

COMPLICACIONES NEFROLOGICAS COVID-19



Dr. René Soto

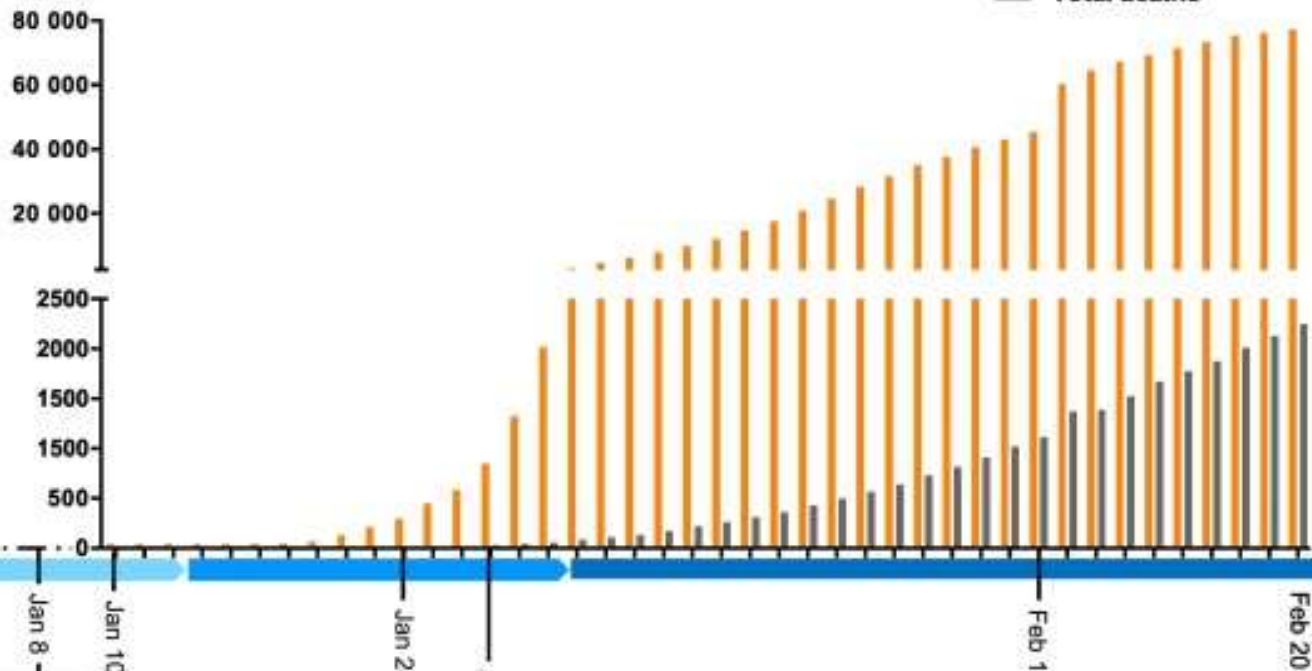
(A)

Wuhan reported 27 unknown pneumonia cases, some had close contact with the Huanan Seafood Wholesale Market and seven of them were serious cases

Dec 31

Huanan Seafood Wholesale Market was closed

Jan 1



Confirmed cases
Total deaths

First phase

Second phase

Third phase

The unknown pathogen was confirmed as a novel coronavirus by China CDC

Human to human transmissions were officially reported

Wuhan confirmed 41 cases caused by the novel coronavirus and one of them died

1. Ten family cluster infection cases were reported in Guangdong;
2. Wuhan goes into lock-down

1. WHO officially named this new disease as Coronavirus Disease 2019, abbreviated COVID-19; 2. ICTV named this novel coronavirus as Severe acute respiratory syndrome coronavirus 2, abbreviated SARS-CoV-2

Novel Coronavirus 2019 Epidemic and the Kidneys

Presentation

- Mild, flu-like illness**
- Fever (98%)**
- Cough (76%)**
- Myalgia (18%)**
- Fatigue (18%)**
- Leukopenia (25%)**
- Lymphopenia (63%)**

Diagnosis

- History of contact**
- Clinical manifestations**
- Laboratory examinations**
 - Hemogram
 - Chest CT
 - **Virological examinations**

Several COVID-19 nucleic acid detection assays have been developed, both in-house and commercial
- Of note, there are recent cases without any travel history or apparent contact with infected individuals**
- Pregnant women, newborns, elderly patients, and those with comorbidities like DM, HTN, CVD, are susceptible to COVID-19 infection and likely to have more severe illness often requiring ICU care**

AKI in COVID-19 infections

- AKI was an independent risk factor for patients' in-hospital mortality** *(Ref 13,14)*
- "Postulated" mechanisms**
 - Sepsis leading to cytokine storm syndrome
 - Direct cellular injury due to the virus
- Isolated SARS-CoV-2 from the urine sample of an infected patient suggests the kidney as a target of this novel coronavirus** *(Ref 19)*
- Treatment**
 - General and supportive management
 - Kidney replacement therapy
 - No effective antiviral therapy available at present

The impact of COVID-19 on CKD has not been reported

Conclusions COVID-19, a disease caused by a novel coronavirus, is a major global human threat with a potential to turn into a pandemic. Kidney involvement seems to be frequent in this infection and AKI is an independent predictor of mortality. The impact of this infection in those with CKD has not been studied, and the management of patients on dialysis who have been suspected to have been in contact with COVID-19 should be carried out according to strict protocols to minimize risk to other patients and healthcare personnel taking care of these

Naicker S, Yang C-W, Hwang S-J, Liu B-C, Chen J-H, Jha V. **The Novel Coronavirus 2019 Epidemic and the Kidneys.** *Kidney Int* (2020) <https://doi.org/10.1016/j.knt.2020.03.001>
Visual Graphic by Edgar Lerma, MD, FASN

How does COVID-19 affect kidneys and what can we do?

Kidney Involvement



15% Creatinine rise
14% - 27% Raised BUN



44% - 63%
Proteinuria



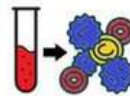
26%
Hematuria



AKI independent risk factor for mortality

*Data from various studies

What damages kidneys?



Sepsis & Cytokine storm



Direct cellular injury

(Postulated mechanisms)



Binding on tubules via ACE & DPP 4



Virus isolated from urine and kidney tissue

Increased COVID-19 susceptibility in



Uremia



Newborn



Pregnancy



Elderly



Comorbidities (DM/HTN/CVD)



In-center HD increases risk of transmission in pts and staff

Impact of COVID-19 on CKD is not well known

Management



Quarantine & supportive care



Experimental

Antivirals
Chloroquine
CRRT, HVHF
Trastuzumab



HD centers

- ✓ Educate the team
- ✓ No group activities
- ✓ Personal protection
- ✓ Screen all febrile
- ✓ Equipment cleaning

Conclusion: Kidney involvement seems to be frequent in COVID-19 infection and AKI is an independent predictor of mortality. Uremic patients are particularly vulnerable and strict protocols in HD units are required.



kidney
INTERNATIONAL

OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

Naicker S et al, 2020

Visual Abstract by Divya Bajpai



COVID-19



Incidencia de IRA

0.5-23%

*Naicker S, et al. Kidney Int 2020; doi.org/10.1016/j.kint.2020.03.001
Yang X, et al. Lancet; doi.org/10.1016/S2213-2600(20) 30079-5*

Injuria Renal Aguda (IRA) y #Covid-19

Necesidad de TRRC

0.8-17%



*Cheng Y, et al. Kidney Int 2020; doi.org/10.1016/j.kint.2020.03.005
Guan W, et al. NEJM 2020; doi:10.1056/NEJMoa2002032
Yang X, et al. Lancet; doi.org/10.1016/S2213-2600(20) 30079-5*



**Más común en el
contexto de la UCI**

8.3% vs 2.0%

Wang D, et al. JAMA 2020; 323 (11): 1061-69



Anormalidades urinarias

Albuminuria 34%

Proteinuria 63%

Hematuria 26.7%

ambas 44%



Naicker S, et al. Kidney Int 2020; doi.org/10.1016/j.kint.2020.03.001

Comorbilidades

*Arentz M, et al. JAMA 2020; doi:10.1001/jama.20204326
Chen H, et al. Lancet 2020; 395 (10226): 809-15
Cheng Y, et al. Kidney Int 2020; doi.org/10.1016/j.kint.2020.03.005
Guan W, et al. NEJM 2020; doi:10.1056/NEJMoa2002032
Huang C, et al. Lancet 2020; 395 (10223): 497-506*



**ECV
40%**



**ERC
0.7-48%**



**DM
7.4-20%**



**HTA
15-33%**



60 years
1960-2020

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Acute kidney injury in patients hospitalized with COVID-19

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¹Division of Kidney Diseases and Hypertension, Department of Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Great Neck, New York, USA; ²Institute of Health Innovations and Outcomes Research, Feinstein Institutes for Medical Research, Manhasset, New York, USA; and ³Department of Information Services, Northwell Health, New Hyde Park, New York, USA

Table 1 | Clinical characteristics of the study cohort

Variables	Overall (n = 5449)
Age (yr)	64.0 (52.0, 75.0)
Male	3317 (60.9)
Race	
Asian	466 (8.6)
Black	1123 (20.6)
White	2112 (38.8)
Declined	32 (0.6)
Other/multiracial	1494 (27.4)
Other/unknown	222 (4.1)
Comorbid conditions ^a	
HTN	3037 (55.7)
CAD	600 (11.0)
HF	349 (6.4)
PVD	98 (1.8)
Diabetes	1797 (33.0)
HIV	35 (0.6)
Chronic liver disease	114 (2.1)
COPD	296 (5.4)
Asthma	460 (8.4)
OSA	164 (3.0)
Cancer	327 (6.0)
Obesity	1475 (27.1)
Morbid obesity	456 (8.4)
BMI (kg/m ²)	28.6 (25.4, 33.1)
Admission SCr (mg/dl)	1.01 (0.80, 1.34)
Medications	
No. of medications	4 (1, 8)
ACE-I	654 (13.3)
ARB	902 (18.3)
ICU	1395 (25.6)

Table 2 | Baseline characteristics of study cohort, by AKI status

Variables	No AKI (n = 3456)	AKI (n = 1993)	Stages of AKI			P value ^a (no AKI vs. all AKI)	P value ^b (trend)
			1 (n = 927)	2 (n = 447)	3 (n = 619)		
Age (yr)	61.0 (50.0, 72.0)	69.0 (58.0, 78.0)	69.0 (58.0, 79.0)	71.0 (58.5, 79.0)	67.0 (58.0, 76.0)	<0.001	<0.001
Male	2047 (59.2)	1270 (63.7)	556 (60.0)	266 (59.5)	448 (72.4)	0.001	<0.001
Comorbid conditions ^c							
HTN	1745 (50.5)	1292 (64.8)	624 (67.3)	287 (64.2)	381 (61.6)	<0.001	<0.001
CAD	311 (9.0)	289 (14.5)	136 (14.7)	72 (16.1)	81 (13.1)	<0.001	<0.001
HF	141 (4.1)	208 (10.4)	112 (12.1)	47 (10.5)	49 (7.9)	<0.001	<0.001
PVD	37 (1.1)	61 (3.1)	22 (2.4)	18 (4.0)	21 (3.4)	<0.001	<0.001
Diabetes	967 (28.0)	830 (41.6)	368 (39.7)	193 (43.2)	269 (43.5)	<0.001	<0.001
HIV	25 (0.7)	10 (0.5)	5 (0.5)	4 (0.9)	1 (0.2)	0.42	0.36
Chronic liver disease	72 (2.1)	42 (2.1)	27 (2.9)	8 (1.8)	7 (1.1)	1.00	0.11
COPD	149 (4.3)	147 (7.4)	74 (8.0)	36 (8.1)	37 (6.0)	<0.001	<0.001
Asthma	317 (9.2)	143 (7.2)	74 (8.0)	35 (7.8)	34 (5.5)	0.012	0.02
OSA	99 (2.9)	65 (3.3)	27 (2.9)	20 (4.5)	18 (2.9)	0.46	0.31
Cancer	194 (5.6)	133 (6.7)	65 (7.0)	25 (5.6)	43 (6.9)	0.13	0.30
Obesity	916 (26.5)	559 (28.0)	244 (26.3)	132 (29.5)	183 (29.6)	0.23	0.25
Morbid obesity	276 (8.0)	180 (9.0)	81 (8.7)	42 (9.4)	57 (9.2)	0.20	0.57
BMI (kg/m ²)	28.4 (25.3, 32.8)	29.0 (25.4, 33.5)	28.7 (25.5, 33.2)	28.7 (24.7, 33.6)	29.5 (25.9, 34.0)	0.09	0.04
Kidney function							
Admission SCr (mg/dl)	0.95 (0.77, 1.16)	1.24 (0.91, 1.82)	1.26 (0.91, 1.83)	1.30 (0.95, 1.86)	1.19 (0.90, 1.79)	<0.001	<0.001
Discharge SCr (mg/dl)	0.80 (0.66, 0.98)	1.42 (0.84, 3.16)	1.02 (0.72, 1.57)	1.38 (0.80, 2.26)	4.00 (2.21, 6.12)	<0.001	<0.001
Peak SCr (mg/dl)	0.98 (0.80, 1.20)	2.23 (1.40, 4.12)	1.50 (1.10, 2.16)	2.13 (1.59, 2.91)	5.20 (3.40, 7.24)	<0.001	<0.001
Median SCr (mg/dl)	0.86 (0.70, 1.03)	1.20 (0.82, 2.00)	1.04 (0.75, 1.53)	1.10 (0.80, 1.53)	2.05 (1.11, 3.55)	<0.001	<0.001
Admission eGFR (ml/min/1.73 m ²)	82.5 (62.0, 98.0)	56.0 (34.0, 80.0)	54.0 (33.0, 81.0)	53.0 (32.0, 79.0)	62.0 (37.0, 81.0)	<0.001	<0.001
Discharge eGFR (ml/min/1.73 m ²)	94.0 (77.0, 107.0)	45.0 (17.0, 86.0)	69.0 (39.0, 97.0)	50.0 (27.0, 89.0)	14.0 (8.0, 27.0)	<0.001	<0.001
Medications							
No. of medications	3 (1, 7)	6 (2, 10)	6 (2, 10)	6 (2, 10)	5 (1, 9)	<0.001	<0.001
ACE-I	385 (11.9)	269 (15.9)	119 (14.4)	51 (13.4)	99 (20.2)	<0.001	<0.001
ARB	516 (16.0)	386 (22.8)	184 (22.3)	84 (22.1)	118 (24.0)	<0.001	<0.001
ICU	335 (9.7)	1060 (53.2)	320 (34.5)	244 (54.6)	496 (80.1)	<0.001	<0.001
Mechanical ventilator	122 (3.5)	1068 (53.6)	288 (31.1)	262 (58.6)	518 (83.7)	<0.001	<0.001
ECMO	0 (0.0)	10 (0.5)	3 (0.3)	5 (1.1)	2 (0.3)	<0.001	<0.001
Inotropes ^d	3 (0.1)	51 (2.6)	10 (1.1)	12 (2.7)	29 (4.7)	<0.001	<0.001
Vasopressor ^e	119 (3.4)	1049 (52.6)	278 (30.0)	252 (56.4)	519 (83.8)	<0.001	<0.001

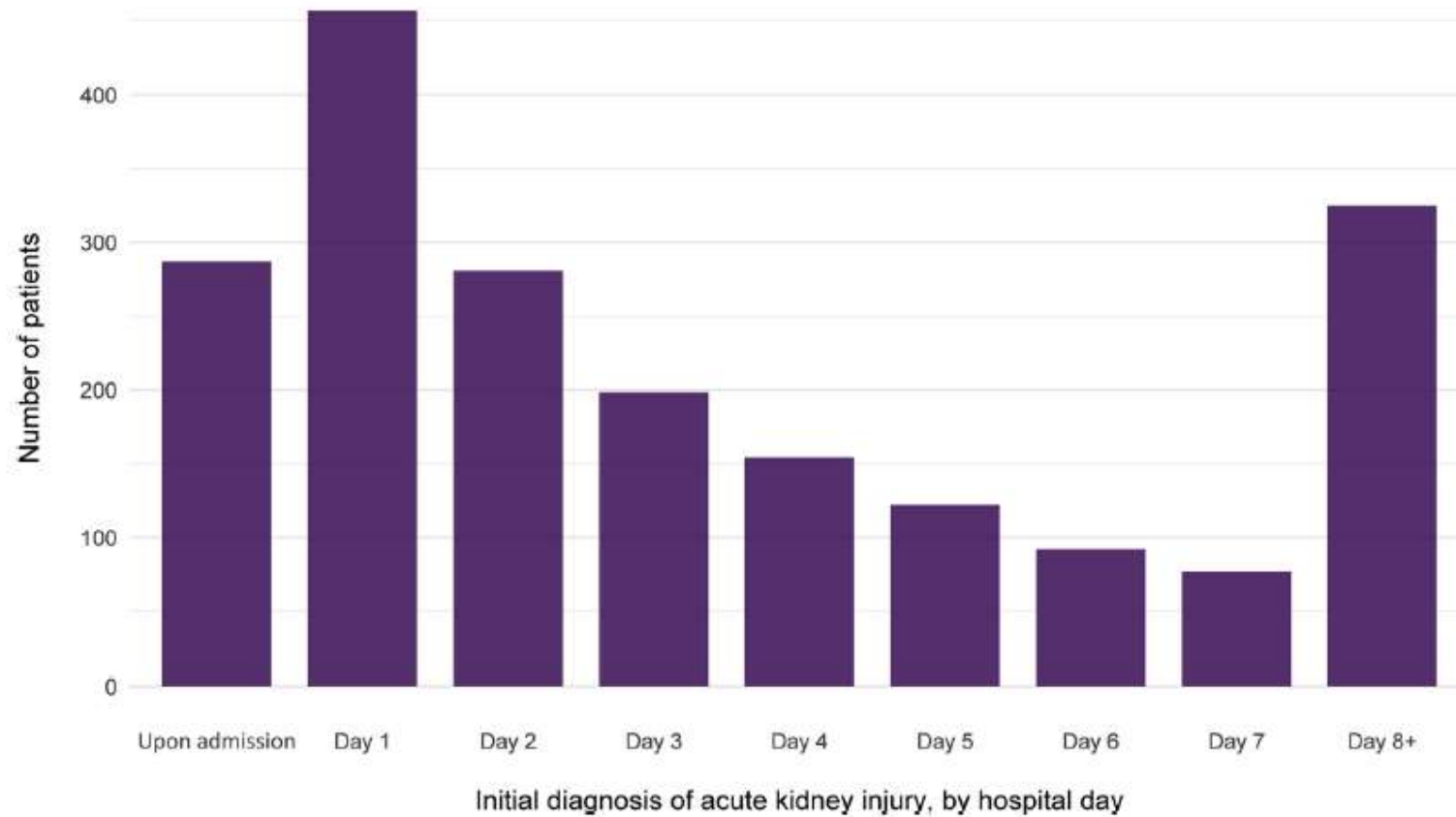


Figure 2 | The number of patients with initial diagnosis of acute kidney injury, by hospital day of admission.

Table 3 | The proportion of patients with AKI, by requirement for invasive mechanical ventilation

	No use of invasive mechanical ventilation (n = 4259)	Required invasive mechanical ventilation (n = 1190)	<i>P</i> value ^a
No AKI	3334 (78.3)	122 (10.3)	<0.001
AKI			
Any stage	925 (21.7)	1068 (89.7)	<0.001
Stage 1	639 (15.0)	288 (24.2)	<0.001
Stage 2	185 (4.3)	262 (22.0)	<0.001
Stage 3	101 (2.4)	518 (43.5)	<0.001
Required renal replacement therapy ^b	9 (0.2)	276 (23.2)	<0.001

AKI, acute kidney injury.

^aData were compared using the Fisher exact test.

^bRenal replacement therapy includes intermittent hemodialysis and continuous renal replacement therapy.

Values are n (%).

Table 5 | Univariate and multivariate logistic regression analyses of risk factors associated with the development of AKI

Variable	Unadjusted OR	95% CI	P value	Adjusted OR ^a	95% CI	P value
Age (yr)	1.03	1.02–1.03	<0.001	1.03	1.03–1.04	<0.001 ^b
Male	1.21	1.08–1.35	0.001	1.14	0.97–1.33	0.10
White race	Reference	Reference	Reference	Reference	Reference	Reference
Asian	0.84	0.68–1.04	0.11	0.83	0.61–1.12	0.23
Black	0.93	0.80–1.08	0.32	1.23	1.01–1.50	0.04 ^b
Other/mixed	0.81	0.71–0.93	0.003	0.84	0.69–1.03	0.09
Unknown	0.9	0.69–1.18	0.44	0.74	0.50–1.11	0.15
Tertiary hospital	0.89	0.79–1.00	0.05	0.90	0.77–1.06	0.20
Diabetes	1.84	1.64–2.06	<0.001	1.76	1.49–2.07	<0.001 ^b
Hypertension	1.81	1.61–2.02	<0.001	1.25	1.04–1.50	0.02 ^b
Cardiovascular disease ^c	2.05	1.77–2.37	<0.001	1.48	1.22–1.80	<0.001 ^b
Respiratory disease ^d	1.09	0.93–1.26	0.29	—	—	—
Obesity, BMI ≥ 30 kg/m ²	1.12	1.00–1.26	0.05	1.11	0.94–1.31	0.22
HIV	0.69	0.33–1.44	0.33	—	—	—
Cancer	1.2	0.96–1.51	0.11	1.09	0.82–1.45	0.54
Chronic liver disease	1.01	0.69–1.49	0.95	—	—	—
Mechanical ventilation	31.60	25.80–38.60	<0.001	10.7	6.81–16.70	<0.001 ^b
Vasoactive medication ^e	31.40	25.60–38.40	<0.001	4.53	2.88–7.13	<0.001 ^b
ACE-I or ARB use	1.61	1.42–1.82	<0.001	0.87	0.73–1.04	0.12

ACE-I, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; BMI, body mass index; CI, confidence interval; OR, odds ratio.

^aVariables were entered into the model when the α level of risk factor was less than 0.15. Age, sex, and race were added into the model regardless of α level.

^bIndependent risk factors include increased age, black race, diabetes, hypertension, cardiovascular disease, mechanical ventilation, and vasoactive medication.

^cCardiovascular diseases include coronary artery disease, heart failure, and peripheral vascular disease.

^dRespiratory diseases include asthma and chronic obstructive pulmonary disease.

^eVasoactive medications include inotropes and vasopressors.

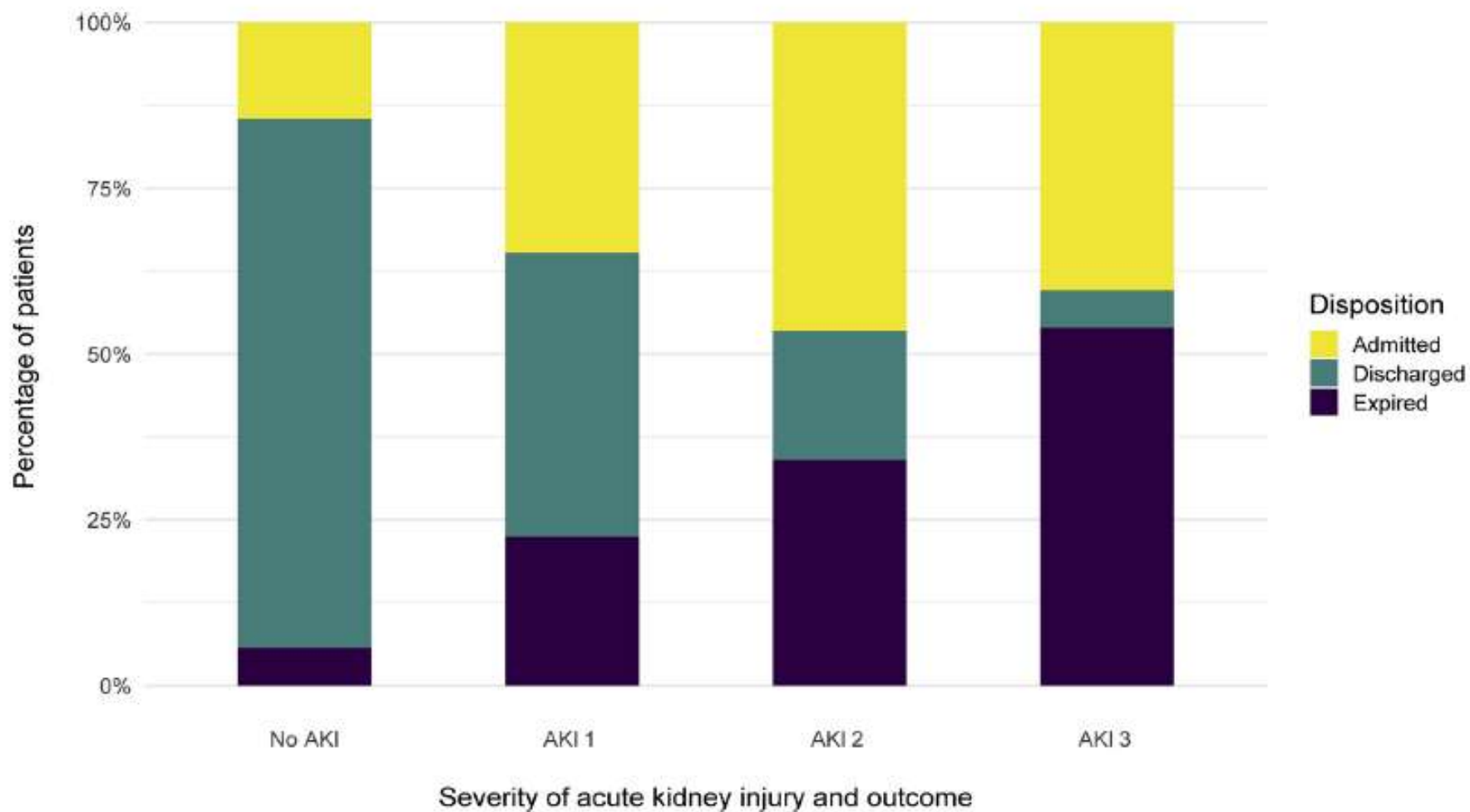
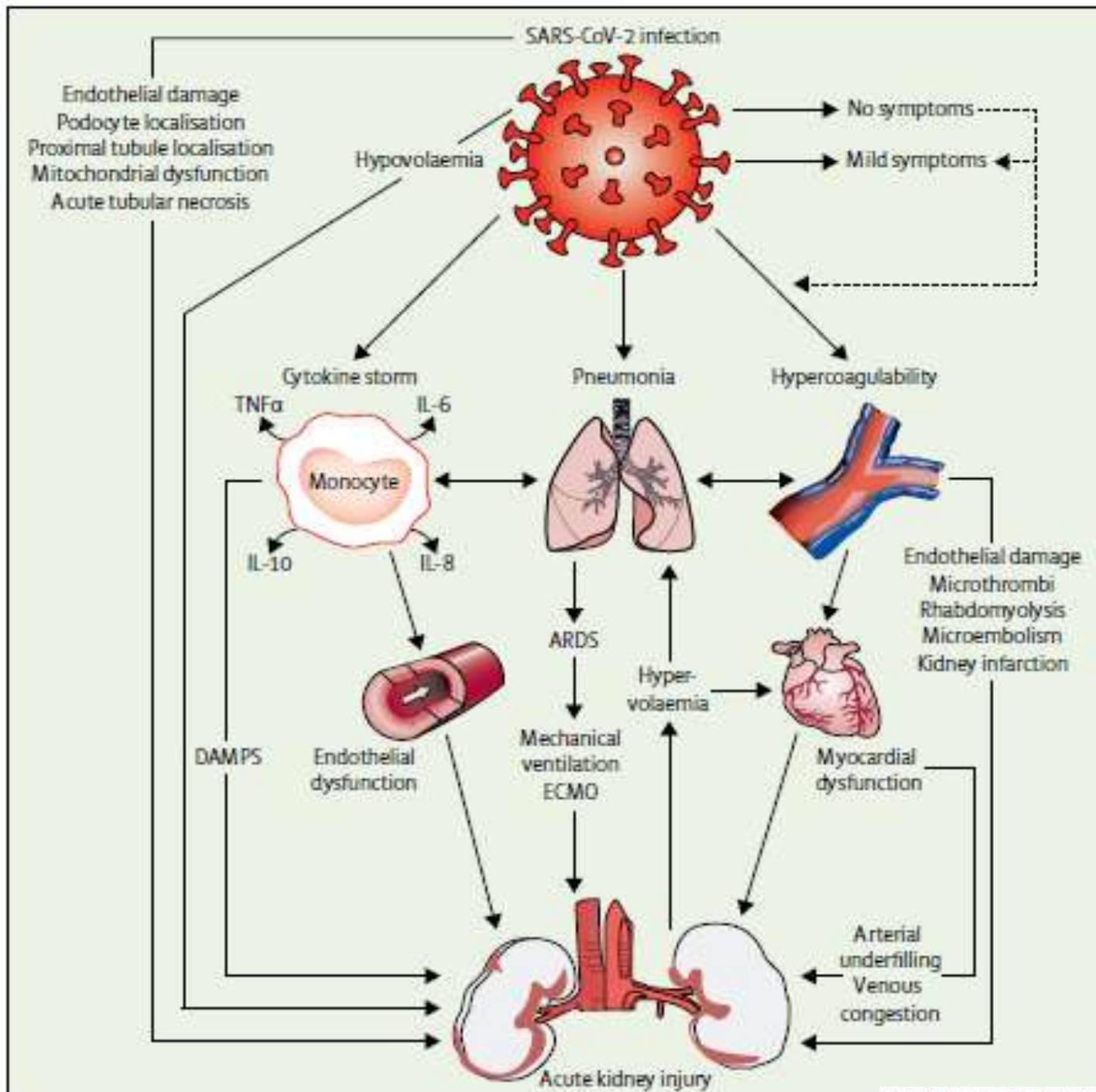



Figure 4 | The proportion of disposition type, by stages (1–3) of acute kidney injury (AKI).



Renal Involvement and Early Prognosis in Patients with COVID-19 Pneumonia

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Table 1. Clinical characteristics of patients with COVID-19

Variables	All Patients	Moderate	Severe	Critically Ill	P Value
N	333	144 (43.2%)	133 (39.9%)	56 (16.8%)	
Days from onset	9 (7–11)	8 (6–11)	10 (7–11)	8 (6–11)	0.12 ^a
Age, yr	56.3±13.4	50.9±12.5	58.1±12.3	63.1±11.0	<0.001 ^a
Male patient, %	182/333 (54.7%)	67/144 (46.5%)	79/133 (59.4%)	36/56 (64.3%)	0.03 ^b
Hypertension, %	107/332 (32.2%)	37/144 (25.7%)	43/133 (32.3%)	27/55 (49.1%)	0.003 ^b
ACEI/ARB history, %	37/321 (11.5%)	12/143 (8.4%)	14/126 (11.1%)	11/52 (21.2%)	0.02 ^b
ACEI/ARB	11/26	0/12	6/8	5/6	
Diabetes, %	76/332 (22.9%)	20/144 (13.9%)	32/133 (24.1%)	24/55 (43.6%)	<0.001 ^b
SPO ₂ (%)	93 (91.0–97.0)	97.0 (96.0–98.0)	92.0 (90.0–93.0)	89.5 (80.0–93.0)	<0.001 ^a
Systolic BP, mm Hg	126 (115–138)	124 (114–132)	128 (116–141)	135 (118–145)	0.001 ^a
Diastolic BP, mm Hg	78 (72–86)	77 (72–86)	78 (71–87)	79 (73–86)	0.76 ^a
Blood sugar, mmol/L	6.6 (5.7–8.1)	6.0 (5.4–7.1)	6.9 (5.9–8.6)	7.8 (6.3–12.4)	<0.001 ^a
CRP, mg/L	44.1 (16.3–90.8)	22.1 (7.5–45.3)	58.1 (32.5–101.4)	69.7 (42.9–119.6)	<0.001 ^a
Erythrocyte sedimentation rate, mm/h	31.0 (18.0–58.8)	27.0 (14.3–50.3)	39.0 (22.0–64.0)	31.0 (22.0–58.0)	0.004 ^a
ALT, U/L	24.0 (15.0–38.3)	20.0 (13.0–33.0)	26.0 (18.5–39.5)	29.0 (18.0–43.0)	0.001 ^a
AST, U/L	31.0 (22.0–48.0)	24.0 (20.0–38.0)	33.0 (24.0–50.5)	40.5 (25.5–62.3)	<0.001 ^a
HsTnl, pg/ml	5.4 (3.3–14.0)	4.6 (2.5–7.0)	4.8 (3.1–11.7)	11.4 (6.3–21.6)	<0.001 ^a
NT-proBNP, pg/ml	139.0 (52.0–392.5)	76.0 (23.0–152.0)	157.5 (55.5–333.8)	372.5 (155.3–758.3)	0.002 ^a
Serum albumin, g/L	34.5±4.7	36.6±4.9	33.6±4.2	32.9±4.3	<0.001 ^a
BUN, mmol/L	4.3 (3.2–5.7)	3.9 (3.1–5.0)	4.4 (3.2–5.5)	5.9 (4.6–8.6)	<0.001 ^a
SCR, μmol/L	70.0 (57.0–84.0)	66.5 (56.0–81.0)	69.0 (57.0–84.0)	77.0 (60.0–89.0)	<0.001 ^a
Proteinuria, %	219/333 (65.8%)	63/144 (43.8%)	108/133 (81.2%)	48/56 (85.7%)	<0.001 ^b
Hematuria, %	139/333 (41.7%)	48/144 (33.3%)	52/133 (39.1%)	39/56 (69.6%)	<0.001 ^b
AKI, %	35/333 (10.5%)	5/144 (3.5%)	6/133 (4.5%)	24/56 (42.9%)	<0.001 ^b
Renal involvement, %	251/333 (75.4%)	89/144 (61.8%)	111/133 (83.5%)	51/56 (91.1%)	<0.001 ^b
Death, %	29/333 (8.7%)	0	0	29/56 (52.8%)	<0.001 ^b

Table 2. Characteristics of patients with AKI according to two different criteria

Variables	KDIGO AKI Criteria	Expanded Criteria
N	22	35
AKI occurrence on admission	3/22 (13.6%)	13/35 (37.1%)
AKI occurrence during hospital stay	19/22 (86.4%)	22/35 (62.9%)
Classification		
Prerenal AKI	0/22 (0%)	2/35 (5.7%)
Rhabdomyolysis-induced AKI	4/22 (18.2%)	4/35 (11.4%)
Suspected intrinsic AKI	18/22 (81.8%)	29/35 (82.9%)
AKI stage		
1	4/22 (18.2%)	16/35 (45.7%)
2	7/22 (31.8%)	8/35 (22.9%)
3	11/22 (50.0%)	11/35 (31.4%)
AKI recovery (total)	4/22 (18.2%)	16/35 (45.7%)
Prerenal AKI recovery	—	2/2 (100%)
Rhabdomyolysis-induced AKI recovery	1/4 (25%)	1/4 (25%)
Suspected intrinsic AKI recovery	3/18 (16.7%)	13/29 (44.8%)
Stage 1 recovery	1/4 (25.0%)	12/16 (75.0%)
Stage 2 recovery	3/7 (42.9%)	4/8 (50.0%)
Stage 3 recovery	0/11 (0%)	0/11 (0%)
The mean time for AKI recovery	6 (5–8) ^a	6 (5–11) ^a
Total death	19/22 (86.4%)	20/35 (57.1%)
Death in prerenal AKI	0/0 (0%)	0/2 (0%)
Death in rhabdomyolysis-induced AKI	3/4 (75.0%)	3/4 (75.0%)
Death in suspected intrinsic AKI	16/18 (88.9%)	17/29 (58.6%)
Death in AKI stage 1	3/4 (75.0%)	4/16 (25.0%)
Death in AKI stage 2	6/7 (85.7%)	6/8 (75.0%)
Death in AKI stage 3	10/11 (90.9%)	10/11 (90.9%)

