Akut vesekárosodás (AKI) COVID 19-ben

Leiner Tamás, Ruszkai Zoltán, Tánczos Krisztián, Molnár Zsolt

TM KETLAK
KORONAVÍRUS
ELLENI TRANSZLÁCIÓS
LAKOSSÁGTÁMOGATÓ
AKCIÓ- ÉS KUTATÓCSOPORT

Kidney Disease Improving Global Outcomes (KDIGO) classification

Table 2 | Staging of AKI

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ⩾0.3 mg/dl (⩾26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ⩾12 hours
3	3.0 times baseline OR Increase in serum creatinine to ⩾4.0 mg/dl (⩾353.6 μmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ⩾24 hours OR Anuria for ⩾12 hours

Clinical Practice Guidelines for Acute Kidney Injury 2012. http://www.kdigo.org/clinical_practice guidelines/AKI.php.

ARDS és AKI (LUNG SAFE study)

Crit Care Med. 2019 Sep;47(9):1216-1225. doi: 10.1097/CCM.0000000000003832.

Impact of Early Acute Kidney Injury on Management and Outcome in Patients With Acute Respiratory Distress Syndrome: A Secondary Analysis of a Multicenter Observational Study.

McNicholas BA, Rezoagli E, Pham T, Madotto F, Guiard E, Fanelli V, Bellani G, Griffin MD, Ranieri M, Laffey JG; ESICM Trials Group and the Large observational study to UNderstand the Global impact of Severe Acute respiratory FailurE (LUNG SAFE) Investigators.

⊕ **Collaborators (888)**

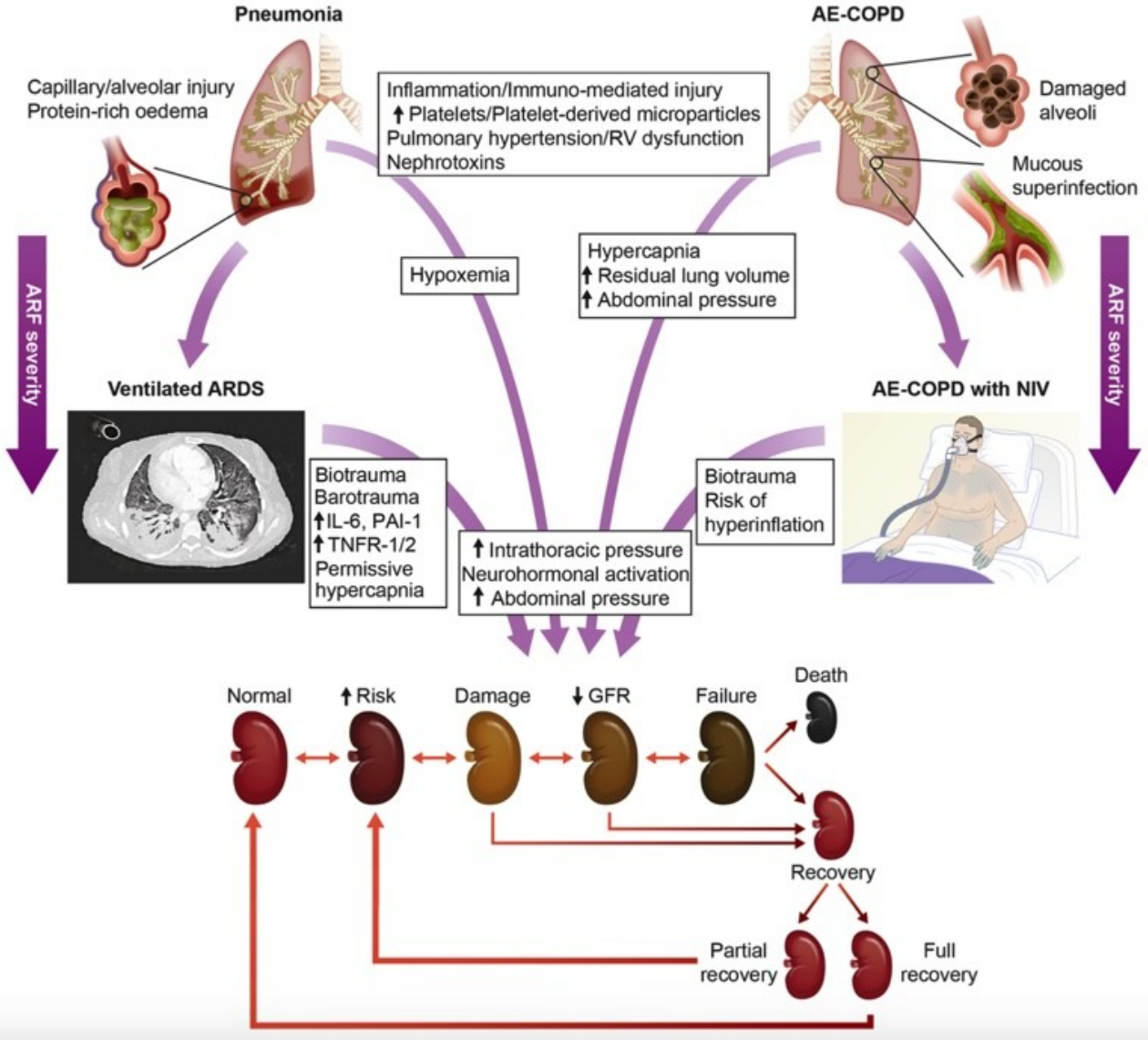
Hospital mortality increased from 31% in acute respiratory distress syndrome patients with no acute kidney injury to 50% in mild-moderate acute kidney injury ($p \leq 0.001$ vs no acute kidney injury) and 58% in severe acute kidney injury ($p \leq 0.001$ vs no acute kidney injury and mild-moderate acute kidney injury). In multivariate analyses, both mild-moderate (odds ratio, 1.61; 95% CI, 1.24-2.09; $p < 0.001$) and severe (odds ratio, 2.13; 95% CI, 1.55-2.94; $p < 0.001$) acute kidney. injury were independently associated with mortality.

Tüdő- vese interakció ARDS- ben

CONFERENCE REPORTS AND EXPERT PANEL

Lung–kidney interactions in critically ill patients: consensus report of the Acute Disease Quality Initiative (ADQI) 21 Workgroup

https://doi.org/10.1007/s00134-019-05869-7



COVID 19 AKI - ETIOLÓGIA

Table 1 | **Potential mechanisms of kidney damage and treatment strategies in COVID-19**

Pathway[a]	Mechanism of kidney damage	Suggested treatment strategy
Cytokine damage		
Cytokine release syndrome	Direct cytokine lesion	Cytokine removal using various approaches: direct haemoperfusion using a neutro-macroporous sorbent; plasma adsorption on resin after separation from whole blood; CKRT with hollow fibre filters with adsorptive properties; high-dose CKRT with MCO or HCO membranes
Increased cytokine generation owing to ECMO, invasive mechanical ventilation and/or CKRT		
Haemophagocytic syndrome		
Organ crosstalk		
Cardiomyopathy and/or viral myocarditis	Cardiorenal syndrome type 1	LVAD, arteriovenous ECMO
Alveolar damage	Renal medullary hypoxia	Venovenous ECMO
High peak airway pressure and intra-abdominal hypertension	Renal compartment syndrome	Venovenous ECMO, extracorporeal CO_2 removal, CKRT
Rhabdomyolysis	Tubular toxicity	CKRT using a HCO or MCO membrane
Systemic effects		
Positive fluid balance	Renal compartment syndrome	Continuous ultrafiltration and diuretics
Endothelial damage, third-space fluid loss and hypotension	Renal hypoperfusion	Vasopressors and fluid expansion
Rhabdomyolysis	Tubular toxicity	CKRT using a HCO or MCO membrane
Endotoxins	Septic AKI	Endotoxin removal using polysterene fibres functionalized with polymyxin-B

AKI, acute kidney injury; CKRT, continuous kidney replacement therapy; ECMO, extracorporeal membrane oxygenation; HCO, high cut-off; LVAD, left ventricular assist device; MCO, medium cut-off. [a]The pathways and mechanisms are interconnected and treatment strategies will influence different aspects simultaneously.

NATURE REVIEWS | NEPHROLOGY

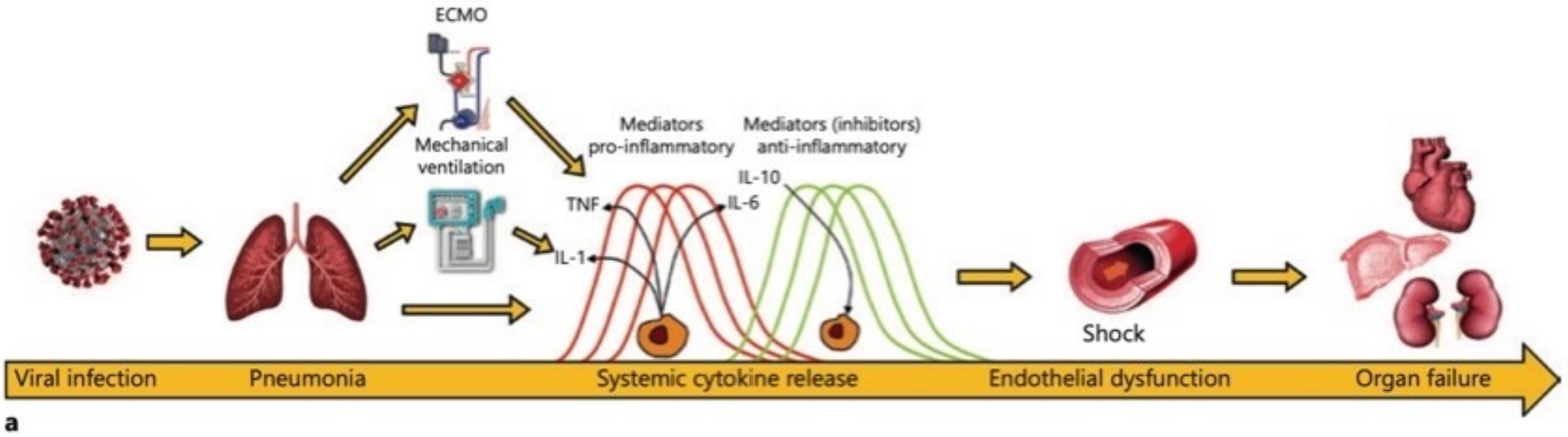
https://doi.org/10.1038/s41581-020-0284-7

COVID 19 AKI – Etiológia – cytokin hatás

Editorial

Blood Purif
DOI: 10.1159/000507039

Received: March 9, 2020
Accepted: March 9, 2020
Published online: March 13, 2020



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COVID 19 AKI - ETIOLÓGIA

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NATURE REVIEWS | NEPHROLOGY

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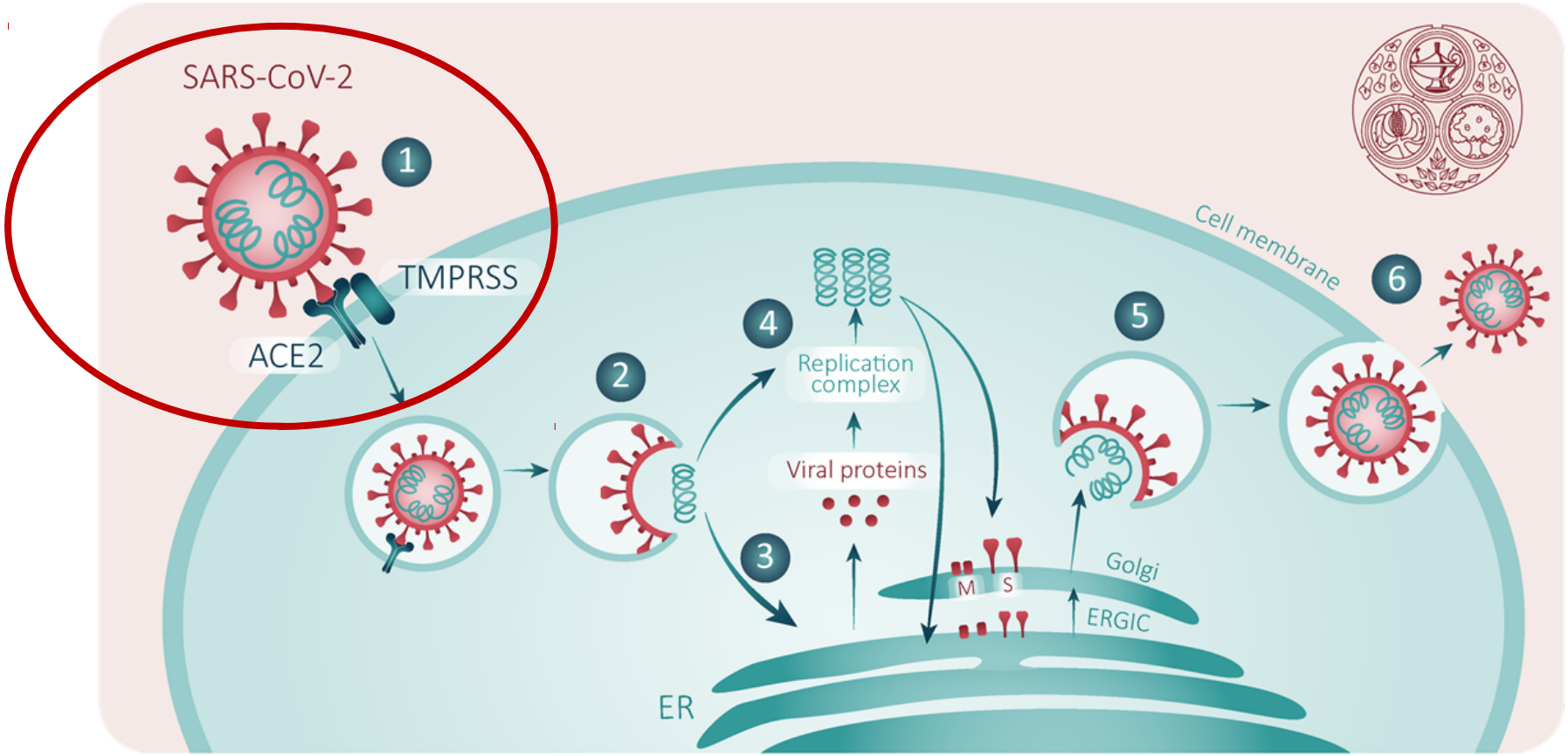
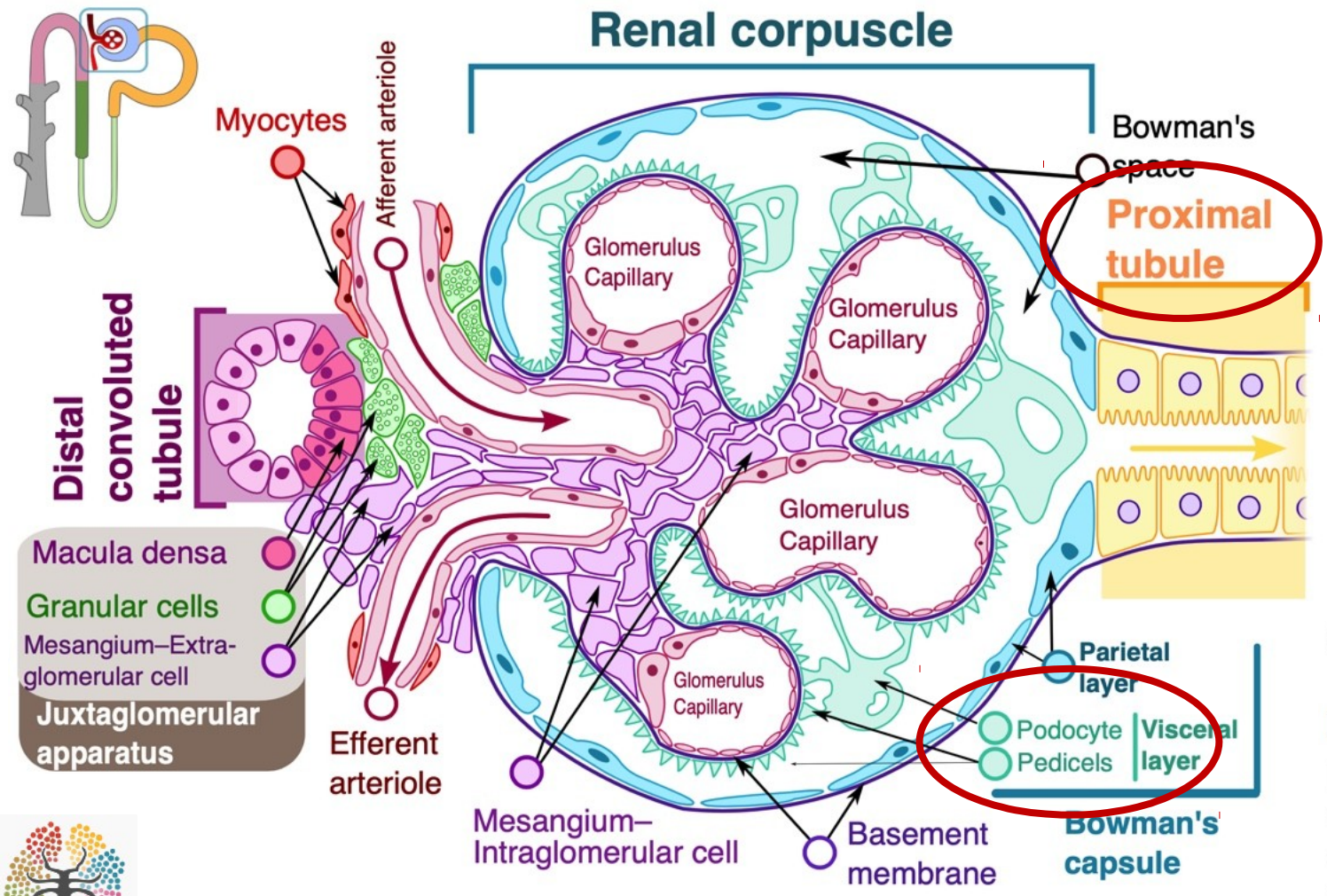
COVID 19 AKI – Etiológia – direkt vírus hatás



Ward, P et al. (2020), 'COVID-19/SARS-CoV-2 Pandemic', Faculty of Pharmaceutical Medicine blog, 6 April. Available at: https://www.fpm.org.uk/blog/covid-19-sars-cov-2-pandemic/

Song et al., 'Viruses', 2019; Jiang et al., 'Emerging Microbes and Infections, 2012; 'The Economist'.

COVID 19 AKI – Etiológia – direkt vírus hatás



ACE 2 és TMPRSS2

expresszió

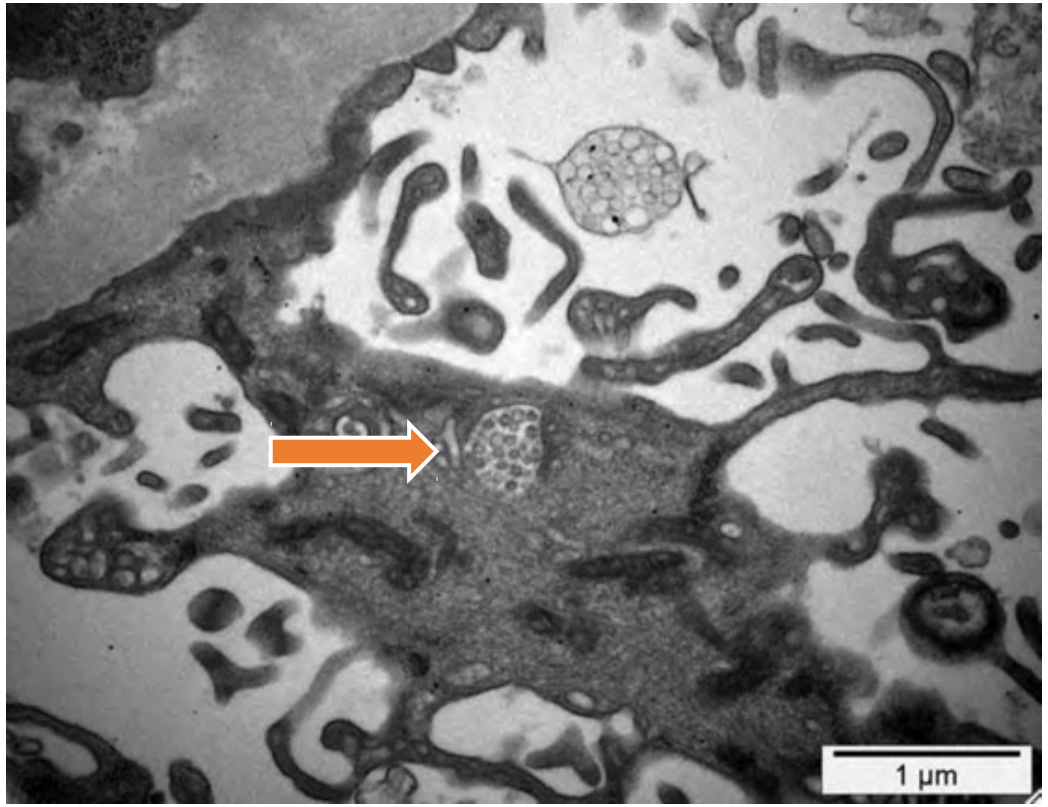
Intensive Care Med
https://doi.org/10.1007/s00134-020-06026-1

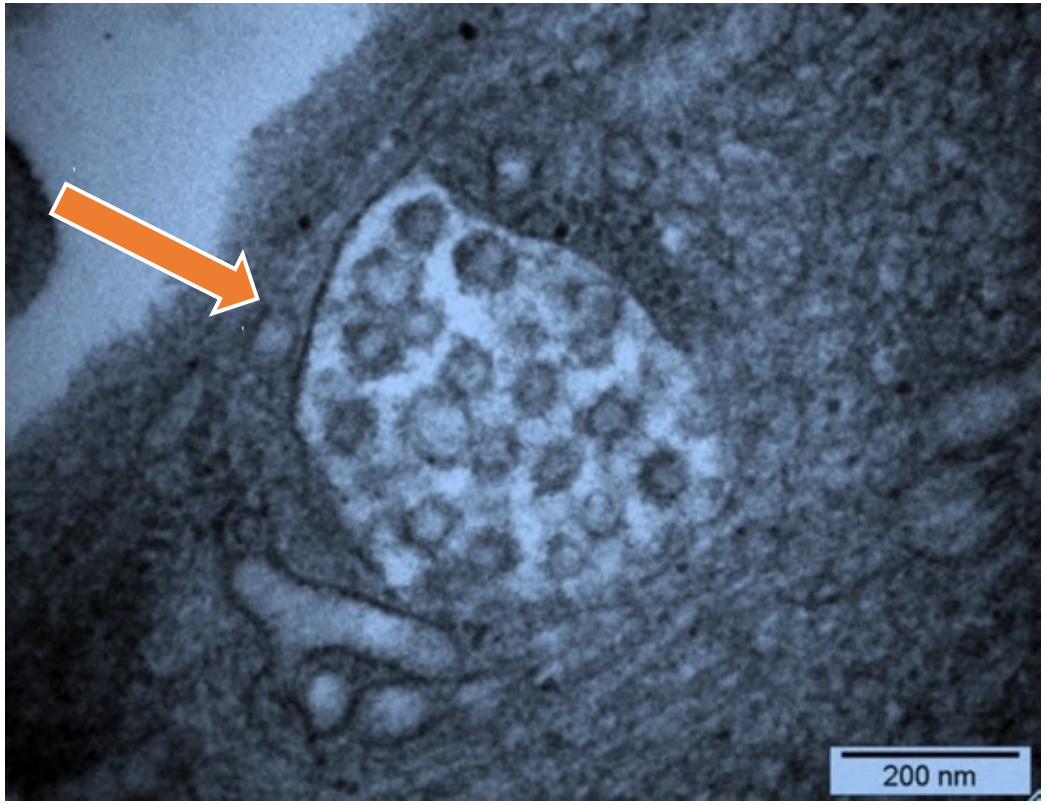
LETTER

Identification of a potential mechanism of acute kidney injury during the COVID-19 outbreak: a study based on single-cell transcriptome analysis

Xiu-wu Pan[1,2], Da Xu[2,5], Hao Zhang[4,5], Wang Zhou[2,5*], Lin-hui Wang[3*] and Xin-gang Cui[2*]

COVID 19 AKI – Etiológia – direkt vírus hatás





Electron microscopy study: In the podocytes cytoplasm, vacuoles containing numerous spherical particles that had the typical appearance of viral inclusion bodies reported with SARS-CoV-2.

https://doi.org/10.1016/j.kint.2020.04.006

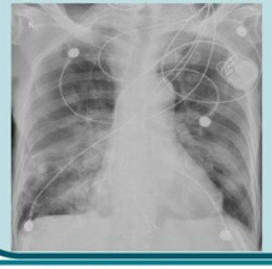
COVID 19 AKI – Etiológia – direkt vírus hatás

Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China

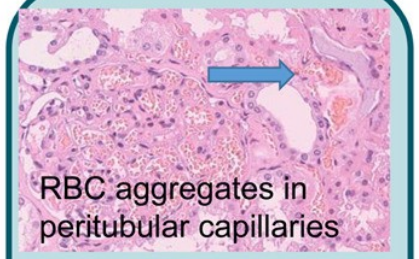
Study Cohort

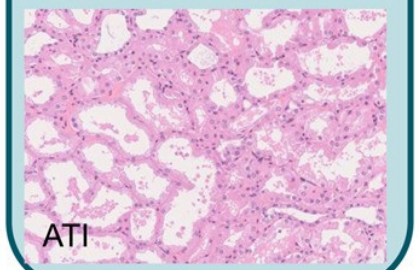
26 autopsies in COVID-19 patients

-death due to respiratory failure
-average age 69 years
-19 males; 7 females
-9/26 showed clinical signs of kidney injury

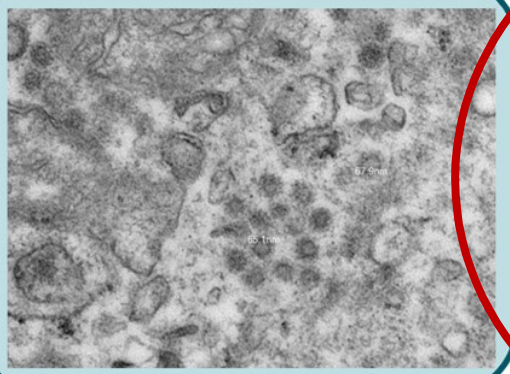


Light microscopy: ATI, RBC aggregates

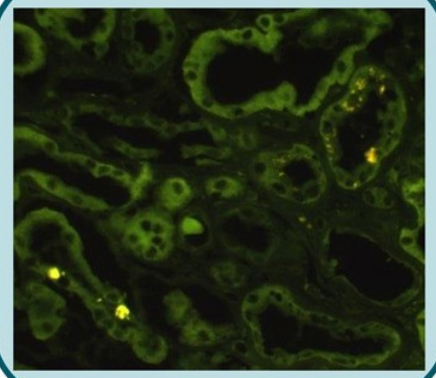




Electron microscopy: virus in tubules and podocytes



SARS-CoV nuclear protein detection



CONCLUSION:

Direct parenchymal infection of tubular epithelial cells and podocytes with marked acute tubular injury (ATI) and erythrocyte aggregation occurs in severe lethal COVID-19.

ISN kidney INTERNATIONAL
OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

Su et al, 2020

EPIDEMIOLOGIA- AKI előfordulása COVID 19-ben

Patient-Oriented, Translational Research: Research Article

American Journal of Nephrology

Am J Nephrol
DOI: 10.1159/000507471

Received: March 11, 2020
Accepted: March 24, 2020
Published online: March 31, 2020

Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China

Luwen Wang[a] Xun Li[a] Hui Chen[c] Shaonan Yan[a] Dong Li[b] Yan Li[b]
Zuojiong Gong[a]

In this study, the effects of SARS-CoV-2 infection on renal function were explored through analyzing the clinical data of 116 hospitalized COVID-19-confirmed patients. However, the results of common renal impairment in COVID-19 patients were not observed in this study. Although 12 patients (10.8%) without CKD showed mild increase of BUN or SCr (<26 μmol/L within 48 h), and 8 patients (7.2%) showed trace or 1+ albuminuria after infection with the virus and during the treatment of pneumonia, all these patients did not meet the diagnostic criteria of AKI. Moreover, these patients gradually returned to normal after a follow-up without receiving special treatment for the kidneys. The temporary abnormal renal function is probably supposed as secondary injury duo to hypoxemia in these patients.

EPIDEMIOLÓGIA

ARTICLE IN PRESS

www.kidney-international.org editorial: special report

Kidney disease is associated with in-hospital death of patients with COVID-19

Yichun Cheng[1,2], Ran Luo[1,2], Kun Wang[1,2], Meng Zhang[1], Zhixiang Wang[1], Lei Dong[1], Junhua Li[1], Ying Yao[1], Shuwang Ge[1] and Gang Xu[1]

OPEN

COVID-19. In this cohort, approximately 13% of patients had underlying kidney disease. More than 40% had evidence of abnormal kidney function and 5.1% had acute kidney injury (AKI) during their hospital stay. There was a dose-dependent relationship between AKI stages and death, with an excess risk of mortality by at least 4 times among those with stage 3 AKI. Kidney disease is a major complication of COVID-19 and a significant risk factor of death. How-

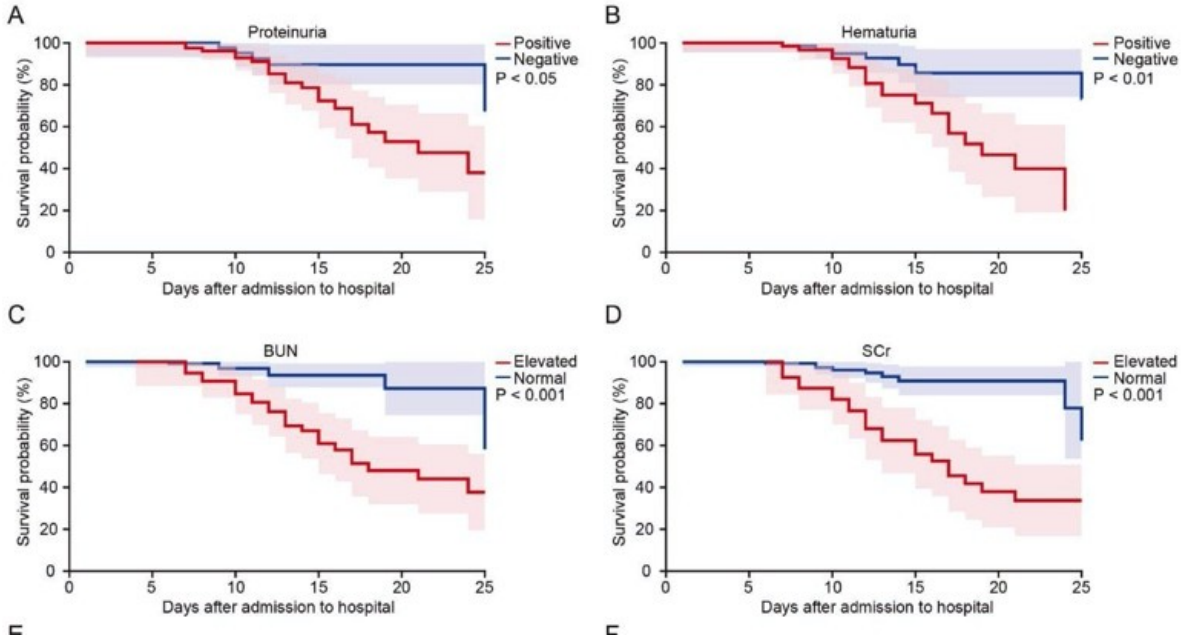
EPIDEMIOLÓGIA

The Lancet Infectious Diseases

Caution on Kidney Dysfunctions of COVID-19 Patients

https://ssrn.com/abstract=3559601

On hospital admission, a remarkable fraction of patients had signs of kidney dysfunctions, including 59% with proteinuria, 44% with hematuria, 14% with increased levels of blood urea nitrogen, and 10% with increased levels of serum creatinine, although mild but worse than that in cases with other pneumonia.



EPIDEMIOLÓGIA –Olaszország

Characteristics of SARS-CoV-2 patients dying in Italy
Report based on available data on April 16th , 2020

The present report describes characteristics of 19,996 SARS-CoV-2 patients dying in Italy.* Geographic distribution across the 19 regions and 2 autonomous provinces of Trento and Bozen is presented in the table below. Data are update to April 16^{6h}, 2020.

Acute Respiratory Distress syndrome was observed in the majority of patients (96.7% of cases), followed by acute renal failure (22.9%). Superinfection was observed in 12.4% and acute cardiac injury in 9.5% of cases.

EPIDEMIOLÓGIA -UK

Table 7 Outcome, length of stay and organ support* for patients admitted to critical care with confirmed COVID-19

Critical care unit outcome	Patients with confirmed COVID-19 and critical care outcome reported (N=2936)		Patients with viral pneumonia (non-COVID-19), 2017-19 (N=5367)	
Outcome at end of critical care, n (%)				
Alive	1437	(48.9)	4184	(78.0)
Dead	1499	(51.1)	1183	(22.0)
Length of stay				
Length of stay in critical care (days), median (IQR)				
Survivors	5	(2, 9)	6	(3, 12)
Non-survivors	6	(4, 10)	6	(2, 13)
Organ support (Critical Care Minimum Dataset)*				
Receipt of organ support, at any point, n (%)				
Advanced respiratory support	1795	(65.4)	2529	(47.1)
Basic respiratory support	1512	(55.1)	4375	(81.5)
Advanced cardiovascular support	698	(25.4)	1178	(21.9)
Basic cardiovascular support	2469	(90.0)	4978	(92.8)
Renal support	558	(20.3)	902	(16.8)
Liver support	10	(0.4)	44	(0.8)
Neurological support	139	(5.1)	292	(5.4)

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www.icnarc.org

ICNARC report on COVID-19 in critical care
17 April 2020

EPIDEMIOLÓGIA -UK

Table 8 Critical care outcomes, by receipt of respiratory support*

Critical care unit outcome	Patients receiving advanced respiratory support* (N=1795)	Patients receiving only basic respiratory support* (N=821)
Outcome at end of critical care, n (%)		
Alive	586 (32.6)	661 (80.5)
Dead	1209 (67.4)	160 (19.5)
Length of stay		
Length of stay in critical care (days), median (IQR)		
Survivors	9 (6, 14)	3 (2, 5)
Non-survivors	7 (4, 10)	3 (2, 5)
Organ support (Critical Care Minimum Dataset)*		
Receipt of organ support, at any point, n (%)		
Basic respiratory support	690 (38.4)	821 (100.0)
Advanced cardiovascular support	684 (38.1)	11 (1.3)
Basic cardiovascular support	1677 (93.4)	733 (89.3)
Renal support	517 (28.8)	31 (3.8)
Liver support	9 (0.5)	0 (0.0)
Neurological support	133 (7.4)	5 (0.6)

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17 April 2020

EPIDEMIOLÓGIA -UK

TRANSLATIONAL MEDICINE

Table 9 Critical care outcomes, by receipt of renal support*

Critical care unit outcome	Patients receiving any renal support* (N=558)	Patients not receiving any renal support* (N=2186)
Outcome at end of critical care, n (%)		
Alive	111 (19.9)	1233 (56.4)
Dead	447 (80.1)	953 (43.6)
Length of stay		
Length of stay in critical care (days), median (IQR)		
Survivors	10 (4, 16)	5 (2, 9)
Non-survivors	8 (5, 12)	5 (3, 8)
Organ support (Critical Care Minimum Dataset)*		
Receipt of organ support, at any point, n (%)		
Advanced respiratory support	517 (92.7)	1278 (58.5)
Basic respiratory support	168 (30.1)	1344 (61.5)
Advanced cardiovascular support	282 (50.5)	416 (19.0)
Basic cardiovascular support	519 (93.0)	1950 (89.2)
Liver support	7 (1.3)	3 (0.1)
Neurological support	47 (8.4)	92 (4.2)

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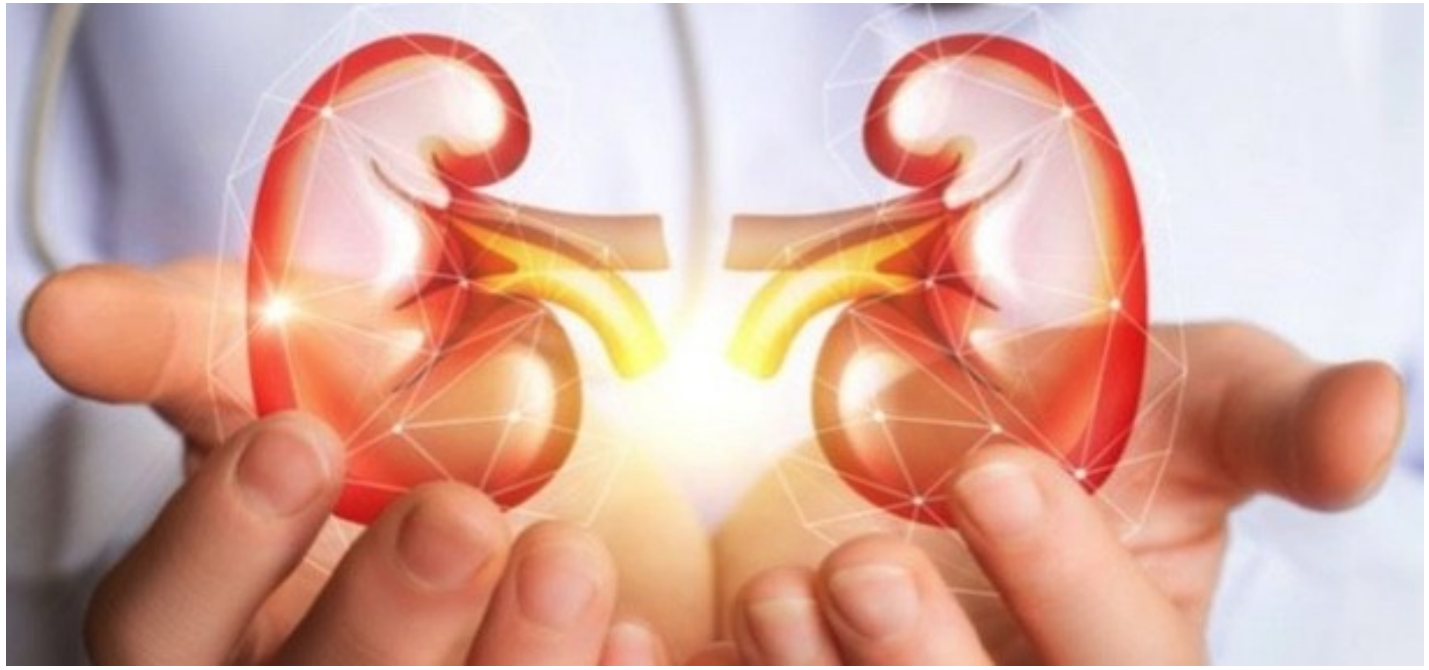
17 April 2020

Akkor mit tehetünk ?



Kockázat Felismerés – akut vesekárosodás kialakulásának kockázat becslése

Van –e vesekárosodásra hajlamosító tényező?

ANAMNÉZIS

Krónikus vesebetegség eGFR < 45 ml/perc/1,73 m^2
Cukorbetegség
Akut vesekárosodás az anamnézisben
Szívelégtelenség
65 év feletti életkor
Rendszeresen szedett:
- NSAID
- ACE gátló
- ARB
- SGLT2 gátlók

TERÁPIA

Diuretikum alkalmazá
NIV

FONTOS !
Láz, megnövekedett légzésszám
↓
Perspiratio insensibilis ↑

NEM

Obszerváció
Vesefunkció (Creatinin és urea) /48-72 h
Folyadékegyenleg !!

IGEN

Obszerváció
Vesefunkció (Creatinin és urea) /24h
Folyadékegyenleg !!
Napi testsúly mérés !
Hólyag katéter behelyezés megfontolandó !

Vizsgálatok és kezelés ha AKI kialakult

Fontos, hogy mindig követni kell a adott kórházban érvényes eljárásrendet !

Állhat dehidráció a vesekárosodás hátterében ?

NEM

Vizelet gyors teszt (fehérje, vér, ...) és egyéb okok keresése

Képalkotó (UH vagy nem kontrasztos CT) ha:

1. Alsó húgyúti tünetek
2. Szóló vese
3. Prosztata betegség
4. Vesekövesség
5. Állandó hólyag katéter
6. Kismedencei malignitás
7. Gyorsan romló vesefunkció (nem reagál folyadékra)

NINCS szükség további extra folyadék adására ha keringési peraméterek megfelelőek.

IGEN

Folyadék „challenge” megfontolandó ha a beteg légzési elégtelensége ezt lehetővé teszi.

Krisztalloid!

Hypernatraemia!

Alkalmazott gyógyszerek felülvizsgálata ! ⟶ Dózis módosítása

Konzílium kérés -eszkaláció

AKI 1-es stádium ÖNMAGÁBAN nem indikáció – szoros obszerváció!

Légzési elégtelenség és AKI 2-es, 3-as stádiuma

↓

ITO konzílium

Nincs légzési elégtelenség de

1. Hyperkalaemia (K 6mmmol/L)
2. AKI 2-es, 3-as stádiuma
3. AKI + haematuria és proteinuria
4. Progrediaáló AKI
5. AKI más okból

↓

Nefrológiai konzílium

Akut vesekárosodás kezelése

Konzervatív kezelések

Kacs diuretikum adása megfontolható folyadék túltelítődésben.

Hyperkalaemia kezelése: Kálium- kötők
Calcium glükonát vagy calcium klorid
Inzulin – dextróz
Inh. salbutamol
Nátrium – bikarbonát

Vesepótló kezelés indításának hagyományos idikációi:

1. Életet veszélyeztető refrakter hyperkalaemia
2. kezelésre nemreagáló folyadék telítettség
3. Súlyos metabolikus acidózis

COVID 19 Akut vesekárosodás – vesepótló kezelések módjai

Folyamatos kezelések	Intermittáló kezelések	Peritoneális Kezelések
CVVH CVVHDF CVVHD	IHD IHDF SLED PIRRT	PD APD

Összefoglalás

Az akut vesekárosodás COVID 19 betegségben gyakori.

FONTOS!

- Rizikóbecslés – Betegszelekció
- MEGELŐZÉS !
- Korai eszkaláció !
- Korai vizelet vizsgálat – proteinuria, haematuria ???