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Folate and Reduced Mortality in Adults with Infection-Associated Acute Kidney Injury: a Single-Centre Retrospective Cohort Study

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Introduction

Infection-associated acute kidney injury (AKI) carries high mortality. Preclinical studies suggest folate mitigates oxidative stress and improves kidney recovery, but clinical evidence in AKI is lacking. In patients with infection-associated AKI we aimed to evaluate the association between folate administration and mortality.

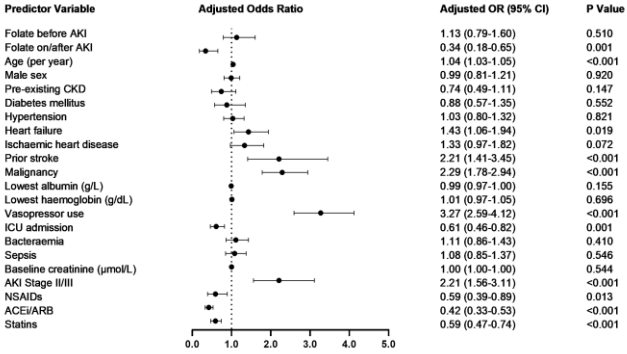
Results

Compared with non-users (n = 2,272), folate started on or after AKI onset was associated with higher 30-day recovery (77.0% vs 65.7%; OR 1.75, 95% CI 1.09-2.81, P = 0.023) and lower 30-day mortality (12.0% vs 25.0%; OR 0.41, 95% CI 0.22-0.75, P = 0.002). These associations persisted after multivariable adjustment (recovery: adjusted OR 1.77, 95% CI 1.08-2.88; mortality: adjusted OR 0.34, 95% CI 0.18-0.65) and in a propensity-score-matched analysis. Folate started before AKI did not differ significantly from non-users. Serum folate was measured in 690 patients (26.7%); pretreatment deficiency was more common in the on-or-after group.

Table. Unadjusted Outcomes of 2,585 Patients with Infection-Associated Acute Kidney Injury, Overall and by Timing of Folate Exposure.

Outcome	Folate users (n=313)		Non-users (n=2,272)	OR – On/After vs non-users	P value
	Before AKI (n=213)	On or After AKI (n=100)			
AKI recovery					
12-hour	7 (3.3%)	9 (9.0%)	113 (5.0%)	1.89 (0.93-3.85)	0.098
24-hour	40 (18.8%)	22 (22.0%)	434 (19.1%)	1.19 (0.74-1.94)	0.440
48-hour	73 (34.3%)	44 (44.0%)	861 (37.9%)	1.29 (0.86-1.93)	0.247
7-day	120 (56.3%)	69 (69.0%)	1370 (60.3%)	1.47 (0.95-2.26)	0.094
30-day	130 (61.0%)	77 (77.0%)	1492 (65.7%)	1.75 (1.09-2.81)	**0.023**
Progression to CKD*	8/169 (4.7%)	5/76 (6.6%)	65/1983 (3.3%)	2.08 (0.81-5.32)	0.182
Cardiovascular events					
Heart failure	9 (4.2%)	3 (3.0%)	68 (3.0%)	1.00 (0.31-3.24)	1.000
IHD	7 (3.3%)	5 (5.0%)	89 (3.9%)	1.29 (0.51-3.25)	0.595
Stroke	2 (0.9%)	1 (1.0%)	24 (1.1%)	0.95 (0.13-7.06)	1.000
Mortality					
In-hospital	44 (20.7%)	14 (14.0%)	476 (21.0%)	0.61 (0.35-1.09)	0.101
30-day	54 (25.4%)	12 (12.0%)	569 (25.0%)	0.41 (0.22-0.75)	**0.002**
90-day	83 (39.0%)	25 (25.0%)	771 (33.9%)	0.65 (0.41-1.03)	0.066
180-day	95 (44.6%)	30 (30.0%)	886 (39.0%)	0.67 (0.43-1.04)	0.075
365-day	110 (51.6%)	41 (41.0%)	1033 (45.5%)	0.83 (0.55-1.25)	0.412

Figure. Multivariable-adjusted odds ratios for 30-day mortality in patients with infection-associated acute kidney injury (full cohort, n=2,585).



Methods

This single-centre retrospective cohort study included 2,585 adults with presumed infection (blood culture obtained plus ≥4 qualifying antimicrobial days) and KDIGO creatinine-defined AKI admitted to Queen Mary Hospital, Hong Kong, in 2023. Folate during the index admission was classified by first-dose timing relative to AKI onset: before AKI (n=213), on or after AKI (n=100), or no folate (n=2,272). Most treated patients (247/313; 79%) received oral folic acid 5 mg daily (median 18 days; IQR 7-61). The primary outcome was 30-day all-cause mortality; secondary outcomes were longer term mortality, AKI recovery, and cardiovascular events. Analyses used chi-square tests and multivariable logistic regression adjusted for age, sex, comorbidities, severity markers, AKI stage, and concurrent medications, with propensity-score matching as a sensitivity analysis.

Conclusions

Folate started on or after AKI onset was associated with lower 30-day mortality and higher 30-day recovery; folate started before AKI was not. These observational findings may be influenced by residual confounding and time-related bias and require confirmation in randomised controlled trials.

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