Association of thiamine use with outcomes in septic patients with alcohol use disorder: an analysis of the MIMIC-III database

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Supplementary Material

Supplementary Tables and Figures cited in main text

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Table S1: Diagnostic criteria for alcohol use disorder

	ICD-9	Description
AUD diagnosis	2910	Alcohol withdrawal delirium
	2911	Alcohol-induced persisting amnestic disorder
	2912	Alcohol-induced persisting dementia
	2913	Alcohol-induced psychotic disorder with hallucinations
	2915	Alcohol-induced psychotic disorder with delusions
	29181	Alcohol withdrawal
	29182	Alcohol induced sleep disorders
	29189	Other alcohol-induced mental disorders
	2919	Unspecified alcohol-induced mental disorders
	30300	Acute alcoholic intoxication in alcoholism, unspecified
	30301	Acute alcoholic intoxication in alcoholism, continuous
	30302	Acute alcoholic intoxication in alcoholism, episodic
	30303	Acute alcoholic intoxication in alcoholism, in remission
	30390	Other and unspecified alcohol dependence, unspecified
	30391	Other and unspecified alcohol dependence, continuous
	30392	Other and unspecified alcohol dependence, episodic
	30393	Other and unspecified alcohol dependence, in remission
	30500	Alcohol abuse, unspecified
	30501	Alcohol abuse, continuous
	30502	Alcohol abuse, episodic
	30503	Alcohol abuse, in remission

AUD was confirmed according to the criteria of International Classification of Diseases, 9th edition [ICD-9].

Abbreviations: AUD, alcohol use disorder; ICD-9, International Classification of Diseases, 9th edition.

Table S2: Thiamine administration in this study

Variable	Thiamine, n=233
The first time of intravenous thiamine received in ICU	
Within 24 hours, %	175/223(75.1)
Within 48 hours, %	201/233(86.3)
Within 72 hours, %	215/233(92.3)
Daily dose of thiamine use in ICU, mg	100(100-100)
<100 mg, %	24/233(10.3)
=100 mg, %	179/233(76.8)
101-200 mg, %	18/233(7.7)
＞200 mg, %	12/233(5.2)
Cumulative dose of thiamine use in ICU, mg	200(100-345)
<100 mg, %	10(4.3)
=100 mg, %	83(35.6)
100-200 mg, %	44(18.9)
200-345 mg, %	38(16.3)
≥345 mg, %	58(24.9)
Days of thiamine use in ICU, day	1(1-3)
1 day, %	125/233(53.6)
2 day, %	41/233(17.6)
3 day, %	33/233(14.2)
4 day, %	16/233 (6.9)
≥5 day, %	18/233(7.7)
Cumulative duration of thiamine use in ICU, hours	18(7-63)

Abbreviations: ICU, intensive care unit.

Table S3: Vasopressors use for septic patients with AUD during ICU stay

Duration of vasopressors use during ICU stay, hours	All, n=944	Non-thiamine, n=711	Thiamine, n=233	P value
Norepinephrine	27(9-60) (n=323)	26(9-54) (n=247)	30(7-86) (n=76)	0.404
Phenylephrine	16(6-39) (n=184)	15(6-38) (n=133)	20(4-40) (n=51)	0.909
Vasopressin	27(14-62) (n=89)	23(11-51) (n=67)	33(21-96) (n=22)	0.165
Dopamine	6(2-30) (n=53)	6(2-30) (n=45)	11(2-73) (n=8)	0.728
Epinephrine	11(2-30) (n=10)	12(3-53) (n=8)	-/(n=2)	0.296
Milrinone	119(47-147) (n=6)	110(43-151) (n=5)	-/(n=1)	0.770
Dobutamine	1(0.3-18) (n=5)	-/(n=1)	1.2(0.4-27) (n=4)	0.480

Abbreviations: AUD, alcohol use disorder; ICU, intensive care unit.

Table S4: Changes in variables among patients during ICU stay

Variables change	All, n=944	Non-thiamine, n=711	Thiamine, n=233	P value
△Lactate, mmol/L	-1.2(-2.9 to -0.1)	-1.3(-3.3 to 0)	-0.9(-2.7 to -0.1)	0.987
△Heart rate, bpm	-6(-19 to 5)	-5(-18 to 5)	-7(-19 to 5)	0.621
△Respiratory rate	0(-4 to 4)	0(-4 to 4)	1(-4 to 5)	0.232
△Systolic blood pressure, mmHg	5(-5 to 18)	5(-5 to 18)	7(-6 to 18)	0.912
△Diastolic blood pressure, mmHg	0(-8 to 7)	0(-7 to 7)	0(-10 to 7)	0.696
△Serum creatine, mg/dL	-0.2(-0.6 to 0)	-0.3(-0.6 to 0)	-0.2(-0.5 to 0)	0.341
△Blood urea nitrogen, mg/dL	-2(-12 to 6)	-2(-12 to 7)	-2(-10 to 5)	0.992
△White blood cell count, $\times 10^3$/uL	-2.4(-6.9 to 1.0)	-2.3(-0.4 to 0.8)	-2.6(-7.2 to 1.2)	0.726
△Serum magnesium, mg/dL	-0.1(-0.4 to 0.1)	-0.1(-0.4 to 0.1)	-0.1(-0.4 to 0.2)	0.287

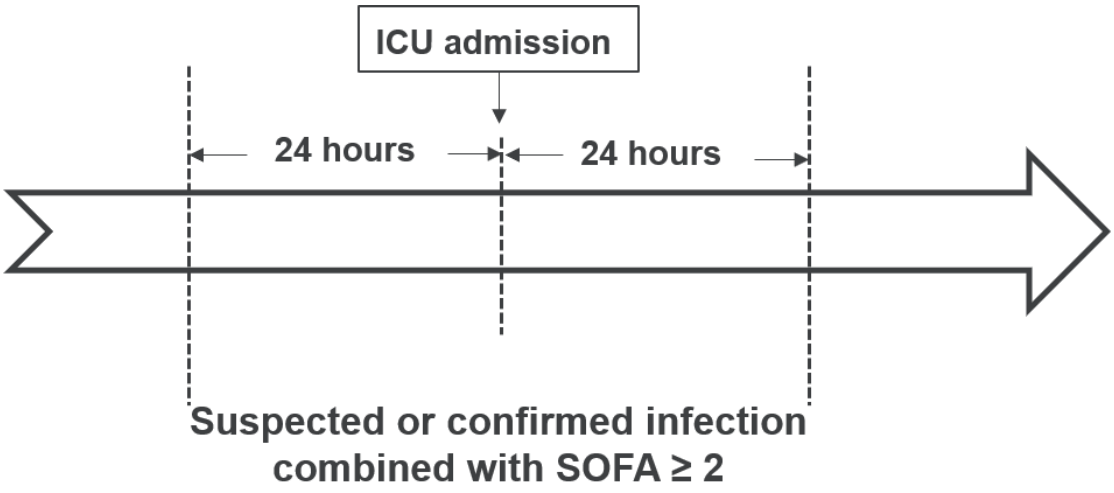
△ represented the change between Day 7 and Day 1

Table S5: Daily trends in GCS score.

	Intervention group	Control group
Day 1 GCS, medium (IQR)	14(13-15)	15(13-15)
Day 2 GCS, medium (IQR)	15(13-15)	15(14-15)
Day 3 GCS, medium (IQR)	15(13-15)	15(14-15)
Day 4 GCS, medium (IQR)	15(13-15)	15(14-15)
Day 5 GCS, medium (IQR)	15(12-15)	15(14-15)
Day 6 GCS, medium (IQR)	14.5(13-15)	15(14-15)
Day 7 GCS, medium (IQR)	15(13.5-15)	15(14-15)

Abbreviations: GCS, Glasgow Coma Scale.

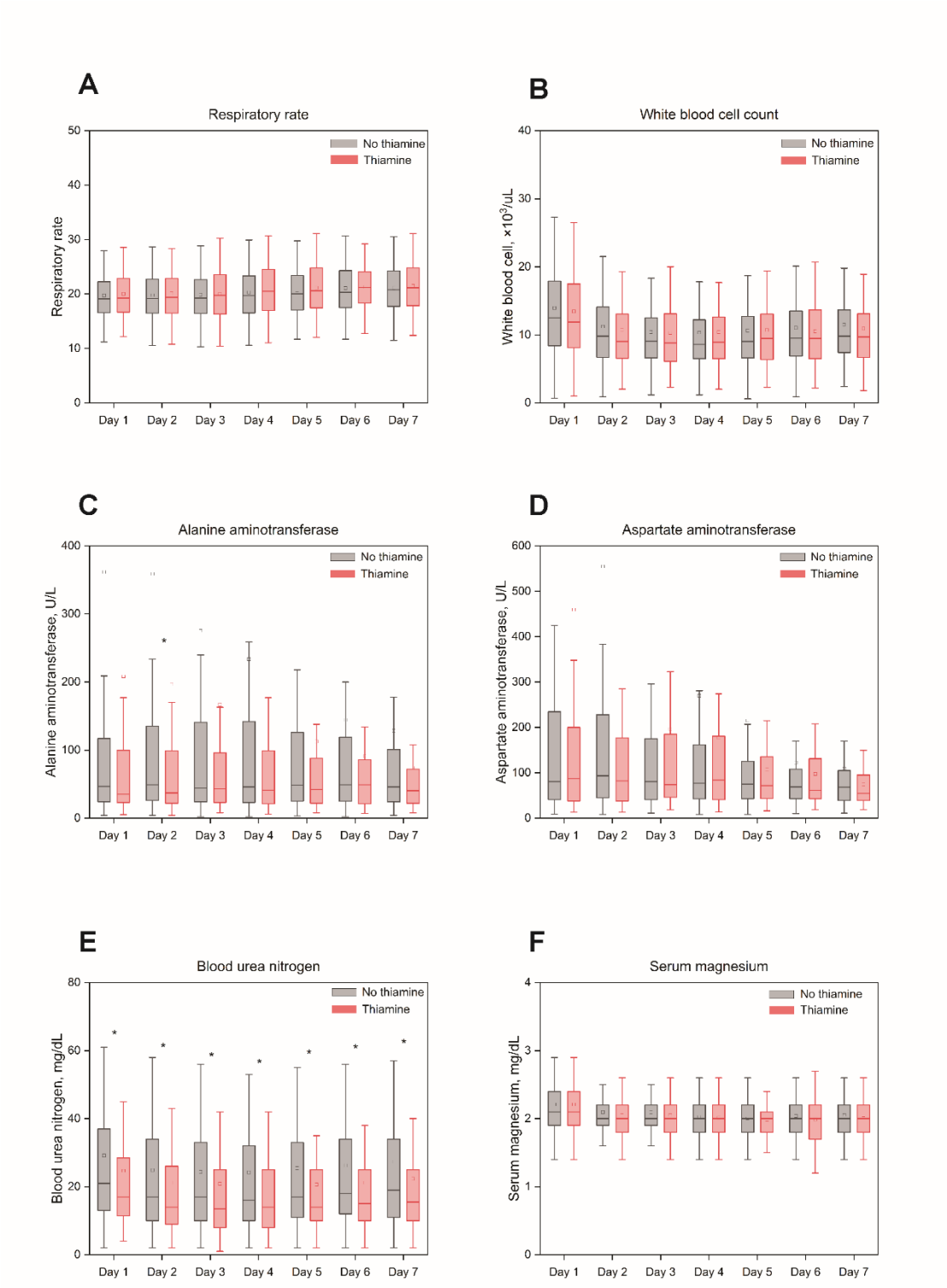
Figure S1: Diagnostic criteria for sepsis



Patients with suspected or documented infection combined SOFA score no less than 2 points were diagnosed sepsis (Diagnosis time between 24 hours before ICU admission and 24 hours after ICU admission).

Abbreviations: SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit.

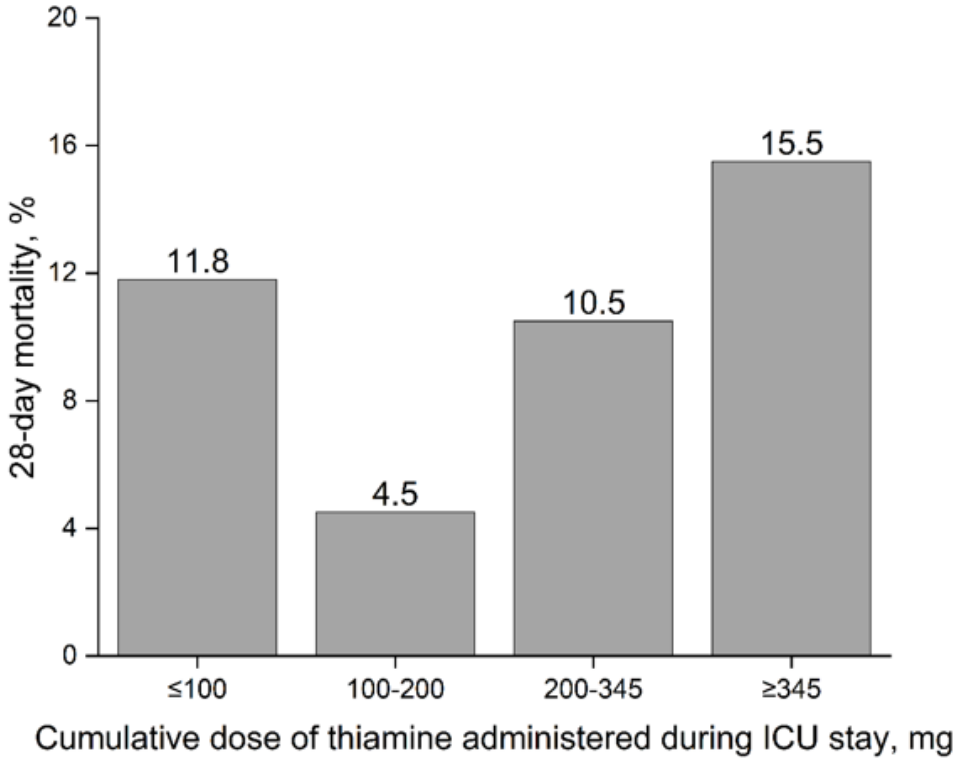
Figure S2: The dynamic changes up to day 7 for prespecified variables



* represented p <0.05

The square icon in each group represented mean value.

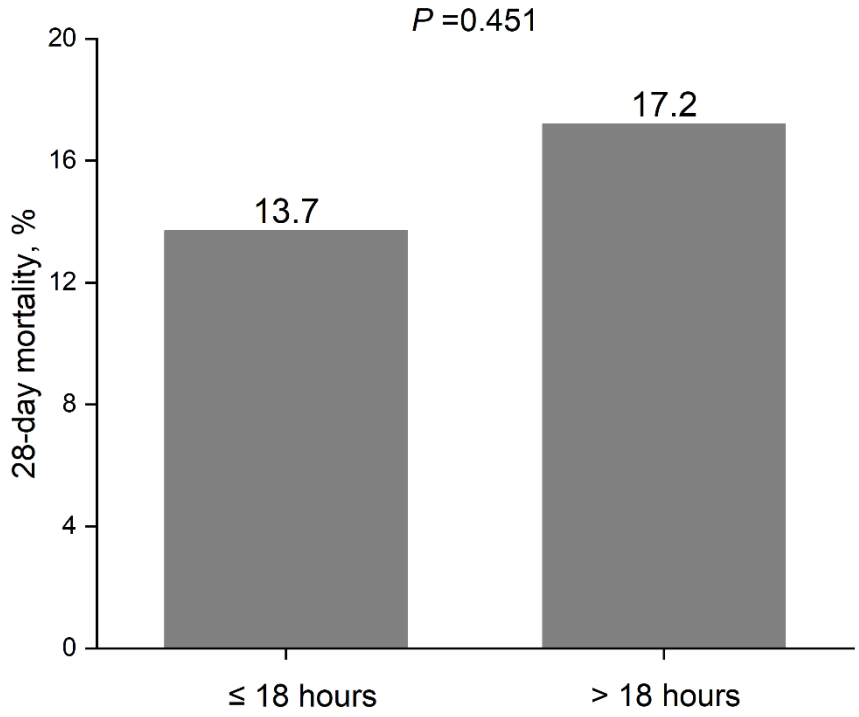
Figure S3: Association between the cumulative dose of thiamine administered during ICU stay and 28-day mortality among septic patients with AUD



Dose	No. of patients	28-day mortality	P value
≤100 mg	93	11/93(11.8%)	
100-200 mg	44	2/44(4.5%)	
200-345 mg	38	4/38(10.5%)	0.375
≥345 mg	58	9/58(15.5%)	
Total	233	26/233(11.2%)	

Abbreviations: AUD, alcohol use disorder; ICU, intensive care unit.

Figure S4: Association between the duration of thiamine use during ICU stay and 28-day mortality among septic patients with AUD



Abbreviations: AUD, alcohol use disorder; ICU, intensive care unit.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	8-10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	10
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	10-11
Outcome data	15*	Report numbers of outcome events or summary measures over time	10-11

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: As the checklist was provided upon initial submission, the page number reported may be changed due to copyediting and may not be referable in the published version.