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NEPHROLOGY - LETTER TO THE EDITOR

Relationship between chronic kidney disease and adverse outcomes of coronavirus disease 2019: a meta-analysis based on adjusted risk estimates

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Recently, there are several studies reporting that pre-existing chronic kidney disease (CKD) was related to the adverse outcomes of patients with coronavirus disease 2019 (COVID-19) [1, 2]. Moreover, a meta-analysis has indicated that CKD was associated with poor prognosis in patients with COVID-19 on the basis of unadjusted effect estimates [3]. To the best of our knowledge, several factors including age, gender and underlying diseases were reported to have effects on the clinical outcomes of COVID-19 patients [4]. Therefore, in this present meta-analysis, we aimed to investigate the relationship between CKD and the adverse outcomes in COVID-19 patients on the basis of adjusted effect estimates by performing a quantitative meta-analysis.

The electronic databases including PubMed, Web of Science, EMBASE and Chinese National Knowledge Infrastructure (CNKI) were searched by two independent authors to screen out eligible articles, using the keywords of "coronavirus disease 2019" OR "SARS-CoV-2" OR "2019 novel coronavirus" OR "2019-nCoV" OR "COVID-19" AND "chronic kidney disease" OR "chronic renal disease" (up to July 15th, 2020). The adverse outcomes were defined as severe illness, critical illness or death. Studies reporting the adjusted effect estimates (odds ratio (OR) or hazard ratio (HR)) on the association between CKD and adverse outcomes of COVID-19 patients were eligibly included. All analyses were performed by STATA 11.2. A fixed-effects model was used if I^2 was < 50%. Otherwise, a random-effects model was applied. The stability of results was assessed by sensitivity analysis. Publication bias was evaluated by Begg's test and Egger's test.

A total of 179 articles were identified. Finally, 13 articles with 12,999 patients were included in the study. The main characteristics of the included studies are shown in Table 1. Our results indicated that COVID-19 patients with a history of CKD had an increased risk for adverse outcomes (pooled effect = 1.64, 95% CI 1.28–2.09) (Fig. 1a). We also observed that CKD was significantly associated with an increased risk for COVID-19 death while adverse outcomes were only restricted to death (pooled effect = 1.67, 95% CI 1.28–2.17) (Fig. 1b). There was no publication bias (Begg's test, $P = 0.855$ (Fig. 1c) and Egger's test, $P = 0.655$). Sensitivity analysis exhibited that our results were stable (Fig. 1d).

Previous meta-analyses have reported the association of CKD with poor outcomes including mortality among COVID-19 patients, but their findings were based on unadjusted effect estimates [5–10]. Our present study based on adjusted effect estimates indicated that pre-existing CKD was independently associated with an increased risk for adverse outcomes, especially for mortality. Thus, co-existing CKD patients should be taken care not to get COVID-19 infection. Of course, there are some limitations to this study. First, the patients in each article might be in different stages of the disease, which may have a certain impact on the overall effects. Second, supportive treatment and medications are not clear in the included studies, thus, the data could not be analyzed currently. Third, the included studies were mainly from China, USA and Italy. As a result, it should be cautious to extrapolate the inclusion to other regions. Fourth, the findings were based on the adjusted effect estimates, but the adjusted factors were not completely consistent. This issue should be addressed in the future studies. Taken together, our current study is needed to be verified by further well-designed studies with a large sample size.

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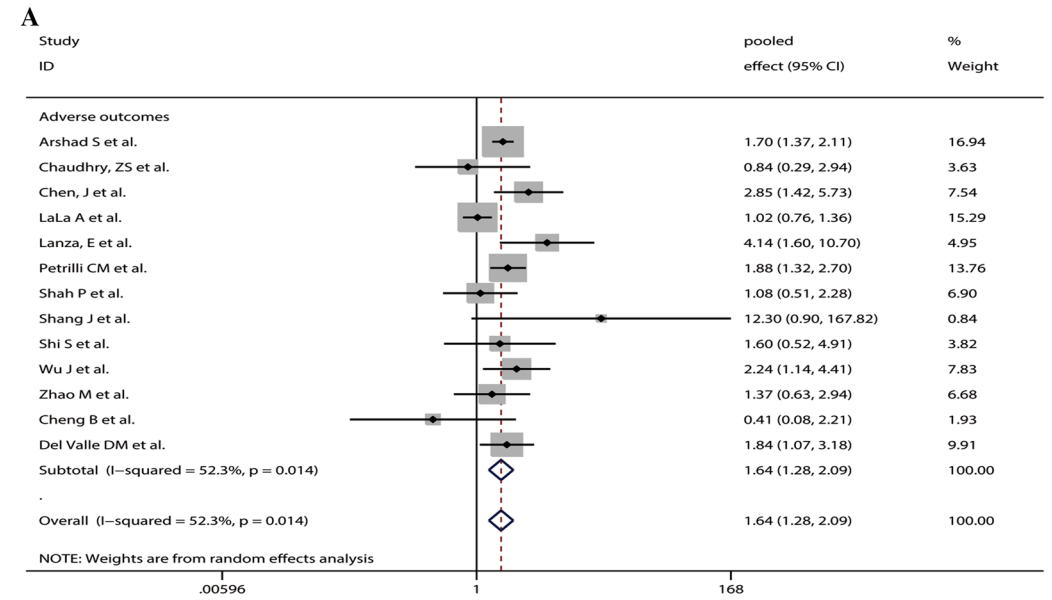
Table 1 Characteristics of the included studies

Author	Country	Cases (*n*)	Age (years)	Male (%)	Study design	CKD (%)	Adjusted effect estimates (95% CI)	Confounders	NOS score
Arshad et al. (PMID: 32623082)	USA	2541	64 (53–76)	1243 (48.9)	R	1099 (43.3)	HR 1.699 (1.370–2.108)	HCQ alone, AZM alone, HCQ + AZM, age, gender, race, BMI, lung comorbidity, immunodeficiency comorbidity, CVD, HTN, asthma, DM, percent O_2 saturation, admitted to ICU, ventilator, given steroid, given tocilizumab	6
Chaudhry et al. (PMID: 32654332)	USA	135	NA	73 (54.1)	R	88 (65.2)	OR 0.84 (0.29–2.94)	Age, diabetes, HFH COVID-19 severity score, transplant status	7
Chen et al. (PMID: 32634830)	China	3309	62 (49–69)	1642 (49.6)	R	57 (1.7)	OR 2.85 (1.42–5.73)	Gender, age, comorbidities, days from onset to clinics, days from onset to admission	6
Cheng et al. (PMID: 32622952)	China	456	54.97 ± 18.59	211 (46.27)	R	19 (4.16)	OR 0.415 (0.078–2.206)	Age, gender, comorbidities, neutrophil count, lymphocyte count, NLR, CRP, procalcitonin	5
Del Valle et al. (PMID: 32511562)	USA	1268	63 (53–72)	787 (60.1)	P	167 (13.2)	HR 1.84 (1.07–3.18)	Cytokines, demographics, comorbidities, laboratory measurements	5
LaLa et al. (PMID: 32517963)	USA	2736	48.9 ± 16.3	1630 (59.6)	R	273 (10.0)	OR 1.02 (0.76–1.36)	Troponin strata, gender, age, race, CAD, diabetes, heart failure, HTN, atrial fibrillation, BMI, CURB-65 score, ACE-I or ARB use, statin use	7
Lanza et al. (PMID: 32591888)	Italy	222	66.4 (53.8–75.8)	334 (55)	R	10 (4.5)	OR 4.14 (1.6–10.7)	Compromised lung volume, age, sex, smoke habit, CRP, heart disease, lung disease, cancer, diabetes, CURB-65[a]1, CURB-65[a]2, urea at admission, BMI	6
Petrilli et al.	Italy	1603	58.0 ± 20.9	758 (47.3)	R	69 (6)	OR 1.88 (1.32–2.7)	Age, cancer, CAD, diabetes, gender, heart failure, hyperlipidemia, HTN, BMI, pulmonary disease, race, tobacco use, CRP, creatinine, ferritin, lymphocyte count, procalcitonin, oxygen saturation on presentation, temperature	7

Table 1 (continued)

Author	Country	Cases (*n*)	Age (years)	Male (%)	Study design	CKD (%)	Adjusted effect estimates (95% CI)	Confounders	NOS score
Shah et al. (PMID: 32620056)	USA	552	63 (50–72)	218(58.2)	R	78 (14.9)	OR 1.08 (0.51–2.28)	Age, BMI, gender, race, comorbidities, tobacco smoking	5
Shang et al. (PMID: 32653423)	China	584	NA	277 (47.4)	R	8 (1.4)	HR 12.301 (0.902–167.823)	Age, sex, HTN, CVD, diabetes, chronic respiratory diseases, chronic liver diseases, acute kidney injury, acute liver injury, respiratory failure, acute cardiac injury	8
Shi et al. (PMID: 32391877)	China	671	63 (50–72)	322 (48.0)	R	28 (4.2)	HR 1.6 (0.52–4.91)	Male, age, HTN, diabetes, coronary heart disease, chronic heart failure, cerebrovascular diseases, procalcitonin, CRP, CK-MB, MYO, cTnl, NT-proBNP	8
Wu et al. (PMID: 32503812)	China	865	61 (50–69)	825 (48.8)	P	33 (2.0)	HR 2.24 (1.14–4.41)	Glu level, gender, age, diabetes, HTN, smoking history, insulin treatment, systemic glucocorticoids, COPD, cancer, admission white cell counts, admission lymphocyte counts, admission d-dimer, admission AST, admission ALT, admission creatinine	7
Zhao et al. (PMID: 32499448)	China	1000	61 (46–70)	466 (46.6)	R	24 (2.4)	HR 1.365 (0.634–2.942)	Age	8

All values are *n* (%), mean ± SD (standard deviation) or median (interquartile range, IQR); *NA* not available, *P* prospective, *R* retrospective, *HR* hazard ratio, *OR* odds ratio, *CK-MB* creatinine kinase-myocardial band, *MYO* myoglobin, *cTnl* cardiac troponin I, *NT-proBNP* N-terminal pro-B-type natriuretic peptide, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *CVD* cardiovascular diseases, *COPD* chronic obstructive pulmonary diseases, *CAD* coronary artery disease, *CRP* C-reactive protein, *Glu* glucose, *BMI* body mass index, *HCQ* hydroxychloroquine, *AZM* azithromycin, *ICU* intensive care unit, *HFH* Henry Ford Hospital, *NLR* neutrophil count/lymphocyte count ratio, *ACE* angiotensin-converting enzyme, *ARB* angiotensin II receptor blocker, *NOS* Newcastle–Ottawa scale, *CKD* chronic kidney disease, *HTN* hypertension


A
Study
ID
pooled
effect (95% CI)
%
Weight
Adverse outcomes
Arshad S et al. 1.70 (1.37, 2.11) 16.94
Chaudhry, ZS et al. 0.84 (0.29, 2.94) 3.63
Chen, J et al. 2.85 (1.42, 5.73) 7.54
LaLa A et al. 1.02 (0.76, 1.36) 15.29
Lanza, E et al. 4.14 (1.60, 10.70) 4.95
Petrilli CM et al. 1.88 (1.32, 2.70) 13.76
Shah P et al. 1.08 (0.51, 2.28) 6.90
Shang J et al. 12.30 (0.90, 167.82) 0.84
Shi S et al. 1.60 (0.52, 4.91) 3.82
Wu J et al. 2.24 (1.14, 4.41) 7.83
Zhao M et al. 1.37 (0.63, 2.94) 6.68
Cheng B et al. 0.41 (0.08, 2.21) 1.93
Del Valle DM et al. 1.84 (1.07, 3.18) 9.91
Subtotal (I–squared = 52.3%, p = 0.014) 1.64 (1.28, 2.09) 100.00
Overall (I–squared = 52.3%, p = 0.014) 1.64 (1.28, 2.09) 100.00
NOTE: Weights are from random effects analysis
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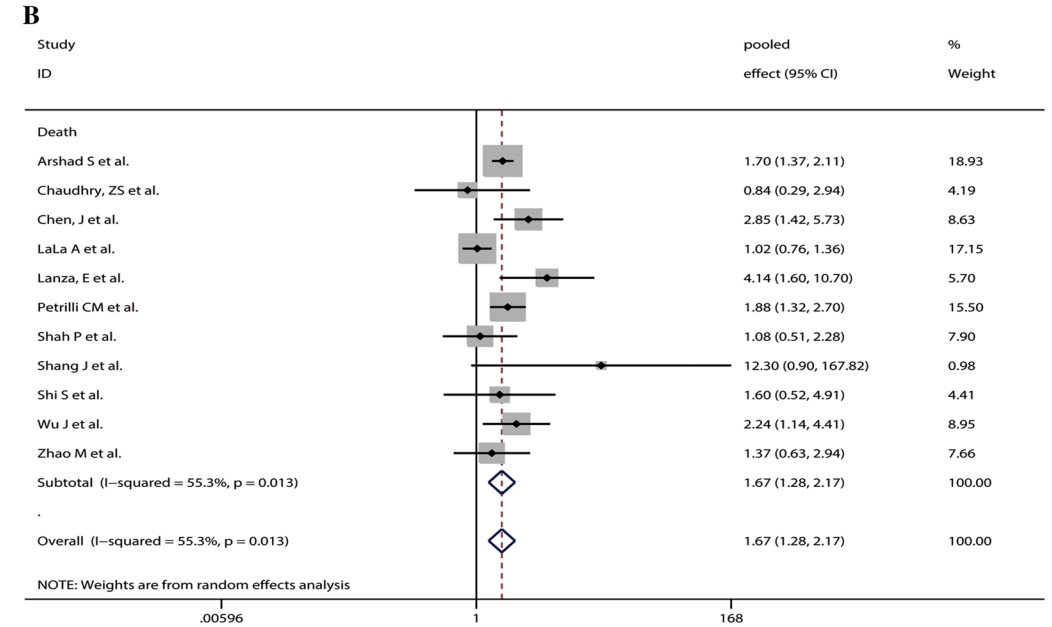
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Study
ID
pooled
effect (95% CI)
%
Weight
Death
Arshad S et al. 1.70 (1.37, 2.11) 18.93
Chaudhry, ZS et al. 0.84 (0.29, 2.94) 4.19
Chen, J et al. 2.85 (1.42, 5.73) 8.63
LaLa A et al. 1.02 (0.76, 1.36) 17.15
Lanza, E et al. 4.14 (1.60, 10.70) 5.70
Petrilli CM et al. 1.88 (1.32, 2.70) 15.50
Shah P et al. 1.08 (0.51, 2.28) 7.90
Shang J et al. 12.30 (0.90, 167.82) 0.98
Shi S et al. 1.60 (0.52, 4.91) 4.41
Wu J et al. 2.24 (1.14, 4.41) 8.95
Zhao M et al. 1.37 (0.63, 2.94) 7.66
Subtotal (I–squared = 55.3%, p = 0.013) 1.67 (1.28, 2.17) 100.00
Overall (I–squared = 55.3%, p = 0.013) 1.67 (1.28, 2.17) 100.00
NOTE: Weights are from random effects analysis
.00596
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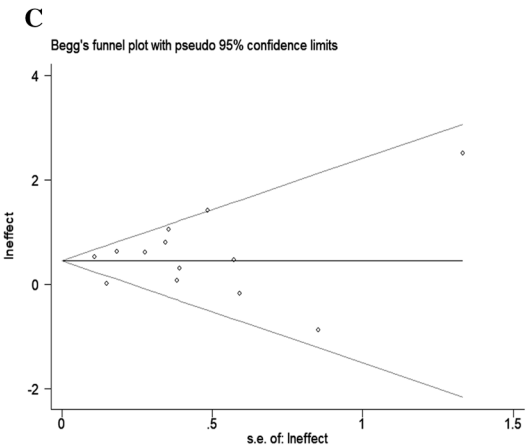
168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Begg's funnel plot with pseudo 95% confidence limits
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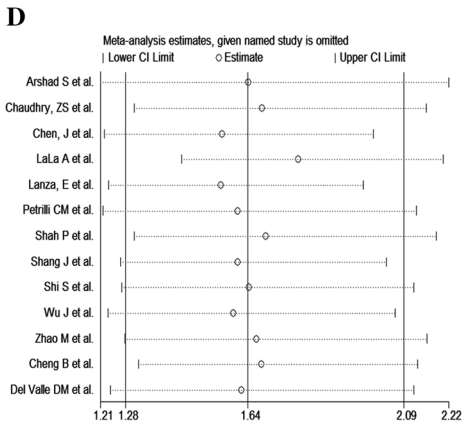
D
Meta-analysis estimates, given named study is omitted
Lower CI Limit
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Arshad S et al.
Chaudhry, ZS et al.
Chen, J et al.
LaLa A et al.
Lanza, E et al.
Petrilli CM et al.
Shah P et al.
Shang J et al.
Shi S et al.
Wu J et al.
Zhao M et al.
Cheng B et al.
Del Valle DM et al.
1.21
1.28
1.64
2.09
2.22

◂**Fig. 1** The pooled effects and 95% confidence interval (CI) of the relationship between chronic kidney disease (CKD) and adverse outcomes in patients with coronavirus disease 2019 (COVID-19) (**a**); The pooled effects and 95% CI of the relationship between CKD and death in patients with COVID-19 (**b**); Publication bias was assessed by Begg's funnel plot (**c**); Sensitivity analysis of the relationship between CKD and adverse outcomes in patients with COVID-19 (**d**)

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Compliance with ethical standards

Conflict of interest All the authors declare that there is no potential conflict of interest.

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