

Supplementary Material

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eTable 1. Participant Characteristics by Quartiles of Traditional Anion Gap in 11,957 participants of NHANES 1999-2004

Characteristic	Traditional Anion Gap (mEq/L)				P
	≤ 10.0	10.1 – 12.0	12.1 – 14.0	≥ 14.1	
Number	3346	3339	2864	2408	
Age (years)	46.4 (0.3)	46.3 (0.4)	46.3 (0.5)	45.5 (0.5)	0.18
Women (%)	51.3 (1.0)	51.6 (0.9)	50.1 (1.0)	49.7 (0.9)	0.18
Race/Ethnicity (%)					0.34
<i>Non-Hispanic White</i>	72.2 (2.1)	72.7 (0.2)	72.4 (2.3)	72.1 (2.7)	
<i>Mexican American</i>	6.7 (1.0)	7.8 (1.0)	7.4 (1.1)	7.0 (1.4)	
<i>Non-Hispanic Black</i>	11.7 (1.3)	10.7 (1.1)	9.1 (1.1)	8.5 (1.8)	
Body-mass index (kg/m²)					0.09
< 20	4.3 (0.3)	5.7 (0.6)	5.9 (0.6)	5.6 (0.7)	
20 – 25	30.6 (1.0)	29.2 (1.1)	29.7 (1.0)	26.4 (1.3)	
25 – 29	36.3 (0.9)	34.4 (1.2)	32.7 (1.1)	36.0 (1.2)	
30 – 35	17.5 (0.7)	19.0 (0.9)	19.1 (0.8)	18.7 (1.0)	
> 35	11.3 (0.8)	11.8 (0.9)	12.7 (1.0)	13.3 (0.9)	
Less than high-school diploma (%)	17.6 (1.2)	18.5 (0.9)	23.1 (1.0)	22.1 (1.2)	0.002
Activity Level (MET-min/wk, %)					0.004
0	14.1 (0.8)	15.7 (0.9)	18.8 (1.0)	18.6 (1.7)	
< 500	21.6 (0.9)	21.8 (0.9)	20.1 (1.0)	19.5 (0.8)	
500 – 2000	36.2 (1.0)	37.2 (0.7)	33.3 (1.1)	33.1 (1.4)	
> 2000	28.1 (1.1)	25.3 (1.2)	27.9 (1.3)	28.8 (1.7)	
Smoking (%)					0.12
<i>Never</i>	52.2 (0.9)	48.5 (0.9)	48.7 (1.6)	50.0 (2.5)	
<i>Former</i>	24.7 (1.0)	27.0 (0.9)	25.2 (1.1)	23.5 (1.6)	
<i>Current</i>	23.0 (1.1)	24.5 (1.0)	26.1 (1.4)	26.5 (1.3)	
Hypertension (%)	37.0 (1.2)	40.1 (1.3)	40.8 (1.3)	43.9 (1.7)	0.001
Diabetes mellitus (%)	5.7 (0.5)	7.6 (0.6)	7.5 (0.6)	8.1 (0.6)	0.006
Cardiovascular disease (%)	7.3 (0.6)	8.3 (0.7)	9.5 (0.7)	8.8 (0.7)	0.07
eGFR (mL/min/1.73m²)					0.55
15 – 59	5.6 (0.4)	6.0 (0.5)	6.8 (0.4)	7.1 (0.5)	
60 – 89	35.3 (1.2)	35.5 (1.4)	35.7 (1.4)	34.1 (1.1)	
90 – 119	49.4 (1.3)	48.2 (1.4)	48.1 (1.4)	49.2 (1.2)	

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≥ 120	9.7 (0.7)	10.3 (0.7)	9.4 (0.7)	9.5 (0.8)	
UACR > 30 mg/g (%)	7.2 (0.6)	9.4 (0.5)	10.0 (0.7)	11.1 (0.9)	0.001
Hemoglobin (g/dL)	14.33 (0.05)	14.47 (0.06)	14.61 (0.05)	14.79 (0.07)	<0.001
Serum bicarbonate (mEq/L)	25.4 (0.1)	24.4 (0.1)	23.6 (0.1)	22.6 (0.1)	<0.001
Serum albumin (g/dL)	4.24 (0.01)	4.33 (0.01)	4.39 (0.01)	4.47 (0.02)	<0.001
Serum calcium (mg/dL)	9.45 (0.02)	9.49 (0.02)	9.47 (0.02)	9.54 (0.03)	0.008
Serum phosphate (mg/dL)	3.64 (0.02)	3.70 (0.02)	3.65 (0.02)	3.64 (0.02)	0.68

Abbreviations: MET, metabolic equivalent; eGFR, estimated glomerular filtration rate; UACR, urinary albumin-creatinine ratio.

Data are expressed as mean (SE) or percent (SE).

eTable 2. Participant Characteristics by Quartiles of Albumin-Adjusted Anion Gap in 11,957 participants of NHANES 1999-2004

Characteristic	Albumin-Adjusted Anion Gap (mEq/L)				P
	≤ -0.50 9.55	$9.55-0.45$ 11.05	$11.05-10.06$ 12.95	> 10.06 12.95	
Number	3124	2716	3042	3075	
Age (years)	45.1 (0.3)	46.1 (0.4)	46.3 (0.4)	47.3 (0.6)	0.001
Women (%)	45.0 (1.0)	52.1 (1.1)	51.7 (1.0)	55.0 (0.9)	<0.001
Race/Ethnicity (%)					0.52
<i>Non-Hispanic White</i>	73.6 (1.9)	72.6 (2.0)	71.6 (2.3)	71.6 (2.6)	
<i>Mexican American</i>	7.2 (0.9)	7.7 (1.1)	7.5 (1.1)	6.7 (1.3)	
<i>Non-Hispanic Black</i>	9.8 (1.1)	11.1 (1.0)	10.6 (1.1)	9.4 (1.8)	
Body-mass index (kg/m²)					<0.001
< 20	5.4 (0.4)	5.3 (0.6)	5.3 (0.6)	5.2 (0.6)	
20 – 25	33.7 (1.1)	30.0 (1.2)	28.4 (1.1)	24.2 (1.1)	
25 – 29	36.8 (0.7)	34.3 (1.2)	34.0 (1.3)	34.0 (1.1)	
30 – 35	15.6 (0.6)	19.9 (1.1)	19.3 (0.8)	19.7 (0.9)	
> 35	8.6 (0.7)	10.4 (0.8)	13.0 (1.0)	17.0 (0.9)	
Less than high-school diploma (%)	16.9 (1.1)	18.8 (1.0)	22.8 (1.0)	22.0 (1.2)	<0.001
Activity Level (MET-min/wk, %)					<0.001
0	12.8 (0.8)	15.5 (0.8)	17.9 (1.1)	20.2 (1.6)	
< 500	20.9 (1.0)	22.2 (1.0)	20.6 (1.1)	20.1 (0.9)	
500 – 2000	37.3 (1.0)	36.8 (1.0)	33.9 (1.1)	32.4 (1.1)	
> 2000	29.0 (1.1)	25.4 (1.3)	27.7 (1.1)	27.3 (1.5)	
Smoking (%)					0.16
<i>Never</i>	52.4 (0.9)	49.9 (1.1)	47.3 (1.2)	49.8 (2.5)	
<i>Former</i>	24.9 (1.1)	25.4 (0.8)	25.6 (1.1)	25.1 (1.5)	
<i>Current</i>	22.7 (1.2)	24.7 (0.9)	27.1 (1.2)	25.1 (1.4)	
Hypertension (%)	33.9 (1.2)	38.5 (1.3)	42.2 (1.3)	46.5 (1.7)	<0.001
Diabetes mellitus (%)	4.6 (0.5)	6.6 (0.6)	7.7 (0.7)	9.9 (0.7)	<0.001
Cardiovascular disease (%)	6.3 (0.6)	7.8 (0.7)	9.6 (0.7)	10.2 (0.7)	<0.001
eGFR (mL/min/1.73m²)					<0.001
15 – 59	4.4 (0.4)	5.8 (0.6)	6.8 (0.5)	8.4 (0.5)	
60 – 89	35.4 (1.2)	35.1 (1.5)	35.7 (1.2)	34.7 (1.1)	
90 – 119	50.5 (1.2)	49.0 (1.6)	48.0 (1.3)	47.3 (1.3)	

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≥ 120	9.8 (0.7)	10.1 (0.7)	9.6 (0.6)	9.6 (0.8)	
UACR > 30 mg/g (%)	6.7 (0.5)	8.0 (0.6)	10.2 (0.6)	12.3 (0.8)	<0.001
Hemoglobin (g/dL)	14.53 (0.05)	14.44 (0.05)	14.55 (0.05)	14.59 (0.07)	0.28
Serum bicarbonate (mEq/L)	25.5 (0.1)	24.6 (0.1)	23.8 (0.1)	22.6 (0.1)	<0.001
Serum albumin (g/dL)	4.38 (0.01)	4.33 (0.01)	4.35 (0.01)	4.33 (0.01)	0.05
Serum calcium (mg/dL)	9.50 (0.02)	9.49 (0.01)	9.48 (0.02)	9.47 (0.02)	0.13
Serum phosphate (mg/dL)	3.64 (0.02)	3.68 (0.02)	3.65 (0.02)	3.66 (0.02)	0.57

Abbreviations: MET, metabolic equivalent; eGFR, estimated glomerular filtration rate; UACR, urinary albumin-creatinine ratio.

Data are expressed as mean (SE) or percent (SE).

eTable 3. Relative Hazard of All-Cause Mortality with Revised Model 3

Anion Gap	Relative Hazard (95% CI)			
	Model 1	Model 2	Model 3	Model 4
Traditional				
Continuous*	1.15 (1.02-1.29)	1.15 (1.03-1.29)	1.09 (0.97-1.23)	1.08 (0.94-1.24)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	0.86 (0.66-1.12)	0.86 (0.67-1.10)	0.81 (0.62-1.05)	0.83 (0.64-1.07)
Quartile 3	1.01 (0.76-1.35)	0.99 (0.75-1.32)	0.90 (0.67-1.21)	0.90 (0.66-1.23)
Quartile 4	1.30 (0.96-1.74)	1.32 (1.01-1.72)	1.16 (0.89-1.51)	1.20 (0.89-1.61)
P for trend	0.04	0.02	0.15	0.15
Albumin adjusted				
Continuous*	1.40 (1.25-1.58)	1.28 (1.14-1.44)	1.21 (1.07-1.36)	1.19 (1.03-1.38)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	1.36 (1.05-1.76)	1.29 (0.99-1.67)	1.23 (0.95-1.59)	1.24 (0.97-1.59)
Quartile 3	1.30 (1.00-1.70)	1.19 (0.91-1.56)	1.09 (0.84-1.42)	1.07 (0.82-1.38)
Quartile 4	2.17 (1.62-2.91)	1.82 (1.37-2.41)	1.58 (1.18-2.12)	1.62 (1.19-2.21)
P for trend	<0.001	<0.001	0.004	0.007
Full				
Continuous*	1.50 (1.33-1.68)	1.29 (1.15-1.45)	1.21 (1.07-1.37)	1.20 (1.03-1.41)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	1.67 (1.22-2.29)	1.40 (1.01-1.94)	1.31 (0.92-1.85)	1.31 (0.97-1.79)
Quartile 3	1.59 (1.19-2.13)	1.28 (0.95-1.72)	1.18 (0.87-1.60)	1.19 (0.90-1.57)
Quartile 4	2.68 (1.87-3.83)	1.88 (1.31-2.70)	1.62 (1.12-2.35)	1.64 (1.17-2.31)
P for trend	<0.001	0.001	0.01	0.01

Abbreviations: CI, Confidence Interval. **Bold** values indicate $p < 0.05$.

Quartile cutoff levels for each anion gap definition: Traditional: Q1 ≤ 10 ; Q2 10.1-12; Q3 12.1-14; Q4 ≥ 14.1 mEq/L; Albumin adjusted: **Q1 ≤ -0.50 ; Q2 -0.45-1.05; Q3 1.10-2.95; Q4 ≥ 3 mEq/L; Full: Q1 ≤ 3.61 ; Q2 3.62-5.34; Q3 5.35-7.23; Q4 > 7.23 mEq/L; Q1 ≤ 9.5 ; Q2 9.55-11.05; Q3 11.10-12.95; Q4 ≥ 13 mEq/L; Full: Q1 ≤ 13.61 ; Q2 13.62-15.34; Q3 15.35-17.23; Q4 > 17.23 mEq/L.**

* Per standard deviation higher anion gap (traditional SD = 2.55 mEq/L; Albumin adjusted SD = 2.47 mEq/L; Full SD = 2.49 mEq/L).

Model 1: unadjusted

Model 2: adjusted for age, sex, race/ethnicity

Model 3: adjusted for age, sex, race/ethnicity, eGFR categories, and log-transformed urine albumin-creatinine ratio

Model 4: adjusted for age, sex, race/ethnicity, eGFR categories, BMI, education, activity level, smoking status, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, log-transformed urine albumin-creatinine ratio, serum bicarbonate, and hemoglobin

eTable 4. Relative Hazard of All-Cause Mortality by Serum Bicarbonate Quartiles in 11,957 participants of NHANES 1999-2004

Serum Bicarbonate	Relative Hazard (95% CI)			
	Model 1	Model 2	Model 3	Model 4
Continuous*	1.19 (1.04-1.36)	0.94 (0.84-1.06)	0.96 (0.86-1.07)	1.01 (0.89-1.13)
≤ 23 mEq/L (n=4468)	Ref	Ref	Ref	Ref
24 mEq/L (n=2116)	1.00 (0.72-1.39)	0.85 (0.63-1.15)	0.87 (0.65-1.18)	0.89 (0.68-1.16)
25-26 mEq/L (n=3536)	1.22 (0.93-1.59)	0.86 (0.66-1.13)	0.88 (0.69-1.13)	0.98 (0.77-1.25)
≥ 27 mEq/L (n=1837)	1.72 (1.25-2.36)	0.94 (0.71-1.24)	0.97 (0.73-1.27)	1.12 (0.82-1.53)
P for trend	0.005	0.53	0.64	0.58

Abbreviations: CI, Confidence Interval. **Bold** values indicate $p < 0.05$.

* Per standard deviation higher serum bicarbonate (SD = 2.28 mEq/L).

Model 1: unadjusted

Model 2: adjusted for age, sex, race/ethnicity

Model 3: adjusted for age, sex, race/ethnicity, and eGFR categories

Model 4: adjusted for age, sex, race/ethnicity, eGFR categories, BMI, education, activity level, smoking status, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, log-transformed urine albumin-creatinine ratio, and hemoglobin