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LETTER TO THE EDITOR

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Acute kidney injury is associated with the mortality of coronavirus disease 2019

To the Editor,

We read with great interest the recent article "Analysis of 92 deceased patients with COVID-19" by Yang et al published in the *Journal of Medical Virology*. The authors observed that 14 patients suffered from renal injury after the infection of SARS-CoV-2 in 92 deceased patients with coronavirus disease 2019 (COVID-19), although none of them had chronic renal insufficiency.[1] Studies have shown that the kidneys may be at high risk for viral invasion.[2] However, some studies are indicating that there might not be an association between acute kidney injury (AKI) and the risk of mortality in patients with COVID-19.[3,4] Thus, the association of AKI with the risk of mortality in patients with COVID-19 is still inconclusive. Moreover, the incidence of AKI has been reported to vary among different clinical centers.[5,6] To obtain a definite conclusion on the association between AKI and the risk of mortality in patients with COVID-19, a meta-analysis was performed, which may provide an evidence-based medicine proof for clinicians in the management of COVID-19 patients with AKI.

We selected relevant studies published until 26 April 2020, by searching PubMed, Web of Science, and China National Knowledge Infrastructure, using the searching terms: "coronavirus" or "COVID-19" or "SARS-CoV-2" or "2019-nCoV" and "laboratory" or "clinical" and "mortality" or "outcome". Articles reporting in patients with COVID-19 on AKI and creatinine for both non-survival and survival patients were included. The combined effects were estimated as odds ratio (OR) along with its 95% confidence interval (CI) for AKI. The weighted mean difference (WMD) and 95% CI were calculated for the combined effects of creatinine. Subgroup analysis of the creatinine levels of the patients was performed according to the severity of COVID-19 graded by the Guidance for Corona Virus Disease 2019 (edition 7) of the China National Health Commission,[7] which were divided into severe and non-severe patients, critical and non-critical patients, and survival and non-survival patients. Heterogeneity was assessed with the I^2 test. The potential sources of heterogeneity were investigated by meta-regression, subgroup analysis, and sensitivity analysis. The sample size, median, and interquartile range (IQR) were used to estimate the mean and standard deviation when the articles reported data with median and IQR.[8] All analyses were performed using the Stata 11.2 (StataCorp, College Station, TX), and statistical significance was set as $P < .05$.

The AKI definition and comorbidity characteristics of patients in the included studies are shown in Table S1. The basic characteristics of AKI are shown in Table S2. There were 11 studies with a total of 7437 patients including 573 (34.0%) patients with AKI and 532 (9.3%) without AKI in non-survivors (Table S3). This meta-analysis showed that AKI was associated with a higher risk of mortality in COVID-19 patients (OR = 15.93, 95% CI: 7.69-32.98, $P < .001$; $I^2 = 78.1\%$, $P < .001$) (Figure 1A). None of these factors (such as sample size, AKI definition, and location) could explain the significant heterogeneity by meta-regression and subgroup analysis (Table S4). In addition, sensitivity analysis indicated that the combined OR did not change significantly when a single study was removed one by one, indicating that our results were reliable and robust (Figure 1B). No publication bias was found (Egger's test $P = .266$; Begg's test $P = .436$).

The level of creatinine elevation is related to the severity of AKI[9] and the serum creatinine level is used as a criterion for AKI.[10,11] Our results showed that the level of creatinine was significantly higher in non-survivors compared to survivors (WMD = 19.69, 95% CI: 13.90-25.47, $P < .001$; $I^2 = 47.9\%$, $P = .073$). To further elucidate the relationship between creatinine levels and COVID-19 progression, subgroup analysis was performed. The results demonstrated the higher the creatinine value, the more severe the patients' condition (critical WMD = 7.27, 95% CI: 2.79-11.75, $P = .001$; $I^2 = 17.8\%$, $P = .294$; severe WMD = 6.57, 95% CI: 1.43-11.72, $P = .012$; $I^2 = 38.9\%$, $P = .109$) (Figure 1C, Table S5). This observation supported the notion that AKI was associated with the risk of mortality in patients with COVID-19 in the other aspect to a certain extent.

In summary, our findings demonstrated that AKI was associated with the mortality in patients with COVID-19, which can be a predictor for poor outcomes in patients with COVID-19. Hence, clinicians should increase their awareness of AKI in patients with COVID-19. However, there are also some limitations to our meta-analysis. First, the meta-analysis result of AKI with mortality in patients with COVID-19 had high heterogeneity. Second, the included studies for this present meta-analysis failed to describe comorbidity characteristics of individual patients, and it was hard to adjust for confounding factors at present. Further analyses including more studies are needed to verify our findings.

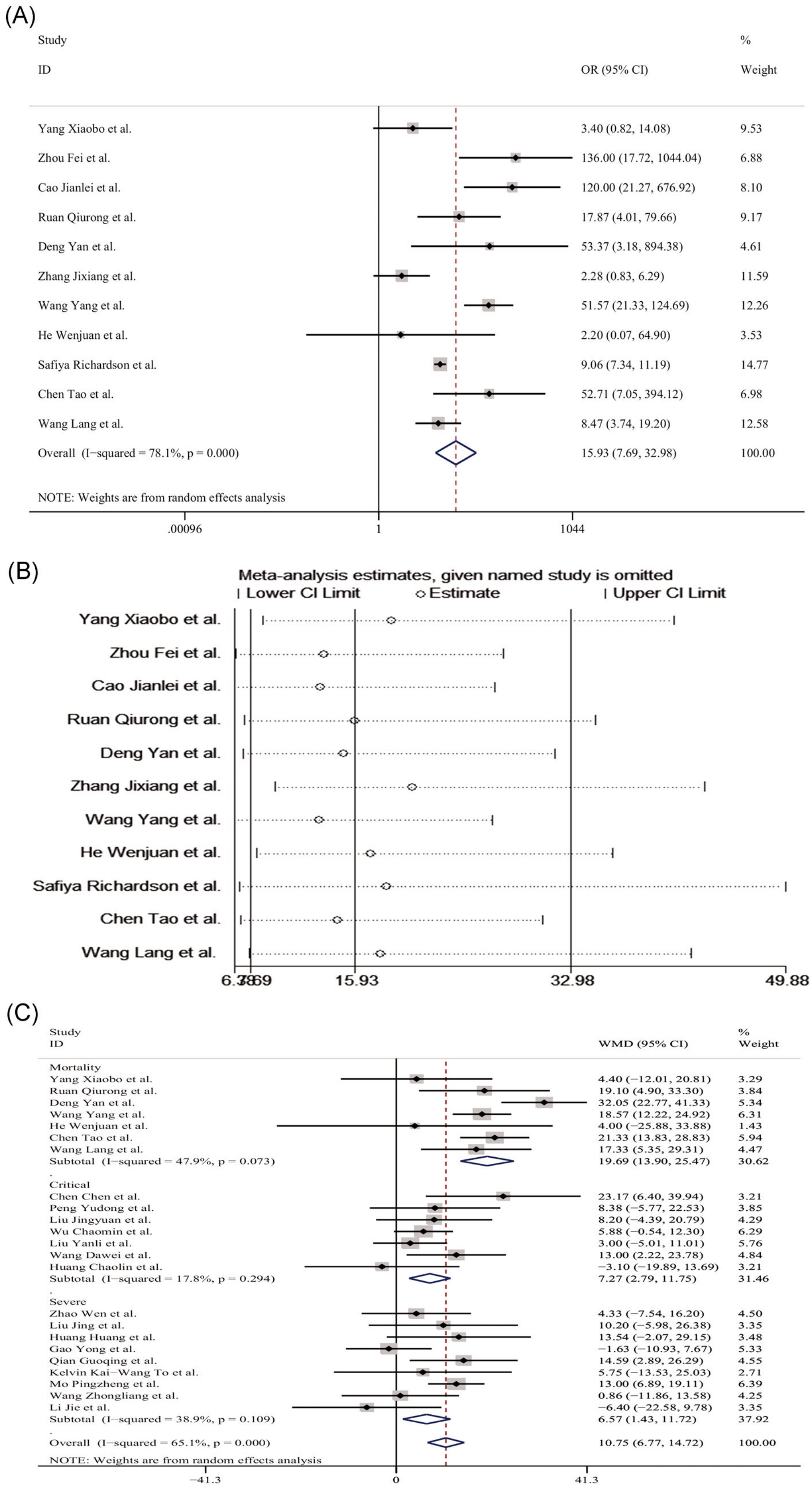

FIGURE 1 Odds ratio (OR) along with its 95% confidence interval (CI) for acute kidney injury (A), sensitivity analysis for acute kidney injury (B), weighted mean difference (WMD), and 95% CI for creatinine by subgroup analysis, and (C) creatinine levels between coronavirus disease 2019 patients with non-survival and survival by random-effects model

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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SUPPORTING INFORMATION

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