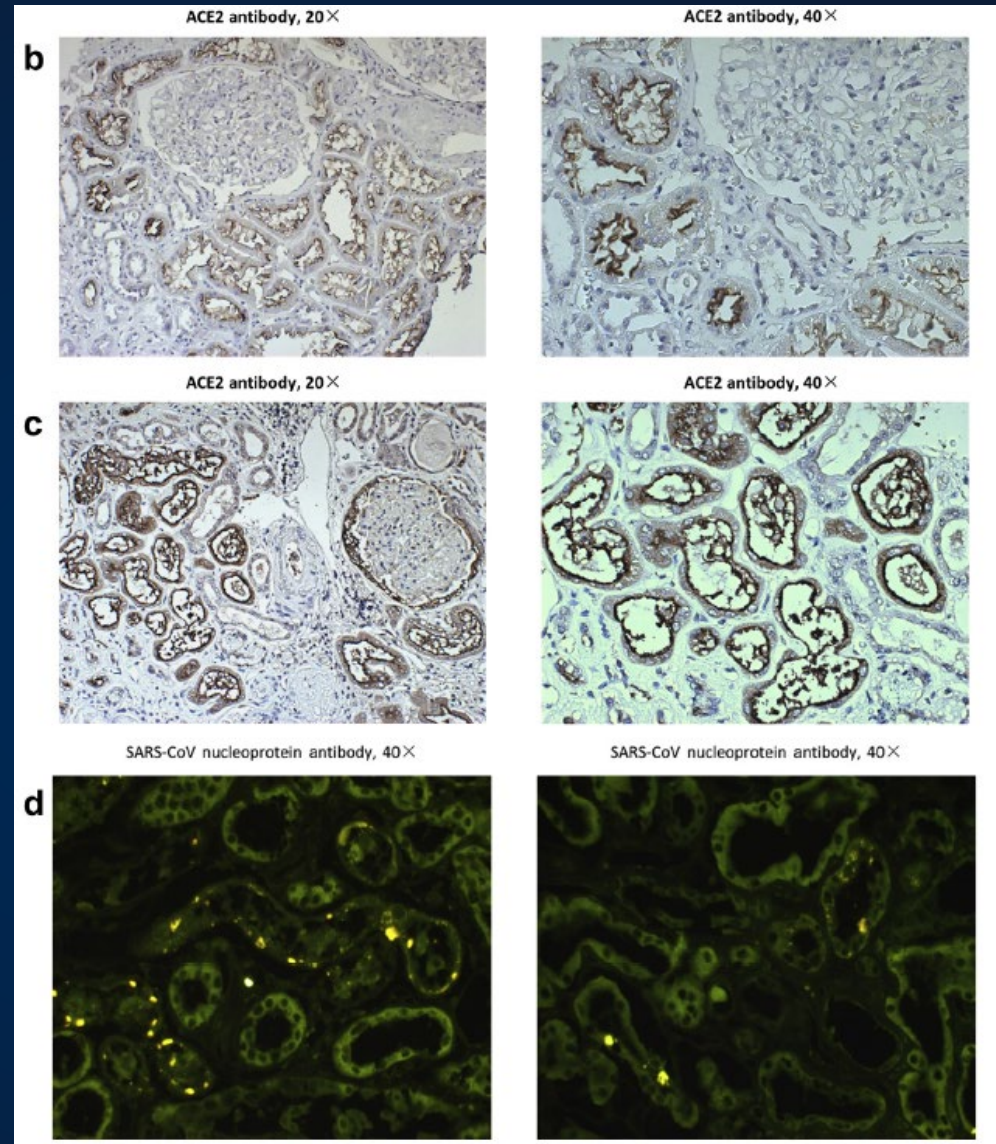
# Pathology

Clusters of coronavirus-like particles with distinctive spikes in the tubular epithelium and podocytes



# Pathology

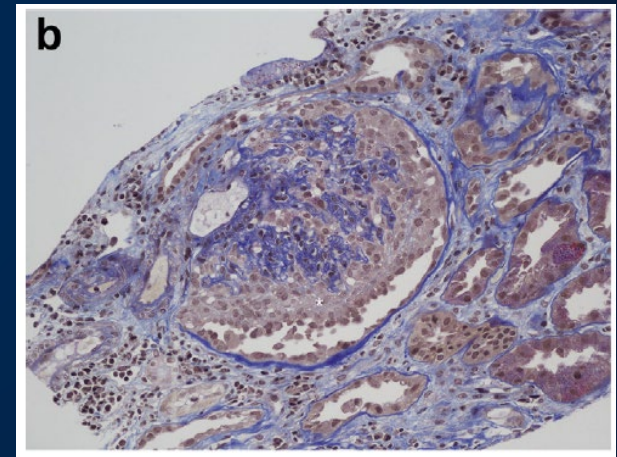
- Receptor ACE2 upregulated
- Positive immunostaining with SARS-CoV nucleoprotein antibody in tubules



# Case Reports

- Collapsing Glomerulopathy – association with high risk APOL1 genotype (Larson et al. KI Reports. 2020) (Kissling et al. KI. 2020)

- African American
- Significant proteinuria



- Patients in both reports noted to be homozygous for the at-risk apolipoprotein A (APOL1)

# Mechanism of Injury

- Interaction between angiotensin II (AngII) over activity, innate/adaptive immune and complement pathways, and the dysregulation of the coagulation system
- Decreased activity of ACE2
- Balance shifts from vasodilatory to vasoconstrictive

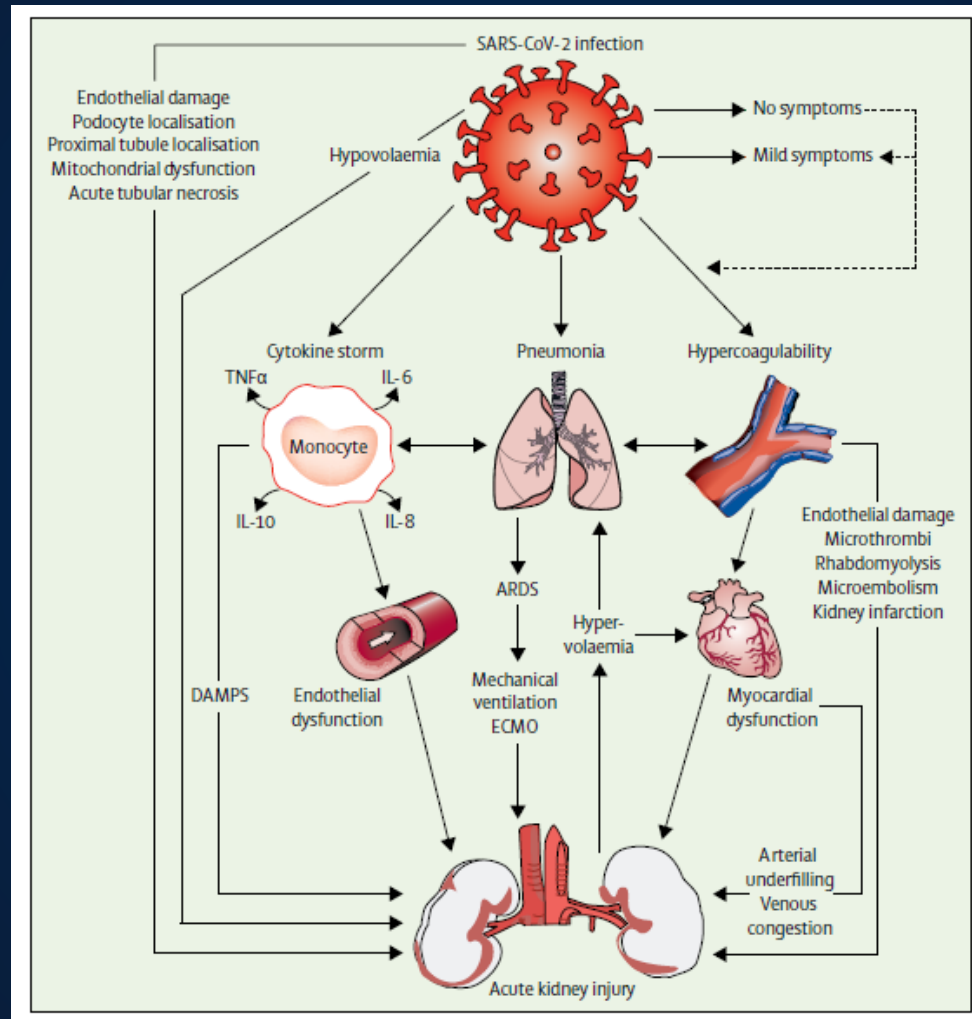


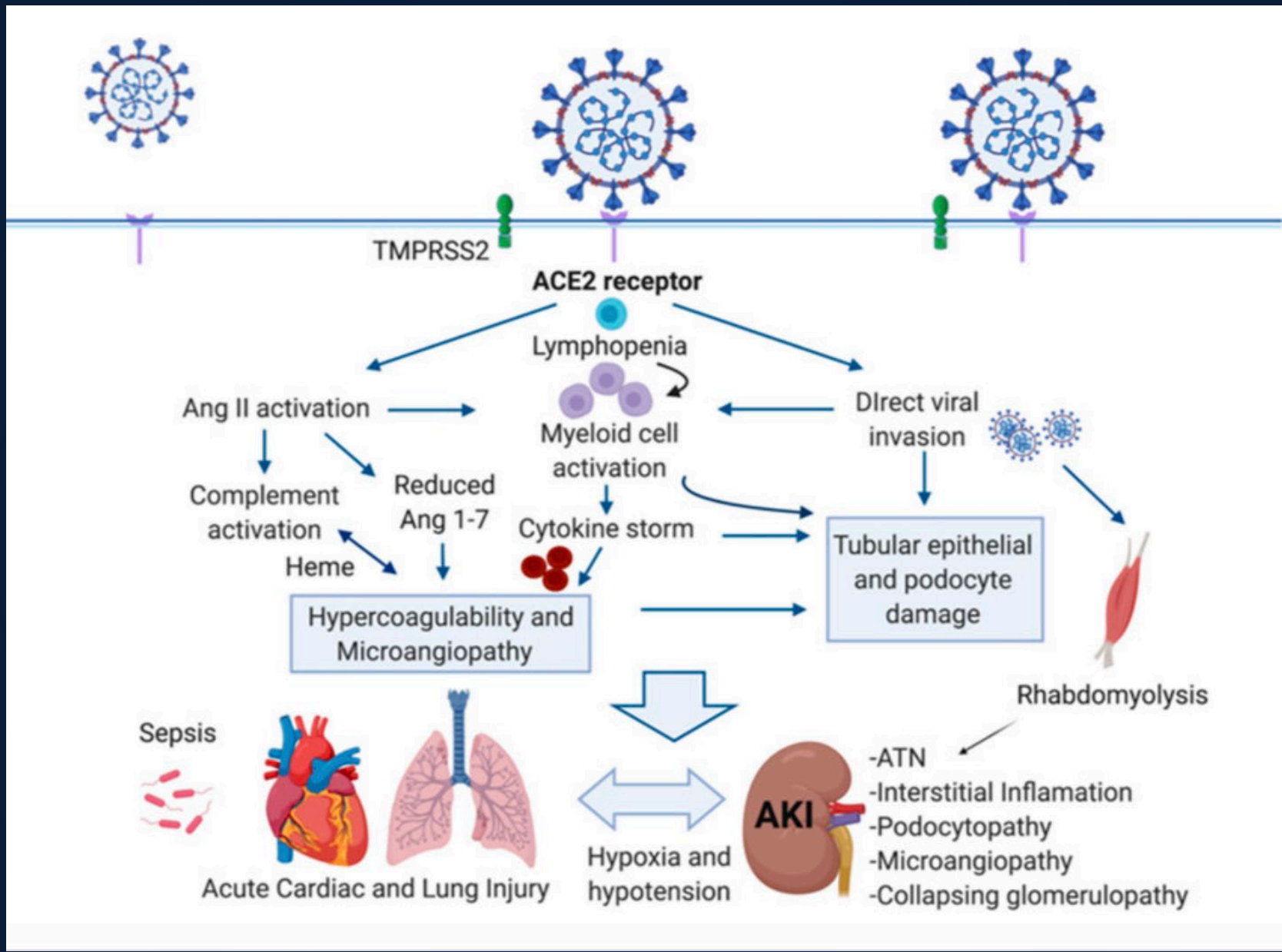
# Multifactorial Causes of AKI

- Prerenal azotemia
- Proximal tubular injury
- Glomerulopathy
- Thrombotic microangiopathy
- Complications of treatment



# Proposed Mechanisms of kidney injury





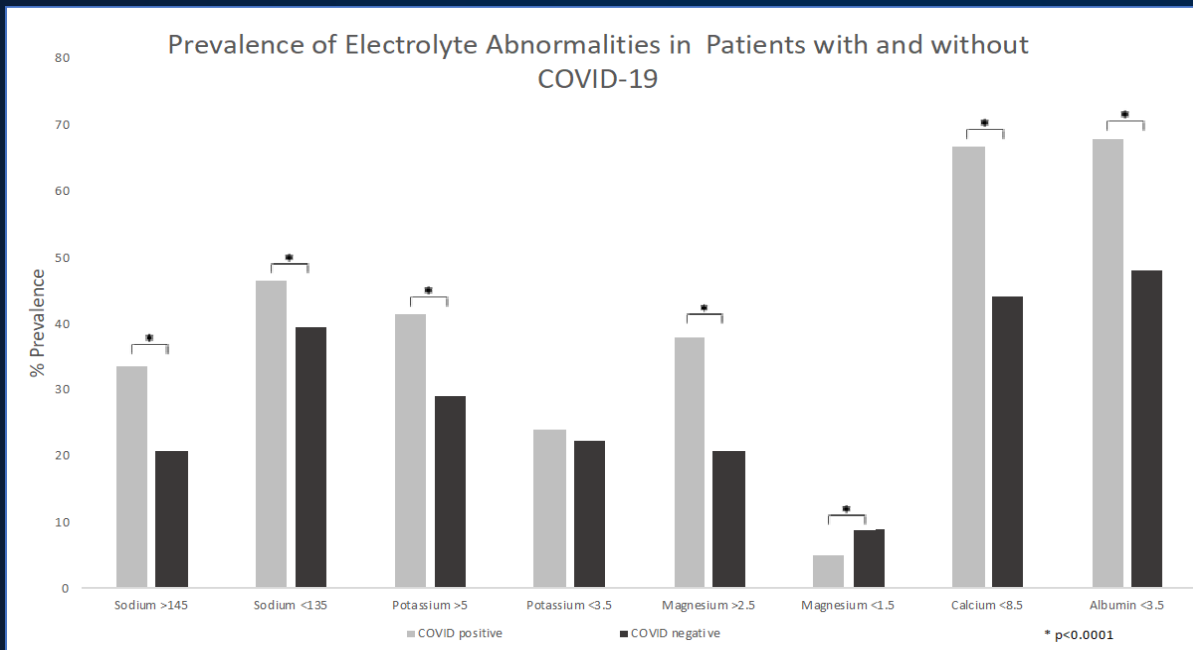
# Clinical Presentation

# Clinical Presentation

- Elevated levels of BUN and Creatinine
- Decreased urinary output
- Proteinuria
- Hematuria
- High blood pressure
- Reduced density on CT scan

# High prevalence of electrolyte abnormalities in hospitalized patients with COVID-19

4579 patients, compared COVID + to COVID -



- Dysnatremias
- Hyperkalemia
- Hypermagnesemia
- Hypocalcemia
- Hypoalbuminemia

D Liu et al. manuscript in process

# Coagulopathy and Kidney Injury?

- Retrospective cohort 183 patients, overall mortality 11.5%
- non-survivors compared to survivors on admission
  - ↑ D-dimer
  - ↑ fibrin degradation product (FDP) levels
  - ↑ prothrombin time and activated partial thromboplastin time

# Thromboses and COVID 19

- Both macro and micro vascular thromboses have been described
- Analysis of 181 critically ill ICU patients, 31% developed thromboses despite prophylaxis

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

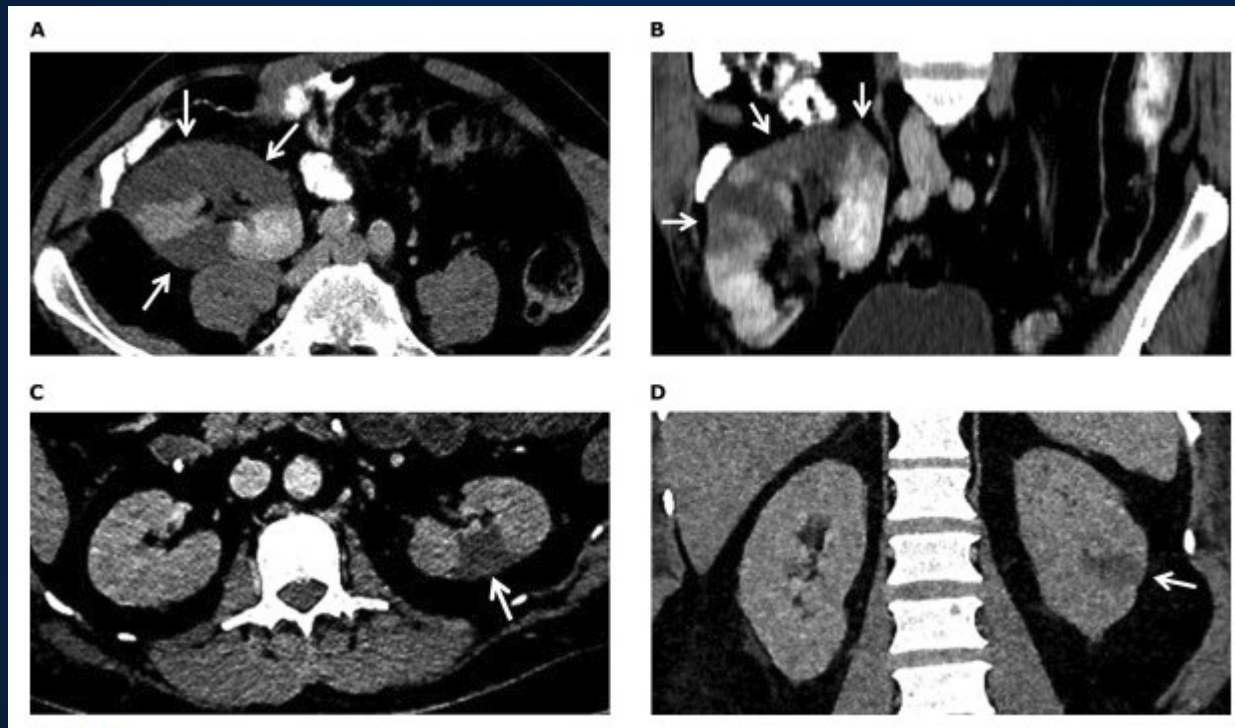
# Renal Artery Thrombosis/Infarction

- 69 yr old female initially had mild COVID-19 symptoms which improved
- One week later presented with acute abdominal pain





- Case Series from Netherlands
- COVID -19 patients with multiple renal infarctions



# Management of AKI in COVID-19

# Management of AKI in COVID 19

- Early recognition
- Fluid challenge
- Regular monitoring of Creatinine and Urine output
- Renal Replacement Therapy- Continuous dialysis modalities in hemodynamically unstable patients
  - Extracorporeal treatments do not compromise the experimental antibody-based therapies such as tocilizumab, intravenous immunoglobulins, and convalescent plasma administration
- \*\*Haemoperfusion with sorbent cartridges might prevent cytokine induced kidney damage
- Anticoagulation



# MonteNephrology