



Long-Covid bei nierenkranken Patienten

46.
Nephrologisches
Seminar in
Heidelberg

19. März 2022

M. Zeier

Themen zu Post-Covid bei nierenkranken Patienten

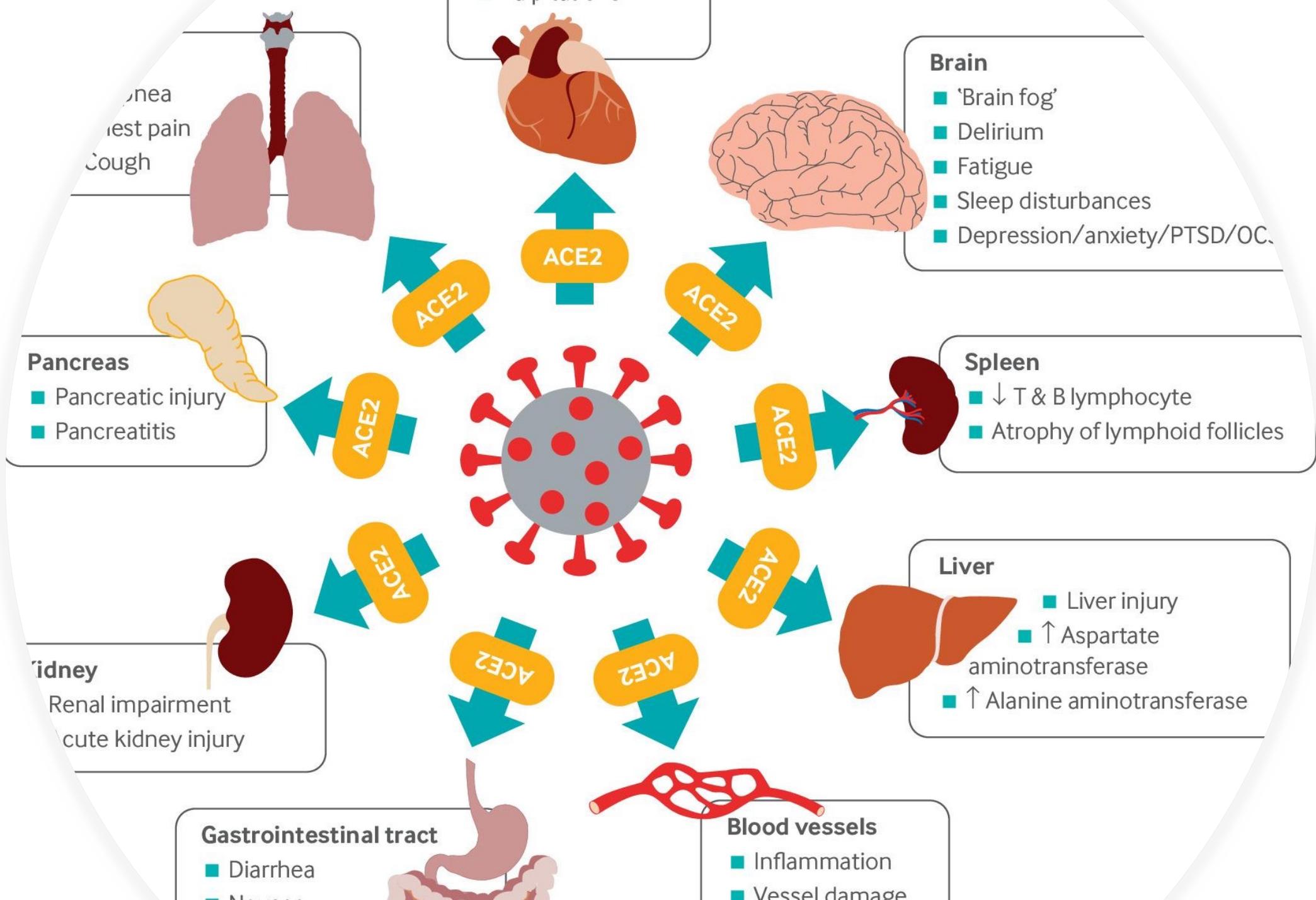
Post-Covid/Long-Covid – eine
Einteilung

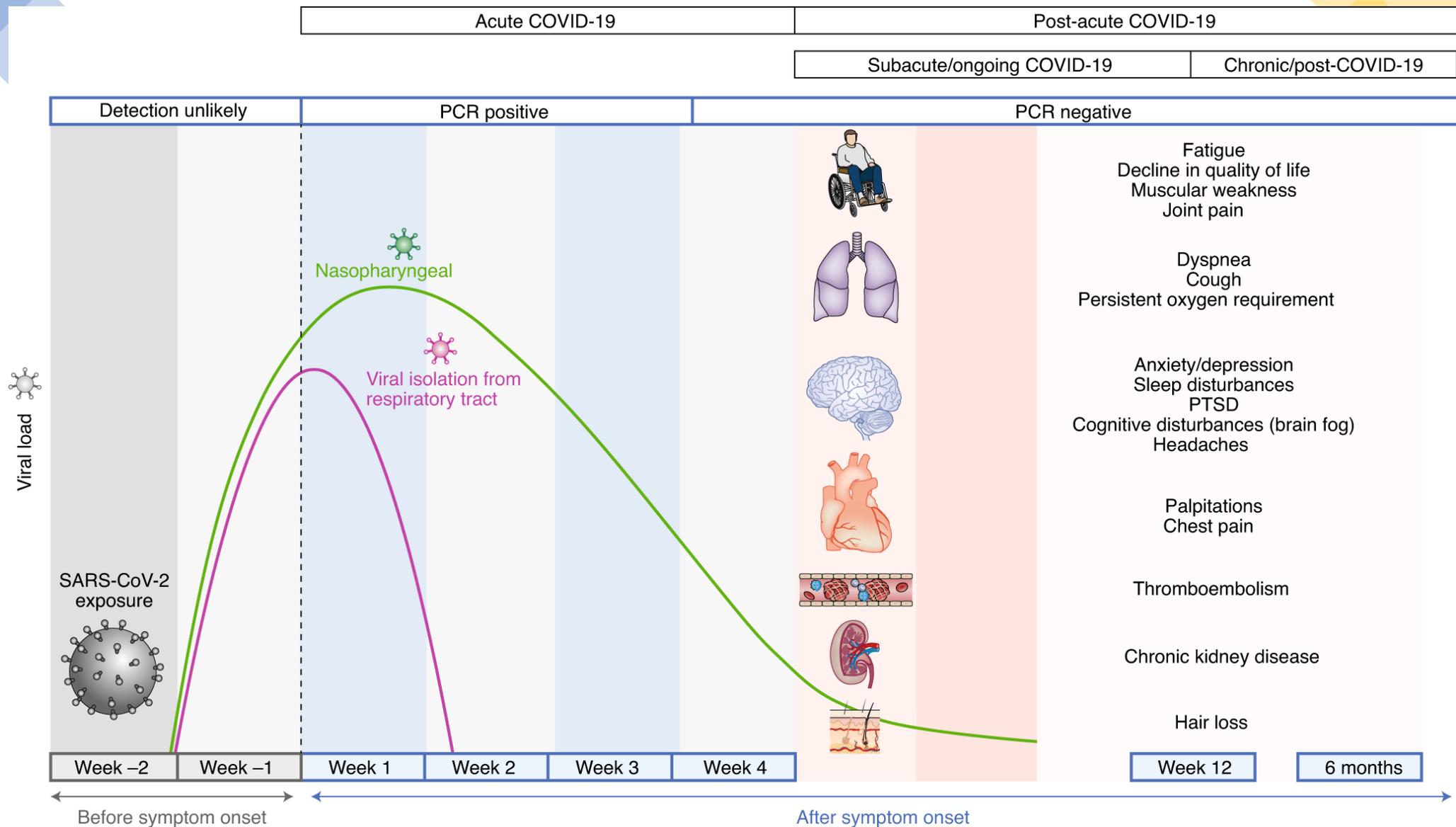
Long-Covid und Niere

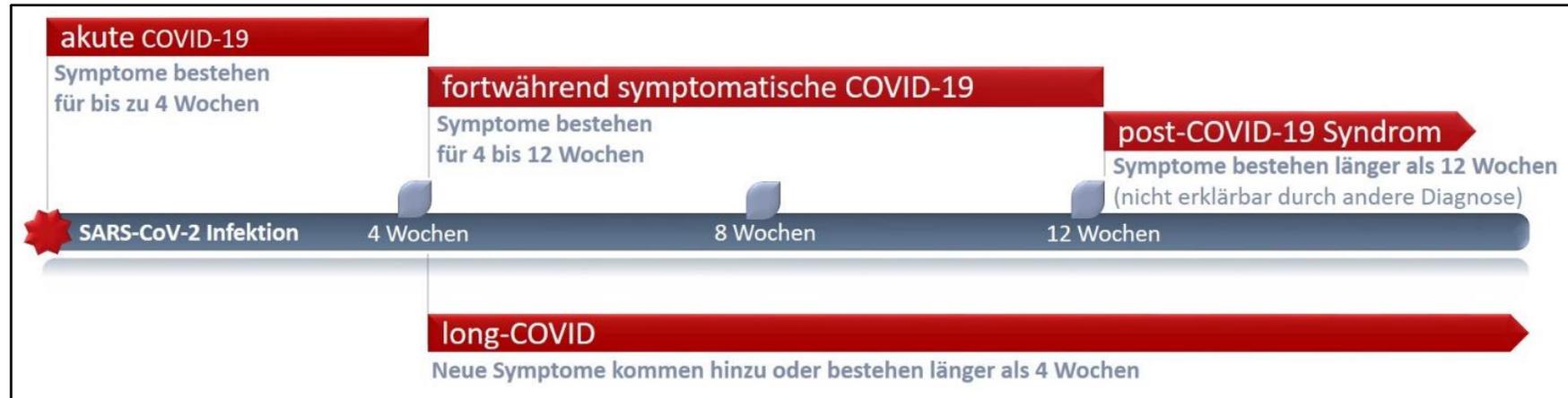
Impfantwort

Covid-Infektion der Nieren,

Akutes Nierenversagen und
die Entwicklung einer
chronischen Niereninsuffizienz







AWMF Leitlinie zu Covid/Post-Covid/Long-Covid

NICE Guideline on long covid BMJ 2020

Zwischen-Fazit

Bestehen mehr als 12 Wochen nach einer aktiven Infektion Symptome, deviante Laborwerte bzw. deren Kombination wird allgemein von einem Post-Covid-Syndrom gesprochen. Andere Erklärungen für den Zustand wurden ausgeschlossen

Co-Morbidität und Schwere der Erkrankung sind Determinanten des Post-Covid-Syndroms

Alter

Vorbestehende Niereninsuffizienz CKD

Diabetes und Hypertonie mit oder ohne CKD

Erkrankungsdauer

Stationäre Behandlung

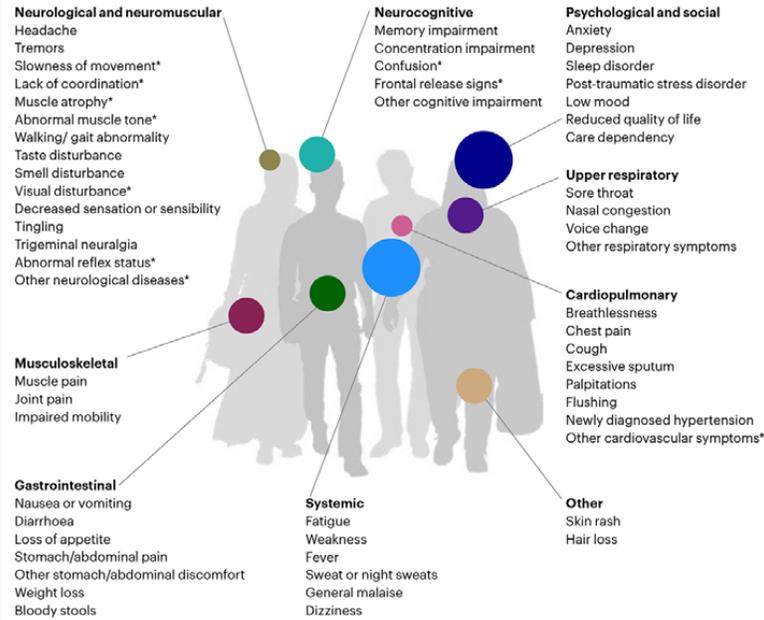
Intensivmedizinische Behandlung incl. Beatmungstherapie

Long Covid symptoms and signs

Frequency: Very common Common Less common

People hospitalised during acute phase of Covid-19

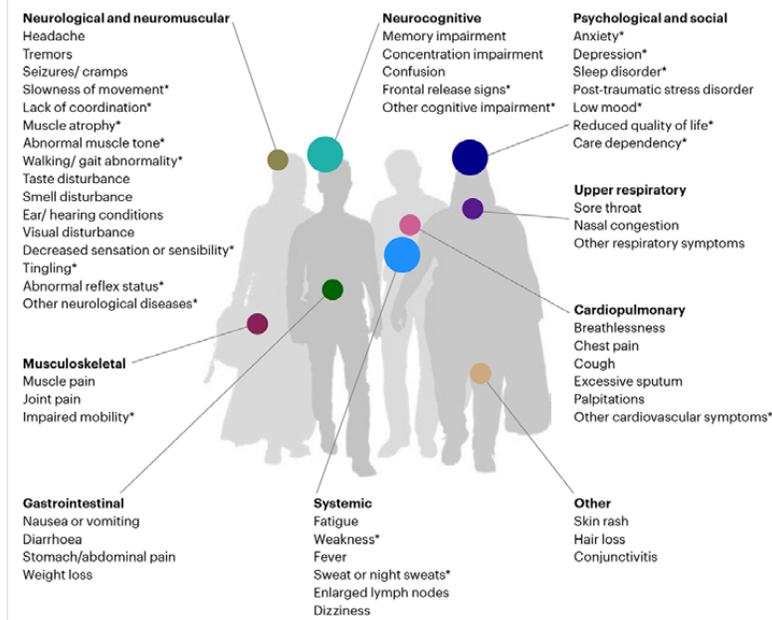
Based on 26 studies with 7147 people*



* Identified only in studies including both hospitalised and non-hospitalised people (9 studies including 2636 people)

People non-hospitalised during acute phase of Covid-19

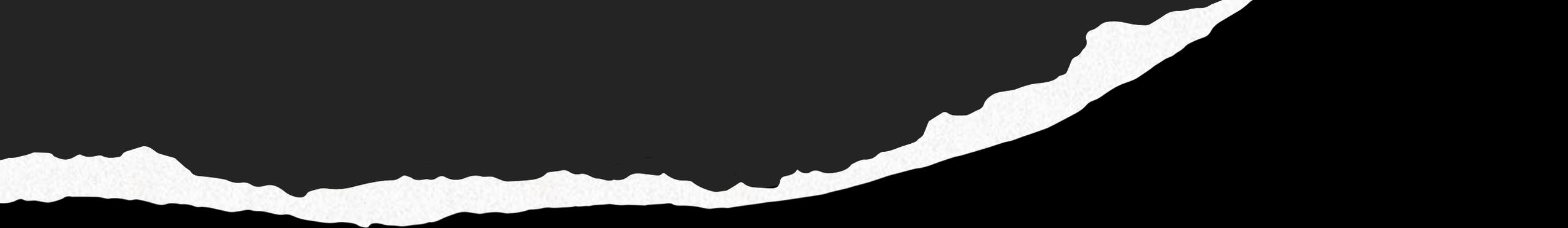
Based on 4 studies with 1168 people*



Last updated 17 Mar 2021

Symptome von Long-Covid – Vergleich von hospitalisierten und nicht-hospitalisierten Patienten

- Besonderer Fokus auf den neurologischen und psychischen Auswirkungen
- Die Nieren und die Nierenfunktion sind nicht im Fokus
- BMJ Global Health 2021



Die Infektion der Nieren und potentielle Auswirkungen

Direkte
Auswirkungen
auf die Nieren –
Infektion
parenchymaler
Strukturen

ACE2-Rezeptor – Eintrittspforte für SARS-Cov-2 Virus

- Bürstensaum von proximalen Tubuluszellen, Podozyten

SARS-Cov-2 Infektion von Nierenzellen

- Glomerulonephritis
- Akute Tubulus-Nekrose
- Infektionsnachweis in tubulären Epithelzellen und Podozyten

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

Study Cohort

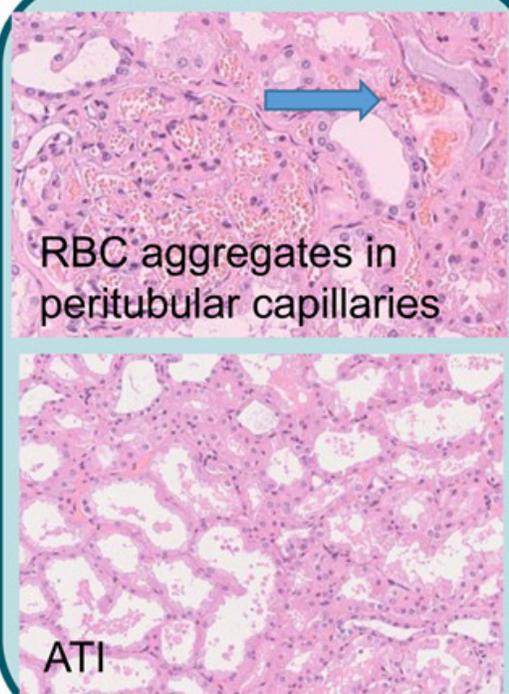


26 autopsies in COVID-19 patients

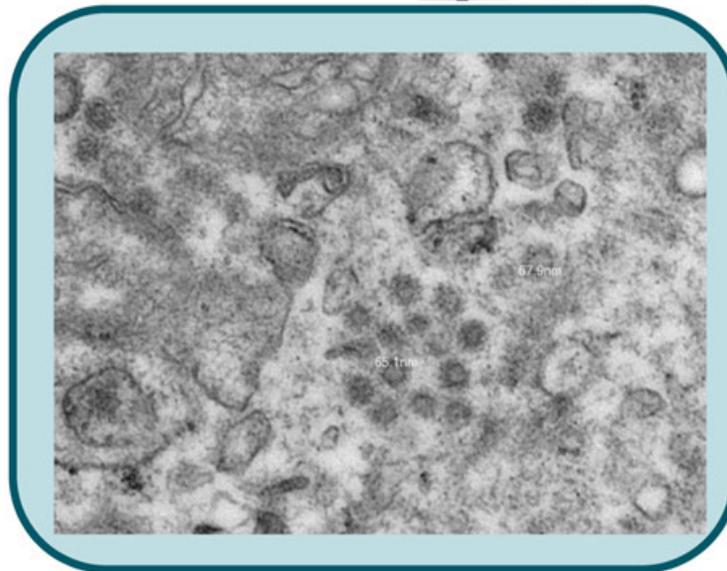
- death due to respiratory failure
- average age 69 years
- 19 males; 7 females
- 9/26 showed clinical signs of kidney injury



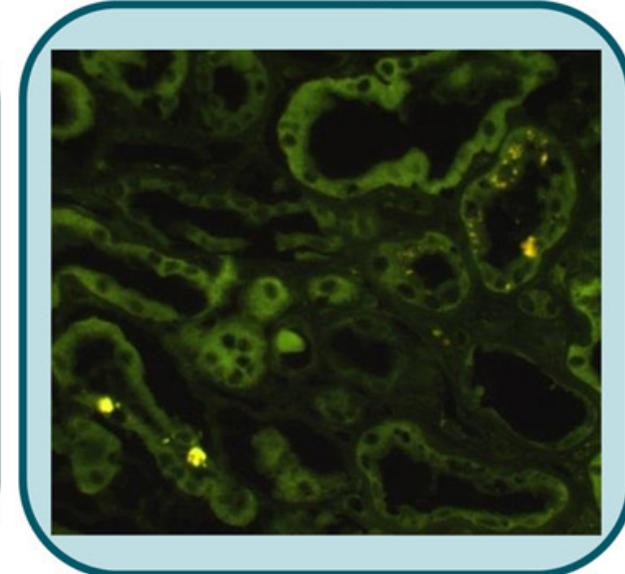
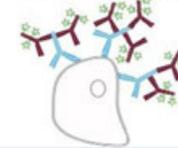
Light microscopy: ATI, RBC aggregates



Electron microscopy: virus in tubules and podocytes



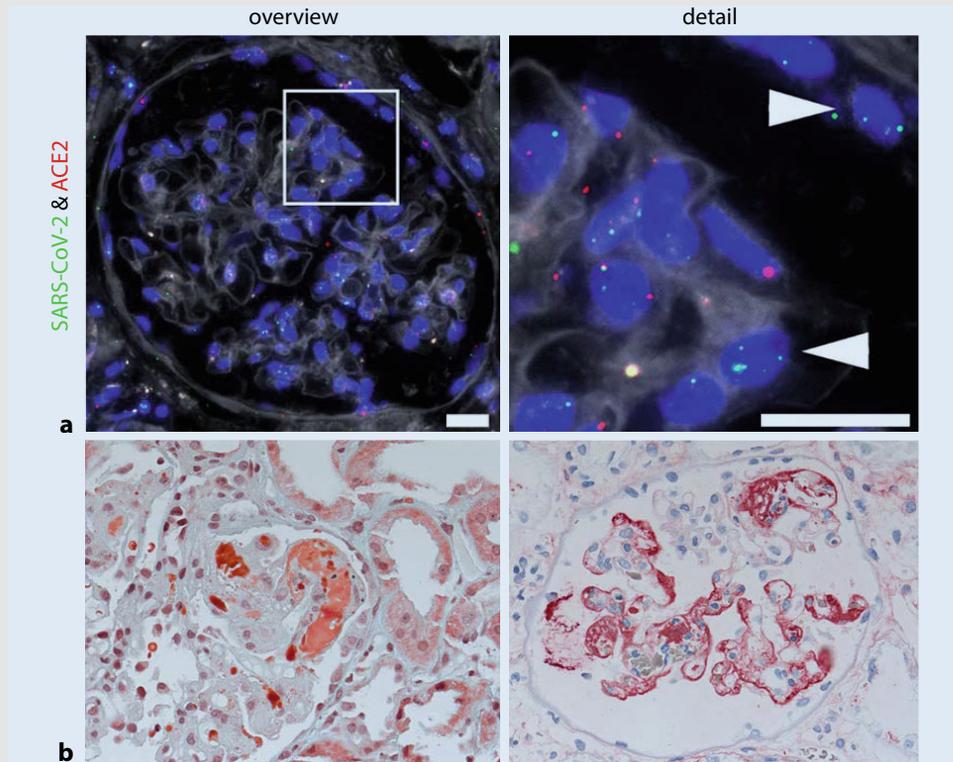
SARS-CoV nuclear protein detection



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.

SARS-Cov-2 Infektion von Nierenzellen



- SARS-Cov-2-Virusnachweis in glomerulären Zellen (ACE-Rezeptor)
- Thrombotisches Material in glomerulären Kapillaren. NPE eines 38-jährigen mit AKI
- Amann; Pathologe 2020

Case series of 10 native kidney biopsies in patients with COVID-19 and AKI

Cohort



10 patients with COVID-19

Mean age = 65 years

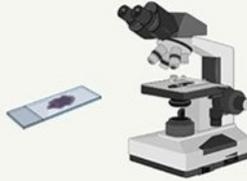


AKI, proteinuria ± hematuria



8 required dialysis

Kidney Biopsy Findings



Pathologic Findings

- All patients had varying degree of ATN
- 2 had TMA
- 1 had myoglobin cast nephropathy
- 1 had pauci-immune crescentic GN
- 1 had FSGS with features of collapsing glomerulopathy



SARS-CoV-2

- All negative for SARS-CoV-2 by immunohistochemistry
- No viral particles identified via electron microscopy

Conclusion: This kidney biopsy series showed ATN as the most common finding in patients with COVID-19 and AKI. We found no evidence of significant viral presence in the kidney.

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JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

Nephropathology of Coronavirus 2019 Disease (COVID-19): A Multi-Center Retrospective Cohort Study by the COVID-19 Kidney Biopsy Consortium

kidney
INTERNATIONAL



Study population:



COVID-19 patients with kidney failure from 10 institutions (n=240 native, 44 allografts)

Methods:



Kidney biopsy evaluation, APOL1 genotyping, and SARS-CoV-2 immunohistochemistry

Results:



Collapsing glomerulopathy (COVAN)
Myoglobin cast nephropathy
PGMID
Rejection (in allografts)



Arterionephrosclerosis
Diabetic nephropathy
IgA nephropathy

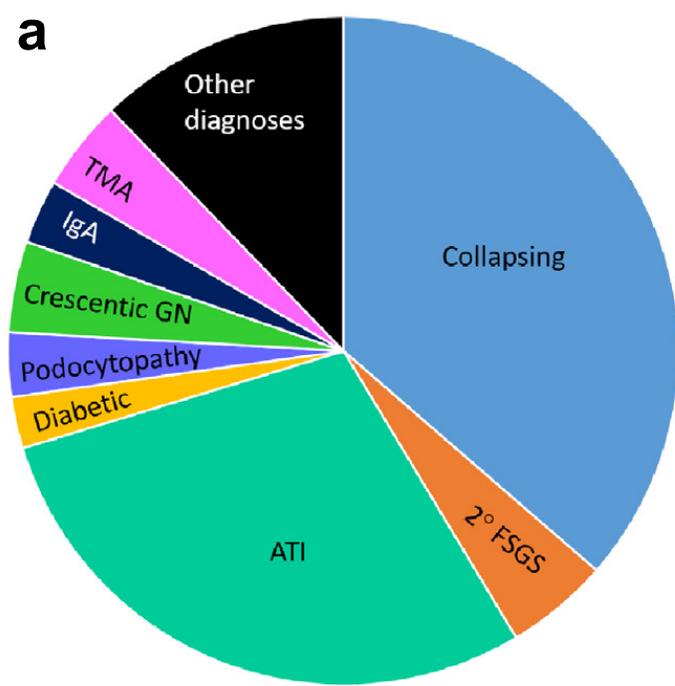


60.7% high-risk
APOL1 genotype

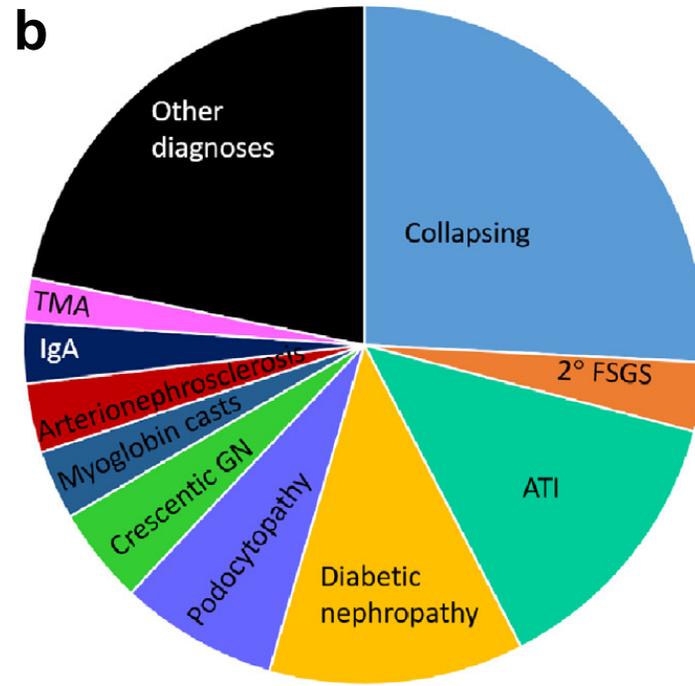


No direct viral
infection in tissue

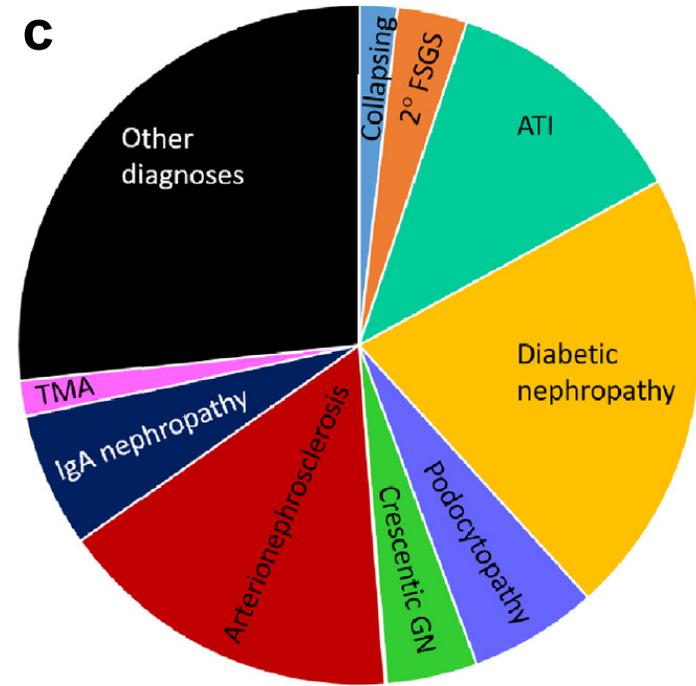
CONCLUSION: There is increased frequency of COVAN associated with a high-risk *APOL1* genotype in COVID-19 patients. Proliferative glomerulonephritis with monoclonal immune deposits (PGMID), and myoglobin cast nephropathy were also enriched and chronic conditions were under-represented in this cohort (n=284 biopsies).



Reported COVID-19 biopsies (n = 159)



COVID-19 biopsies (n = 240)



Control biopsy database (n = 63,575)

Figure 2 | Frequencies of diagnosis in coronavirus disease 2019 (COVID-19) kidney biopsies compared to the pre-pandemic biopsied population. (a) Frequencies of diagnosis of COVID-19 kidney biopsies reported in the literature ($n = 159$ patients). (b) Frequencies of diagnosis of COVID-19 kidney biopsies in our multi-institutional cohort ($n = 240$ patients). (c) Comparison of diagnostic frequencies in the 5-year pre-pandemic biopsy cohort ($n = 63,575$ patients). ATI, acute tubular injury; FSGS, focal segmental glomerular sclerosis; GN, glomerulonephritis; TMA, thrombotic microangiopathy.

Zwischen-Fazit

Autopsie und Biopsie: ATN viel häufiger im Vergleich zu non-Covid-19 Biopsien
Auffallend häufig: Collapsing Nephropathy – vermutlich US-spezifisch

Akutes Nierenversagen und chronische Niereninsuffizienz



The Impact of COVID-19 on Patients With ADPKD

Canadian Journal of Kidney Health and Disease
Volume 8: 1–8
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SAGE

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Abstract

Purpose of review: Patients with autosomal dominant polycystic kidney disease (ADPKD) have kidney cysts and kidney enlargement decades before progressing to advanced chronic kidney disease (CKD), meaning patients live most of their adult life with a chronic medical condition. The coronavirus disease 2019 (COVID-19) pandemic has created common questions among patients with ADPKD. In this review, we discuss COVID-19 concerns centered around a patient with a common clinical vignette.

Sources of information: We performed PubMed and Google scholar searches for English, peer-reviewed studies related to “COVID-19,” “ADPKD,” “CKD,” “tolvaptan,” “angiotensin-converting enzyme inhibitors” (ACEi), “angiotensin receptor blockers” (ARB), and “vaccination.” We also evaluated transplant data provided by the Ontario Trillium Gift of Life Network.

Methods: Following an assessment of available literature, this narrative review addresses common questions of patients with ADPKD in the context of the COVID-19 pandemic.

Key findings: Data regarding the risk of developing COVID-19 and the risk of adverse COVID-19 outcomes in patients with ADPKD remain limited, but patients with ADPKD with impaired estimated glomerular filtration rate (eGFR), kidney transplants, or on dialysis are likely at similar increased risk as those with generally defined CKD. We provide strategies to improve virtual care, which is likely to persist after the pandemic. Current evidence suggests ACEi, ARB, and tolvaptan treatment should be continued unless contraindicated due to severe illness. When available, and in the absence of a severe allergy, vaccination is recommended for all patients with ADPKD.

Limitations: This narrative review is limited by a paucity of high-quality data on COVID-19 outcomes in patients specifically with ADPKD.

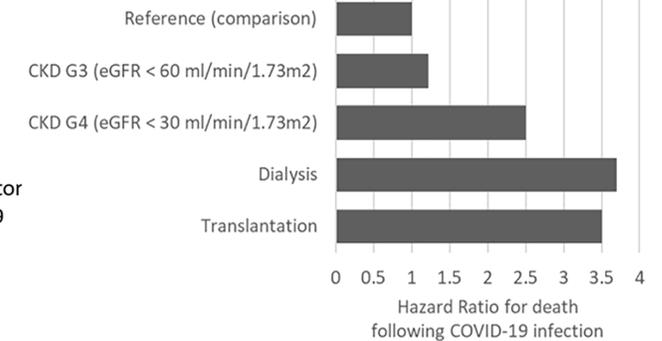
Implications: Patients with ADPKD who have developed advanced CKD, require dialysis, or who have received a kidney transplant are at elevated risk of COVID-19 complications.

Risk of contracting COVID-19



Virus exposure is greatest risk factor
No evidence ↑ risk of COVID-19 infection with ADPKD

Risk of death following hospitalized COVID-19 infection



No evidence of ↑ risk specific to ADPKD beyond kidney dysfunction

Covid-19 Infektion bei Zystennieren Patienten in unterschiedlichen Stadien der Niereninsuffizienz, Dialyse oder Transplantation

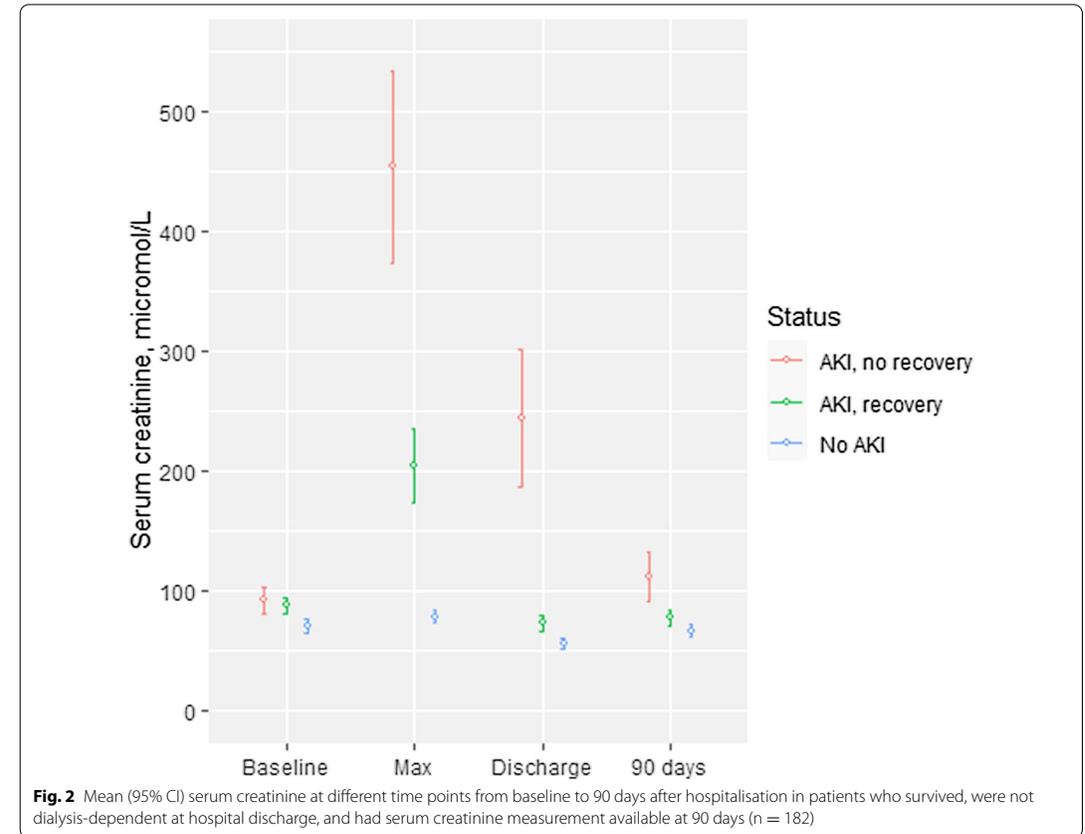
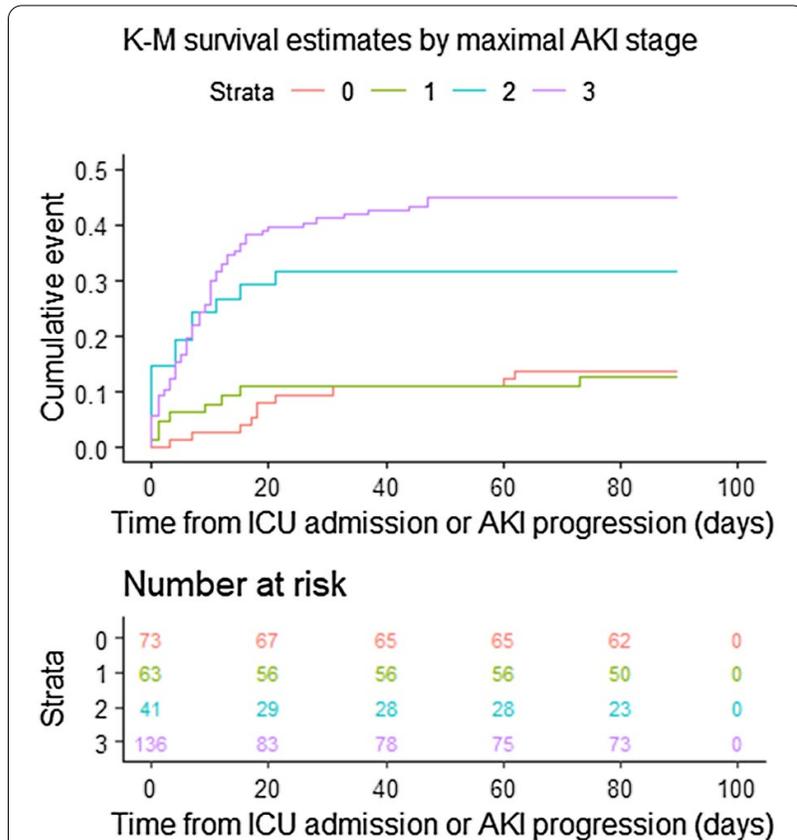
	Total (n=191)	Non-survivor (n=54)	Survivor (n=137)	p value
Treatments*				
Antibiotics	181 (95%)	53 (98%)	128 (93%)	0.15
Antiviral treatment	41 (21%)	12 (22%)	29 (21%)	0.87
Corticosteroids	57 (30%)	26 (48%)	31 (23%)	0.0005
Intravenous immunoglobulin	46 (24%)	36 (67%)	10 (7%)	<0.0001
High-flow nasal cannula oxygen therapy	41 (21%)	33 (61%)	8 (6%)	<0.0001
Non-invasive mechanical ventilation	26 (14%)	24 (44%)	2 (1%)	<0.0001
Invasive mechanical ventilation	32 (17%)	31 (57%)	1 (1%)	<0.0001
ECMO	3 (2%)	3 (6%)	0	0.0054
Renal replacement therapy	10 (5%)	10 (19%)	0	<0.0001
Outcomes				
Sepsis	112 (59%)	54 (100%)	58 (42%)	<0.0001
Respiratory failure	103 (54%)	53 (98%)	50 (36%)	<0.0001
ARDS	59 (31%)	50 (93%)	9 (7%)	<0.0001
Heart failure	44 (23%)	28 (52%)	16 (12%)	<0.0001
Septic shock	38 (20%)	38 (70%)	0	<0.0001
Coagulopathy	37 (19%)	27 (50%)	10 (7%)	<0.0001
Acute cardiac injury	33 (17%)	32 (59%)	1 (1%)	<0.0001
Acute kidney injury	28 (15%)	27 (50%)	1 (1%)	<0.0001

Kohorte von 191 Covid-19 Patienten die intensivmedizinisch in Wuhan behandelt wurden

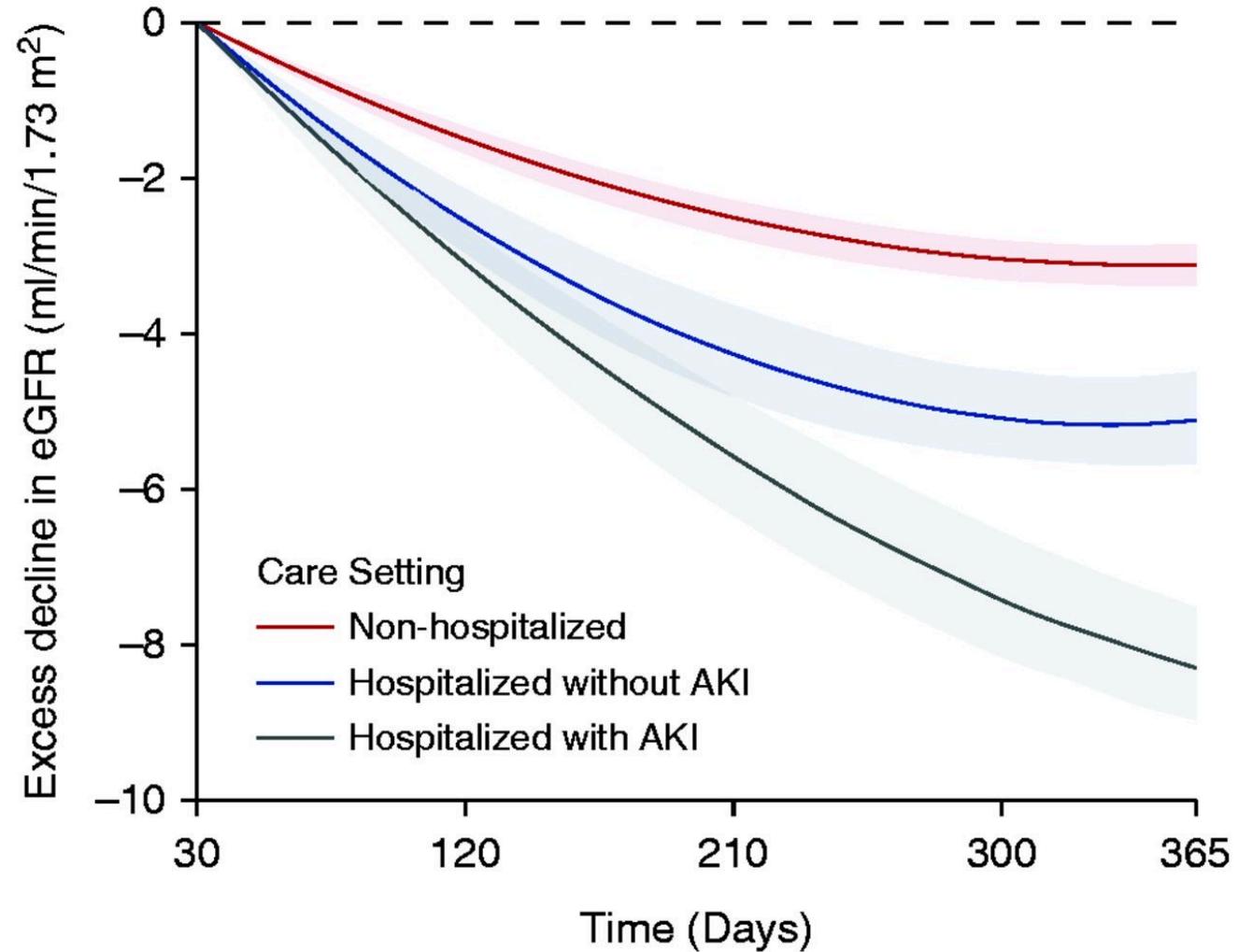
Die Hälfte der Verstorbenen waren dialysepflichtig

Lancet 2020

Retrospektive Analyse, n=313 (222 „Survivors“ Patienten, 16% der „AKI-Survivors“ hatten CKD incl. Dialysepflicht (N=8); In 81% wieder normale Nierenfunktion nach 90 Tagen p.i. ; Ann Int Care 2021



Excess decline in eGFR in postacute COVID-19 by AKI status during the acute phase of the illness.



Benjamin Bowe et al. JASN 2021;32:2851-2862

CKD nach AKI: Vergleich Covid-19 und Influenza KI2021

Introduction: Acute kidney injury (AKI) is a common complication in patients with severe COVID-19. We sought to compare the AKI incidence and outcomes among patients hospitalized with COVID-19 and with influenza.

Methods: This was a retrospective cohort study of patients with COVID-19 hospitalized between March and May 2020 and historical controls hospitalized with influenza A or B between January 2017 and December 2019 within a large health care system. Cox proportional hazards models were used to compare the risk of AKI during hospitalization. Secondary outcomes included AKI recovery, mortality, new-onset chronic kidney disease (CKD), and $\geq 25\%$ estimated glomerular filtration rate (eGFR) decline.

Results: A total of 2425 patients were included; 1091 (45%) had COVID-19, and 1334 (55%) had influenza. The overall AKI rate was 23% and 13% in patients with COVID-19 and influenza, respectively. Compared with influenza, hospitalized patients with COVID-19 had an increased risk of developing AKI (adjusted hazard ratio [aHR] = 1.58; 95% confidence interval [CI], 1.29–1.94). Patients with AKI were more likely to die in the hospital when infected with COVID-19 versus influenza (aHR = 3.55; 95% CI, 2.11–5.97). Among patients surviving to hospital discharge, the rate of AKI recovery was lower in patients with COVID-19 (aHR = 0.47; 95% CI, 0.36–0.62); however, among patients followed for ≥ 90 days, new-onset CKD (aHR = 1.24; 95% CI, 0.86–1.78) and $\geq 25\%$ eGFR decline at the last follow-up (aHR = 1.36, 95% CI, 0.97–1.90) were not significantly different between the cohorts.

Conclusion: AKI and mortality rates are significantly higher in patients with COVID-19 than influenza; however, kidney recovery among long-term survivors appears to be similar.

Risk of AKI

- Stage 1 AKI, univariate model
- Stage 1 AKI, multivariable model
- Stage 2 AKI, multivariable model
- Stage 3 AKI, multivariable model

Hazard ratio (95% CI)

- 1.46 (1.20 – 1.77)
- 1.58 (1.29 – 1.94)
- 2.09 (1.50 – 2.91)
- 2.67 (1.56 – 4.58)

AKI recovery prior to hospital discharge

- AKI recovery to within 20% baseline

0.47 (0.36 – 0.62)

Risk of in-hospital death

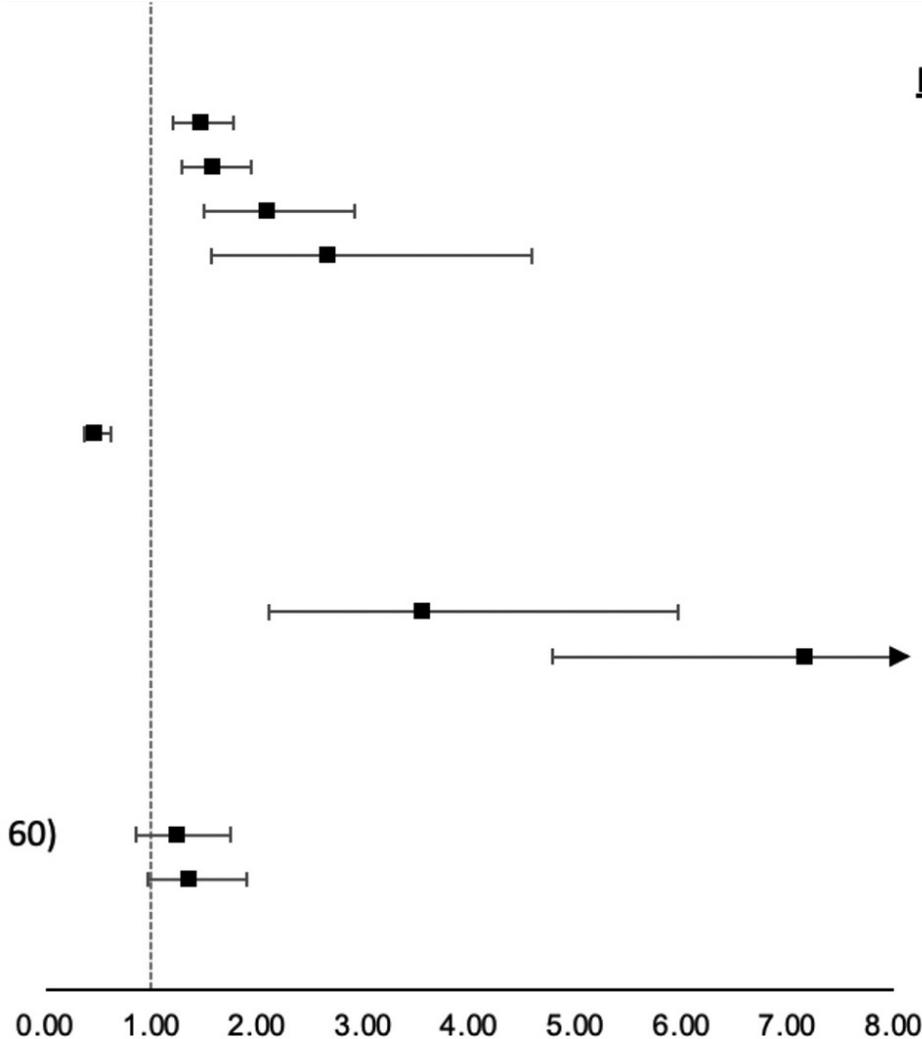
- Among patients with AKI
- Among all patients within hospitalization

3.55 (2.11 – 5.97)
7.17 (4.78 – 10.76)

Risk of long-term kidney outcomes

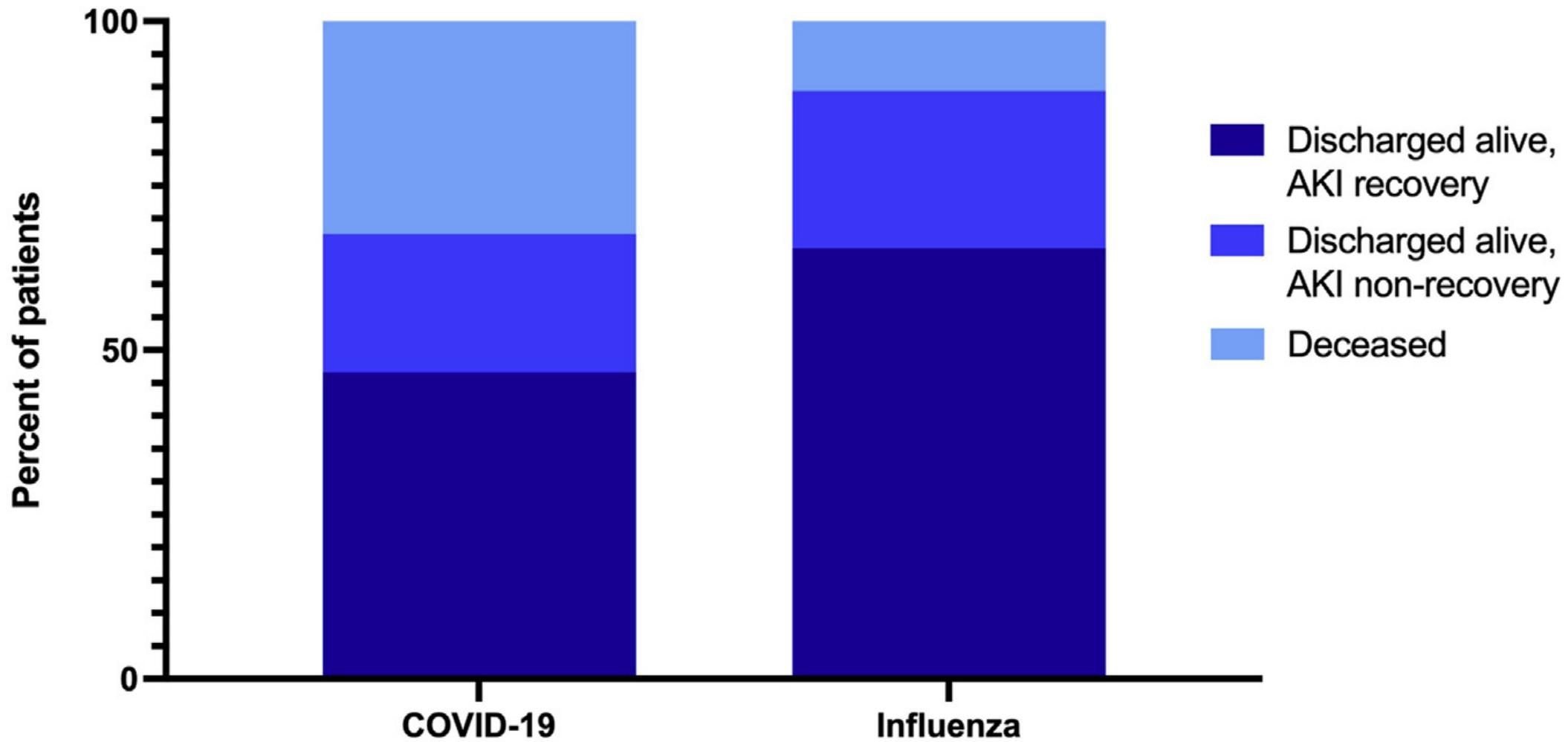
- New onset CKD (among those with baseline eGFR > 60)
- eGFR 25% decline from baseline at last follow-up

1.24 (0.86 – 1.78)
1.36 (0.97 – 1.90)



Favors influenza ←

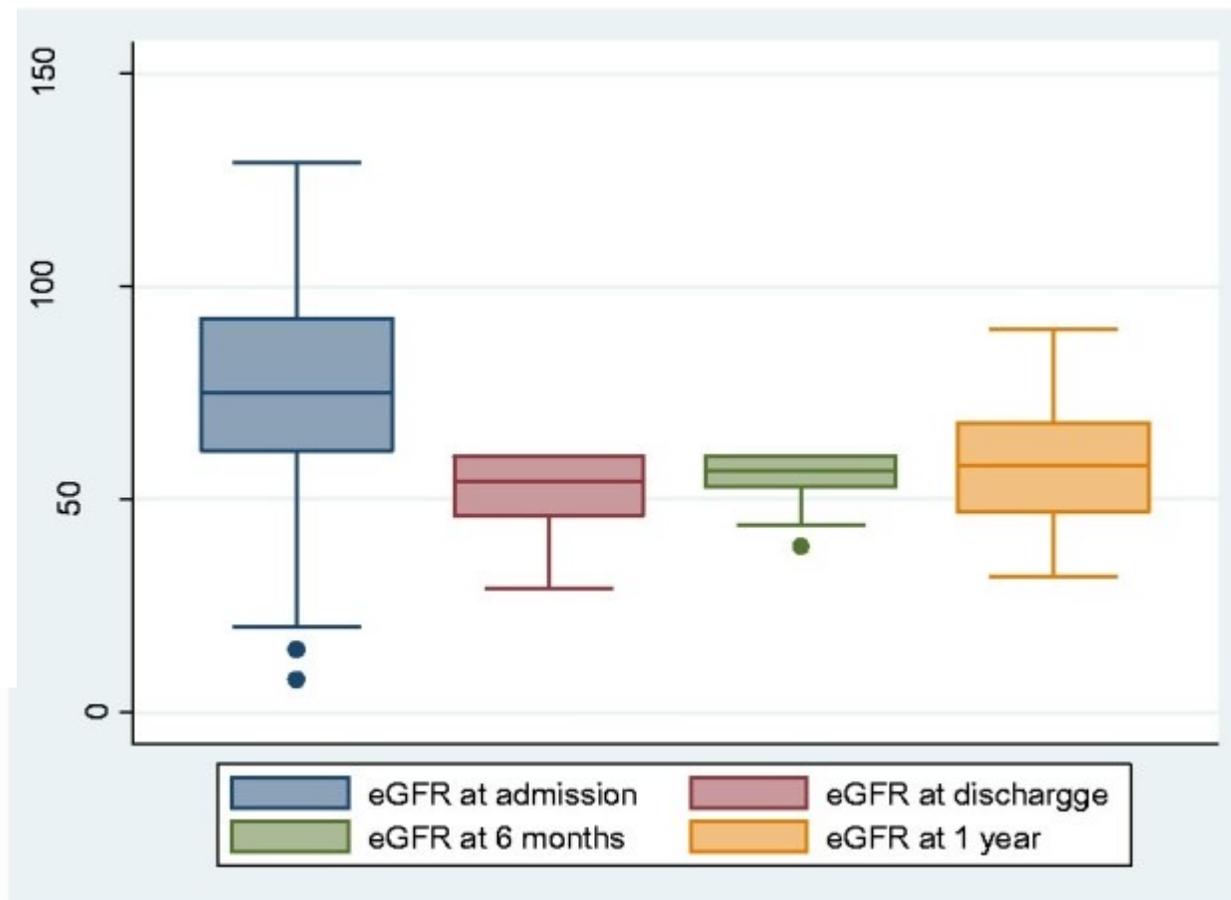
→ Favors COVID-19



Renal long-term outcome of critically ill COVID-19 patients with acute kidney failure and continuous renal replacement therapy

Table 1. Clinical and demographic characteristics of 53 critically ill COVID-19 patients who developed AKI requiring CRRT

Clinical and demographic characteristics	Values
Sex (male/female), n/n	42/11
Age (years), median (IQR)	63 (31–78)
Baseline serum creatinine (mg/dL), mean \pm SD	1.23 \pm 0.93
Baseline eGFR (mL/min/1.73 m ²), mean \pm SD	73.1 \pm 26.7
Diabetes, n (%)	12 (23)
Hypertension, n (%)	40 (75)
Obesity, n (%)	20 (38)
CRRT prescription, %	CVVHD: 85 CVVH: 15
Time on CRRT (days), median (IQR)	18 (1–176)
Mortality, n (%)	39 (73.5)



Kidney Recovery and Death in Critically Ill Patients with Covid-19-associated Kidney Injury treated with dialysis: The STOP-Covid Cohort Study

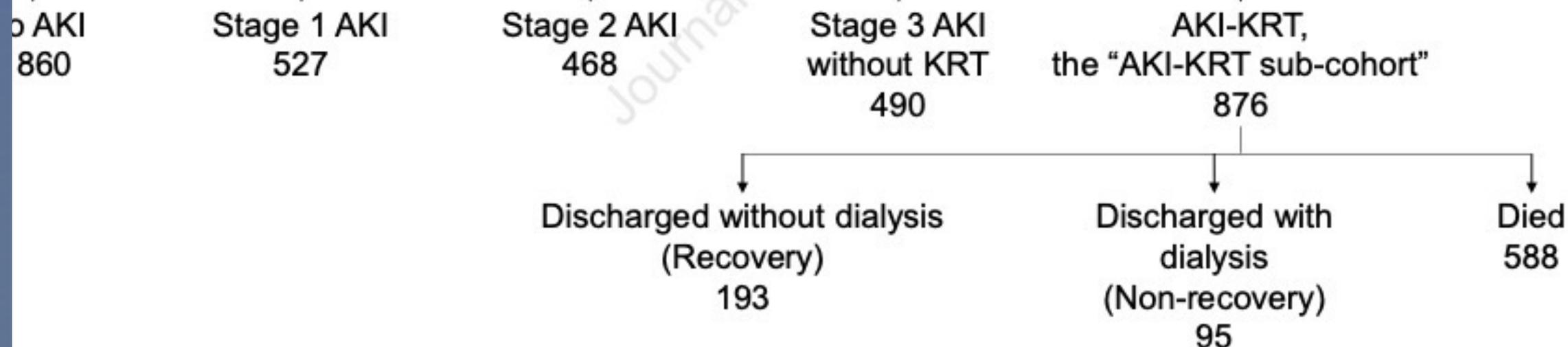
- 4221 adults with Covid-19 not receiving kidney replacement therapy (KRT). In the clinical course 876 developed AKI receiving KRT.
- Conclusion: Lower baseline eGFR and reduced urine output at the time of KRT initiation are strongly and independently associated with kidney nonrecovery among critically ill patients with Covid-19

AJKD Nov. 2021 (Journal Pre Proof)

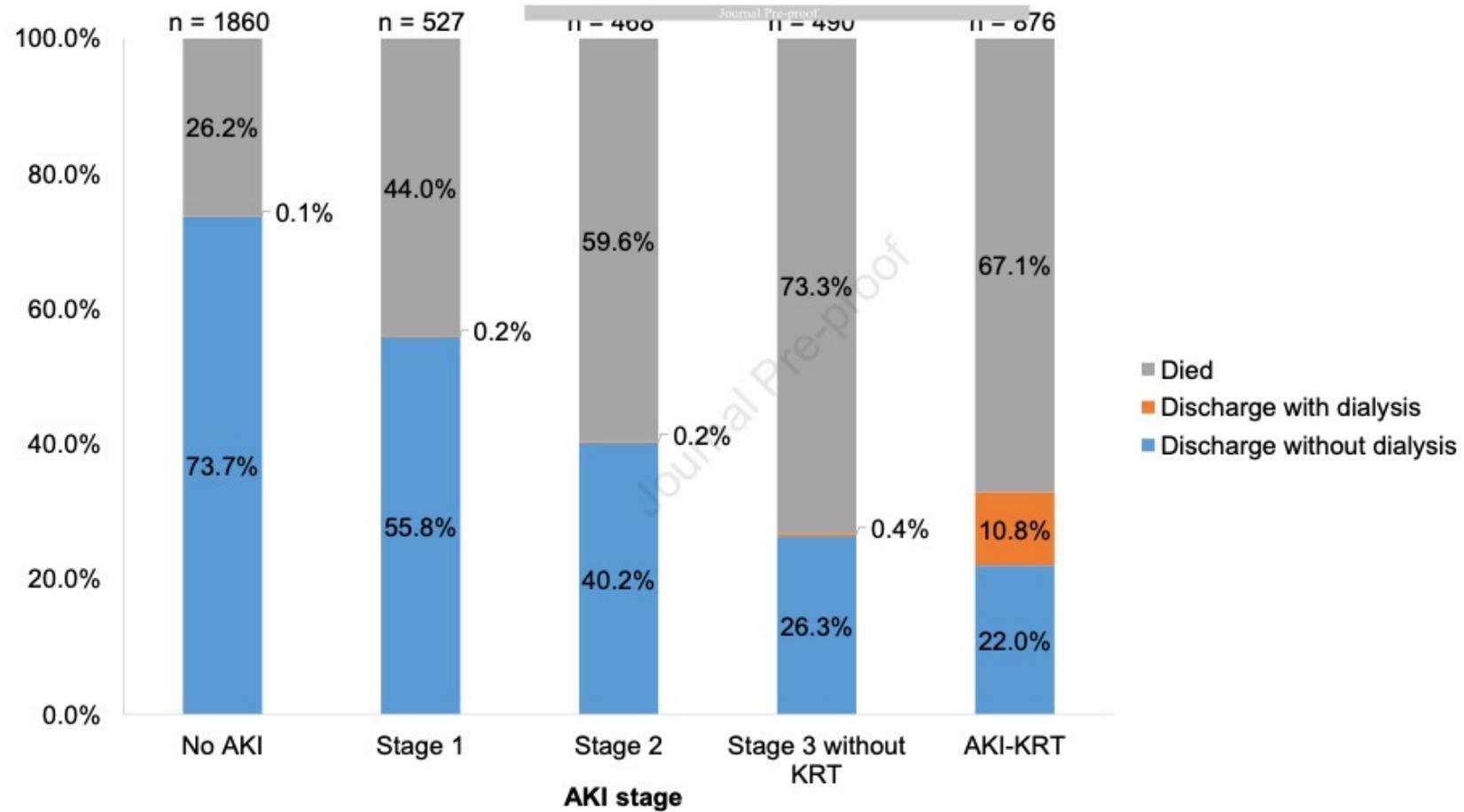
Journal Pre-proof
5154 patients enrolled in STOP-COVID

- 192 patients with ESKD on dialysis
- 39 without outcome data
- 196 still hospitalized at last follow-up
- 444 without kidney function assessment at discharge
- 62 without a baseline SCr

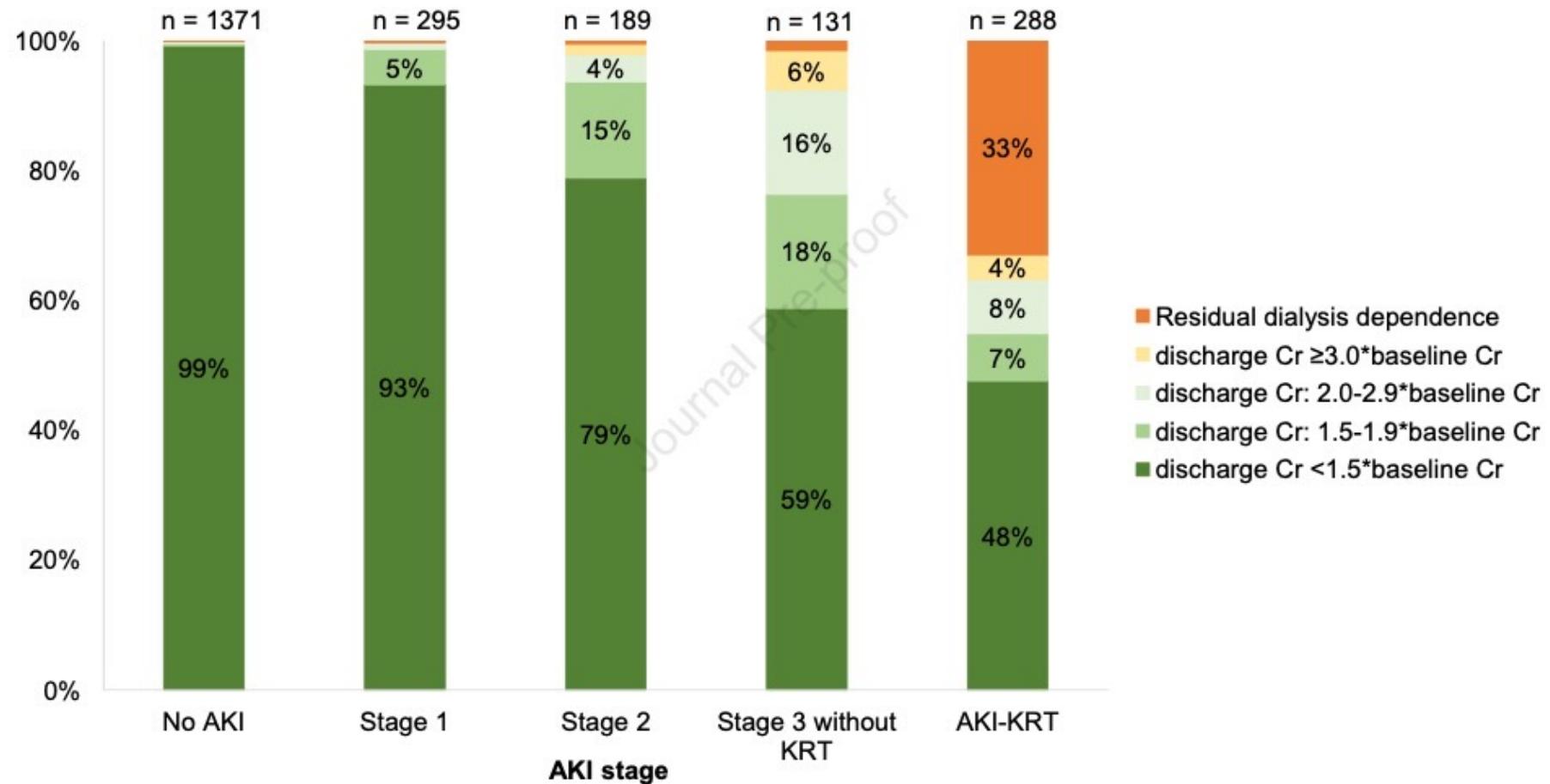
4221 patients at risk for AKI, the "ICU cohort"



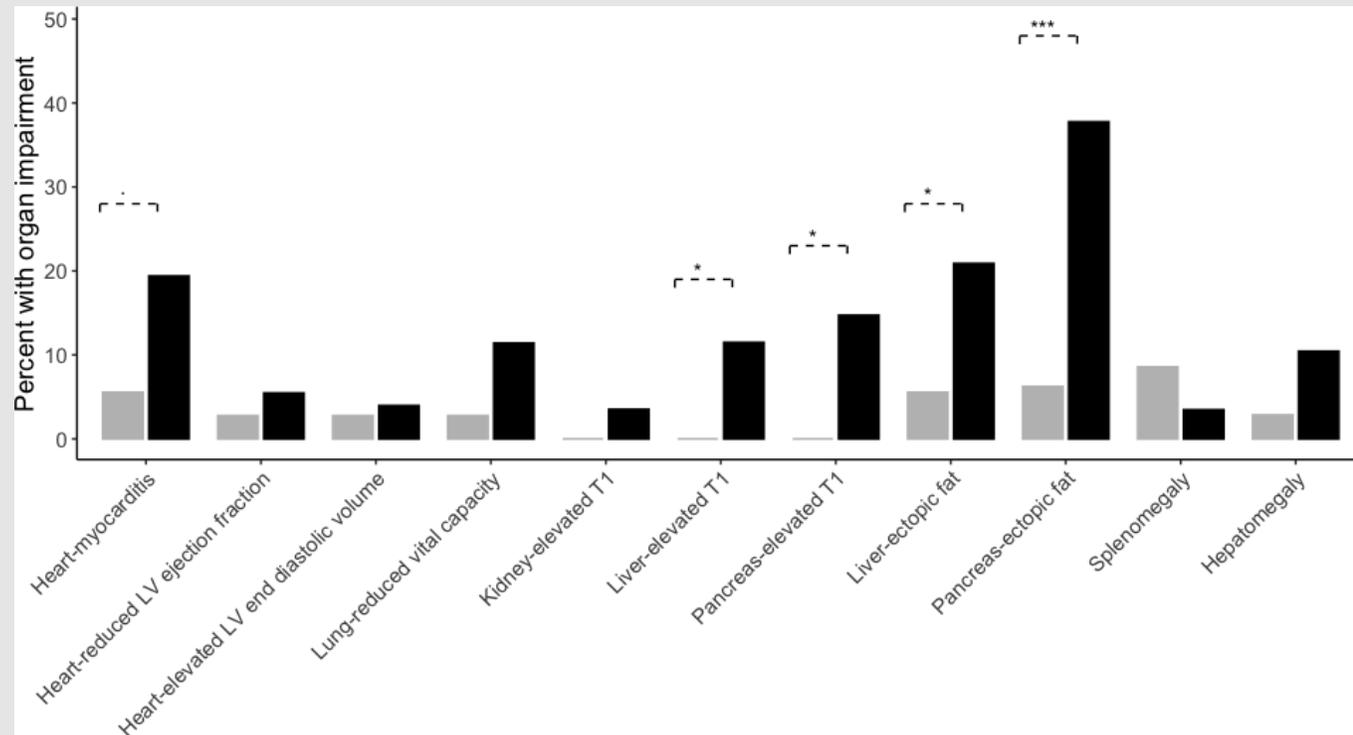
„Outcome“ der ICU-Kohorte



Nierenfunktion der „Survivors“



Morbidität bei mildem Covid-19 Verlauf



- Patienten mit mildem Verlauf haben dennoch in 70% eine Beeinträchtigung von einem oder mehr Organen, vier Monate nach den initialen Covid-19 Symptomen.

- Fallzahl: 201

- Aber: Kaum renale Morbidität

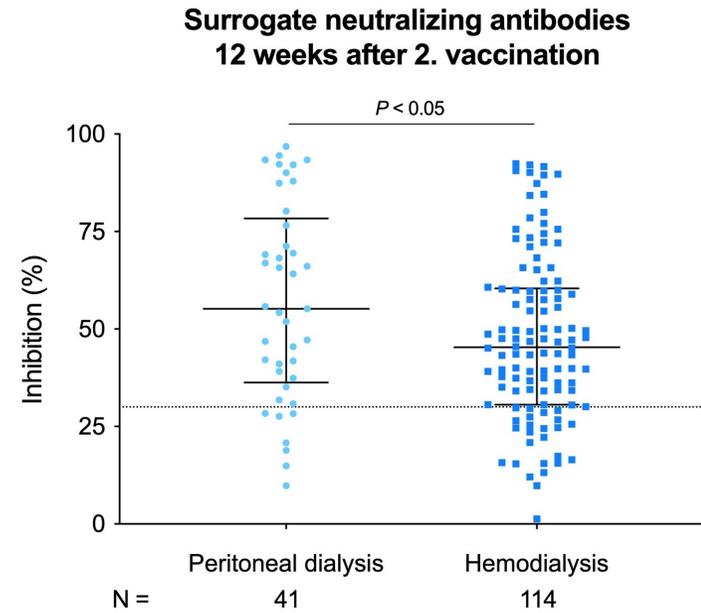
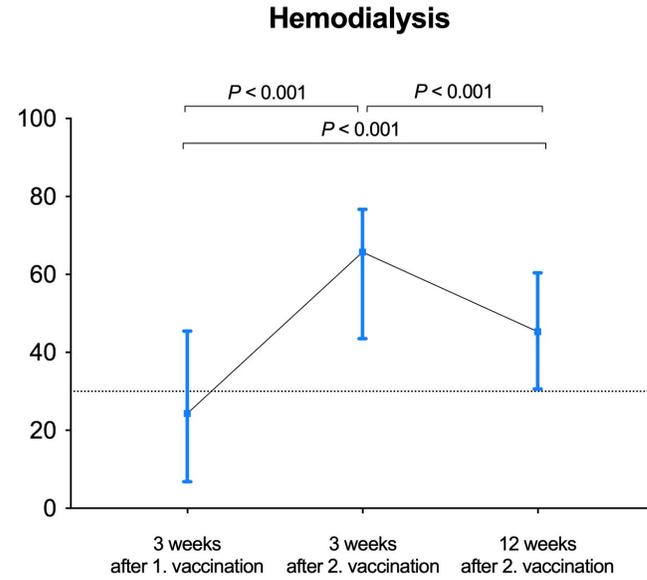
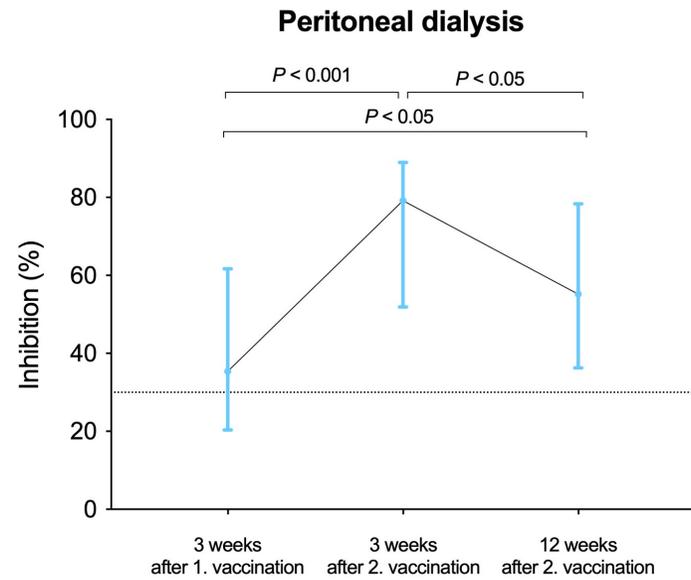
- BMJ Open 2021

Zwischen-Fazit

Die Schwere des AKI gibt einen Hinweis auf Schwere und Progression der nachfolgenden CKD. Milde Verläufe verursachen eher keinen Langzeitschaden

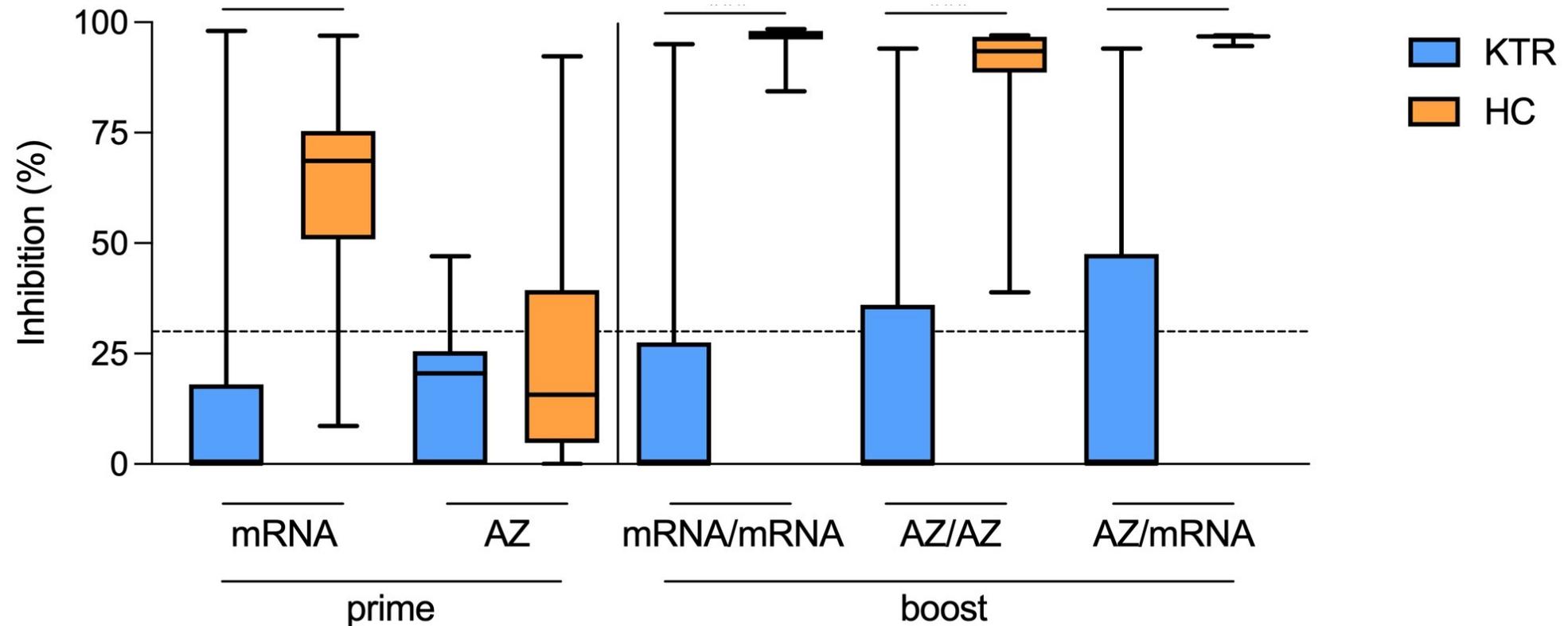
A blue ribbon graphic with a 3D effect, featuring a dark blue shadow on the left side. The ribbon is horizontal and contains white text.

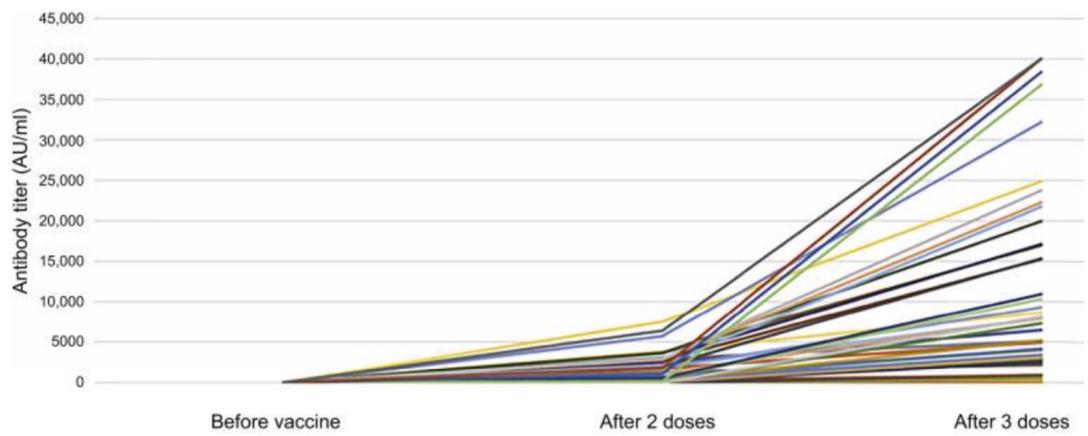
Covid-19 Impfungen und Impfantwort



- Neutralisierende Antikörper im Verlauf über 12 Wochen nach 2. SARS-CoV-2 BNT Impfung bei Peritoneal- und Hämodialyse-Patienten

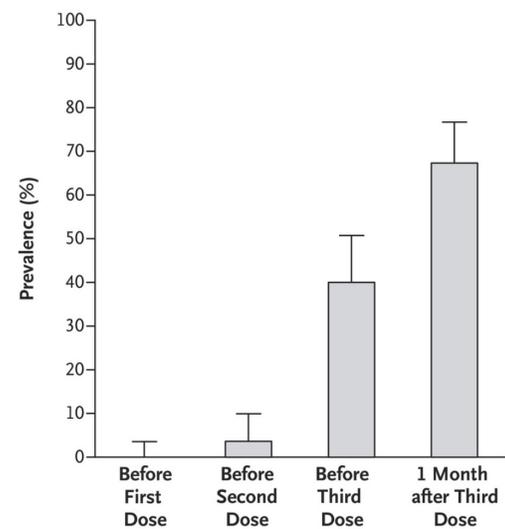
Antikörper nach verschiedenen SARS-CoV-2 Impfschemata bei Nierentransplantierten und gesunden Kontrollen (homolog + heterolog)





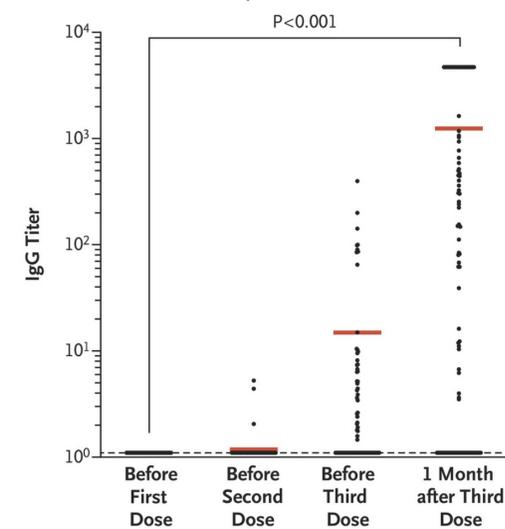
KI 2021

A Prevalence of Anti-SARS-CoV-2 Antibodies



NEJM 2021

B Anti-SARS-CoV-2 Antibody Titers



Zusammenfassung

SARS-Cov-2 infiziert renale Strukturen

- Typisch für viele Virusinfektionen

Im Vordergrund steht das akute Nierenversagen bei schweren Verläufen

- Spezielle Aufmerksamkeit für Patienten die post-AKI eine eingeschränkte Nierenfunktion aufweisen.
- Systematische Beurteilung von dialysepflichtig gebliebenen Patienten im Hinblick auf chronische Lungenschäden

Milde Verläufe verursachen möglicherweise keinen chronischen Nierenschaden

- Keine endgültigen Aussagen, interessant wie sich Omikron auf die Nieren- und Nierenfunktion auswirkt