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COVID, Kidney, Disease & SARS-CoV-2

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An Overlooked, Possibly Fatal Coronavirus Crisis: A Dire Need for Kidney Dialysis

Ventilators aren't the only machines in intensive care units that are in short supply. Doctors have been confronting an unexpected rise in patients with failing kidneys.



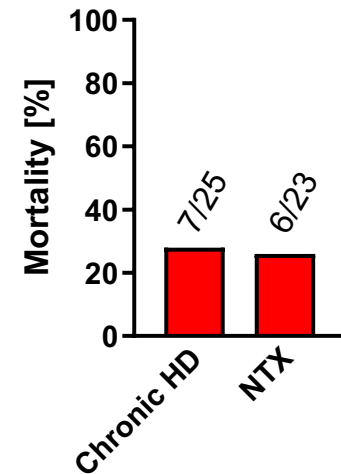
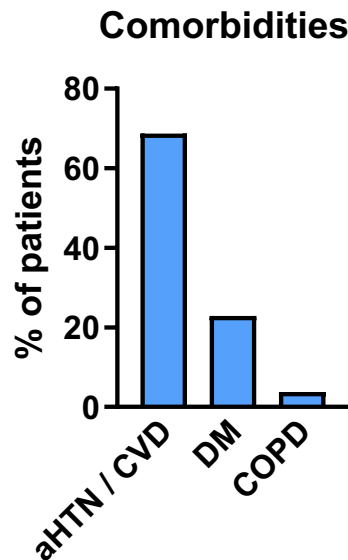
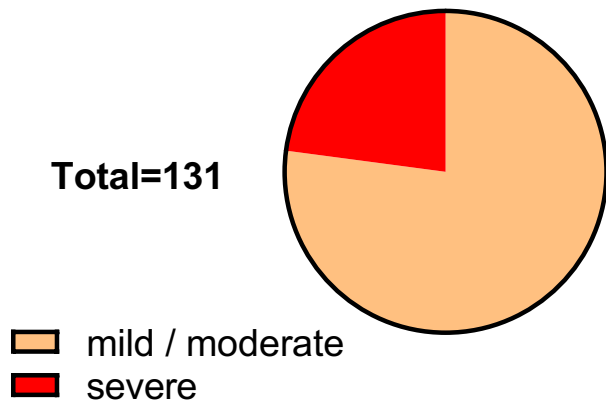
CKD & COVID-19

Italy (Brescia)

- 643 dialysis patients
- 94 (15%) SARS-CoV-2 positive
- 57 (61%) required hospitalization
- Mortality 29%

High risk of severe Covid-19 in patients with Chronic Kidney Disease

- All patients on maintenance hemodialysis in Wuhan, China (n = 7154)
- Incidence of Covid-19 ~2.2%



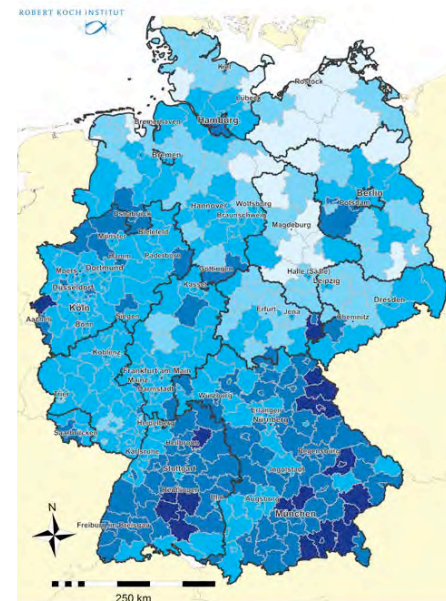
Xiong et al. *J Am Soc Nephrol* 2020

Trujillo et al. *Kidney Int Rep* 2020

COVID-19 in Germany

Up to June 2, 2020

- 182'028 cases
(2'775 cases in the last 7 days)
- 8'522 deaths



Cumulative incidence per 100'000 persons

< 0	-	≤ 50	(23)
> 0	-	≤ 100	(60)
> 100	-	≤ 250	(193)
> 250	-	≤ 500	(104)
> 500	-	≤ 2.000	(21)

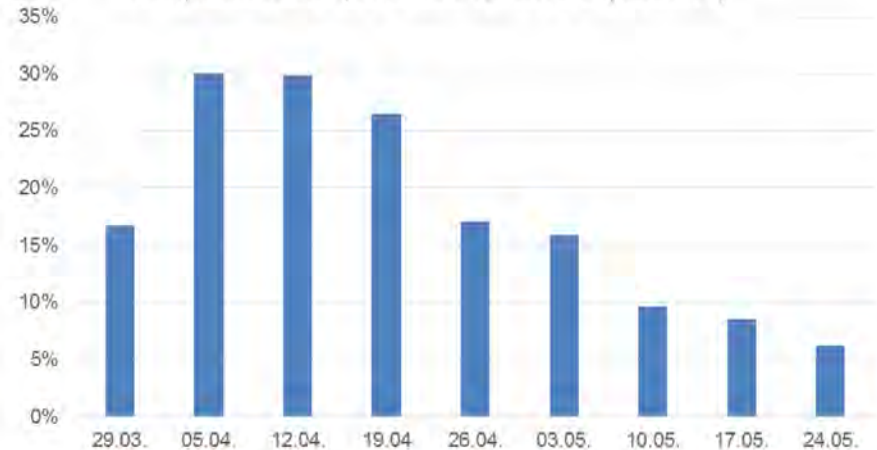
COVID-19 Registry of the German Society of Nephrology

Data available for approx. 14'000 dialysis patients

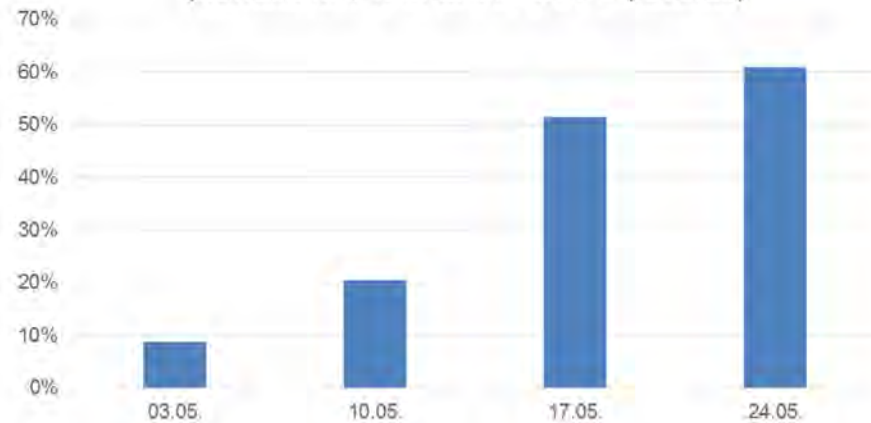
SARS-CoV-2 Patients (% of dialysis patients)



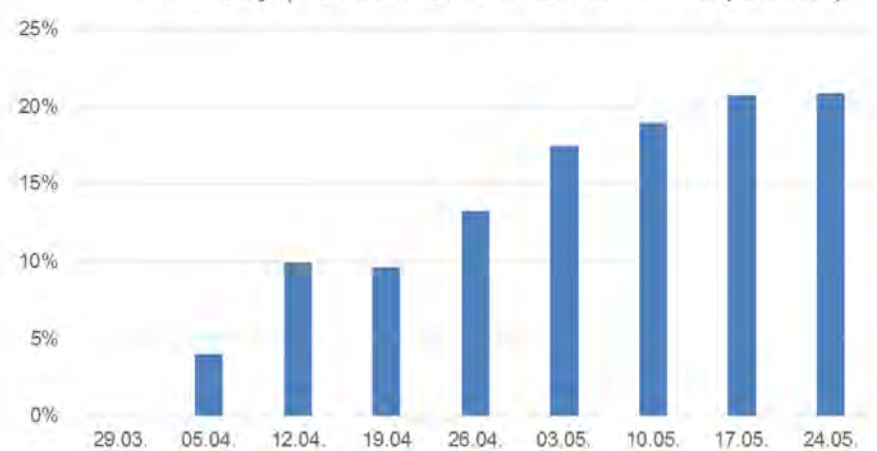
Hospitalization (% of SARS-CoV-2 patients)



Clearance of SARS-CoV-2
(Cumulative, % of SARS-CoV-2 patients)



Mortality (Cumulative, % of SARS-CoV-2 patients)

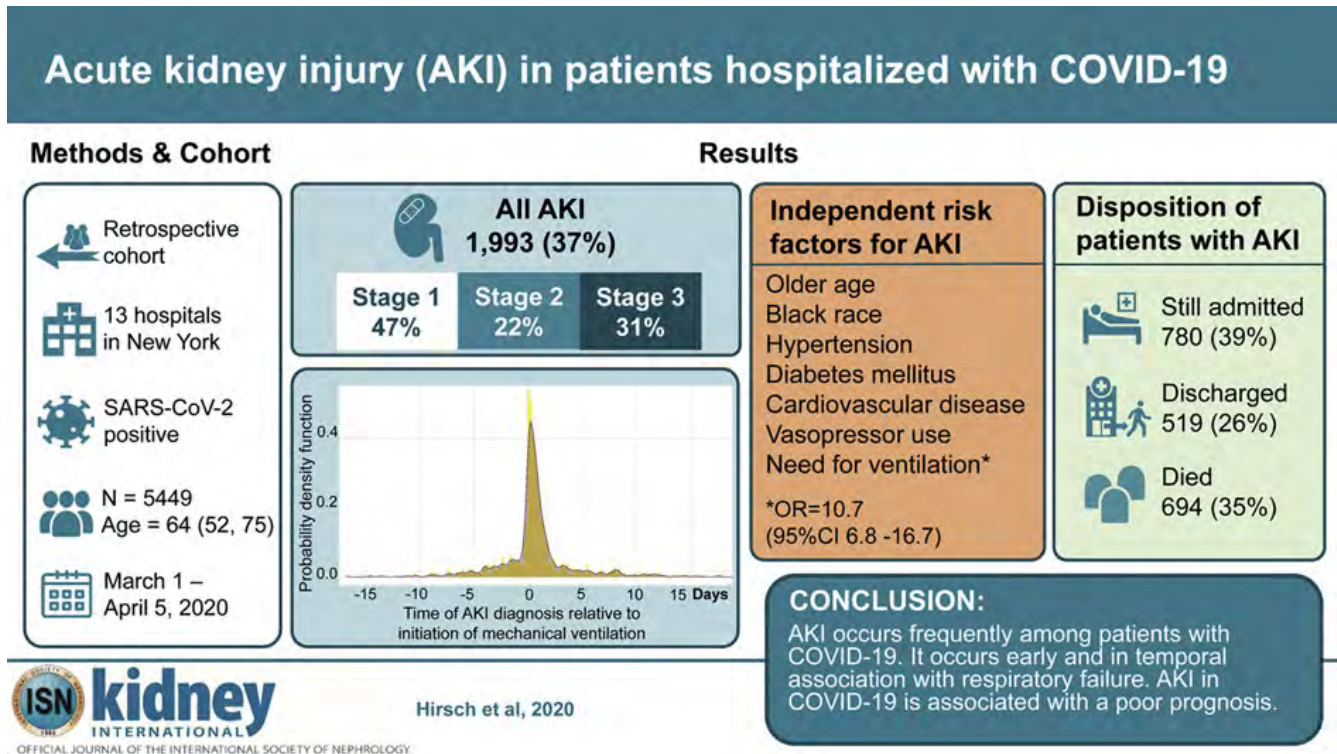


Patients with kidney disease are particularly vulnerable to COVID-19

- Older age, common comorbidities, increased mortality risk
- Impairment of immune system
(because of ESKD, the underlying disease or its treatment)
- No home-isolation possible (esp. in-center dialysis patients)

AKI & COVID-19

Renal involvement in Covid-19 patients is frequent and predicts mortality



ACUTE KIDNEY INJURY IN PATIENTS HOSPITALIZED WITH COVID-19

Jamie S. Hirsch, Jia H. Ng, Daniel W. Ross, Purva Sharma, Hitesh H. Shah, Richard L. Barnett, Azzour D. Hazzan, Steven Fishbane, Kenar D. Jhaveri, on behalf of the Northwell COVID-19 Research Consortium and the Northwell Nephrology COVID-19 Research Consortium

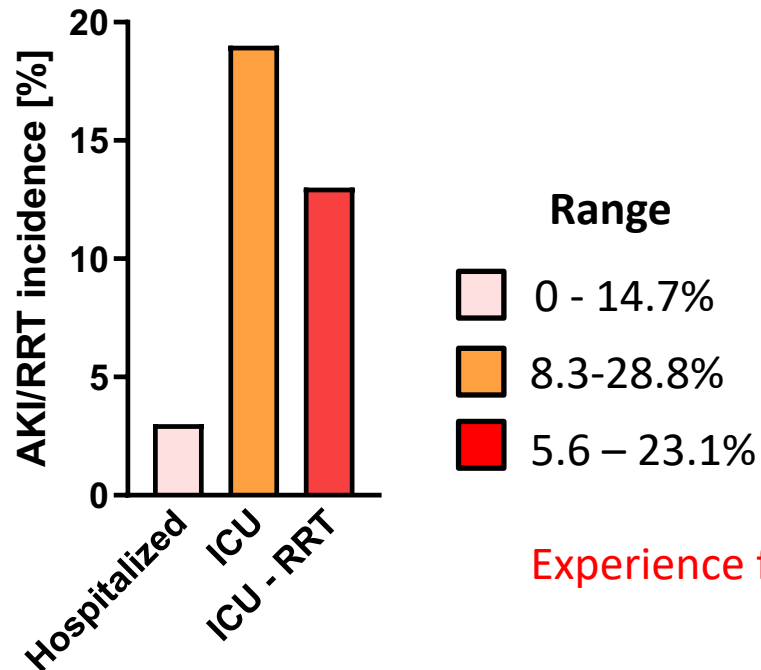
Acute kidney injury in COVID-19 patients

	No use of invasive mechanical ventilation (N=4259)	Required invasive mechanical ventilation (N=1190)
No AKI	3334 (78.3%)	122 (10.3%)
AKI, any stage	925 (21.7%)	1068 (89.7%)
AKI stage 1	639 (15.0%)	288 (24.2%)
AKI stage 2	185 (4.3%)	262 (22.0%)
AKI stage 3	101 (2.4%)	518 (43.5%)
Required renal replacement therapy	9 (0.2%)	276 (23.2%)

Akute Kidney Injury in Covid-19 patients

Metaanalysis of 9 studies
(mostly China) with ~2800
patients.

JASN study not yet included

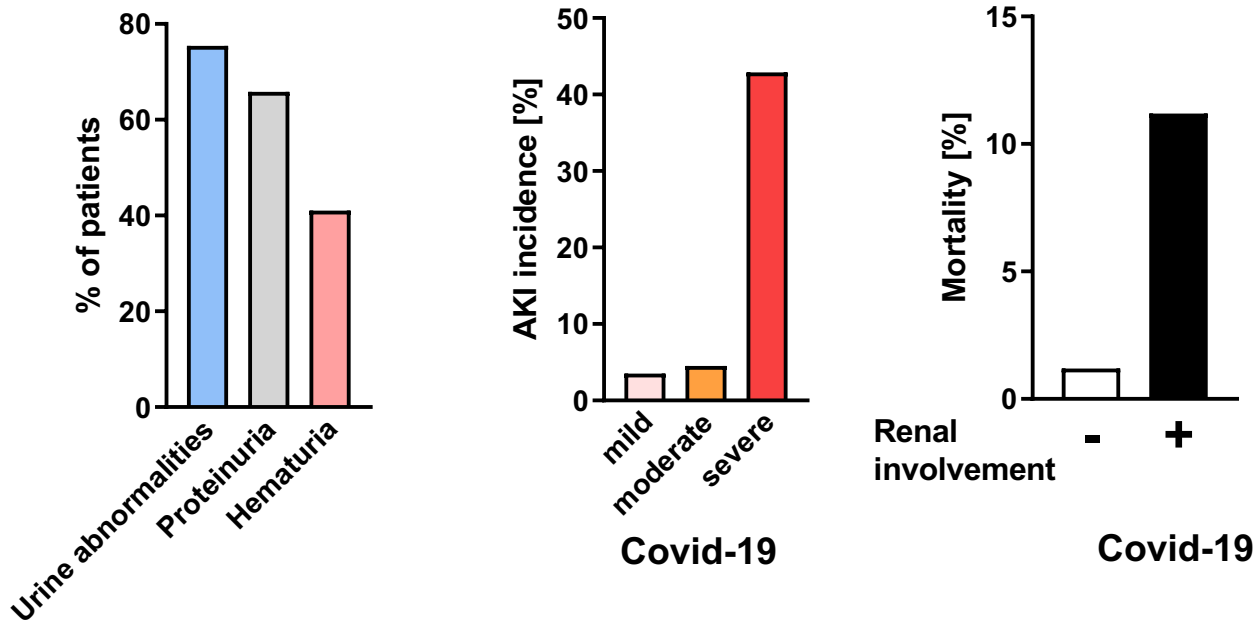


Experience from UKE ICU: 25-30%

Arentz et al. *JAMA* 2020; Cheng et al. *Kidney Int.* 2020; Guan et al. *N Engl J Med.* 2020; Huang *Lancet* 2020; Shi et al. *JAMA Cardiol* 2020; Wang et al. *Am J Nephrol* 2020; Wang et al. *JAMA* 2020; Yang et al. *Lancet Respir Med* 2020; Zhou et al. *Lancet* 2020.

Renal involvement in Covid-19 patients is frequent and predicts mortality

333 hospitalized patients with Covid-19 pneumonia, single center, China



Acute kidney injury in COVID-19 patients

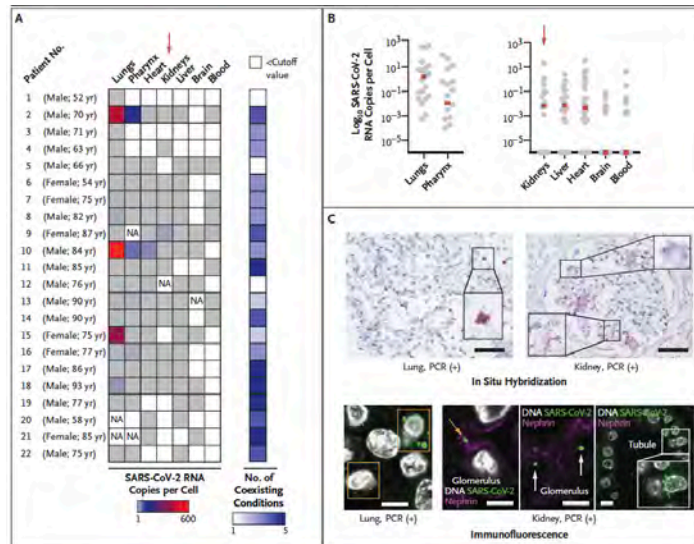
- Acute tubule injury
- Endothelial damage
- Secondary damage
(drug-induced, ischemic injury, secondary infections, rhabdomyolysis, etc.)
- Virulence of SARS-CoV-2 in the kidney?
(tubular epithelium, podocytes, other glomerular cells)

SARS-CoV-2 & Kidney

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Multiorgan and Renal Tropism of SARS-CoV-2



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Multiorgan- and Renal tropism of SARS-CoV-2

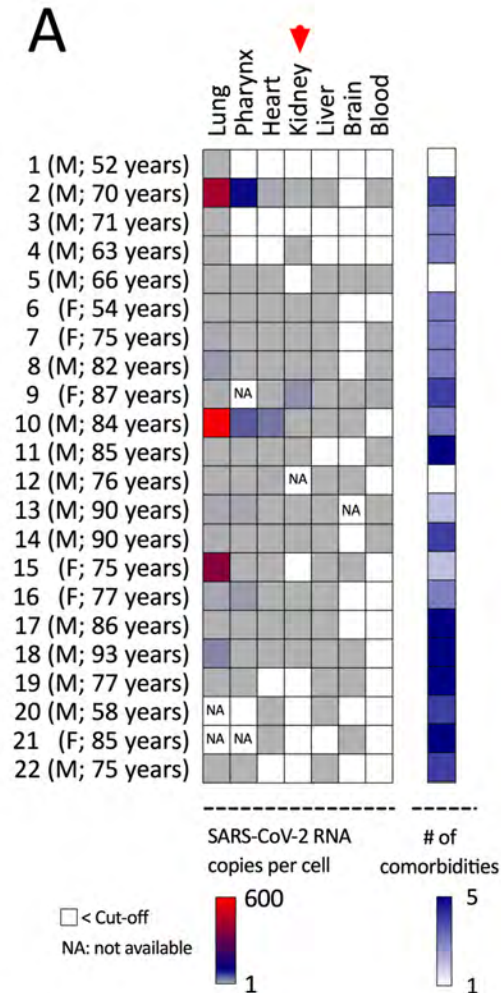
Table S1. This table summarizes post-mortem interval (PMI), number of coexisting conditions highlighting affected organ systems including chronic kidney disease (kidney), and laboratory findings, including urinary analysis, blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR) and SARS-CoV-2 RNA copies per kidney cell.

Identifiers		Number of coexisting conditions						Laboratory findings			
Case	PMI (days)	Respiratory tract	Cardiovascular system	Kidney	Brain	Metabolism	Other	Urine analysis *	BUN (mmol/l)	eGFR (ml/min/1.73m ²)	Kidney PCR [§]
1	1	-	-	-	-	1	-	NA	NA	NA	<DT
2	1	-	2	1	1	-	-	NA	16,84	20	0,0902
3	2	1	1	-	-	-	1	NA	3,50	52,4	<DT
4	1	1	-	-	-	2	-	NA	2,67	92,3	0,0391
5	2	-	1	-	-	-	-	NA	NA	NA	<DT
6	1	-	-	-	2	-	1	NA	NA	88,9	0,3219
7	4	-	2	-	-	-	1	Protein (+), Erythrocytes (++)	NA	55,1	0,0899
8	1	-	1	-	1	1	-	NA	NA	50,8	0,0122
9	4	1	1	1	-	-	1	NA	NA	36,9	18,6932
10	5	-	1	1	-	1	-	NA	NA	36,2	1,2144
11	2	1	3	-	-	-	1	Normal	4,34	60,9	0,0078
12	3	-	-	-	-	1	-	NA	3,00	85,1	NA
13	3	1	1	-	-	-	-	NA	NA	53,0	0,9050
14	2	-	2	-	1	1	-	NA	NA	NA	0,0012
15	2	-	2	-	-	-	-	NA	NA	NA	<DT
16	1	1	1	-	1	-	-	NA	NA	NA	0,0050
17	2	1	1	1	2	-	-	NA	NA	NA	0,0524
18	2	1	3	-	-	1	-	NA	13,84	36,0	0,0066
19	2	1	3	1	-	-	-	NA	10,51	28,0	<DT
20	6	1	1	-	1	-	1	NA	NA	NA	<DT
21	0	-	3	1	-	-	1	Protein (+)	17,18	14,0	<DT
22	4	1	3	1	-	-	-	NA	26,02	26,0	<DT
23	2	-	-	-	1	-	2	NA	10,34	82,0	0,0101
24	NA	-	3	1	-	-	-	NA	NA	NA	<DT
25	3	-	2	1	-	1	-	NA	19,01	8 [§]	0,3395
26	9	-	2	-	1	-	-	NA	9,67	40,0	0,1371
27	9	-	3	1	-	1	-	NA	13,17	20,0	<DT

In number of coexisting conditions (-) represents absence in the clinical records; NA: not available; [#]obtained with urinary stix and sediment, [§]patient was on dialysis since 2014, [&]total SARS-CoV-2 RNA copies corrected for beta β-globin, <DT: below detection threshold.

Patients dying from COVID-19 have a high number of co-morbidities

Multiorgan- and Renal tropism of SARS-CoV-2



Higher number of co-morbidities associates with multiorgan tropism

Multiorgan- and Renal tropism of SARS-CoV-2

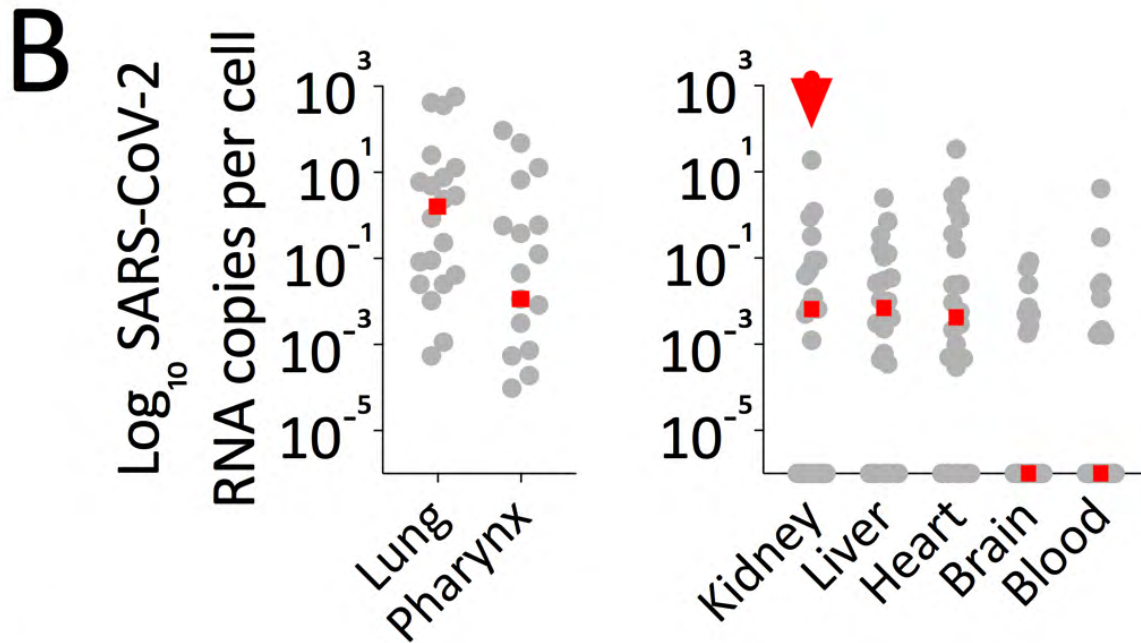
# of coexisting conditions	Heart PCR		Liver PCR		Brain PCR		Kidney PCR	
	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)
1-2	1 (20%)	4 (80%)	1 (20%)	4 (80%)	1 (25%)	3 (75%)	3 (75%)	1 (25%)
3-5	4 (24%)	13 (76%)	4 (24%)	13 (76%)	12 (71%)	5 (29%)	5 (29%)	12 (71%)

Particularly, kidney tropism increases with co-morbidities

Table S3. This table summarizes renal tropism of SARS-CoV-2 [Kidney PCR (+)] in the presence or absence of reported chronic kidney disease (CKD).

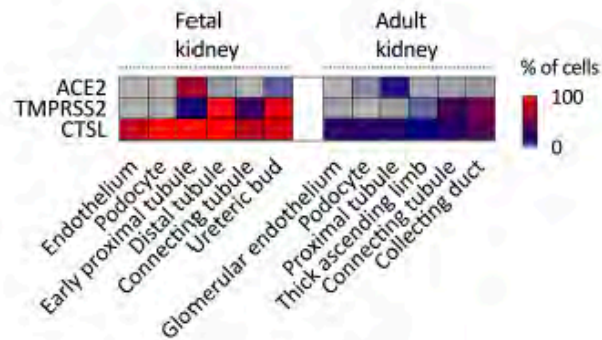
CKD history	# of cases	Kidney PCR	
		(-)	(+)
With history of CKD	8	4 (50%)	4 (50%)
Without history of CKD	10	1 (10%)	9 (90%)

In patients with preexisting CKD, there seems to be less kidney tropism



After the respiratory tract, kidneys exhibits the highest viral load

Fig. S1. SARS-CoV-2 infection adhesion and facilitator genes in renal cells



The high presence of SARS-CoV-2 infection adhesion and facilitator genes throughout different kidney compartments is shown using an in-silico analysis of publicly available single cell RNA sequencing data. Data was retrieved from Muus et al.⁶ and Hochane et al.⁷.

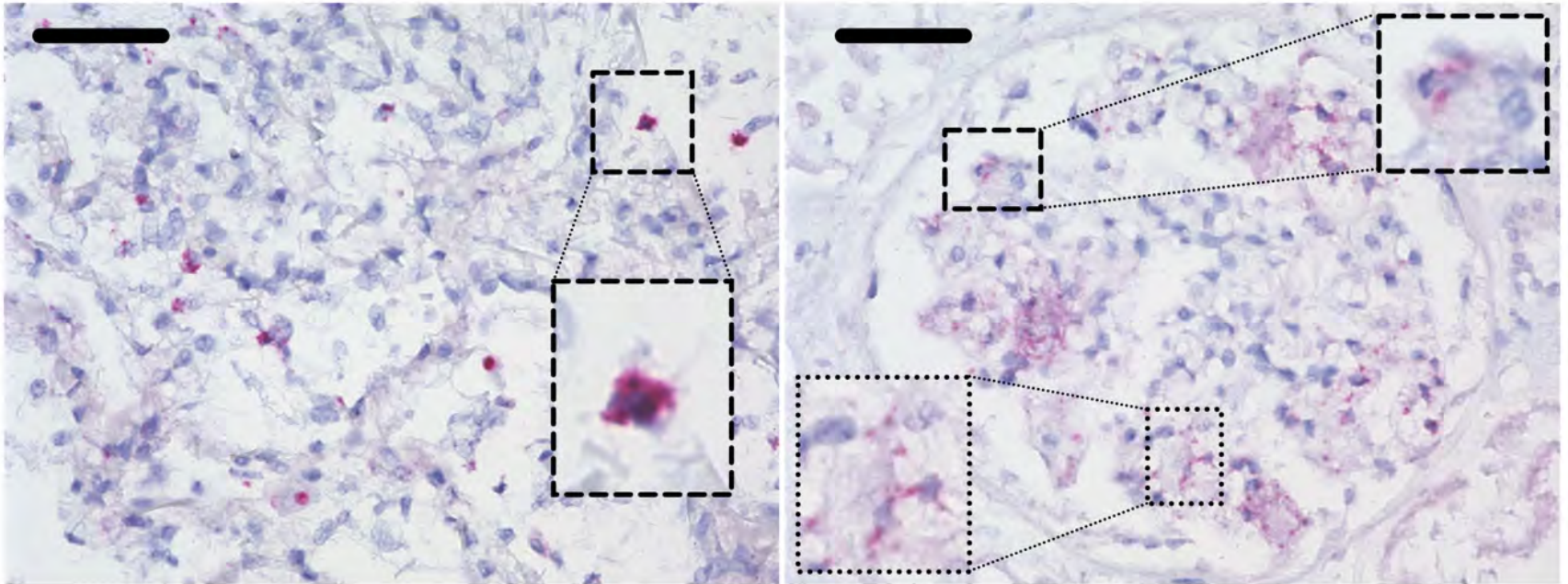
Kidneys do express SARS-CoV-2 adhesion and facilitator genes

C

Lung - PCR (+)

Kidney - PCR (+)

In situ hybridization

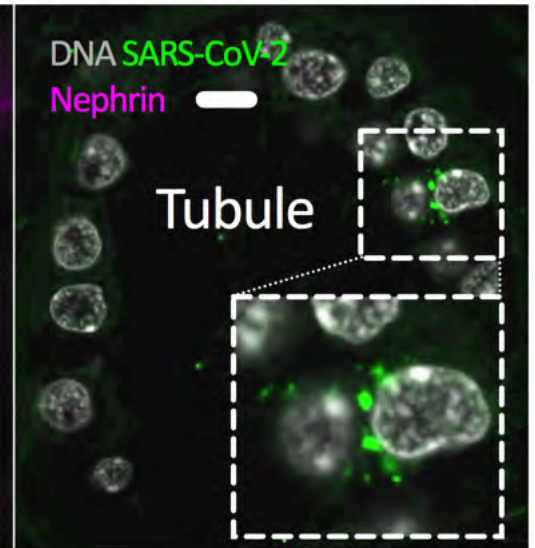
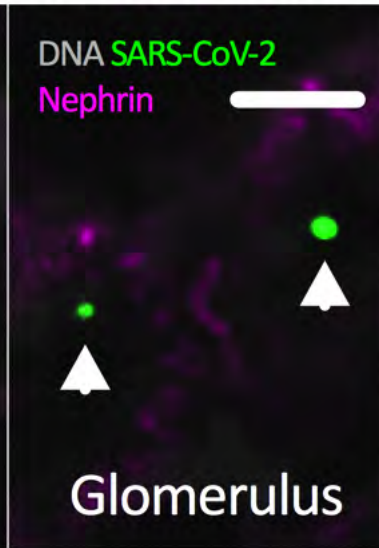
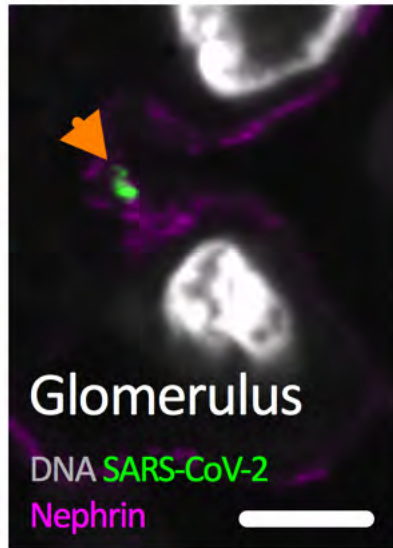
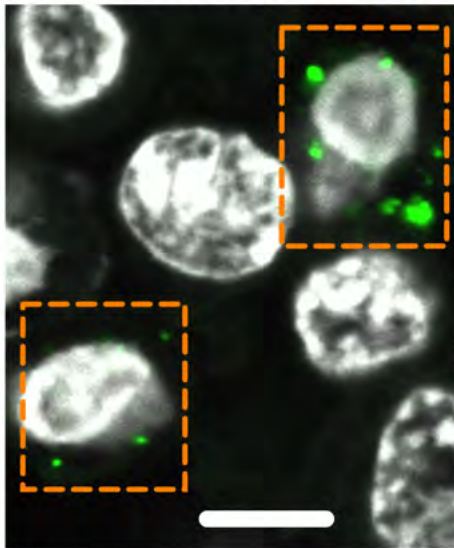


ISH detects SARS-CoV-2 RNA in the kidney

Lung - PCR (+)

Kidney - PCR (+)

Immunofluorescence



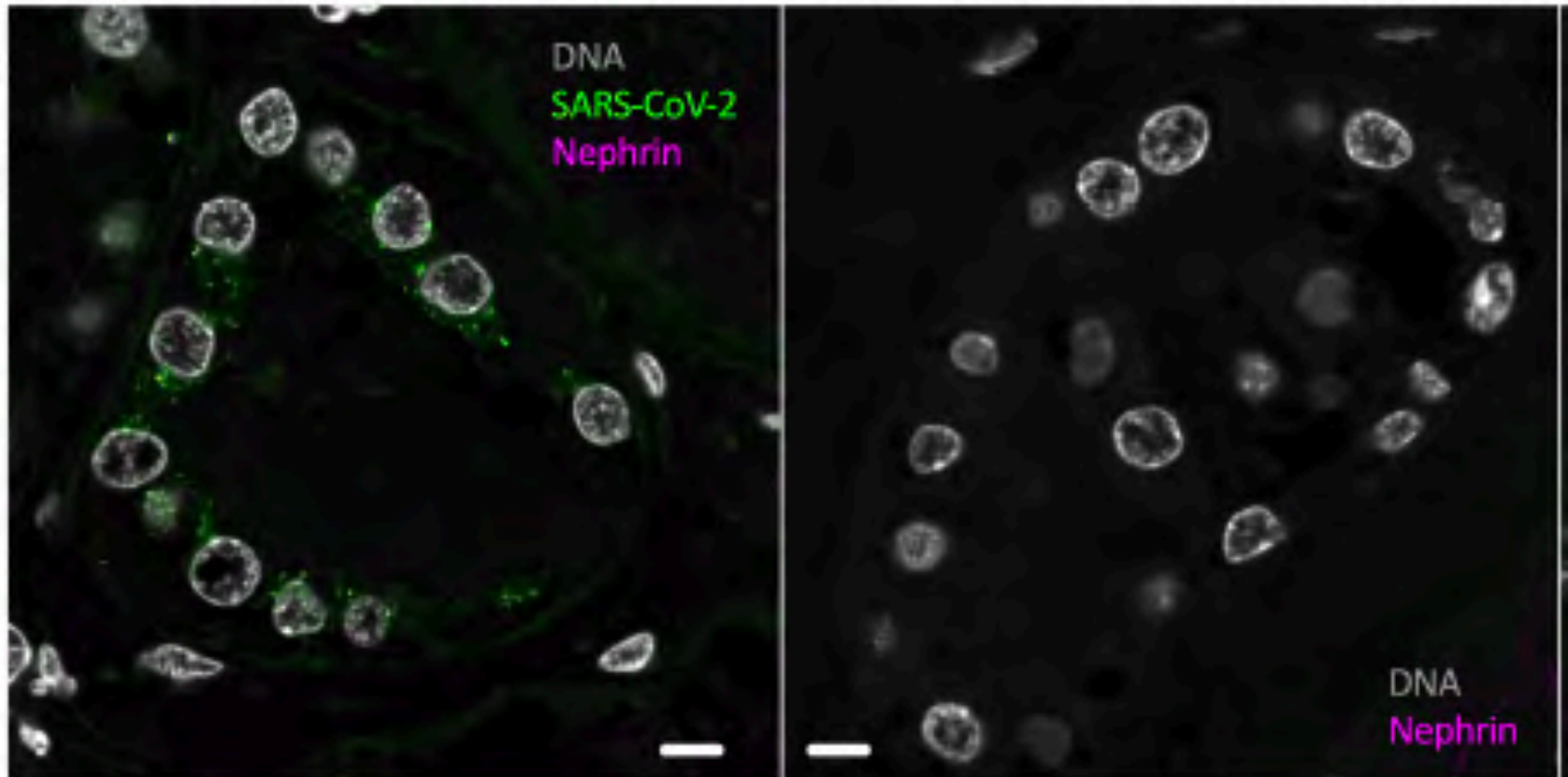
IF confirms SARS-CoV-2 protein in the kidney

Renal tropism of SARS-CoV-2

Tubuli

PCR (+) - primary and secondary antibodies

PCR (-) - primary and secondary antibodies



Renal tropism of SARS-CoV-2

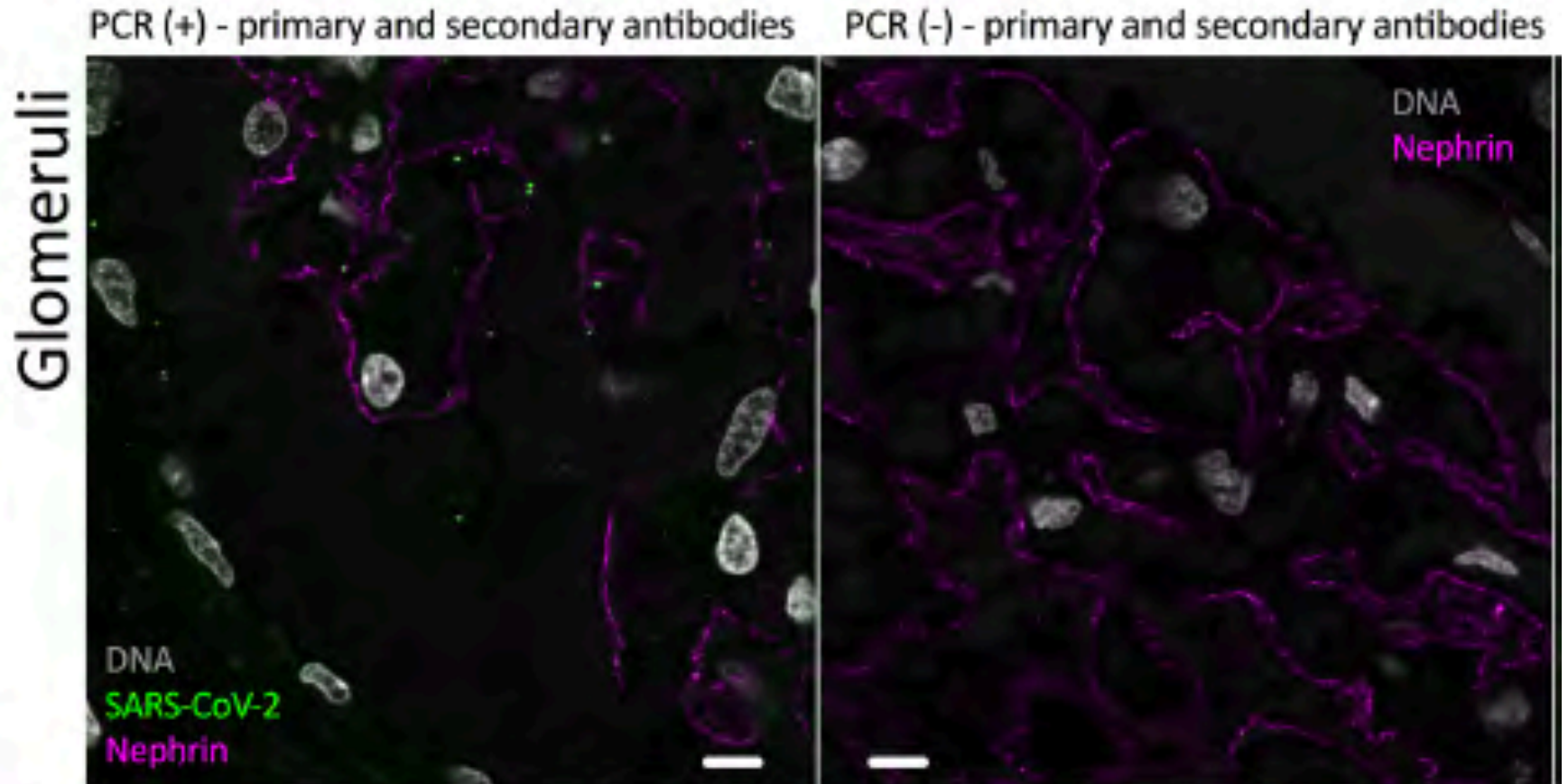
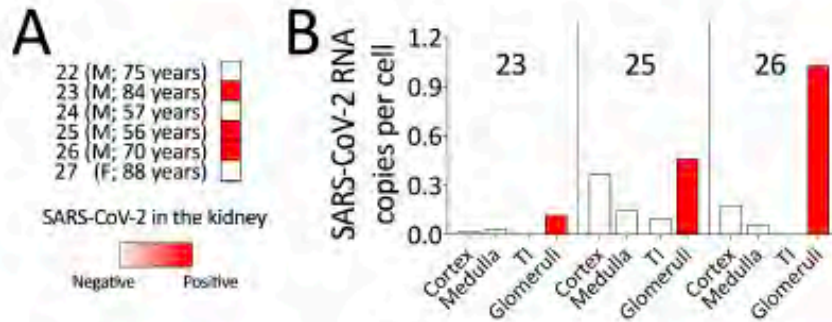


Fig. S2. SARS-CoV-2 is detected in all renal compartments

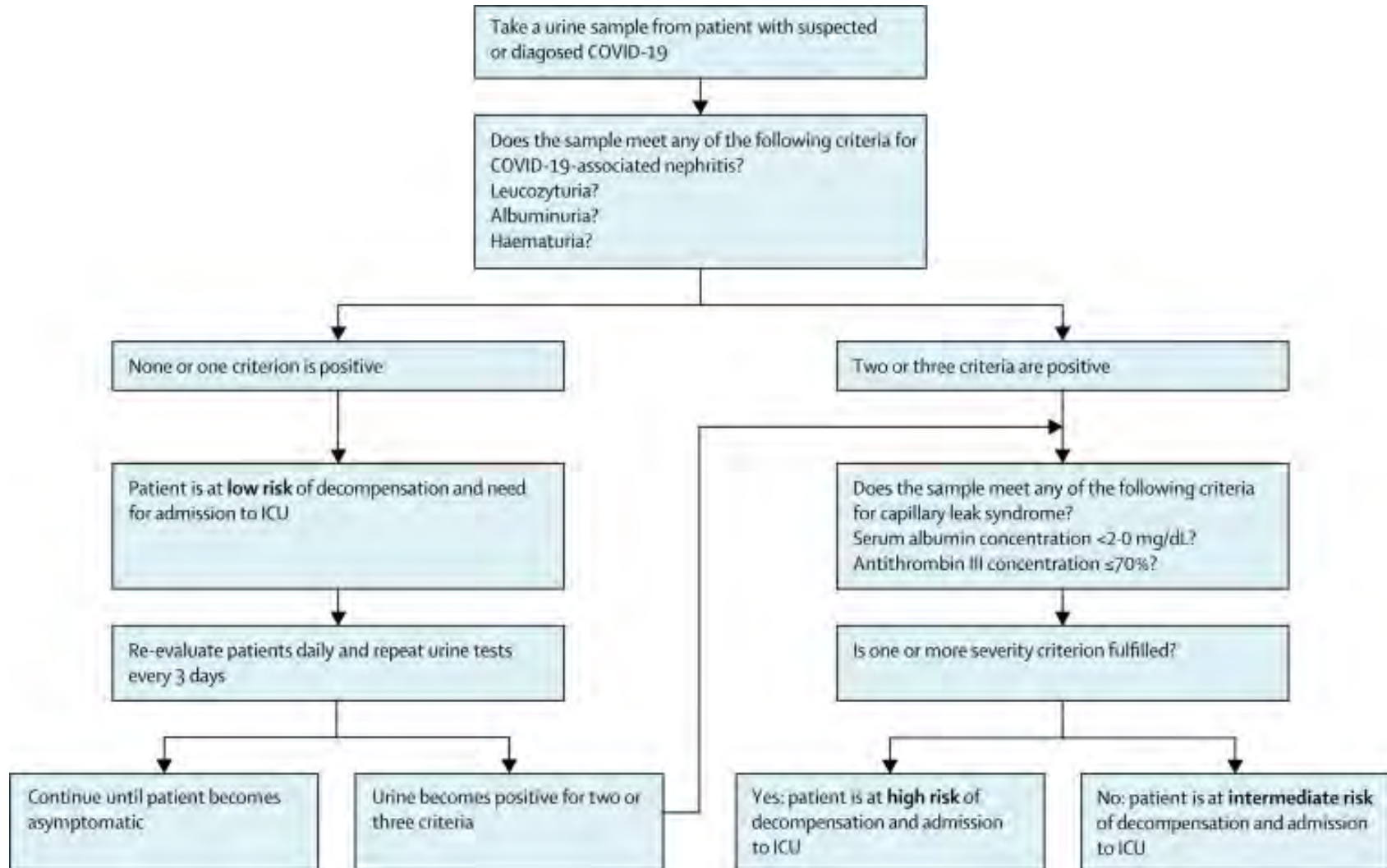


Panel A shows that SARS-CoV-2 is detected in random kidney samples containing both cortex and medulla and Panel B shows SARS-CoV-2 detection in all renal compartments, especially in kidney glomeruli; where TI represents the tubulo-interstitial compartment.

Enrichment of SARS-CoV-2 in the glomerular compartment

SARS-CoV-2 & Kidney Outlook

Can urine abnormalities serve as outcome predictors in COVID-19 patients?



The background is a vibrant, textured collage of colors including green, yellow, blue, and red. The textures are intricate and organic, resembling coral reefs, dense foliage, or perhaps microscopic biological structures. The colors are layered and interwoven, creating a rich, multi-dimensional visual effect.

Questions