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Postoperative acute kidney injury and early and long-term mortality in acute aortic dissection patients

A meta-analysis

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Abstract

Objective: To evaluate the impact of postoperative acute kidney injury (AKI) on early and long-term mortality in patients with acute aortic dissection by conducting a meta-analysis.

Methods: An extensive literature search was performed in PubMed and Embase databases until February 15, 2020. Observational studies that reported the associations between postoperative AKI and early (in-hospital and within 30 days) or long-term mortality in patients with acute aortic dissection were included.

Results: Seven studies comprising 1525 acute aortic dissection patients were identified. A random effect meta-analysis showed that postoperative AKI was significantly associated with higher risk of long-term mortality (risk ratio [RR] 2.32; 95% confidence interval [CI] 1.50–3.59). Subgroup analysis revealed that the pooled RR of long-term mortality was 1.42 (95% CI 0.90–2.22) for stage 1 AKI, 1.72 (95% CI 0.95–3.12) for stage 2 AKI, and 4.46 (95% CI 2.72–7.32) for stage 3 AKI, respectively. Furthermore, postoperative stage 3 AKI was associated with an increased risk of early mortality (RR 11.3; 95% CI 4.2–30.5).

Conclusions: This meta-analysis provided clinical evidence that postoperative stage 3 AKI is associated with higher risk of early and long-term mortality, even after adjusting important confounding factors. However, the current findings should be interpreted with caution due to the retrospective nature and limited number of studies analyzed.

Abbreviations: AAD = acute aortic dissection, AKI = acute kidney injury, CI = confidence interval, NOS = Newcastle Ottawa Scale, RR = risk ratio.

Keywords: acute aortic dissection, acute kidney injury, all-cause mortality, meta-analysis

1. Introduction

Acute aortic dissection (AAD) is characterized by blood entering the medial layer of the wall with the creation of a false lumen. According to the anatomic location, AAD is conventionally classified as Stanford type A and type B aortic dissection. Type A is defined as a dissection proximal to the brachiocephalic artery and type B is defined as a dissection distal to the left subclavian artery (restricted in descending aorta). Surgery is an option for both Stanford type A and complicated type B aortic dissection. Despite the advance of surgery and endovascular technique, mortality from AAD remains substantial.[1] Data analysis of the Nationwide German Diagnosis-Related Group Statistics from 2006 to 2014 showed that in-hospital mortality of 14911 cases type A and 5622 cases type B aortic dissections was 19.5% and 9.3%, respectively.[2] Therefore, early risk stratification is of great need for this complex population.

Acute kidney injury (AKI) is one of the main complications after aortic surgical procedures.[3] Postoperative AKI after open surgery or endovascular aortic repair is associated with adverse clinical outcomes. A number of observational studies[4–12] that reported the associations between postoperative AKI and early or late mortality have yielded conflicting results in patients with AAD. These conflicting findings may be partially explained by the severity of AKI or different definitions of renal impairment.

A well-designed meta-analysis has evaluated the association of postoperative AKI with 30-day postoperative death in patients with type A aortic dissection.[13] No previous meta-analysis has been systematically assessed the value of postoperative AKI in prediction of long-term survival outcome in patients with AAD. This meta-analysis aimed to evaluate the impact of postoperative AKI on early and long-term mortality in patients with AAD.

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WM and RL have contributed equally to this work.

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The authors have no conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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2. Materials and methods

2.1. Data sources and searches

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[14] Ethical approval or informed consent was not necessary due to this article does not involve the individual patient data or animals performed by any of the authors. An extensive literature search was performed in PubMed and Embase databases until February 15, 2020 using the "aortic dissection" in combination of "acute kidney injury" OR "acute renal failure" AND "death" OR "mortality." To identify any possible missing studies, we manually reviewed the references of the related articles.

2.2. Study selection

Inclusion criteria were as follow: original observational study enrolling patients with AAD; AKI after open surgery or minimally invasive endovascular repair as exposure; early or long-term mortality as outcomes; and reporting multivariate-adjusted hazard ratio (HR) or risk ratio (RR) and 95% confidence intervals (CI) of survival outcome associated with AKI. Early mortality was defined as in-hospital death or death occurred within 30 days. Exclusion criteria included: preoperative, perioperative, or uncertain time of AKI; and reporting unadjusted risk estimate.

2.3. Data extraction and quality assessment

A standardized data extraction form was applied to abstract the following information by 2 independent authors: first author's surname, year of publication, study design, origin of study, sample sizes, type of patients, sex, age at baseline, definition of AKI, outcome measures, number of events, multivariable-adjusted risk estimate, length of follow-up, and adjusted confounders. The Newcastle-Ottawa Scale (NOS) was adopted to assess the methodological quality of the included studies by 2 independent authors.[15] Study with a score of 7 to 9 points was considered as high methodological quality. Discrepancies during assessment were settled by census or discussed a third author.

2.4. Statistical analysis

STATA 12.0 (STATA Corp LP, College Station, TX) was used for the data analysis.

Given the likelihood of significant between-study heterogeneity, we selected a random-effect model when pooling each outcome. Statistically significant heterogeneity was defined by the

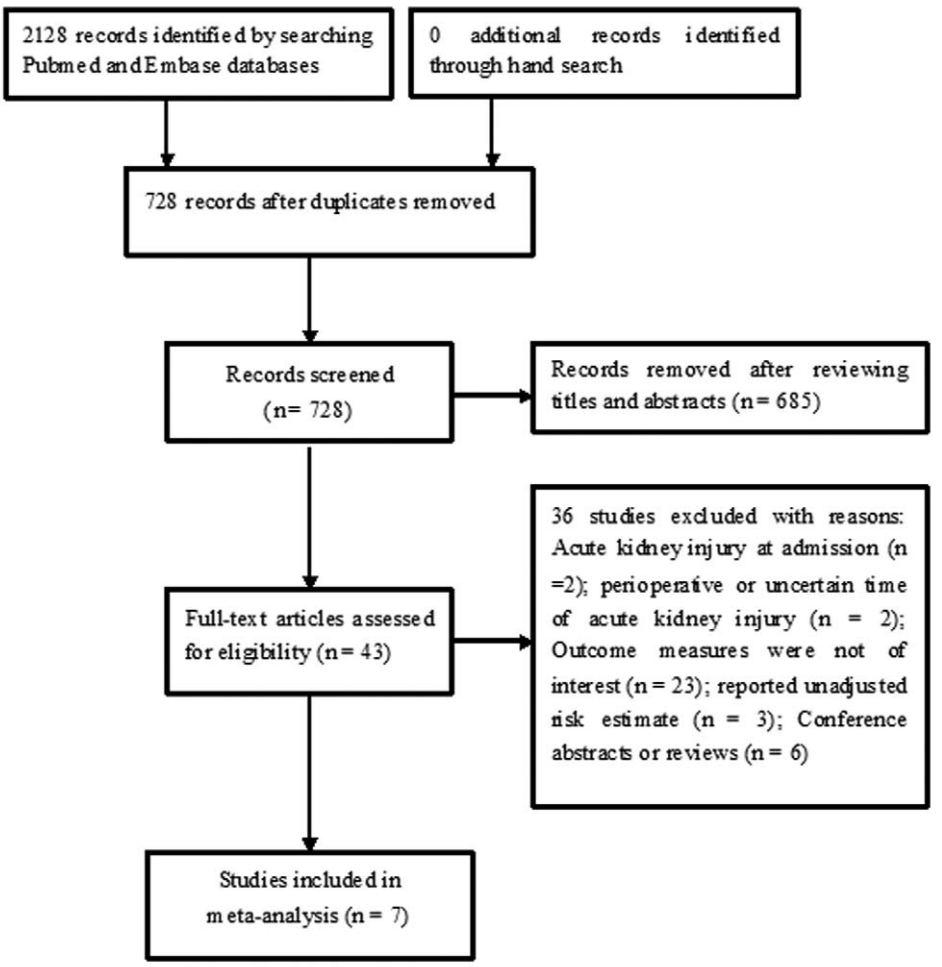

Figure 1. Flow chart showing the study selection process.

I^2 statistic >50% and/or P-value <0.10 of Cochrane Q test. Leave out one study sensitivity analysis was performed to observe the robustness of the pooling outcomes. Subgroup analyses were conducted according to the degree of AKI. Begg test[16] and Egger test[17] were scheduled to check the likelihood of publication bias.

3. Results

3.1. Search results and study characteristics

A detailed process of study selection is summarized in Fig. 1. Briefly, we identified a total of 728 potentially relevant records after removal of duplicate. After screening the titles and abstracts, 685 articles were removed and left 43 articles for full-text evaluation. Thirty-six articles were further removed after adopting the predefined inclusion and exclusion criteria. Finally, 7 studies[4–7,10–12] were included in our meta-analysis.

Table 1 describes the main data of the eligible studies. All studies adopted the retrospective designs and published between 2012 and 2019. The sample sizes ranged from 37 to 375, with a total of 1525 AAD patients. Three studies[6,7,10] enrolled the type A aortic dissection patients, 1 study[5] enrolled the complicated type B aortic dissection patients, and other studies[4,11,12] included all types of patients. The median/mean age of the patients ranged from 50.3 to 69 years. The follow-up duration was up to 4.83 years. According to NOS criteria, the methodological quality of the included studies was moderate to high (6 to 8 points).

3.2. Early mortality

Three studies[7,11,12] reported the association between stage 3 AKI and early mortality. As shown in Fig. 2, no significant heterogeneity (I^2=0%, P=.647) was found across studies. Meta-analysis indicated that AKI stage 3 was associated with an increased risk of early mortality (RR 11.3; 95% CI 4.19–30.48) compared with those without AKI. Leave out one study sensitivity analysis indicated that the pooled RR ranged from 9.02 to 15.9 and low 95% CI ranged from 2.84 to 4.47.

3.3. Long-term mortality

Three studies[4,6,10] reported the association of all stage AKI with long-term mortality and 1 study[5] addressed the stage 3 AKI associated long-term mortality. As shown in Fig. 3, there was statistically significant heterogeneity (I^2=50.6%, P=.059) between studies. Meta-analysis indicated that overall postoperative AKI was associated with higher risk of long-term mortality (RR 2.32; 95% CI 1.50–3.59) compared with those without AKI. Leave out 1 study sensitivity analysis indicated that the pooled RR ranged from 2.11 to 2.78 and low 95% CI ranged from 1.31 to 1.43. Subgroup analysis (Fig. 4) according to the degree of AKI revealed that the pooled RR of long-term mortality was 1.42 (95% CI 0.90–2.22) for stage 1 AKI, 1.72 (95% CI 0.95–3.12) for stage 2 AKI, and 4.46 (95% CI 2.72–7.32) for stage 3 AKI, respectively.

3.4. Publication bias

We did not perform the Begg test and Egger test to check the likelihood of publication bias due to less than the recommended arbitrary minimum number of 10 studies.[18]

Table 1

Main characteristic of the included studies.

Author/year	Region	Study design	Patients (% men)	Age, y	AKI definition	Outcomes OR/HR (95% CI)	Follow-up, y	Adjustment for covariates	NOS score
Tsai 2012[4]	Taiwan	Retrospective	AAD 268 (72.8)	53±14	RIFLE criteria	Long-term death: 50 2.55 (1.04–6.26)	1.0	Age, cardiogenic shock, preoperative ventilator, bypass time, sepsis	7
Ruan 2014[5]	China	Retrospective	Complicated B type AAD 62 (71.0)	56.3±10.3	Not reported	Long-term death: 9 3.98 (1.26–12.1) stage 3	4.4	Multivariate adjusted analysis	6
Ko 2015[6]	Japan	Retrospective	A type AAD 375 (52)	66.4±13.3	KDIGO criteria	Long-term death: 33 1.61 (0.55–4.68) stage 1 1.67 (0.40–6.98) stage 2 6.83 (2.52–18.5) stage 3	2.58	Age, sex, BMI, smoker, hypertension, DM, CHD, CHF, AF, malperfusion, LVEF, CRP, extracorporeal circulation time, coronary dissection, neurologic dysfunction, sepsis	7
Sansone 2015[7]	Italy	Retrospective	A type AAD 37 (83.8)	65±11	RIFLE criteria	30-d death: 10 6.6 (1.35–32.4) stage 3	—	Multivariate adjusted analysis	6
Sasabuchi 2016[10]	Japan	Retrospective	A type AAD 4 03 (51.4)	65 (55–72)	KDIGO criteria	Long-term death: 89 1.38 (0.84–2.26) stage 1 1.73 (0.90–3.33) stage 2 3.84 (1.98–7.45) stage 3	4.83	Age, bicuspid aortic valve, preoperative hemoglobin, perioperative stroke	8
Lingzhi 2016[11]	China	Retrospective	AAD 151 (70.2)	50.3±13.5	KDIGO criteria	In-hospital death: 19 21.3 (3.07–147.9) stage 3	—	Triiodothyronine 3, thyroid-stimulating hormone, d-dimer, pericardial effusion, AD type	6
Baldawi 2019[12]	USA	Retrospective	Isolated AAD 229 (78.6)	69±11	Increase in sCr >2 mg/dL preoperative value	30-d death: 15 12.8 (2.38–68.9) stage 3	—	Multivariate adjusted analysis	7

AD = acute aortic dissection, AKI = acute kidney injury, CHD = coronary heart disease, CHF = chronic heart failure, CI = confidence intervals, CRP = C-reactive protein, DM = diabetes mellitus, HR = hazard ratio, KDIGO = kidney disease improving global outcomes, LVEF = left ventricular ejection fraction, NOS = Newcastle-Ottawa Scale, OR = odds ratio, RIFLE = risk, injury, failure, loss, end stage, sCr = serum creatinine.

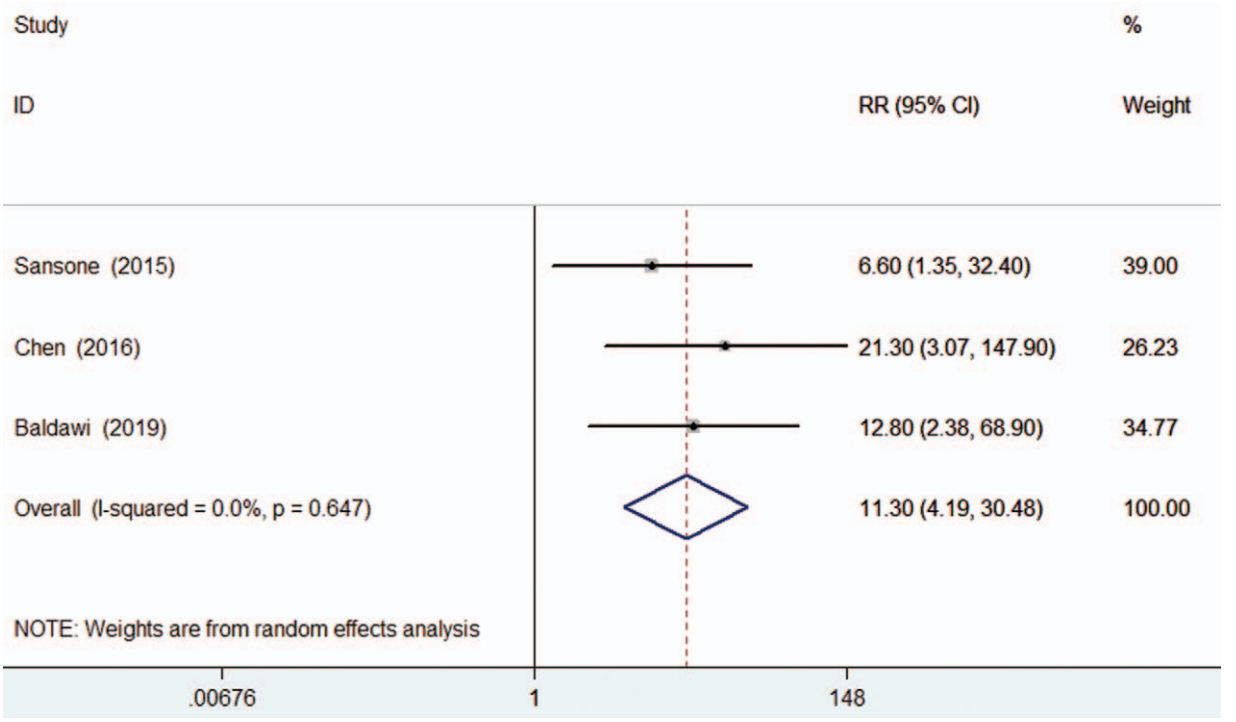

Figure 2. Forest plots showing RR and 95% CI of early mortality associated postoperative stage 3 AKI. AKI = acute kidney injury; CI = confidence interval; RR = risk ratio.

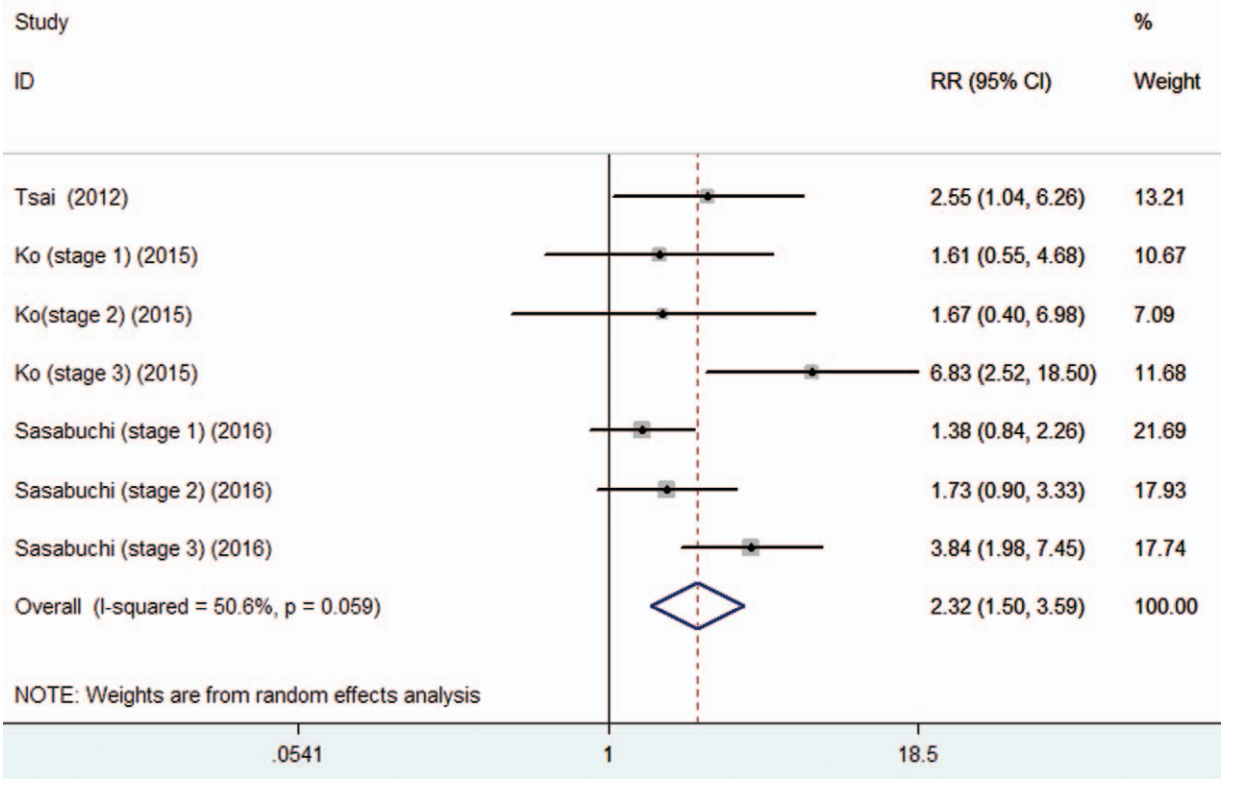

Figure 3. Forest plots showing RR and 95% CI of long-term mortality associated with postoperative AKI. AKI = acute kidney injury; CI = confidence interval; RR = risk ratio.

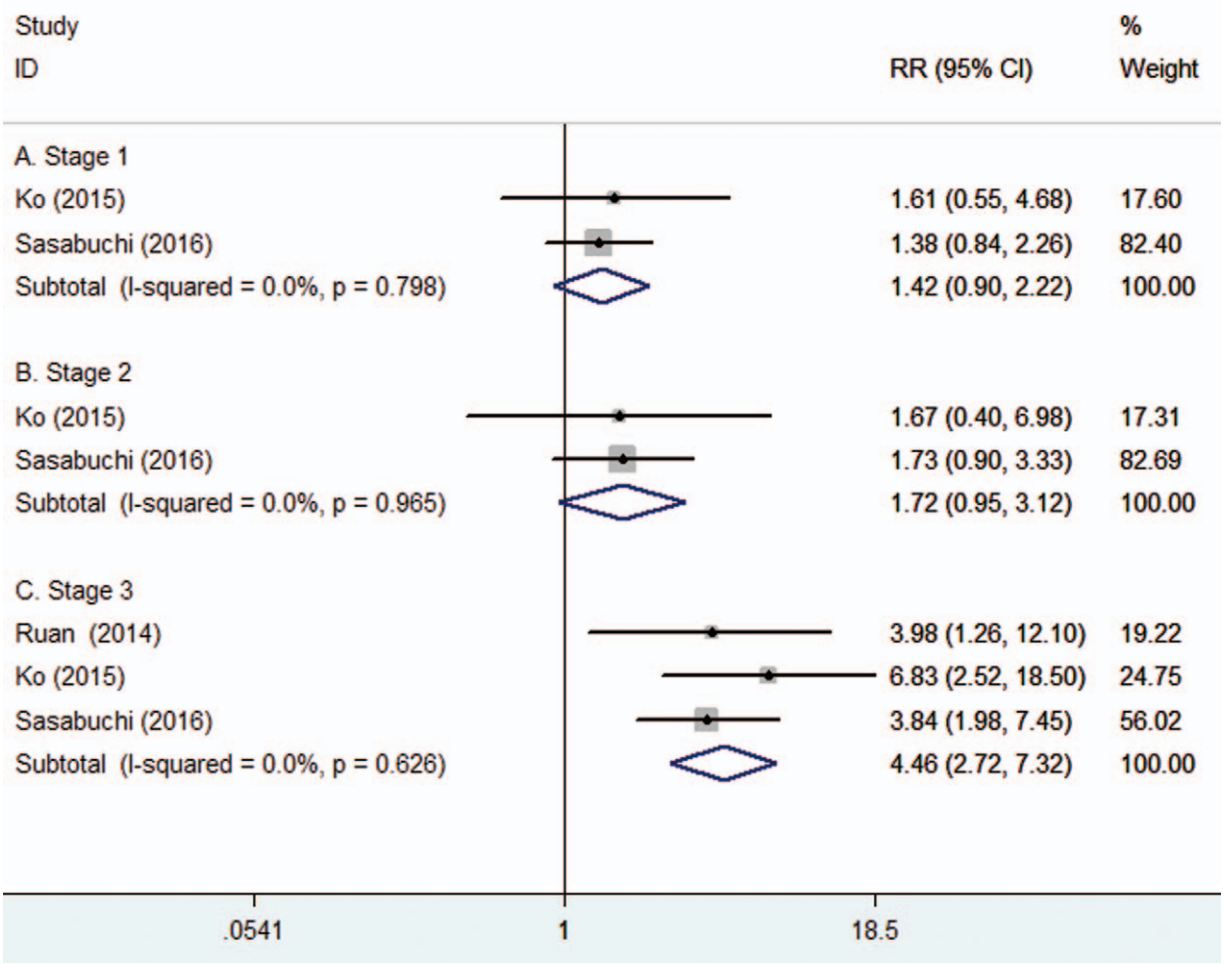

Figure 4. Forest plots showing RR and 95% CI of long-term mortality associated with different degree of postoperative AKI. AKI = acute kidney injury; CI = confidence interval; RR = risk ratio.

4. Discussion

The main findings of this meta-analysis are that: overall postoperative AKI was associated with an increased risk of long-term mortality; presence of postoperative stage 3 AKI markedly increased both early and long-term all-cause mortality in patients with AAD. AAD patients with stage 3 AKI exhibited an 11-fold and 4.46-fold higher risk of early and long-term mortality, respectively. Based on these findings, measurement of renal function after surgery may improve risk stratification in AAD patients.

An early meta-analysis[13] demonstrated that postoperative AKI was associated with 249% increase in 30-day postoperative mortality. However, this result was not established on the multivariate analysis, which may have overestimated the risk estimate. In addition, the long-term mortality outcome was not addressed in this meta-analysis. By contrast, our meta-analysis only selected the studies that reported the multivariate-adjusted results and further extended to the long-term mortality outcome.

The kidney disease improving global outcomes (KDIGO) and risk, injury, failure, loss, end stage (RIFLE) are 2 widely accepted criteria to define AKI in the analyzed studies. In our meta-analysis, overall postoperative AKI was associated with an increased risk of long-term mortality. However, results of subgroup analysis by the degree of AKI indicated lack of significant association between postoperative stage 2/3 AKI and long-term mortality. Therefore, prognostic significance of postoperative AKI appeared to be dominated by the stage 3 AKI. Similarly, the impact of postoperative AKI on early mortality was also dominated by the stage 3 AKI. No statistically significant association of stages 1 and 2 AKI with mortality may be partially explained by the low incidence of death, which may reduce the statistical power. Future studies addressing the prognostic value of postoperative AKI by different stage are strongly required.

Survival after AAD can be affected by preexisting renal impairment. Preoperative stage 3 AKI[19] and perioperative acute renal failure[20] was an independent predictor of in-hospital mortality in type A aortic dissection patients. Apart from AKI, renal malperfusion also affected operative mortality following acute type A aortic dissection repair.[21] Occurrence of AKI in AAD has important clinical implications. Impaired renal function at baseline has been identified as a risk factor for AKI.[22] AAD patients should dynamically monitor renal function and receive an intensive treatment. In addition, hypertension, renal malper-

fusion, long bypass duration, and sepsis all contributed to the development of AKI.[4,6]

Several limitations should be considered in the current meta-analysis. First, all the included studies were retrospective designs and potential selection bias cannot be excluded. Second, some patients may already have AKI on admission, which could lead to overestimate the number of AKI. Third, statistically significant heterogeneity was found in pooling long-term mortality. Different types of AAD, severity of AKI, and duration of follow-up may contribute to the significant heterogeneity. Finally, results from subgroup analysis should be interpreted with caution due to the limited number of study analyzed.

5. Conclusions

Postoperative stage 3 AKI significantly increased both early and long-term mortality in patients with AAD, even after adjusting some important confounding factors. This meta-analysis highlights the urgent need for development of strategies to prevent and decrease postoperative AKI in AAD patients.

Author contributions

Conceptualization: Nashunbayaer Zha.
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Investigation: Lihua E.
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Supervision: Nashunbayaer Zha.
Validation: Wenbin Meng, Rui Li, Lihua E, Nashunbayaer Zha.
Visualization: Wenbin Meng, Rui Li, Lihua E, Nashunbayaer Zha.
Writing – original draft: Rui Li.
Writing – review & editing: Wenbin Meng.

References

[1] Sampson UK, Norman PE, Fowkes FG, et al. Global and regional burden of aortic dissection and aneurysms: mortality trends in 21 world regions, 1990 to 2010. Glob Heart 2014;9:171.e10–80.e10.
[2] Reutersberg B, Salvermoser M, Trenner M, et al. Hospital incidence and in-hospital mortality of surgically and interventionally treated aortic dissections: secondary data analysis of the Nationwide German Diagnosis-Related Group Statistics from 2006 to 2014. J Am Heart Assoc 2019;8:e011402doi: 10.1161/JAHA.118.011402.
[3] Tsai HS, Chen YC, Chu PH. The influence of acute kidney injury on acute cardiovascular disease. Acta Cardiol Sin 2014;30:93–7.
[4] Tsai HS, Tsai FC, Chen YC, et al. Impact of acute kidney injury on one-year survival after surgery for aortic dissection. Ann Thorac Surg 2012;94:1407–12.
[5] Ruan ZB, Zhu L, Yin YG, et al. Risk factors of early and late mortality after thoracic endovascular aortic repair for complicated stanford B acute aortic dissection. J Card Surg 2014;29:501–6.
[6] Ko T, Higashitani M, Sato A, et al. Impact of acute kidney injury on early to long-term outcomes in patients who underwent surgery for type a acute aortic dissection. Am J Cardiol 2015;116:463–8.
[7] Sansone F, Morgante A, Ceresa F, et al. Prognostic implications of acute renal failure after surgery for Type A acute aortic dissection. Aorta (Stamford) 2015;3:91–7.
[8] Zhu JC, Chen SL, Jin GZ, et al. Acute renal injury after thoracic endovascular aortic repair of Stanford type B aortic dissection: incidence, risk factors, and prognosis. J Formos Med Assoc 2014;113:612–9.
[9] Tolenaar JL, Froehlich W, Jonker FH, et al. Predicting in-hospital mortality in acute type B aortic dissection: evidence from International Registry of Acute Aortic Dissection. Circulation 2014;130(11 suppl 1): S45–50.
[10] Sasabuchi Y, Kimura N, Shiotsuka J, et al. Long-term survival in patients with acute kidney injury after acute Type A aortic dissection repair. Ann Thorac Surg 2016;102:2003–9.
[11] Lingzhi C, Hao Z, Weijian H, et al. Outcome predictors in patients presenting with acute aortic dissection. J Cardiothorac Vasc Anesth Oct 2016;30:1272–7.
[12] Baldawi M, Krafcik B, Al-Jubouri M, et al. Factors associated with increased mortality after isolated abdominal aortic dissection repair. Ann Vasc Surg 2019;60:171–7.
[13] Wang J, Yu W, Zhai G, et al. Independent risk factors for postoperative AKI and the impact of the AKI on 30-day postoperative outcomes in patients with type A acute aortic dissection: an updated meta-analysis and meta-regression. J Thorac Dis 2018;10:2590–8.
[14] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100.
[15] Wells G, Shea B, O'Connell D, et al. The Newcastle–Ottawa Scale (NOS) for Assessing the Quality if Nonrandomized Studies in Meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (assessed June 20, 2020).
[16] Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50:1088–101.
[17] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.
[18] Lau J, Ioannidis JP, Terrin N, et al. The case of the misleading funnel plot. BMJ 2006;333:597–600.
[19] Chien TM, Wen H, Huang JW, et al. Significance of preoperative acute kidney injury in patients with acute type A aortic dissection. J Formos Med Assoc 2019;118:815–20.
[20] Apaydin AZ, Buket S, Posacioglu H, et al. Perioperative risk factors for mortality in patients with acute type A aortic dissection. Ann Thorac Surg 2002;74:2034–9. discussion 2039.
[21] Qian SC, Ma WG, Pan XD, et al. Renal malperfusion affects operative mortality rather than late death following acute type A aortic dissection repair. Asian J Surg 2020;43:213–9.
[22] Waikar SS, Liu KD, Chertow GM. Diagnosis, epidemiology and outcomes of acute kidney injury. Clin J Am Soc Nephrol 2008;3:844–61.