The Prevalence of Acute Kidney Injury in Patients Hospitalized With COVID-19 Infection: A Systematic Review and Meta-analysis

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Rationale & Objective: Coronavirus disease 2019 (COVID-19) may be associated with high rates of acute kidney injury (AKI) and kidney replacement therapy (KRT), potentially overwhelming health care resources. Our objective was to determine the pooled prevalence of AKI and KRT among hospitalized patients with COVID-19.

Study Design: Systematic review and meta-analysis.

Data Sources: MEDLINE, Embase, the Cochrane Library, and a registry of preprinted studies, published up to October 14, 2020.

Study Selection: Eligible studies reported the prevalence of AKI in hospitalized patients with COVID-19 according to the Kidney Disease: Improving Global Outcomes (KDIGO) definition.

Data Extraction & Synthesis: We extracted data on patient characteristics, the proportion of patients developing AKI and commencing KRT, important clinical outcomes (discharge from hospital, ongoing hospitalization, and death), and risk of bias.

Outcomes & Measures: We calculated the pooled prevalence of AKI and receipt of KRT along with 95% CIs using a random-effects model. We performed subgroup analysis based on admission to an intensive care unit (ICU).

Results: Of 2,711 records reviewed, we included 53 published and 1 preprint study in the analysis, which comprised 30,657 hospitalized patients with COVID-19. Data for AKI were available for 30,639 patients (n = 54 studies), and receipt of KRT, for 27,525 patients (n = 48 studies). The pooled prevalence of AKI was 28% (95% CI, 22%-34%; I^2 = 99%), and the pooled prevalence of KRT was 9% (95% CI, 7%-11%; I^2 = 97%). The pooled prevalence of AKI among patients admitted to the ICU was 46% (95% CI, 35%-57%; I^2 = 99%), and 19% of all ICU patients with COVID-19 (95% CI, 15%-22%; I^2 = 88%) commenced KRT.

Limitations: There was significant heterogeneity among the included studies, which remained unaccounted for in subgroup analysis.

Conclusions: AKI complicated the course of nearly 1 in 3 patients hospitalized with COVID-19. The risk for AKI was higher in critically ill patients, with a substantial number receiving KRT at rates higher than the general ICU population. Because COVID-19 will be a public health threat for the foreseeable future, these estimates should help guide KRT resource planning.

Visual Abstract included

Complete author and article information provided before references.

Acute kidney injury; COVID-19; SARS-CoV2; Kidney Replacement therapy; Meta-analysis.

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Acute kidney injury (AKI) is a common and serious complication of severe illness. It is associated with higher mortality, prolonged hospital stay, and cardiovascular complications.[1,2] In hospitalized patients, AKI is commonly associated with other markers of disease severity such as sepsis,[3] hypoxemic respiratory failure leading to mechanical ventilation,[4] and hypotension requiring vasopressor support.[5] Consequently, it is not surprising that AKI is also a common complication of coronavirus disease 2019 (COVID-19) infection, which in its most severe presentation leads to multisystem critical illness. Recent reports suggest that COVID-19 may also affect the kidney by direct virus-mediated injury, cytokine storm, dysregulation of complement, and hypercoagulability.[6]

These mechanisms of injury may explain some of the high rates of AKI that have strained nephrology resources. For example, reports from New York City and New Orleans estimate that 20% to 60% of patients with COVID-19 experienced AKI and most patients in an intensive care unit (ICU) received emergent kidney replacement therapy (KRT).[7-10] However, other centers, particularly in China, report much lower rates of AKI and KRT in patients hospitalized with COVID-19.[11,12] This wide variation could be due to differences in patient populations, ascertainment of AKI, geographic variation in practice patterns, and study characteristics.

As the COVID-19 pandemic progresses, accurate estimates of AKI associated with COVID-19 will be needed to ensure sufficient KRT resources and that infection control practices are in place to safely care for hospitalized patients. Accordingly, we performed a systematic review and meta-analysis to determine the pooled prevalence of AKI and KRT in patients with COVID-19.

METHODS

The review was conducted using Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines and reported using Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[13,14]

PLAIN-LANGUAGE SUMMARY

We conducted a meta-analysis and systematic review to determine how common acute kidney injury (AKI) and kidney replacement therapy are among hospitalized patients with coronavirus disease 2019 (COVID-19) infection. We analyzed 54 studies that reported AKI using KDIGO (Kidney Disease: Improving Global Outcomes) stages, comprising 30,657 hospitalized patients with COVID-19. We found that AKI complicated the course of nearly 1 in 3 (28%) patients hospitalized with COVID-19. The risk for AKI was higher in critically ill patients, with a substantial number receiving kidney replacement therapy at rates higher than the non-critically ill population. Because COVID-19 will be a public health threat for the foreseeable future, these estimates should help guide kidney replacement therapy resource planning.

Literature Sources and Search

With the direction of a health informatics specialist (see Item S1 for search strategy), we searched Ovid MEDLINE (1946 to October 14, 2020), Embase (1946 to October 14, 2020), and the Cochrane central register of controlled trials (2019 to October 14, 2020). We did not apply language restrictions. We reviewed the bibliographies of identified articles to locate further eligible studies. In addition, we searched the nephrology section of medRxiv (a pre-print repository of medical articles available at medrxiv.org), and the COVID-19 topic section of the website of the American Society of Nephrology for additional studies.

Study Selection

We included studies that reported the prevalence of AKI among hospitalized patients with COVID-19 according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria.[15]

We excluded case series with fewer than 20 patients, reports on patients younger than 18 years, papers in languages other than English, letters to the editor, commentaries, reviews, and editorials. We also excluded studies with missing data for AKI prevalence after contacting the senior author for clarification. When we suspected multiple reports including the same participants based on the time, location, and authors, we used the most complete publication.

Two reviewers (ZH and SH) individually scanned titles and abstracts for initial selection. We reviewed selected articles in full and independently assessed for confirmation of eligibility. We resolved discrepancies by consensus and involvement of the other authors.

Outcomes

Our 2 outcomes of interest were the prevalence of AKI and KRT initiation among all study patients. We accepted the indication for KRT mentioned in each study because it is difficult to ascertain the reason for KRT from published reports.

Data Extraction and Study Quality Assessment

For each study, we extracted data on study characteristics (location and duration), patient characteristics (age, sex, comorbid conditions including hypertension, cardiovascular disease, chronic kidney disease, diabetes, and baseline serum creatinine value), proportion of patients developing AKI (defined according to KDIGO criteria), proportion of patients receiving KRT, proportion of patients with acute respiratory distress syndrome, proportion of patients requiring ICU admission, and important clinical outcomes (discharge from hospital, ongoing hospitalization, and death).

Because most studies were expected to be case series, we used the National Institutes of Health Quality Assessment Tool for Case Series Studies[16] to assess the risk of bias in included studies. This instrument incorporates 9 domains to yield an overall assessment of study quality (good, fair, or poor). We also assessed the quality of studies that were not case series using this tool.

Statistical Analysis

We conducted meta-analyses of proportions using arcsine transformation. We expected clinical and methodological heterogeneity between studies and so calculated pooled proportions and 95% CIs using a random-effects model. We used inverse variance to weigh each study in the pooled analysis. We assessed statistical heterogeneity using I^2 values. We used a z test to compare differences between subgroups. We assessed for publication bias visually with a funnel plot. We considered $P < 0.05$ as statistically significant. We performed all analyses with R, version 3.6.1 (R Core team), using the *metaprop* command from R package meta version 4.13.[17]

Subgroup Analysis

We planned subgroup analyses across age categories, sex, comorbid conditions (chronic kidney disease, cardiovascular disease, and diabetes), and the specific clinical population (ICU vs non-ICU). We also calculated the pooled prevalence of each KDIGO AKI stage to assess the severity of AKI episodes associated with COVID-19.

RESULTS

Our search strategy yielded 2,711 unique citations (Fig S1a). Of these, we excluded 830 duplicates and 1,645 citations after screening of title and abstract, leaving 236 articles for full-text review. We subsequently excluded 182 studies that did not fulfil our inclusion criteria because they consisted of studies not reporting on AKI as an outcome (N = 66); studies with incomplete data in which the author did not reply to our queries (N = 10); review articles, meta-analyses, and letters to the editor (N = 23);

Table 1. Characteristics of Included Studies

			Patient Characteristics			Comorbid Disease				Complications			Outcomes		
Study	City and Country	Population and Setting	No.	Age, y[a]	Female Sex	HTN	CKD	DM	Admission Scr, mg/dL[a]	AKI[b]	KRT[c]	ARDS	Patients Admitted to ICU	Discharged Alive/Still in Hospital	In-Hospital Deaths
Aggarwal et al[63]	New Delhi, India	Patients with COVID-19 and severe acute respiratory illness admitted to Dr Ram Manohar Lohia hospital 4/10/20-4/30/20	32	*54.5*	41.4%	34.4%	0%	50%	*1.1*	13 (40.6%)	NR	NR	37.5%	1%, D/C; 71%, still hospitalized	28%
Alberici et al[18]	Brescia, Italy	Kidney transplant recipients with COVID-19 admitted to Spedali Hospital 2/27/20-3/24/20	20	*59*	20%	85%	100%	15%	*2*	6 (30%)	1 (5%)	55%	20%	15%, D/C; 60%, still hospitalized	25%
Akalin et al[19]	New York City, USA	Transplant recipients with COVID-19 admitted or treated as outpatients at Montefiore Medical Center 3/16/20-4/1/20	36 (28 admitted)	*60*	28%	94%	100%	69%	*1.4*	NR	6 (21%)	NR	NR	36%, D/C; 43%, still hospitalized	21%
Arentz et al[20]	Seattle, USA	Patients with COVID-19 admitted to ICU at Evergreen Hospital 2/20/20-3/5/20	21	70	48%	NR	47.6%	33.3%	1.5	4 (19%)	3 (14%)	95%	100%	47.6%, still hospitalized	52.4%
Argenziano et al[21]	New York City, USA	Total patients with COVID-19 admitted to New York Presbyterian Hospital Irving Medical Center 3/11/20-4/6/20	1,000	*63*	40.4%	60.1%	13.7%	37.2%	NR	288[d] (33.9%)	117 (13.8%)[d]	35%[d]	23.6%	69.9%, D/C; 9%, still hospitalized	21.1%
Argenziano et al[21]	New York City, USA	ICU Patients with COVID-19 admitted to New York Presbyterian Hospital Irving Medical Center 3/11/20-4/6/20	236	*62*	33.3%	66.9%	11.4%	42.8%	NR	184 (78%)[d]	83 (35.2%)[d]	90%[d]	NR	NR	NR
Argenziano et al[21]	New York City, USA	Non-ICU patients with COVID-19 admitted to New York Presbyterian Hospital Irving Medical Center 3/11/20-4/6/20	614	*64*	42.5%	59.8%	16%	37.8%	NR	104 (16.9%)[d]	34 (5.5%)[d]	14%[d]	NR	NR	NR

(Continued)

Table 1 (Cont'd). Characteristics of Included Studies

			Patient Characteristics			Comorbid Disease				Complications			Outcomes		
Study	City and Country	Population and Setting	No.	Age, y[a]	Female Sex	HTN	CKD	DM	Admission Scr, mg/dL[a]	AKI[b]	KRT[c]	ARDS	Patients Admitted to ICU	Discharged Alive/Still in Hospital	In-Hospital Deaths
Argenziano et al[21]	New York City, USA	Patients with COVID-19 admitted to ED of New York Presbyterian Hospital Irving Medical Center 3/11/20-4/6/20	150	*55*	43.3%	50.7%	8%	27%	NR	NR	NR	NR	NR	NR	NR
Azoulay et al[53]	Paris, France	Patients with COVID-19 admitted to ICU at 4 hospitals 3/11/20-4/6/20	379	62	22.9%	49.6%	16.9%	30.1%	NR	195 (51.5%)	74 (19.5%)	NR	100%	34%, D/C; 27%, still hospitalized	39%
Bhatraju et al[22]	Seattle, USA	Patients with COVID-19 admitted to ICU at 9 hospitals within Seattle region 2/24/20-3/3/20	24	64	38%	NR	21%	58%	NR	6 (25%)	1 (4%)	75%	100%	21%, D/C; 29%, still hospitalized	50%
Cai et al[46]	Shenzhen, China	Patients with COVID-19 admitted to Third People's Hospital 1/11/20-2/6/20	298	*47.5*	51.3%	15.8%	NR	6%	*0.7*	17 (5.7%)	4 (1%)	NR	10%	89.9%, D/C; 8.1%, still hospitalized	1%
Caillard et al[54]	Various cities, France	Kidney transplant recipients with COVID-19 admitted to hospitals in France 3/4/20-4/21/20	243	*61.6*	33.3%	90.1%	41.3%	100%	*2*	106 (43.6%)	27 (11.1%)	NR	35%	82.3%, no. D/C or still hospitalized NR	17.7%
Chan et al[7]	New York City, USA	Patients with COVID-19 admitted to Mount Sinai Health System (5 hospitals) 2/23/20-4/15/20	3235; (976 ICU)	*66.5*	42.3%	36.9%	10%	24.7%	*0.9*	Total: 1,406 (43.4%); stage 1: 492 (15.2%); stage 2: 281 (8.5%); stage 3: 633 (19.7%); ICU: 553; non-ICU: 853	Total: 280 (8.7%); ICU:188; non-ICU: 92	NR	25.2%	61.7%, D/C; 14.5%, still hospitalized	23.8%
Chaudhry et al[33]	Detroit, USA	Transplant recipients with COVID-19 admitted to Henry Ford Hospital 3/20/20-4/18/20	35	*62*	34.3%	94.3%	88.6%	65.7%	*NR*	22 (46.8%)	7 (20%)	35.3%	37%	68.6%, D/C; 8.6%, still hospitalized	22.8%
Cheng et al[66]	Wuhan, China	Patients with COVID-19 admitted to Tongji Hospital 1/18/20-2/28/20	1392	*63*	49%	36%	2%	17%	*0.8*	Total: 99 (7%); stage 1: 42 (3%); stage 2: 22 (2%); stage 3: 35 (3%)	15 (1%)	NR	10	NR	14%

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Table 1 (Cont'd). Characteristics of Included Studies

			Patient Characteristics			Comorbid Disease				Complications			Outcomes		
Study	City and Country	Population and Setting	No.	Age, y[a]	Female Sex	HTN	CKD	DM	Admission Scr, mg/dL[a]	AKI[b]	KRT[c]	ARDS	Patients Admitted to ICU	Discharged Alive/Still in Hospital	In-Hospital Deaths
Cravedi et al[65]	Multiple cities in USA, Spain, Italy	Kidney transplant recipients with COVID-19 admitted to 12 hospitals in USA, Italy, and Spain 3/2/20-5/15/20	144	*62*	34.7%	95.1%	100%	52.1%	*1.5*	74 (52.1%)	NR	NR	NR	68%, distinction NR	32%
Cummings et al[34]	New York City, USA	Patients with COVID-19 admitted to 2 New York Presbyterian hospitals 1/18/20-2/28/20	257	*62*	33%	63%	14%	36%	*1.5*	76 (30%)[f]	76 (30%)[f]	NR	NR	24%, D/C; 37%, still hospitalized	39%
Fava et al[55]	Multiple cities, Spain	Kidney transplant recipients with COVID-19 admitted to 5 hospitals in Spain 3/4/20-4/17/20	104	59.7	42.3%	86.5%	100%	30.8%	1.8	Total: 47 (45%); stage 1: 30 (29%); stage 2: 7 (6%); stage 3: 10 (10%)	NR	54.8%	NR	73.1%, distinction NR	26.9%
Ferguson et al[35]	Palo Alto, USA	Patients with COVID-19 admitted to 2 hospitals in Palo Alto (Stanford University Hospital and Valleycare) 3/13/20-4/11/20	72; (21 ICU)	*60.4*	47.2%	34.7%	12.5%	27.8%	*0.9*	Total: 4 (5.6%)[f]; ICU: 4 (5.6%)[f]	Total: 4 (5.6%)[f] ICU: 4 (5.6%)[f]	18%	29%	86.1%, D/C; 5.6%, still hospitalized	8.3%
Fisher et al[36]	New York City, USA	Patients with COVID-19 admitted to 3 hospitals in Montefiore Health System 3/1/20-4/26/20	3,345	64.4	46.9%	NR	12.2%	27.1%	*NR*	Total: 1,903 (56.9%); stage 1: 942 (49.5%); stage 2: 387 (20.3%); stage 3: 574 (30.2%)	164 (4.9%)	NR	13.1%	64%, D/C; 12.8%, still hospitalized	23.2%
Fominskliy et al[56]	Milan, Italy	Mechanically ventilated patients with COVID-19 admitted to ICU 2/5/20-4/20/20	96	NR	16.7%	43.8%	6.3%	16.6%	*NR*	Total: 72 (75%); stage 1: 33 (34.3%); stage 2: 15 (15.6%); stage 3: 24 (25%)	17 (17.7%)	NR	100%	NR	33.3%
Guan et al[11]	Multiple cities, China	Patients with COVID-19 hospitalized at 552 sites in 30 provinces in China 12/11/19-1/29/20	1,099	*47*	42%	15%	0.7%	7.4%	NR	6 (0.5%)	9 (0.8%)[g]	3.4%	5%	5%, D/C; 93.6%, still hospitalized	1.4%
Gupta et al[37]	Multiple cities, USA	Patients with COVID-19 admitted to ICU 3/4/20-4/11/20	3,099	*62*	35.4%	60.3%	28.9%	40%	*1.5*	637 (20.6%)[f]	637 (20.6%)[f]	NR	100%	NR	NR

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Table 1 (Cont'd). Characteristics of Included Studies

			Patient Characteristics			Comorbid Disease				Complications			Outcomes		
Study	**City and Country**	**Population and Setting**	**No.**	**Age, y[a]**	**Female Sex**	**HTN**	**CKD**	**DM**	**Admission Scr, mg/dL[a]**	**AKI[b]**	**KRT[c]**	**ARDS**	**Patients Admitted to ICU**	**Discharged Alive/Still in Hospital**	**In-Hospital Deaths**
Goyal et al[24]	New York City, USA	Patients with COVID-19 admitted to 2 hospitals in Manhattan (Weill Cornell Medical Center and Lower Manhattan Hospital) 3/3/20-3/27/20	393[e]	*62.2*	39.4%	50.1%	4.6% ESKD	25.2%	16% ≥ 1.5	18 (4.8%)[f]	18 (4.8%)[e]	NR	NR	66.2%, D/C; 23.6%, still hospitalized	10.2%
Hirsch et al[8]	New York City, USA	Patients with COVID-19 admitted to 13 hospitals in Northwell Medical System 3/1/20-4/5/20	5,449; (ICU: 1,395)	*64*	39.1%	55.7%	NR	33%	*1.0*	Total: 1,993 (36.6%); stage 1: 927 (17%); stage 2: 447 (8.2%); stage 3: 619 (11.4%); ICU: 1,060; non-ICU: 993	285 (5.2%)	NR	25.6%	60.2%, D/C; 16.3%, still hospitalized	23.5%
Hoek et al[57]	Multiple cities, Netherlands	Solid organ transplant recipients with COVID-19 admitted to various hospitals in Netherlands 2/27/20-4/30/20	23	59.3	21.7%	83%	NR	43%	2.2	1 (4.3%)[f]	1 (4.3%)[f]	NR	NR	NR	21.7%
Hong et al[25]	Daegu, South Korea	Patients with COVID-19 admitted to Yeungnam University Medical Center through 3/29/20	Total: 98; ICU: 13	55	61.2%	30.6%	NR	9.2%	NR	9 (9.2%); ICU: 8; non-ICU: 1	3 (3%); ICU: 3	18.4%	13.2%	30.6%, D/C; 58.2%, still hospitalized; 6.1%, transferred	5.1%
Huang et al[12]	Wuhan, China	Patients with COVID-19 admitted to Jin Yintan Hospital 12/16/19-1/2/20	Total: 41; (ICU: 13)	*49*	27%	15%	NR	20%	10% > 1.5	3 (7%)[f]; ICU: 3[f]	3 (7%)[f]; ICU: 3[f]	29%	32%	68%, D/C; 17%, still hospitalized	15%
Imam et al[38]	Detroit, USA	Patients with COVID-19 admitted to 8 hospitals in Beaumont Health system 3/1/20-4/17/20	1,305	61	46.2%	56.2%	17.5%	30.1%	*1.2*	76 (5.8%)	NR	NR	26.4%	78.3%, D/C; 6.4%, still hospitalized	15.3%
Joseph et al[58]	Paris, France	Patients with COVID-19 admitted to ICU at Hopital Saint-Louis 3/1/20-6/1/20 0	100	*59*	30%	56%	29%	30%	0.7	Total: 81 (81%); stage 1:44 (44%); stage 2: 10 (10%); stage 3:27 (27%)	13 (13%)	NR	100%	71%, distinction NR	29%
Larsson et al[59]	Stockholm, Sweden	Patients with COVID-19 admitted to ICU of Karolinsk University Hospital 3/9/20-4/20/20	260	*59*	20%	39.6%	1.5%	26.2%	*NR*	59 (22.7%)[f]	59 (22.7%)[f]	NR	100%	31.3%, D/C; 38.4, still hospitalized	30.3%

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Table 1 (Cont'd). Characteristics of Included Studies

			Patient Characteristics			Comorbid Disease				Complications			Outcomes		
Study	**City and Country**	**Population and Setting**	**No.**	**Age, y[a]**	**Female Sex**	**HTN**	**CKD**	**DM**	**Admission Scr, mg/dL[a]**	**AKI[b]**	**KRT[c]**	**ARDS**	**Patients Admitted to ICU**	**Discharged Alive/Still in Hospital**	**In-Hospital Deaths**
Lee et al[39]	NYC, USA	Patients with COVID-19 admitted to New York Presbyterian/Weill Cornell Medical center 3/1/20-4/19/20	1,002	*66*	48%	60%	14%	38%	*0.9*	Total: 294 (29%); stage 1: 182 (18%); stage 2: 29 (3%); stage 3: 83 (8%)	59 (6%)	NR	27%	83%, distinction NR	17%
Lendorf et al[60]	Denmark	Patients with COVID-19 admitted to North Zealand Hospital 3/1/20-5/4/20	111; (20 ICU)	*68*	40%	34%	7%	14%	*0.9*	Total: 13 (12%); ICU: 6; non-ICU: 7	Total: 3 (3%); ICU: 3	NR	18%	81%, D/C; 5%, still hospitalized	14%
Li et al[26]	Wuhan and Chongqing, China	Patients with COVID-19 admitted to 4 hospitals in Hubei province and Chongqing (Tongji, Pulmonary, Central and Chongqing Southwest) 1/6/20-2/21/20	193	57	51%	NR	NR	NR	0.8	55 (28%)	7 (4%)	28%	NR	49%, D/C; 34%, still hospitalized	17%
Liu et al[47]	Wuhan, China	Patients admitted with COVID-19 pneumonia to Wuhan Infectious Disease Hospital 1/31/20-2/20/20	1,190	*57*	46.6%	26.1%	2.6%	12.2%	*1*	51 (4.3%)	NR	19.2%	NR	86.8%, distinction NR	13.2%
Mohamed et al[10]	New Orleans, USA	Patients with COVID-19 admitted to Ochsner Medical Center 3/1/20-3/31/20	575; (ICU: 173)	*65*	45.7%	73.7%	29.9%	48.9%	1, de novo AKI; 1.6, prior CKD	Total: 161 (28%); stage 1: 30 (5%); stage 2: 25 (5%); stage 3: 106 (18%); ICU: 105; non-ICU:56	89 (15%); ICU: 77; non-ICU: 12	30%	65%	50%, D/C or still hospitalized (distinction NR)	50%
Mukherjee et al[40]	New York City, USA	Patients with COVID-19 admitted to ICU at Bellevue Hospital 3/10/20-4/7/20	137	*59*	27.2%	51.1%	14.6%	37.2%	1.1	46 (33.6%)[f]	46 (33.6%)[f]	NR	100%	29.9%, D/C; 10.2%, still hospitalized	59.8%
Naar et al[41]	Boston, USA	Patients with COVID-19 admitted to ICU at Massachusetts General Hospital 3/13/20-4/22/20	206	*60*	34.9%	NR	13.1%	43.2%	NR	148 (71.8%)	46 (22.3%)	NR	100%	NR	NR
Naaraayan et al[42]	New York City, USA	Patients with COVID-19 admitted to a community hospital 3/12/20-5/13/20	370	*71*	44.1%	66.2%	111.1%	42.4%	NR	182 (54.9%) (of 331 eligible)	NR	NR	NR	NR	41.1%

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Table 1 (Cont'd). Characteristics of Included Studies

			Patient Characteristics			Comorbid Disease				Complications			Outcomes		
Study	City and Country	Population and Setting	No.	Age, y[a]	Female Sex	HTN	CKD	DM	Admission Scr, mg/dL[a]	AKI[b]	KRT[c]	ARDS	Patients Admitted to ICU	Discharged Alive/Still in Hospital	In-Hospital Deaths
Nowak et al[61]	Warsaw, Poland	Patients with COVID-19 admitted to Central Clinical hospital 3/16/20-4/7/20	169	63.7	48.5%	47.3%	20.7%	18.9%	NR	17 (10.1%)	1 (0.6%)	24.3%	16%	26.3%, D/C; 45.7%, still hospitalized	27.2%
Okoh et al[43]	Newark, USA	Patients with COVID-19 admitted to a quaternary care hospital 3/10/20-4/10/20	251	*62*	49%	70%	18%	46%	NR	52 (21%)[f]	52 (21%)[f]	33%	33%	61.3%, distinction NR	38.6%
Pelayo et al[67]	Philadelphia, USA	Patients with COVID-19 admitted to a tertiary inner-city hospital	223	*NR*	48.4%	80.7%	17.5%	46.6%	NR	110 (49.3%)	9 (4%)	NR	NR	80.3%, D/C	19.7%
Portoles et al[62]	Madrid, Spain	Patients with COVID-19 admitted to Puerta de Hierro University Hospital 2/25/20-4/24/20	1,603	64.6	40.4%	35.7%	9.5%	15.2%	1	333 (20.8%)	17 (1.1%)	NR	NR	87.3%, D/C	12.3%
Qian et al[52]	Wenzhou, China	Patients with COVID-19 admitted to First Affiliated Hospital of Wenzhou Medical University 1/28/20-2/16/20	37	*55*	31.6%	36.8%	2.6%	21.1%	NR	17 (45.9%)	3 (8.1%)	21.6%	NR	59.1%, D/C; 36.4%, still hospitalized	2.7%
Rubin et al[27]	Bordeaux, France	Patients with COVID-19 admitted to 4 ICUs 3/3/20-4/14/20	71	*61*	23%	61%	6%	30%	0.8	Total: 57 (80%); stage I: 20 (35%); stage 2: 20 (35%); stage 3: 17 (30%)	10 (14%)	NR	100%	79%, D/C or still hospitalized (distinction NR)	21%
Shi et al[48]	Wuhan, China	Patients admitted with COVID-19 to Renmin Hospital 1/20/20-2/10/20	416	*64*	50.7%	30.5%	3.4%	14.4%	0.7	8 (1.9%)	2 (0.4%)	23.3%	NR	9.6%, D/C; 79.6%, still hospitalized	13.7%
Suleyman et al[44]	Detroit, USA	Patients with COVID-19 admitted to Henry Ford Hospital 3/9/20-3/27/20	Total: 355; (ICU: 141)	61.4	53.5%	72.7%	45.4%	43.4%	1.1	Total: 159 (44.7%); ICU 98; non-ICU: 61	Total: 25 (5.4%); ICU: 24; non-ICU: 1	NR	30.4%	65%, D/C; 16.4%, still hospitalized	18.6%
Taher et al[64]	Manama, Bahrain	Patients with COVID-19 admitted to Salmaniya Medical Complex 4/1/20-5/3/20	73	54.3	39.7%	42.5%	8.2%	45.2%	NR	Total: 29 (39.7%); stage 1: 8 (11%); stage 2: 11 (15.1%); stage 3: 10 (13.6%)	7 (9.6%)	NR	31.5%	82.2%, Distinction not specified	17.8%

(Continued)

Table 1 (Cont'd). Characteristics of Included Studies

			Patient Characteristics			Comorbid Disease				Complications			Outcomes		
Study	City and Country	Population and Setting	No.	Age, y[a]	Female Sex	HTN	CKD	DM	Admission Scr, mg/dL[a]	AKI[b]	KRT[c]	ARDS	Patients Admitted to ICU	Discharged Alive/Still in Hospital	In-Hospital Deaths
Tang et al[28]	Wuhan, China	Patients with COVID-19 and ARDS admitted to ICU at Wuhan Pulmonary Hospital 12/24/19-2/7/20	73	*67*	38.4%	52.1%	4.1%	27.4%	*0.9*	13 (17.8%)	NR	100%	100%	35.6%, D/C; 35.6%, still in hospital	28.8%
Wang et al[49]	Wuhan, China	Patients with COVID-19 admitted to Sino-French branch of Tongji Hospital 3/9/20-3/17/20	116	NR	46.6%	40.5%	6.0%	17.2%	0.8	Total: 12 (10.3%); stage 1: 9 (7.7%); stage 2: 3 (2.6%); stage 3: 0 (0%)	1 (0.9%)	NR	16.4%	NR	NR
Xia et al[50]	Wuhan China	Patients with COVID-19 admitted to ICU of Sino-French branch of Tongji Hospital 2/5/20-3/20/20	81	66.6	33.3%	53.1%	3.7%	23.5%	0.9	41 (50.6%)	8 (9.9%)	95.1%	100%	25.9%, distinction not specified	74.1%
Xu et al[51]	Wuhan, China	Patients with COVID-19 admitted to ICU of 3 hospitals (Wuhan Union Hospital, Jinyitan Hospital, Wuhan Third Hospital) 1/12/20-2/3/20	239	62.5	40.2%	42.9%	NR	18.4%	*0.8*	119 (49.8%)	12 (5%)	68.6%	100%	61.5%, distinction not specified	38.4%
Yang et al[29]	Wuhan, China	Patients admitted with COVID-19 in critical condition to ICU of Jin Yintan Hospital late 12/19-1/26/20	52	59.7	33%	NR	NR	17%	NR	15 (29%)	9 (17%)	67%	100%	15.3%, D/C; 23.1%, still hospitalized	61.6%
Yu et al[30]	Wuhan, China	Patients admitted with COVID-19 to 19 ICUs in Wuhan 2/26/20-2/27/20 (cross-sectional study)	226	64	38.5%	42.5%	1.3% non-ESKD; 2.2% ESKD	20.8%	0.7	Total: 57 (25.2%); stage 1: 23 (10.2%); stage 2: 12 (5.3%); stage 3: 22 (9.7%)	24 (10.6%)	71.2%	100%	NR	NR
Zhang et al[45]	Wuhan, China	Patients admitted with COVID-19 pneumonia to Zhongnan Hospital 1/2/20-2/10/20	221	*55*	51.1%	35.3%	2.7%	10%	*0.8*	10 (4.5%)	5 (2.3%)	21.7%	NR	19%, D/C; 75.6%, still hospitalized	5.4%
Zheng et al[31]	Zhejiang, China	Patients admitted to the ICU with COVID-19 at First Affiliated Hospital 1/22/20-3/5/20	34	*66*	32.4%	64.7%	5.9%	23.5%	*0.9*	7 (20.6%)	5 (14.7%)	97.1%	100%	58.8%, D/C; 41.2%, still hospitalized	0%

(Continued)

Table 1 (Cont'd). Characteristics of Included Studies

			Patient Characteristics			Comorbid Disease				Complications		Outcomes			
Study	City and Country	Population and Setting	No.	Age, y[a]	Female Sex	HTN	CKD	DM	Admission Scr, mg/dL[a]	AKI[b]	KRT[c]	ARDS	Patients Admitted to ICU	Discharged Alive/Still in Hospital	In-Hospital Deaths
Zhou et al[32]	Wuhan, China	Patients admitted with COVID-19 to 2 hospitals (Jinyitan Hospital and Wuhan Pulmonary Hospital) who were D/C home or died 12/29/19-1/31/20	191	*56*	38%	30%	1%	19%	4% > 1.5	28 (15%)	10 (5%)	31%	26%	72%, D/C	28%

Note: Disease severity is reported according to the classification used in each study, which is based on the classification scheme of the World Health Organization.
Abbreviations: AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; D/C, discharged; DM, diabetes mellitus; ED, emergency department; ESKD, end-stage kidney disease; HTN, hypertension; ICU, intensive care unit; KDIGO, Kidney Disease: Improving Global Outcomes; KRT, kidney replacement therapy; NR, not reported; Scr, admission serum creatinine [mean (median) unless otherwise specified].
[a]Age is reported as mean, unless *italicized (median)*; Scr is reported as mean, unless otherwise specified or *italicized (median)*.
[b]All AKI was reported according to the KDIGO AKI criteria, but not all studies reported AKI stages.[15]
[c]Denominator is all patients included in each study.
[d]Among 850 patients with available data.
[e]Renal outcomes reported for only 375 patients.
[f]Only KRT reported.
[g]Some patients receiving KRT may have been maintenance dialysis patients, but not reported by the authors.

studies that did not use the KDIGO definition of AKI (N = 54); modelling studies (N = 5); studies comprising maintenance dialysis recipients (N = 10); and studies containing duplicate data (N = 14). This yielded 54[7,8,10-12,18-22,23-28,29-32] studies that included 1 preprint.[26]

Risk of Bias Assessment

Overall, most studies were of good methodological quality (Table S1). Studies determined to be of fair quality most commonly did not report the incidence of KRT. There was no evidence of publication bias suggested by visual inspection of the funnel plot (Fig S1b).

Study and Patient Characteristics

Twenty-one reports were from the United States[7,8,10,19-22,24,33-44]; 17 were from China[11,12,23,26,28,29-45,46-52]; 12 were from Europe[18,27,53-62]; 1 each were from India,[63] Bahrain,[64] and South Korea[25]; and 1 report[65] included multiple cities from the United States and Europe. The studies included 30,657 hospitalized patients, of whom 12,800 (41.8%) were women. In total, 9,650 patients (n = 40 studies) were admitted to the ICU, 15,728 patients (n = 24 studies) were admitted to a non-ICU setting, and 4,991 (n = 14 studies) patients did not have their hospital setting reported. Mean age of patients ranged between 47 and 71 years. Hypertension and diabetes mellitus were common comorbid conditions. Mean baseline serum creatinine values ranged from 0.67 to 2 mg/dL (Tables 1[7,8,10-12,15,18-22,24-28,29,30,45-65,66,67] and 2).

Outcomes

Data for AKI were available for 30,639 patients (n = 54 studies) and data for the receipt of KRT were available for 27,525 patients (n = 48 studies; Table 2). We were able to determine the indication for the initiation of KRT in only 3[20,24,34] of the 48 studies. For the entire hospitalized population, the pooled prevalence of AKI was 28% (95% CI, 22%-34%; $I^2 = 99\%$), and the pooled prevalence of receipt of KRT was 9% (95% CI, 7%-11%; $I^2 = 97$; Figs 1 and 2).

Subgroup Analysis

In subgroup analysis, data were available to report outcomes only for patients admitted to an ICU or non-ICU setting, and AKI severity.

ICU Versus Non-ICU Setting

Of the 9,650 patients admitted to an ICU, ascertainment of AKI and receipt of KRT were feasible for only 8,086 and 6,618 patients, respectively (n = 25 studies for AKI; n = 23 studies for KRT). The pooled prevalence of AKI and KRT for patients receiving care in an ICU was 46% (95% CI, 35%-57%; $I^2 = 99\%$) and 19% (95% CI, 15%-22%; $I^2 = 88\%$), respectively (Fig S2).

Among the 15,728 patients who did not receive care in an ICU, the presence of AKI could be ascertained in 7,799 patients (9 studies), and the receipt of KRT, in 3,745 patients (8 studies). The pooled proportion of AKI and KRT

Table 2. Summary of AKI Events

Characteristic	AKI	KRT
No. of studies	54	49
Pooled prevalence (95% CI)	28% (22%-34%)	9% (7%-11%)
Kidney events in patients admitted to an ICU		
Pooled prevalence (95% CI)	46% (35%-57%)	19% (15%-22%)
Kidney events in patients admitted to a non-ICU setting		
Pooled prevalence (95% CI)	12% (6%-19%)	1% (0%-3%)

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; KRT, kidney replacement therapy.

in non-ICU patients was 12% (95% CI, 6%-19%; $I^2 = 98\%$) and 1% (95% CI, 0%-3%; $I^2 = 88\%$), respectively (Fig S3). There was a significant difference in risk for AKI and KRT between patients admitted versus those not admitted to the ICU ($P < 0.001$ for AKI; $P < 0.001$ for KRT).

AKI Severity

Thirteen studies (n = 6,211 patients) reported on the severity of AKI by KDIGO stage. The pooled prevalence of stage 1 AKI was 44% (95% CI, 38%-50%; $I^2 = 94\%$), stage 2 AKI was 19% (95% CI, 17%-22%; $I^2 = 76\%$), and stage 3 AKI was 34% (95% CI, 28%-40%; $I^2 = 94\%$; Fig S4).

DISCUSSION

In this systematic review and meta-analysis of 54 studies, we found that AKI occurred in ∼30% of patients hospitalized with COVID-19. AKI complicated the course of >45% of patients requiring ICU care, and 1 in 5 patients admitted to the ICU received KRT. Because COVID-19 is expected to remain a public health threat for the foreseeable future and disease surges are anticipated, our data provide important information for clinicians caring for hospitalized patients and administrators who need to marshal KRT resources.

A previous worldwide meta-analysis of 154 studies using KDIGO AKI criteria in patients without COVID-19 reported a pooled incidence rate of 21.6% (95% CI, 19.3%-24.1%), which increased to 31.7% (95% CI, 28.6%-35.0%) in a critical care setting.[70] Approximately 10% of patients with AKI received KRT (2% of all patients). In other prospective studies of critically ill patients, between 15% and 30% of patients with AKI received KRT (5%-15% of all patients).[69-71] Therefore, our reported overall AKI prevalence of 28% in hospitalized patients with COVID-19 is consistent with this prior work, but the rate of AKI in critically ill patients is higher. We also identified more use of KRT in COVID-19–associated AKI. These findings are driven primarily by data from the United States and Europe because most of the studies from China reported less overall AKI and use of KRT, which has been described previously in patients without COVID-19.[68,69,72] These differences could be explained in part by under-recognition of AKI stemming from differences in the frequency of kidney function measurement, as well as KRT resource limitations and practice pattern variation in the initiation of KRT among different centers.[73]

These data suggest that COVID-19–associated AKI contributes to a more severe AKI phenotype, and higher rates of KRT should spur further investigation into the mechanisms underlying this complication. Commonly cited hypotheses include a hypercoagulable state and direct viral invasion related to angiotensin-converting enzyme 2 expression on the proximal tubule,[6,74,75] supported by small autopsy studies that demonstrated severe proximal tubule injury, peritubular erythrocyte aggregation, glomerular fibrin thrombi, and even collapsing glomerulopathy in a subset of patients.[76,77] Notably, pigment casts were present in these reports, suggesting some degree of inflammation and acute tubular necrosis, which is a common cause of AKI in patients with multiorgan failure that is compounded by intravascular volume depletion and mechanical ventilation.[78]

Our data also give health care providers and administrators estimates of KRT capacity needed in future COVID-19 surges. This planning involves considering human resources (ie, nurses), equipment availability (ie, KRT machines and reverse osmosis devices), disposables (ie, filters, dialysate, and anticoagulation), and protocol development for other acute dialysis modalities (ie, sustained low efficiency dialysis and/or acute peritoneal dialysis) in case continuous kidney replacement therapy resources become overwhelmed.[9,79,80] In patients with AKI who survive their COVID-19, there will be increased risks for rehospitalization, recurrent AKI, cardiovascular complications, and death that mostly occur within the first year after hospitalization.[81] Current after-care programs for survivors of COVID-19 focus mainly on respiratory and mental health,[82] and the high rates of AKI reported here suggest that kidney monitoring should also be incorporated.

The strengths of our systematic review include the use of a comprehensive search strategy that incorporated preprints and careful identification of duplicate studies. Some of the studies still temporally overlapped in setting and location, and we included only the most complete reports to avoid double counting. We also ascertained all AKI episodes according to KDIGO criteria.

This study has some limitations. First, there was significant heterogeneity among the included studies that remained unaccounted for in subgroup analysis. Factors that may have contributed to heterogeneity included baseline kidney function ascertainment, hospital setting, and hospital policies. For example, AKI could be underreported in hospitals with less frequent kidney function measurement, and criteria for hospital/ICU admission and KRT initiation are determined locally.

In addition, most studies only reported the presence of AKI based on KDIGO criteria (ie, yes/no) and few

Study	Events	Total	Proportion	95%-CI	Weight
Aggarwal	13	32	0.41	[0.24; 0.59]	1.7%
Alberici	6	20	0.30	[0.12; 0.54]	1.6%
Akalin	6	28	0.21	[0.08; 0.41]	1.7%
Arentz	4	21	0.19	[0.05; 0.42]	1.6%
Argenziano	288	850	0.34	[0.31; 0.37]	1.9%
Azoulay	195	379	0.51	[0.46; 0.57]	1.9%
Bhatraju	6	24	0.25	[0.10; 0.47]	1.6%
Cai	17	298	0.06	[0.03; 0.09]	1.9%
Caillard	106	243	0.44	[0.37; 0.50]	1.9%
Chan	1406	3235	0.43	[0.42; 0.45]	1.9%
Chaudhry	22	35	0.63	[0.45; 0.79]	1.7%
Cheng	99	1392	0.07	[0.06; 0.09]	1.9%
Cravedi	74	144	0.51	[0.43; 0.60]	1.9%
Cummings	76	257	0.30	[0.24; 0.36]	1.9%
Fava	47	104	0.45	[0.35; 0.55]	1.9%
Ferguson	4	72	0.06	[0.02; 0.14]	1.8%
Fisher	1903	3345	0.57	[0.55; 0.59]	1.9%
Fominsky	72	96	0.75	[0.65; 0.83]	1.9%
Guan	6	1099	0.01	[0.00; 0.01]	1.9%
Gupta	637	3099	0.21	[0.19; 0.22]	1.9%
Goyal	18	375	0.05	[0.03; 0.07]	1.9%
Hirsch	1993	5449	0.37	[0.35; 0.38]	1.9%
Hoek	1	23	0.04	[0.00; 0.22]	1.6%
Hong	9	98	0.09	[0.04; 0.17]	1.9%
Huang	3	41	0.07	[0.02; 0.20]	1.7%
Imam	76	1305	0.06	[0.05; 0.07]	1.9%
Joseph	81	100	0.81	[0.72; 0.88]	1.9%
Larsson	59	260	0.23	[0.18; 0.28]	1.9%
Lee	294	1002	0.29	[0.27; 0.32]	1.9%
Lendorf	13	111	0.12	[0.06; 0.19]	1.9%
Li	55	193	0.28	[0.22; 0.35]	1.9%
Liu	51	1190	0.04	[0.03; 0.06]	1.9%
Mohamed	161	575	0.28	[0.24; 0.32]	1.9%
Mukherje	46	137	0.34	[0.26; 0.42]	1.9%
Naar	148	206	0.72	[0.65; 0.78]	1.9%
Naaraaya	182	370	0.49	[0.44; 0.54]	1.9%
Nowak	17	169	0.10	[0.06; 0.16]	1.9%
Okoh	52	251	0.21	[0.16; 0.26]	1.9%
Pelayo	110	223	0.49	[0.43; 0.56]	1.9%
Portoles	333	1603	0.21	[0.19; 0.23]	1.9%
Qian	17	37	0.46	[0.29; 0.63]	1.7%
Rubin	57	71	0.80	[0.69; 0.89]	1.8%
Shi	8	416	0.02	[0.01; 0.04]	1.9%
Suleyman	159	355	0.45	[0.40; 0.50]	1.9%
Taher	29	73	0.40	[0.28; 0.52]	1.8%
Tang	13	73	0.18	[0.10; 0.29]	1.8%
Wang	12	116	0.10	[0.05; 0.17]	1.9%
Xia	41	81	0.51	[0.39; 0.62]	1.8%
Xu	119	239	0.50	[0.43; 0.56]	1.9%
Yang	15	52	0.29	[0.17; 0.43]	1.8%
Yu	57	226	0.25	[0.20; 0.31]	1.9%
Zhang	10	221	0.05	[0.02; 0.08]	1.9%
Zheng	7	34	0.21	[0.09; 0.38]	1.7%
Zhou	28	191	0.15	[0.10; 0.20]	1.9%
Random effects model		**30639**	**0.28**	**[0.22; 0.34]**	**100.0%**

Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.0546$, $p = 0$

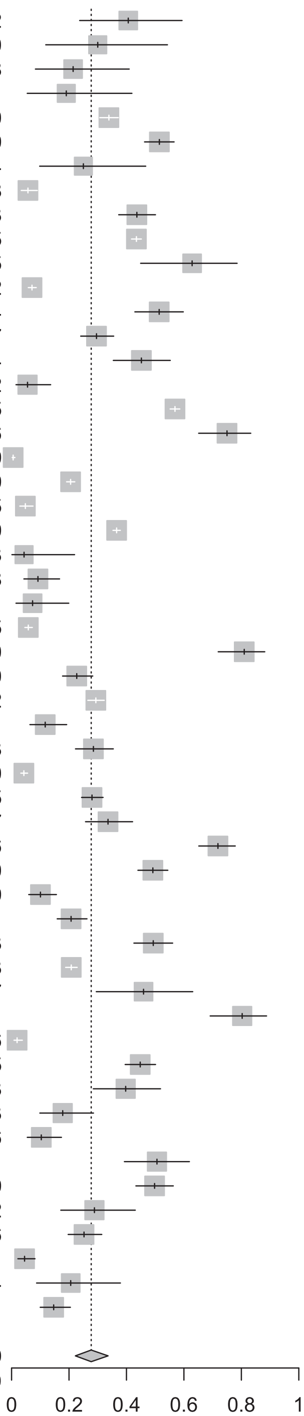

Figure 1. Pooled prevalence of acute kidney injury among all patients with coronavirus disease 2019 (COVID-19) using a random-effects model.

provided data on the severity of AKI by KDIGO stage. However, we estimated the point prevalence of each KDIGO AKI stage among studies reporting these data, as well as the use of KRT, which is a marker of severe AKI. Second, detailed information on the subset of patients who received KRT, including modality and prescription used, was limited; therefore, the optimal method of KRT delivery remains an important knowledge gap. Third, data for kidney recovery and mortality were incomplete, with many patients still hospitalized and the follow-up time too short to properly assess these outcomes. Fourth, we may have slightly overestimated KRT rates by virtue of some

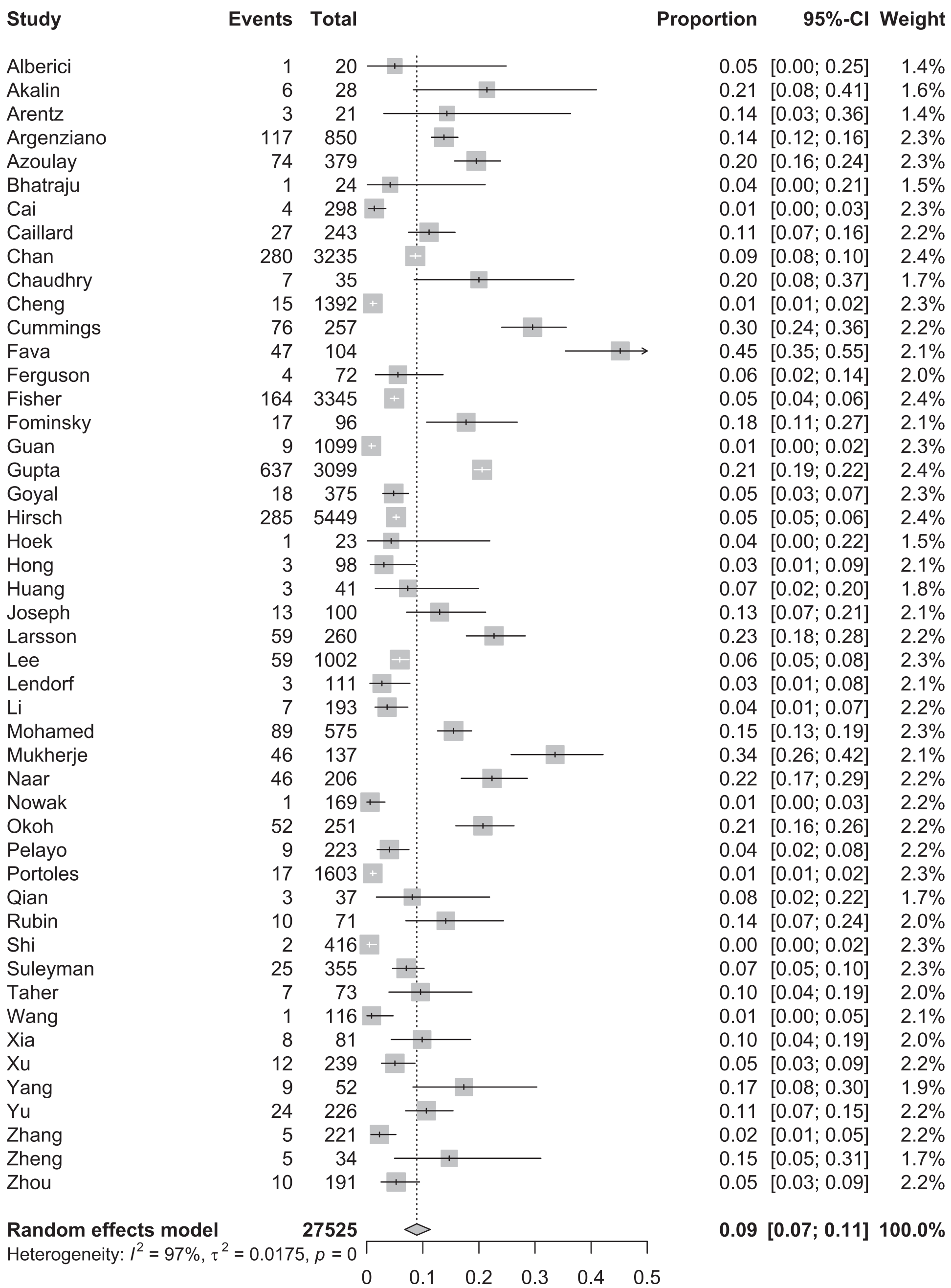

Figure 2. Pooled prevalence of kidney replacement therapy among all patients with coronavirus disease 2019 (COVID-19) using a random-effects model.

patients receiving KRT for end-stage kidney disease. Last, although our study included more than 30,000 patients from 54 studies, our estimates could be affected by the exclusion of 130 studies that did not report on AKI or in which KDIGO criteria were not used.

Our systematic review and meta-analysis provides health care providers and administrators with updated and comprehensive information on the epidemiology of AKI and KRT in hospitalized patients with COVID-19. Approximately 50% of critically ill patients may experience AKI, with almost 20% of all critically ill patients receiving KRT. These data identify targets to guide adequate capacity planning in the face of future COVID-19 surges. Given the prominence of AKI and KRT in hospitalized patients with COVID-19, further work is also needed to better characterize COVID-19–associated AKI and kidney-specific treatments. Future reports should provide detailed data on AKI severity, triggers for KRT, pathology (when performed), and information on the KRT prescription (ie, modality, anticoagulation, and ultrafiltration), as well as data for mortality and kidney recovery.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1: Study flow diagram and funnel plot of included studies.

Figure S2: Pooled prevalence of acute kidney injury and kidney replacement therapy among all patients with COVID-19 admitted to an ICU.

Figure S3: Pooled prevalence of acute kidney injury and kidney replacement therapy among all patients with COVID-19 admitted to a non-ICU setting.

Figure S4: Pooled prevalence of AKI among hospitalized patients with COVID-19 by KDIGO stage.

Item S1: Search strategy.

Table S1: Methodological quality of included studies using the National Institutes of Health (NIH) Quality Assessment Tool.

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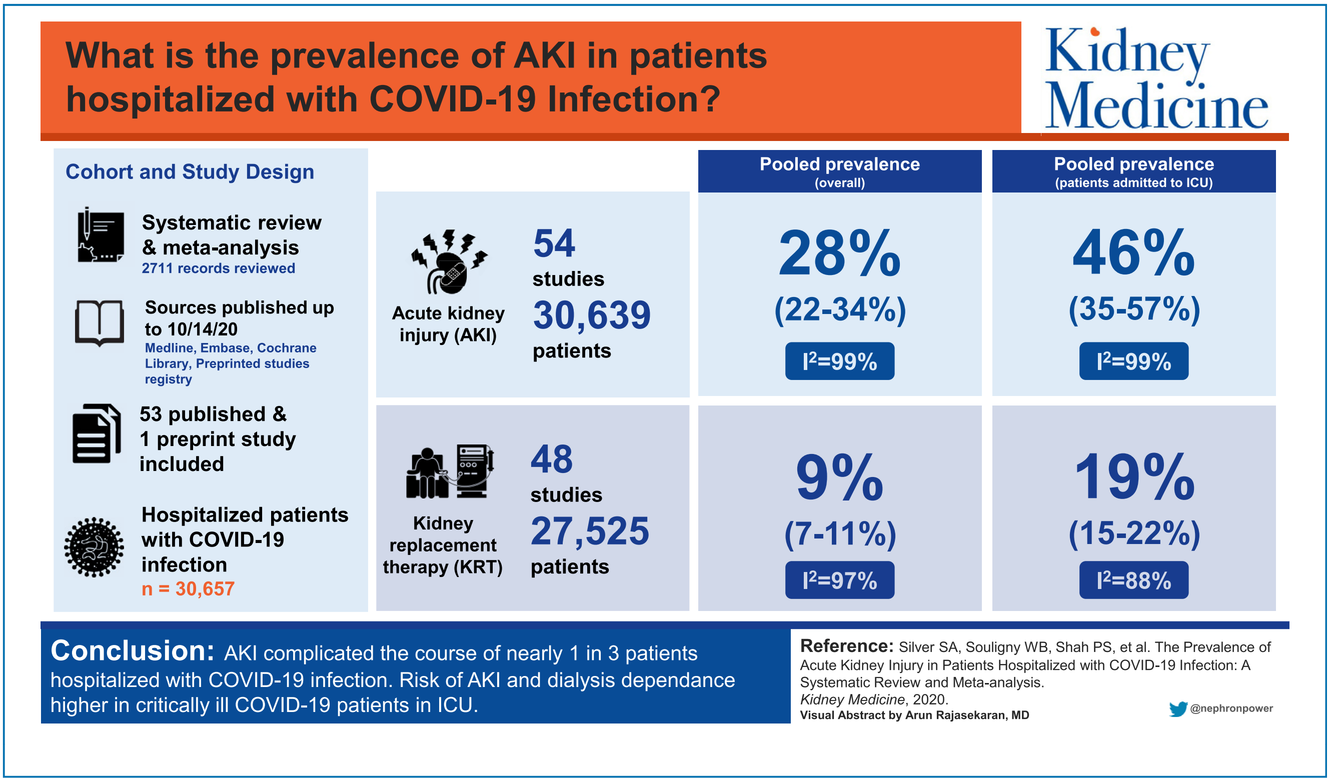
What is the prevalence of AKI in patients hospitalized with COVID-19 Infection?
Kidney Medicine
Cohort and Study Design
Systematic review & meta-analysis
2711 records reviewed
Sources published up to 10/14/20
Medline, Embase, Cochrane Library, Preprinted studies registry
53 published & 1 preprint study included
Hospitalized patients with COVID-19 infection
n = 30,657
Pooled prevalence (overall)
Pooled prevalence (patients admitted to ICU)
Acute kidney injury (AKI)
54 studies
30,639 patients
28%
(22-34%)
I2=99%
46%
(35-57%)
I2=99%
Kidney replacement therapy (KRT)
48 studies
27,525 patients
9%
(7-11%)
I2=97%
19%
(15-22%)
I2=88%
Conclusion: AKI complicated the course of nearly 1 in 3 patients hospitalized with COVID-19 infection. Risk of AKI and dialysis dependance higher in critically ill COVID-19 patients in ICU.
Reference: Silver SA, Souligny WB, Shah PS, et al. The Prevalence of Acute Kidney Injury in Patients Hospitalized with COVID-19 Infection: A Systematic Review and Meta-analysis.
Kidney Medicine, 2020.
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