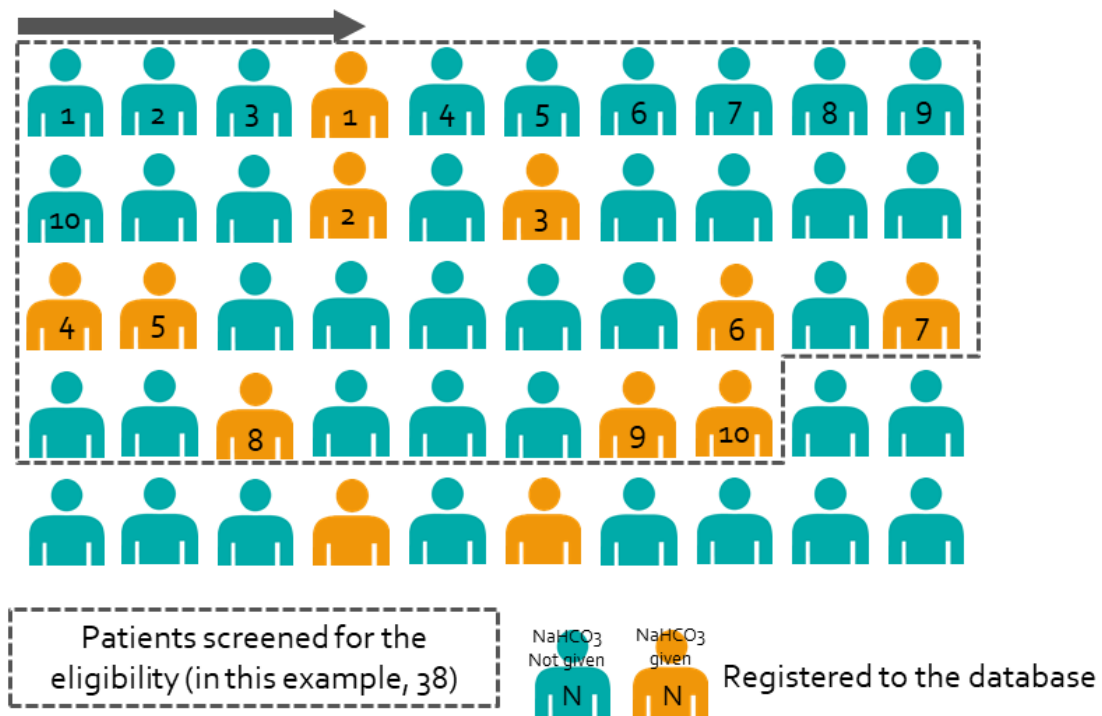
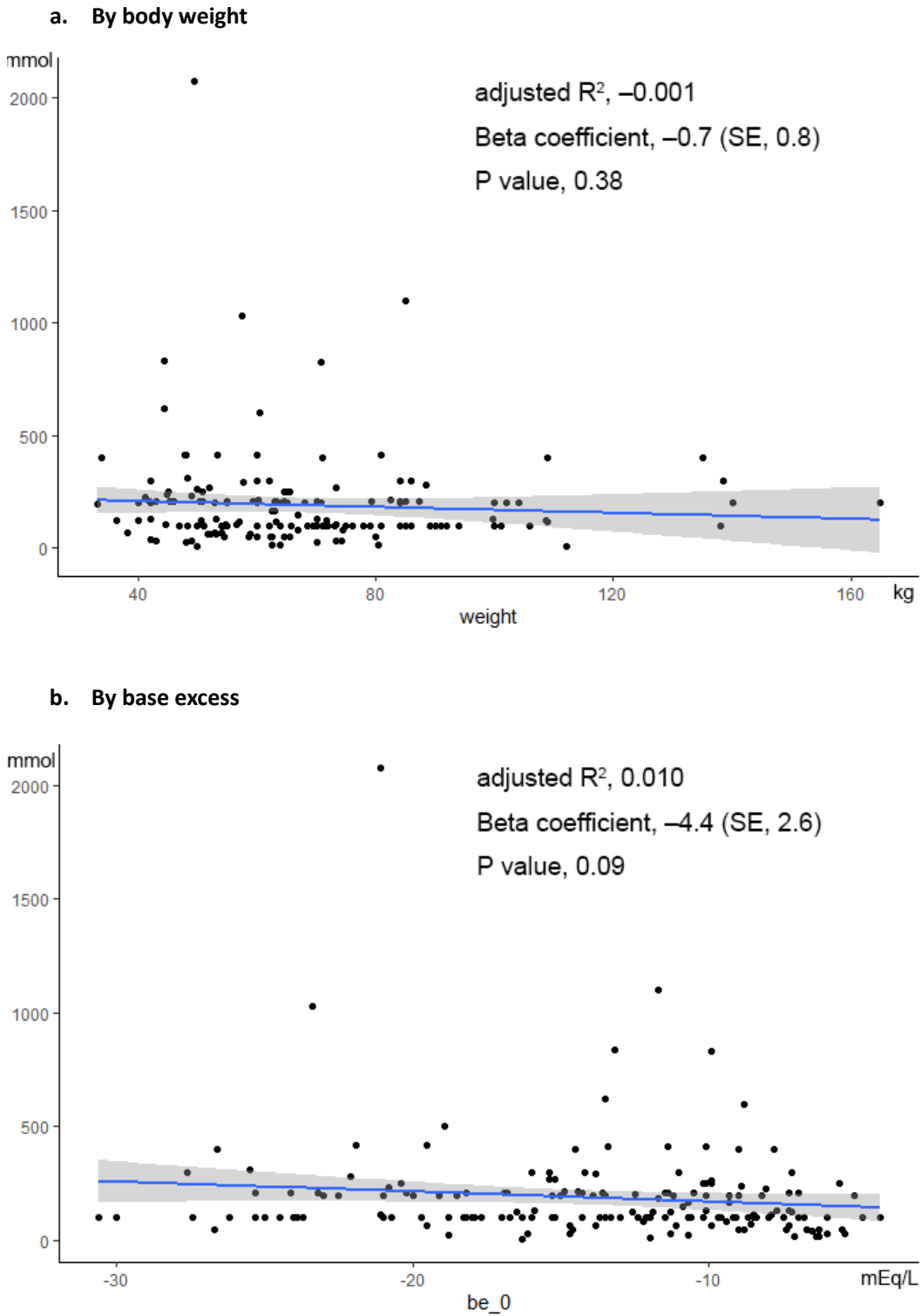


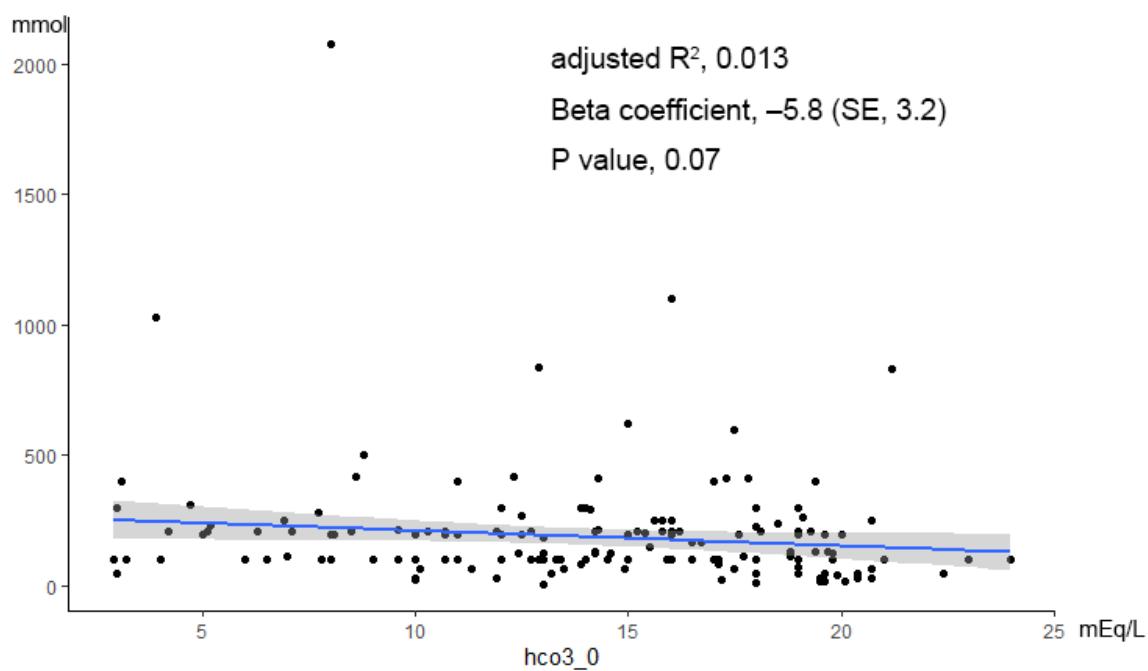
**Supplementary Figure 1.** Diagram of screening and patient data collection. Every patient meeting the criteria were registered until 10 patients in each group (NaHCO<sub>3</sub> vs no-NaHCO<sub>3</sub>)



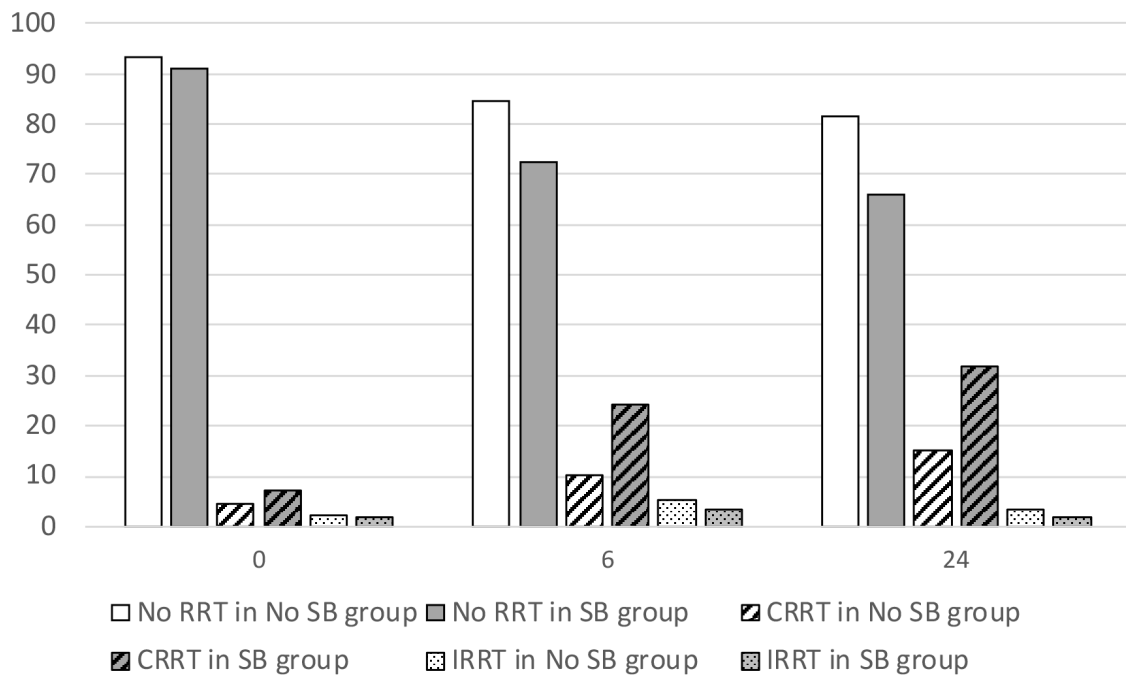
**Supplementary Figure 2.** The total amount of sodium bicarbonate by body weight, base excess or bicarbonate levels.



**c. By bicarbonate levels**

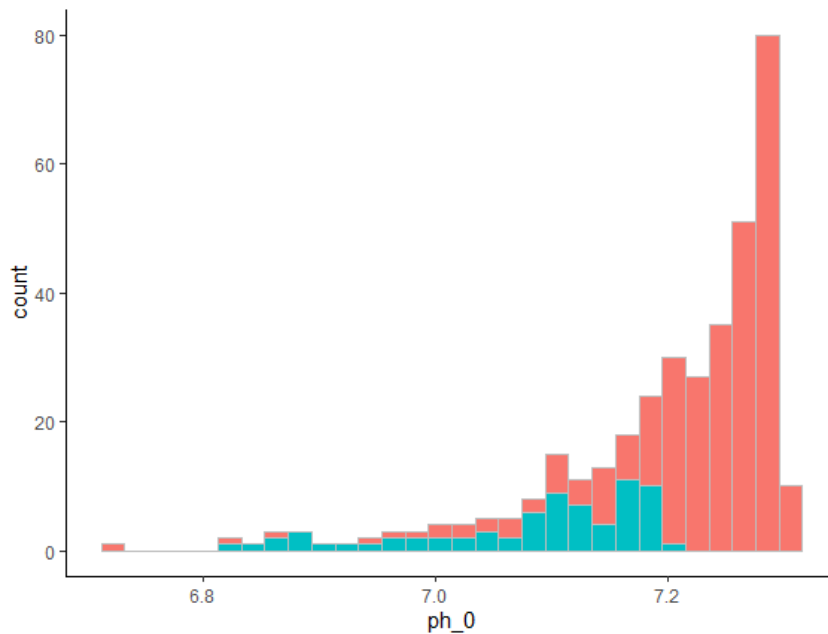


**Supplementary Figure 3.** Need for renal replacement therapy over 24 hours of metabolic acidosis by treatment group.

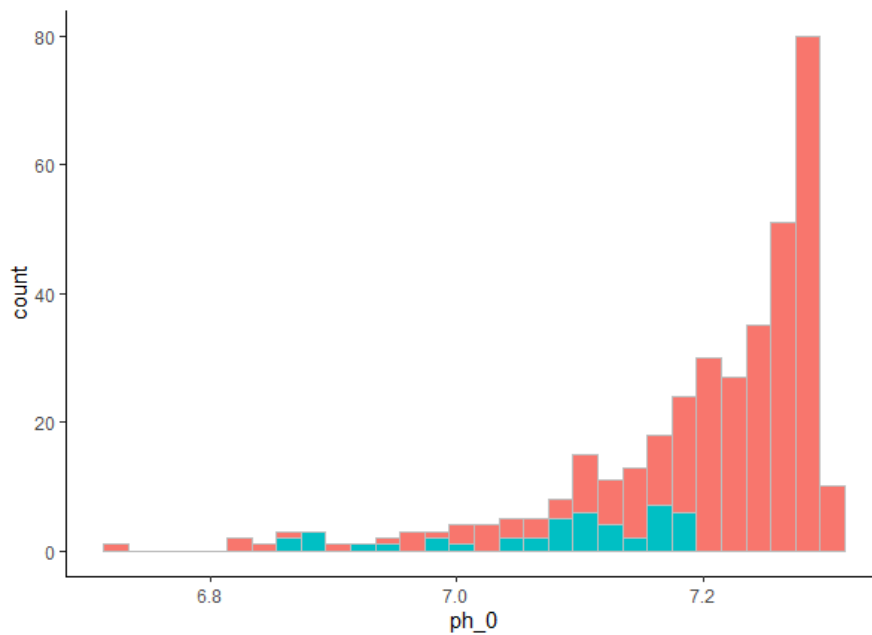


**Supplementary Figure 4.** Distribution of patients with severe metabolic acidosis. Red bar = overall population, blue bar= subpopulation with the criteria.

a.  $\text{pH} < 7.2$  and  $\text{PaCO}_2 \leq 45$  mmHg



b.  $\text{pH} < 7.2$  AND  $\text{PaCO}_2 \leq 45$  mmHg AND  $\text{HCO}_3 \leq 20$  mEq/L AND Lactate  $\geq 2.0$  mmol/L



**Supplementary Table 1.** Characteristics at ICU admission in patients with vasopressor dependency at the diagnosis of metabolic acidosis

	No SB (N=77)	SB (N=110)	p value
Age, years	69.6 [59.4, 81.0]	66.1 [53.0, 76.1]	0.04
Sex, male	52 (67.5)	60 (54.5)	0.10
Weight, kg	73.0 [59.2, 85.0]	64.0 [52.0, 81.0]	0.05
Height, cm	164 [158, 172]	166 [155, 172]	0.99
ICU admission source			0.05
Operation theatre	32 (41.6)	24 (21.8)	
Emergency department	22 (28.6)	46 (41.8)	
Ward	16 (20.8)	32 (29.1)	
Other hospital	5 ( 6.5)	6 ( 5.5)	
ICU in other hospital	2 ( 2.6)	2 ( 1.8)	
Treatment goals on admission			0.21
Full active management	68 (88.3)	94 (85.5)	
Treatment limitation order	9 (11.7)	10 ( 9.1)	
Palliative care	0 ( 0.0)	5 ( 4.5)	
Potential organ donation	0 ( 0.0)	1 ( 0.9)	
Cardiac arrest in 24 hours prior to ICU admission			0.34
Yes	14 (18.2)	28 (25.5)	
No	63 (81.8)	81 (73.6)	
Unknown	0 ( 0.0)	1 ( 0.9)	
Chronic hemo/peritoneal-dialysis	6 ( 7.8)	4 ( 3.6)	0.36
Baseline creatinine, mmol/L	93.0 [74.3, 185.4]	97.0 [57.1, 142.0]	0.27
AKI			0.08
No AKI	24 (45.3)	23 (29.5)	
Stage 1	15 (28.3)	17 (21.8)	
Stage 2	3 ( 5.7)	8 (10.3)	
Stage 3	11 (20.8)	30 (38.5)	
APACHE III score	70 [51, 95]	99 [71, 129]	<0.001

**Supplementary Table 2.** Arterial blood gas analysis and electrolytes in patients with vasopressor dependency at the diagnosis of metabolic acidosis. pH, PaO<sub>2</sub>, PaCO<sub>2</sub>, HCO<sub>3</sub>, Base Excess, and lactate were only measured for arterial blood samples.

	No SB (N=77)	SB (N=110)	p value
pH	7.26 [7.22, 7.28]	7.19 [7.13, 7.25]	<0.001
PaO <sub>2</sub> , mmHg	109.7 [83.1, 182.2]	113.8 [82.4, 209.8]	0.45
PaO <sub>2</sub> /FiO <sub>2</sub>	238.8 [144.8, 323.3]	230.9 [126.8, 370.8]	0.95
PaCO <sub>2</sub> , mmHg	43.8 [37.6, 49.0]	39.5 [32.1, 47.3]	0.04
HCO <sub>3</sub> , mEq/L	18.2 [16.0, 20.7]	15.0 [11.9, 18.0]	<0.001
Base Excess, mEq/L	-7.9 [-10.0, -6.0]	-12.3 [-16.1, -9.3]	<0.001
SID, mEq/L	29.7 [25.8, 32.5]	27.6 [23.4, 31.6]	0.03
Sodium, mEq/L	137.0 [135.0, 140.0]	137.0 [134.0, 140.0]	0.59
Potassium, mEq/L	4.2 [3.8, 4.8]	4.3 [3.8, 5.1]	0.67
Chloride, mEq/L	109.0 [106.3, 113.0]	107.0 [103.0, 112.0]	0.07
Lactate, mmol/L	2.9 [1.8, 5.1]	6.6 [2.3, 10.2]	0.001
Ionised Calcium, mmol/L	1.1 [1.0, 1.2]	1.1 [1.0, 1.2]	0.62

SB denotes sodium bicarbonate; SID, strong ion difference = Sodium + Potassium + Ionised calcium - Chloride – Lactate.

**Supplementary Table 3.** ICU interventions in patients with vasopressor dependency at the time of metabolic acidosis diagnosis

	No SB (N=77)	SB (N=110)	p value
Vasopressor dose, $\mu\text{g}/\text{kg}/\text{min}$	0.12 [0.05, 0.28]	0.25 [0.13, 0.47]	<0.001
Cardiac index monitored	8 (12.1)	11 (12.2)	> 0.99
Cardiac index, L/min/m <sup>2</sup>	2.6 [2.4, 3.0]	3.2 [2.4, 3.8]	0.33
Invasive mechanical ventilation	60 (77.9)	82 (74.5)	
Noninvasive mechanical ventilation	3 ( 3.9)	1 ( 0.9)	
ECMO	0 ( 0.0)	5 ( 4.5)	
Neuromuscular blockade	13 (17.1)	12 (11.0)	0.33
Renal replacement therapy			0.71
Not on RRT	69 (90.8)	96 (87.3)	
CRRT	6 ( 7.9)	11 (10.0)	
IRRT	1 ( 1.3)	3 ( 2.7)	

SB denotes sodium bicarbonate; ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy; CRRT, continuous renal replacement therapy; IRRT, intermittent renal replacement therapy.



**Supplementary Table 4.** Characteristics at ICU admission in patients with severe metabolic acidosis.

	No SB (N=7)	SB (N=39)	p value
Age, years	52.4 [47.7, 65.2]	63.3 [49.2, 70.8]	0.47
Sex, male	3 (42.9)	13 (33.3)	0.68
Weight, kg	74.0 [63.5, 81.2]	63.3 [53.8, 80.9]	0.22
Height, cm	162 [160, 172]	162 [156, 170]	0.76
BMI, kg/m <sup>2</sup>	25.0 [25.0, 28.1]	22.3 [21.1, 26.6]	0.09
ICU admission source			0.80
Operation theatre	1 (14.3)	3 (7.7)	
Emergency department	4 (57.1)	24 (61.5)	
Ward	2 (28.6)	7 (17.9)	
Other hospital	0 (0)	2 (5.1)	
ICU in other hospital	0 (0)	3 (7.7)	
Treatment goals on admission			>0.999
Full active management	7 (100)	32 (82.1)	
Treatment limitation order	0 (0)	4 (10.3)	
Palliative care	0 (0)	3 (7.7)	
Cardiac arrest in 24 hours prior to ICU admission	3 (42.9)	10 (25.6)	0.39
Chronic hemo/peritoneal-dialysis	4 (57.1)	3 (7.7)	0.01
Baseline creatinine, mmol/L	259.0 [104.0, 342.0]	117.5 [72.6, 157.4]	0.23
AKI			0.70
No AKI	3 (60.0)	8 (29.6)	
Stage 1	0 (0)	5 (18.5)	
Stage 2	0 (0)	5 (18.5)	
Stage 3	2 (40.0)	9 (33.3)	
APACHE III score	96 [81, 120]	106 [92, 134]	0.56

**Supplementary Table 5.** Arterial blood gas analysis and electrolytes in patients with severe metabolic acidosis. pH, PaO<sub>2</sub>, PaCO<sub>2</sub>, HCO<sub>3</sub>, Base Excess, and lactate were only measured for arterial blood samples.

	No SB (N=7)	SB (N=39)	p value
pH	7.12 [7.04, 7.19]	7.11 [7.06, 7.16]	0.42
PaO <sub>2</sub> , mmHg	87.5 [83.7, 257.7]	153.0 [113.1, 288.0]	0.42
PaO <sub>2</sub> /FiO <sub>2</sub>	142.2 [136.7, 284.9]	310.0 [215.3, 456.9]	0.12
PaCO <sub>2</sub> , mmHg	36.6 [27.8, 38.0]	33.0 [26.0, 39.2]	0.80
HCO <sub>3</sub> , mEq/L	13.0 [6.6, 13.8]	9.6 [6.7, 12.5]	0.49
Base Excess, mEq/L	-15.2 [-24.5, -13.6]	-19.5 [-23.7, -16.3]	0.58
SID, mEq/L	25.4 [21.4, 27.6]	24.1 [21.0, 29.1]	0.80
Sodium, mEq/L	134.0 [126.8, 136.5]	136.0 [133.5, 138.0]	0.15
Potassium, mEq/L	5.2 [4.1, 6.0]	4.5 [4.1, 4.9]	0.33
Chloride, mEq/L	99.0 [96.0, 106.5]	105.0 [100.0, 111.5]	0.13
Lactate, mmol/L	7.0 [4.2, 16.6]	9.0 [4.5, 13.4]	0.95
Ionised Calcium, mmol/L	1.1 [1.1, 1.2]	1.1 [1.0, 1.2]	0.13

SB denotes sodium bicarbonate; SID, strong ion difference = Sodium + Potassium + Ionised calcium - Chloride - Lactate.

**Supplementary Table 6.** ICU interventions in patients with severe metabolic acidosis at the time of metabolic acidosis diagnosis

	No SB (N=7)	SB (N=39)	p value
Vasopressor dose, µg/kg/min	0.00 [0.00, 0.22]	0.11 [0.00, 0.40]	0.28
Cardiac index monitored	0 (0)	0 (0)	N/A
Respiratory support			0.51
Not on mechanical ventilation	2 (28.6)	12 (30.8)	
Invasive mechanical ventilation	4 (57.1)	25 (64.1)	
Noninvasive mechanical ventilation	1 (14.3)	1 (2.6)	
ECMO	0 (0)	1 (2.6)	
Neuromuscular blockade	2 (28.6)	3 (7.7)	0.16
Renal replacement therapy			0.57
Not on RRT	7 (100)	33 (84.6)	
CRRT	0 (0)	6 (15.4)	

SB denotes sodium bicarbonate; N/A, not applicable; ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy; CRRT, continuous renal replacement therapy.

**Supplementary Table 7.** Characteristics at ICU admission in patients with Stage 2 or 3 AKI at the diagnosis of metabolic acidosis

	No SB (N=34)	SB (N=50)	p value
Age, years	67.6 [55.3, 80.3]	67.3 [55.4, 72.7]	0.43
Sex, male	26 ( 76.5)	23 ( 46.0)	0.01
Weight, kg	61.8 [54.4, 76.4]	63.6 [53.1, 74.0]	0.91
Height, cm	166.5 [156.6, 174.3]	164.0 [149.6, 171.5]	0.17
ICU admission source			0.92
Operation theatre	8 ( 23.5)	9 ( 18.0)	
Emergency department	14 ( 41.2)	19 ( 38.0)	
Ward	10 ( 29.4)	19 ( 38.0)	
Other hospital	1 ( 2.9)	1 ( 2.0)	
ICU in other hospital	1 ( 2.9)	2 ( 4.0)	
Treatment goals on admission			0.46
Full active management	28 ( 82.4)	41 ( 82.0)	
Treatment limitation order	6 ( 17.6)	7 ( 14.0)	
Palliative care	0 ( 0.0)	2 ( 4.0)	
Cardiac arrest in 24 hours prior to ICU admission	5 ( 14.7)	8 ( 16.0)	>0.99
Chronic hemo/peritoneal-dialysis	13 ( 39.4)	3 ( 6.0)	<0.001
Baseline creatinine, mmol/L	271.4 [98.7, 524.9]	87.2 [54.2, 144.3]	<0.001
AKI			>0.99
Stage 2	8 ( 23.5)	11 (22.0)	
Stage 3	26 ( 76.5)	39 ( 78.0)	
APACHE III score	91.5 [69.3, 107.3]	110.0 [88.0, 144.5]	0.002

**Supplementary Table 8.** Arterial blood gas analysis and electrolytes in patients with Stage 2 or 3 AKI. pH, PaO<sub>2</sub>, PaCO<sub>2</sub>, HCO<sub>3</sub>, Base Excess, and lactate were only measured for arterial blood samples.

	No SB (N=34)	SB (N=50)	p value
pH	7.27 [7.20, 7.29]	7.19 [7.12, 7.25]	0.001
PaO <sub>2</sub> , mmHg	111.50 [82.83, 143.22]	109.90 [83.10, 158.25]	0.902
PaO <sub>2</sub> /FiO <sub>2</sub>	251.23 [182.46, 342.11]	255.00 [150.00, 372.22]	0.86
PaCO <sub>2</sub> , mmHg	38.05 [35.80, 46.38]	37.05 [31.05, 43.38]	0.314
HCO <sub>3</sub> , mEq/L	16.90 [14.40, 20.48]	13.95 [10.03, 17.18]	0.001
Base Excess, mEq/L	-8.95 [-12.72, -6.27]	-13.45 [-17.88, -10.05]	<0.001
SID, mEq/L	32.89 [28.02, 36.30]	27.95 [23.57, 31.85]	0.066
Sodium, mEq/L	137.00 [134.00, 140.00]	136.00 [133.00, 138.00]	0.22
Potassium, mEq/L	4.70 [4.16, 5.43]	4.30 [3.80, 5.12]	0.108
Chloride, mEq/L	107.00 [104.50, 112.50]	104.00 [102.00, 110.00]	0.103
Lactate, mmol/L	1.60 [1.20, 4.05]	6.33 [1.40, 11.38]	0.022
Ionised Calcium, mmol/L	1.12 [1.06, 1.21]	1.11 [1.02, 1.21]	0.271

SB denotes sodium bicarbonate; SID, strong ion difference = Sodium + Potassium + Ionised calcium - Chloride – Lactate.

**Supplementary Table 9.** ICU interventions in patients with Stage 2 or 3 AKI at the time of metabolic acidosis diagnosis

	No SB (N=34)	SB (N=50)	p value
Vasopressor dose, µg/kg/min	0.00 [0.00, 0.10]	0.20 [0.01, 0.35]	0.001
Cardiac index monitored	0 ( 0.0)	6 ( 12.0)	0.10
Respiratory support			0.61
Not on mechanical ventilation	17 ( 50.0)	20 ( 40.0)	
Invasive mechanical ventilation	16 ( 47.1)	29 ( 58.0)	
Noninvasive mechanical ventilation	1 ( 2.9)	1 ( 2.0)	
Neuromuscular blockade	6 ( 17.6)	3 ( 6.1)	0.19
Renal replacement therapy			0.57
Not on RRT	22 ( 64.7)	34 ( 68.0)	
CRRT	8 ( 23.5)	13 ( 26.0)	
IRRT	4 ( 11.8)	3 ( 6.0)	

SB denotes sodium bicarbonate; N/A, not applicable; ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy; CRRT, continuous renal replacement therapy; IRRT, intermittent renal replacement therapy.

**Supplementary Table 10.** Association between administration of sodium bicarbonate and clinical

outcomes in patients with Stage 2 or 3 AKI (N = 84).

	aOR, $\beta$	95% CI	p-value
ICU mortality	0.72	0.21 to 2.58	0.59
Hospital mortality	1.13	0.37 to 4.14	0.83
Vasopressor dose at 6h	0.06	-0.02 to 0.14	0.15
Vasopressor dose at 24h	0.07	-0.02 to 0.16	0.15
Mean arterial pressure at 6h	-1.13	-8.09 to 5.39	0.73
Mean arterial pressure at 24h	-6.54	-13.49 to 0.42	0.07
Delta mean arterial pressure per vasopressor dose at 6h	1.89	-6.85 to 10.41	0.67
Delta mean arterial pressure per vasopressor dose at 24h	2.83	-7.53 to 13.19	0.60

Delta mean arterial pressure per vasopressor dose = mean arterial pressure at 24h/(vasopressor dose at 24h +1) – mean arterial pressure at 6h/(vasopressor dose at 6h +1)