

Supplementary Information

ICU day-1 arterial bicarbonate and 30-day mortality in adults with acute pancreatitis discharge diagnoses

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Supplementary Table S1 | Missingness of variables used in the principal and alternative models.

Variable	Missing, n	Missing, %
Arterial bicarbonate	17	1.33
Age	0	0.0
Sex	0	0.0
Weight	1	0.08
Charlson score	0	0.0
ICU day-1 SOFA	2	0.16
Creatinine	17	1.33
Blood urea nitrogen	19	1.48
Glucose	16	1.25
Total calcium	30	2.34
White blood cell count	20	1.56
Platelet count	19	1.48

Percentages use the 1,280-patient cohort before exclusion for missing ICU day-1 arterial bicarbonate as the denominator.

Supplementary Table S2 | Sensitivity analyses using alternative ICU day-1 bicarbonate summaries.

Bicarbonate summary	n	Events	OR (95% CI)	P value
First	1260	201	1.73 (1.20–2.49)	0.003
Min	1260	201	1.88 (1.25-2.81)	0.002
Avg	1260	201	2.07 (1.40-3.04)	<0.001
Median	1260	201	2.05 (1.40-2.99)	<0.001
Last	1260	201	1.80 (1.25-2.58)	0.001
Max	1260	201	1.49 (1.05-2.11)	0.027

Each summary was dichotomized at 22 mmol/L. Models adjusted for age, sex, weight, Charlson score, and ICU day-1 SOFA.

Supplementary Table S3A | Unadjusted exploratory renal outcomes.

Outcome	Bicarbonate ≥ 22	Bicarbonate < 22	P value
CRRT during index hospitalization	38/642 (5.9%)	127/621 (20.5%)	< 0.001
RRT during index hospitalization	58/642 (9.0%)	156/621 (25.1%)	< 0.001
AKI during ICU stay	407/642 (63.4%)	477/621 (76.8%)	< 0.001

AKI, acute kidney injury; CRRT, continuous renal replacement therapy; RRT, renal replacement therapy.

Supplementary Table S3B | Exploratory association between bicarbonate <22 mmol/L and CRRT during the index hospitalization.

Outcome	Model	n	Events	OR (95% CI)	P value
CRRT during index hospitalization	Model 1	1263	165	4.09 (2.79-5.98)	<0.001
CRRT during index hospitalization	Model 2	1262	165	3.98 (2.69-5.88)	<0.001
CRRT during index hospitalization	Model 3	1260	165	1.90 (1.18-3.05)	0.008

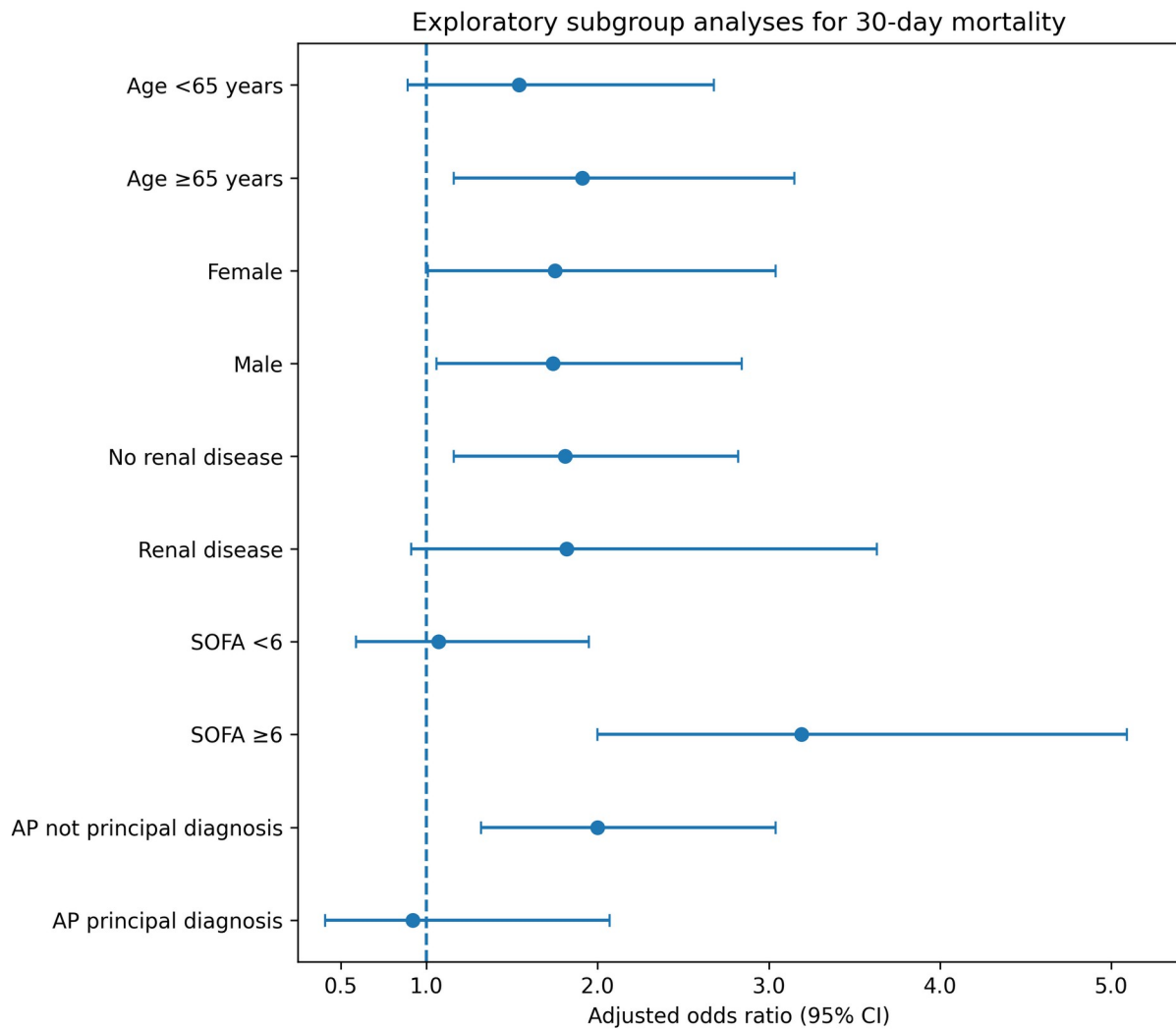
Model 1 was unadjusted. Model 2 adjusted for age, sex, weight, and Charlson score. Model 3 additionally adjusted for ICU day-1 SOFA. The temporal order between bicarbonate measurement and CRRT initiation was unavailable for all patients; this analysis is hypothesis-generating.

Supplementary Table S4 | Exploratory subgroup analyses for 30-day mortality.

Subgroup	n	Events	OR (95% CI)	P value	P for interaction
Age <65 years	764	83	1.54 (0.89-2.68)	0.122	0.689
Age ≥65 years	496	118	1.91 (1.16-3.15)	0.011	
Female	536	88	1.75 (1.01-3.04)	0.047	0.847
Male	724	113	1.74 (1.06-2.84)	0.027	
No renal disease	1010	138	1.81 (1.16-2.82)	0.009	0.841
Renal disease	250	63	1.82 (0.91-3.63)	0.089	
SOFA <6	701	56	1.07 (0.59-1.95)	0.819	0.004
SOFA ≥6	559	145	3.19 (2.00-5.09)	<0.001	
AP not principal diagnosis	832	160	2.00 (1.32-3.04)	0.001	0.124
AP principal diagnosis	428	41	0.92 (0.41–2.07)	0.841	

Subgroup estimates used Model 3 except that the stratifying variable was omitted when appropriate. The SOFA subgroup analysis used Model 2. Interaction tests were not adjusted for multiplicity.

Supplementary Figure S1 | Exploratory subgroup analyses for 30-day mortality.



Points show adjusted odds ratios and horizontal bars show 95% confidence intervals. The dashed vertical line indicates an odds ratio of 1. Subgroup estimates used Model 3 except that the stratifying variable was omitted when appropriate; the SOFA subgroup analysis used Model 2. AP, acute pancreatitis; CI, confidence interval; SOFA, Sequential Organ Failure Assessment.

Supplementary Table S5 | Apparent model performance before and after adding arterial bicarbonate.

Model	C-statistic	Brier score	Likelihood-ratio P
Age, sex, weight, Charlson score, day-1 SOFA	0.815	0.1094	
Base model plus arterial bicarbonate	0.816	0.1085	0.032
Change after adding bicarbonate	0.001 (-0.004 to 0.006)	-0.0009	

The base model included age, sex, weight, Charlson score, and ICU day-1 SOFA. Arterial bicarbonate was entered as a continuous variable. Performance was evaluated in the development dataset and should be interpreted as exploratory. The confidence interval for the change in C-statistic was estimated using 500 bootstrap samples.

Supplementary Table S6 | Operational definitions and extraction windows.

Variable	Operational definition	Source	Time window
Acute pancreatitis cohort	ICD-9 577.0 or ICD-10 K85.x; age >18 years; first hospital admission and first ICU stay retained	MIMIC-IV diagnosis and ICU records	Index hospitalization
Primary exposure	First bicarbonate value from arterial blood gas analysis	MIMIC-IV arterial blood gas records	ICU admission -6 h to +24 h
Day-1 SOFA	Maximum dynamic SOFA score	Derived from MIMIC-IV ICU records	ICU admission 0 h to +24 h
Primary outcome	30-day all-cause mortality	MIMIC-IV mortality records	From ICU admission
Secondary mortality	90-day, in-hospital, and ICU mortality	MIMIC-IV mortality records	As defined
CRRT	Any CRRT during index hospitalization	MIMIC-IV treatment records	Entire index hospitalization
Early ventilation	Invasive ventilation hours >0	MIMIC-IV ventilation records	ICU admission 0 h to +24 h
Early vasopressor	Any selected vasopressor administered	MIMIC-IV medication records	ICU admission 0 h to +24 h
Comorbidity burden	Charlson comorbidity score	MIMIC-IV diagnosis records	Index hospitalization
Enzyme-supported AP phenotype	AP discharge code plus maximum blood amylase ≥ 300 U/L or lipase ≥ 180 U/L	MIMIC-IV laboratory records	Hospital admission to ICU admission +24 h

Diagnosis-derived variables were based on discharge coding and did not provide exact diagnosis onset times.

Supplementary Table S7 | Fixed-threshold enzyme-supported analyses for 30-day mortality.

Analysis	n	Events	Effect (95% CI)	P value	Adjustment
Fixed-threshold enzyme-supported phenotype: bicarbonate <22 vs ≥22 mmol/L	489	77	2.16 (1.13–4.15)	0.020	Model 3
Fixed-threshold enzyme-supported phenotype: per 5 mmol/L lower bicarbonate	489	77	1.22 (0.92–1.63)	0.170	Model 3
Lipase-supported phenotype: bicarbonate <22 vs ≥22 mmol/L	475	75	2.34 (1.20-4.57)	0.013	Model 3
Amylase-supported phenotype: bicarbonate <22 vs ≥22 mmol/L	167	27	2.38 (0.83-6.87)	0.108	Model 3
ICU-proximate first-enzyme phenotype: bicarbonate <22 vs ≥22 mmol/L	387	58	2.15 (0.94-4.93)	0.071	Model 3
Principal AP diagnosis plus enzyme support: bicarbonate <22 vs ≥22 mmol/L	205	20	2.31 (0.71-7.52)	0.163	Age, sex, and day-1 SOFA

The primary fixed-threshold enzyme-supported phenotype required an acute pancreatitis discharge code and a maximum blood amylase concentration ≥300 U/L or lipase concentration ≥180 U/L from hospital admission through 24 h after ICU admission. The ICU-proximate phenotype required the first qualifying enzyme value to occur from 6 h before to 24 h after ICU admission. Model 3 adjusted for age, sex, weight, Charlson score, and ICU day-1 SOFA. The principal-diagnosis-plus-enzyme analysis used a parsimonious model because only 20 deaths occurred. Assay-specific upper reference limits were unavailable; the fixed thresholds approximate three times commonly used upper reference limits. These analyses are supportive and do not constitute confirmation of all revised Atlanta criteria.