Influence of sodium bicarbonate on mortality in general intensive care patients with metabolic acidosis

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Online-Supplement

	Age	APACHE	Admin_aBE	Admin_apH	Admin_aHCO3	Admin_apCO2	Admin_aLac	Admin_HkB	Admin_Na	Admin_K	Admin_KreaS	BMI
0.03 - 0.02 - 0.01 -	\square	Corr: 0.301	Corr: 0.0868	Corr: 0.102	Corr: 0.0727	Corr: 0.0405	Corr: -0.0304	Corr: 0.0772	Corr: 0.0859	Corr: 0.0861	Corr: 0.0987	Corr: 2
40 - 30 - 20 -		\square	Corr: -0.0436	Corr: -0.205	Corr: -0.0188	Corr: -0.0265	Corr: 0.0962	Corr: -0.00315	Corr: 0.00481	Corr: -0.00392	Corr: 0.172	Corr: 0.0537
10 0 -10 -20			\bigwedge	Corr: 0.644	Corr: 0.965	Corr: 0.628	Corr:	Corr: 0.105	Corr: 0.0526	Corr: -0.0585	Corr: -0.209	Corr: 0.0423
-30 7.3 7.2 7.1 7.0 6.9 6.8			F	Λ	Corr: 0.541	Corr: 0.238	Corr. -0.344	Corr. 0.0569	Corr.	Corr. 0.0193	Corr. -0.09	Corr. 0.0167
6.7 30 20 ⁻ 10 ⁻			1		\square	Corr: 0.692	Corr:	Corr: 0.151	Corr: 0.0689	Corr: -0.0542	Corr: -0.217	Corr: 0.0473
0 40 30 20 10			ø			$ \land $	Corr: -0.0946	Corr: 0.238	Corr: 0.144	Corr: 0.126	Corr: -0.0802	Corr: 0.111
25 20 15 10 5-		1						Corr: 0.0209	Corr: 0.068	Corr: 0.237	Corr: 0.144	Corr: -0.0383
0.5 0.4 0.3 0.2								\bigwedge	Corr: 0.0641	Corr: 0.0278	Corr: 0.0251	Corr. 0.0804
150 140 130 120 110				- A-					\square	Corr: -0.055	Corr: -0.0222	Corr: 0.0335
6 5 4 3 2		-		12. 2			Č.			\bigwedge	Corr: 0.331	Corr: 0.101
750 500 - 250 - 0 -				-		J	in.	ä.			\bigwedge	Corr: 0.0985
60 50 40 30 20	25 50 75	10 20 30 40	-30-20-10 0 6		30 10 20 30	10 20 30 40	6 5 10 15 20 2	5 0.20.30.40 5	110/20130140150	2 3 4 5 6	0 250500 750	203040 50 60

Suppl. Figure 1: Marginal distributions of continuous variables in the full sample.

Correlations are in the upper triangle, univariate estimated densities on the diagonal and bivariate clouds in the lower triangle.

	ATE ("crude" sample), n=971	p-value	ATT("crude" sample), n=971	p-value
ICU mortality	1.54 (1.26, 1.88)	<.001	1.56 (1.17, 2.07)	.002
Hospital death	0.81 (0.60, 1.08)	.15	0.67 (0.43, 1.03)	.07
30d death	0.63 (0.45, 0.87)	.005	0.52 (0.32, 0.84)	.007
Death d31 to 365	1.43 (0.99, 2.05)	.06	1.31 (0.74, 2.31)	.36
Death at last follow-up*	0.83 (0.63, 1.09)	.18	0.72 (0.47, 1.09)	.12

Suppl. Table 1: Odds ratios (OR) for treatment effects for mortality in the "crude" dataset.

Reported are the odds ratios (OR) for the treatment effects for mortality at various stages in presence of sodium bicarbonate treatment for the "crude" dataset. Estimated by logit logistic regressions, regressing mortality outcome on SB treatment status, sex, age, BMI and APACHE. * Last follow up: September 2019.

ATE Average Treatment Effect, ATT Average Treatment effect in Treated



Supplement Figure 2: Distributions of the constructed propensity scores.

Distributions are given on the log scale. A and B - in the original sample; C and D - in the matched sample; E and F- with inverse weighting by ATE weights. ATE Average Treatment Effect.

Variable	n(no SB) =356	n(SB) =267	р
Gender	female: 109 (31%)	female: 104 (39%)	.04
BMI (kg/m2)	26.23 [23.65, 29.39]	25.95 [23.2, 29.38]	.51
Age (years)	67 [57.75, 74]	64 [53.5, 72]	.08
APACHE II	32 [27, 35]	30 [25, 36]	.11
DG Cardiovasc.	123 (35%)	96 (36%)	.78
DG Respiratory	96 (27%)	29 (11%)	<.001
DG Gastroint.	22 (6%)	32 (12%)	.02
DG Neurological	48 (13%)	7 (3%)	<.001
DG Trauma&TBI	6 (2%)	33 (12%)	<.001
DG Metabolic&	10 (6%)	33 (12%)	.67
Intox			
DG Haemat.	6 (2%)	5 (2%)	1
disease			
DG Renal	4 (1%)	6 (2%)	.43
DG Sepsis	25 (7%)	41 (15%)	<.001
apH	7.24 [7.19, 7.28]	7.12 [7.05, 7.18]	<.001
aHCO3 (mmol/l)	19.15 [17, 21.5]	10.6 [8.1, 12.5]	<.001
aLactate (mmol/l)	0.9 [0.7, 1.2]	1.4 [0.8, 4.55]	<.001
apCO2 (mmHg)	32.1 [28.08, 36.4]	24.8 [20, 28.5]	<.001
BE	-6.6 [-9.22, -3.68]	-17.4 [-21.3, -14.35]	<.001
Hc	0.28 [0.24, 0.33]	0.26 [0.23, 0.3]	<.001
Na (mmol/l)	134 [131, 137]	134 [131, 137]	.54
K (mmol/l)	3.6 [3.3, 3.9]	3.6 [3.27, 4.1]	.35
CreaS (mmol/l)	90.5 [59.75, 144]	116 [80.75, 174]	<.001
Adrenaline (y/n)	117 (33%)	162 (61%)	<.001
Adrenaline CD (µg)	1238.38 [183.3, 3818.12]	6658.19 [2575.14, 13312.91]	<.001
Noradrenaline (y/n)	231 (65%)	201 (75%)	.01
Noradrenaline CD (µg)	1838.96 [358.17, 7252.5]	4790.74 [1491.42, 17500.32]	<.001
Ventilation (y/n)	246 (69%)	157 (59%)	.01
Blood Products (y/n)	143 (40%)	167 (63%)	<.001
RRT (y/n)	44 (12%)	91 (34%)	<.001
ICU days	2.51 [1.07, 5.38]	2.26 [0.9, 5.73]	.34
Hospital days	8 [3, 16]	8 [2, 18]	.08
ICU Mortality	109 (31%)	130 (49%)	<.001
InHospital death	41 (12%)	22 (8%)	.23
30d death	34 (10%)	19 (7%)	.35
Death d31 to 365	28 (8%)	14 (5%)	.26
Death at last follow up*	48 (13%)	25 (9%)	.15
Time to death(days)	9.01 [1.28, 285.47]	2.03 [0.33, 22.07]	<.001

Suppl Table 2: Patient demographics, ICU treatment, and follow-up data of patients dropped during matching (n=623).

Median values [interquartile ranges] or counts (percentages) are given. 'p' refers to Kolmogorov-Smirnov test for continuous variables, or to chi-squared test for categorical variables (for the null hypothesis of equal categorical frequencies between two groups). Laboratory data are at admission to ICU. DG Diagnosis Group is referring to the APACHE IV-classification of diagnosis ad admission with a separate sepsis group (all groups include operative and non-operative diagnoses). NoSB non sodium bicarbonate recipients, SB sodium-bicarbonate recipients, APACHE II Acute Physiology and Chronic Health Evaluation II Score, Cardiovasc. Cardiovascular, Gastroint. Gastrointestinal, Haemat. Haematological, Hc hematocrit, Na sodium, K potassium, CreaS serum creatinine, TBI traumatic brain injury, CD cumulative dose, RRT renal replacement therapy, ICU intensive care unit. * Last follow up was in September 2019.



Supplement Figure 3: Kaplan–Meier survival curves (until last follow-up) obtained using different propensity score methods.

In the top-left panel crude Kaplan–Meier survival curves for treated and untreated subjects in the "crude" original sample (n=971) are reported (log-rank test: p = 0.047). In the top right panel Kaplan–Meier survival curves for treated and untreated subjects in the propensity score matched sample (n=348) are described (stratified log-rank test p = 0.75). In the bottom-left and bottom-right panels survival curves in the sample weighted using the ATE weights (n=971) and the sample weighted using

the ATT weights (n=971) are reported (adjusted log-rank test with p-values 0.82 and 0.84). ATE Average Treatment Effect, ATT Average Treatment effect in Treated.