CHEST Critical Care

Severe Metabolic Acidosis in the ICU

Boris Jung, MD, PhD; Maxime Fosset, MD; Tomoko Fujii, MD, PhD; Jeffrey A. Kraut, MD; Samir Jaber, MD, PhD

Severe acidemia (pH < 7.20) involving metabolic acidosis affects 2% to 10% of patients in the ICU and is associated with high mortality rates. This condition can arise from various clinical contexts and often accompanies organ dysfunction, particularly cardiovascular impairment. Although addressing the underlying cause is crucial, the role of adjunctive interventions like buffer therapy or renal replacement therapy (RRT) remains debated. This article presents a clinical case to illustrate the diagnostic workup and provides an evidence-based update on current management strategies. It discusses phenotyping metabolic acidosis, consequences of severe metabolic acidemia, and available therapeutic strategies in the ICU. Buffers to mitigate acidemia in certain patients and the pros and cons of sodium bicarbonate (HCO_3^-) infusion vs RRT are considered. A tailored approach, considering sodium HCO_3^- use to raise and maintain blood pH to > 7.20 in some patients, potentially delaying or avoiding RRT, may be useful. However, the optimal dose and duration of sodium HCO_3^- infusion remain unestablished, and further research is needed to refine decision-making processes in managing severe metabolic acidosis.

CHEST Critical Care 2026; 4(3):100271

KEY WORDS: acute kidney injury; metabolic acidosis; renal replacement therapy; sodium bicarbonate

In this article, we use the term *acidosis* to refer to any pathophysiologic process that tends to lower plasma pH, regardless of the measured pH level. The term *acidemia* denotes the presence of plasma pH of < 7.38 whatever the cause. Severe metabolic acidemia (defined as pH < 7.20 with metabolic origin) is observed in approximately 2% to 10% of patients in the ICU, depending on the population characteristics, and is associated with high mortality rates, sometimes reaching 60%, depending on the underlying cause and comorbidities.[1-6]

Severe metabolic acidemia arises in a wide range of clinical contexts and often is accompanied by organ dysfunction, most notably cardiovascular impairment, including arterial vasodilation, decreased myocardial contractility and cardiac output, and an increased risk of ventricular arrhythmias.[7,8] Correction of the underlying cause remains the cornerstone of management. In critically ill patients with severe metabolic acidemia, adjunctive interventions such as buffer therapy with sodium bicarbonate (HCO_3^-) infusion or renal replacement therapy (RRT) often are

Abbreviations: AKI = acute kidney injury; RCT = randomized clinical trial; RRT = renal replacement therapy

AFFILIATIONS: From the Medical Intensive Care Unit (B. J. and M. F.), Lapeyronie Teaching Hospital, the PhyMedExp Laboratory (B. J. and S. J.), the Desbrest Institute of Epidemiology and Public Health (M. F.), INRIA; the Saint Eloi Department of Anesthesiology and Critical Care Medicine (S. J.), Saint Eloi Teaching Hospital, University of Montpellier, France; the Center for Anesthesia Research Excellence (M. F.), Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; the Nephrology Section (J. A. K.), VA Greater Los Angeles Healthcare System and Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, CA; and the Department of Intensive Care (T. F.), Jikei University Hospital, Tokyo, Japan.

CORRESPONDENCE TO: Boris Jung; email: b-jung@chu-montpellier.fr

DOI: https://doi.org/10.1016/j.chstcc.2026.100271

considered. Evidence supporting these interventions remains limited. Sodium HCO_3^- has been evaluated against no sodium HCO_3^- or saline solution in a few physiologic or observational studies, as well as in 2 large randomized clinical trials (RCTs)[4,9] and 1 target trial emulation.[10] Although these studies did not demonstrate a consistent mortality benefit, they suggested a possible benefit of avoiding the use of RRT and did not identify major safety concerns of sodium HCO_3^- as long as contraindications are respected. Ongoing randomized trials continue to explore the potential role of sodium HCO_3^- in this setting.[11,12]

In this How I Do It article, we present a clinical case to illustrate our diagnostic approach and to describe our current management strategy for severe metabolic acidemia, based on our interpretation of the available evidence. Sodium HCO_3^- therapy is widely accepted and recommended if acidemia results from gastrointestinal losses (eg, from diarrhea) and will not be discussed any further herein.[2]

Case Presentation

Mr Y, a 51-year-old man, 175 cm, 100 kg, with a history of atrial fibrillation and alcohol-related liver disease complicated by dilated cardiomyopathy, sought treatment at the emergency department in shock status. His baseline serum creatinine was 100 μmol/L. On arrival, he was hypothermic (34.6° C), hypotensive (BP, 75/30 mm Hg; mean pressure, 45 mmHg), and tachycardic (150 beats/min, irregular) with altered mental status and mottling extending to the knees. Arterial blood gas showed severe metabolic acidemia (Table 1): pH of 7.19, HCO_3^- of 12 mM, P_{CO_2} of 30 mm Hg, and P_{O_2} of 70 mm Hg. He received 30 mL/kg isotonic fluid resuscitation, broad-spectrum antibiotics, and a norepinephrine infusion. CT scan revealed left-sided hydronephrosis resulting from a ureteral stone with perinephric stranding and gas in the collecting system, consistent with obstructive urosepsis. He was intubated in the emergency department because of altered mental status and persistent shock.

How Do We Phenotype Metabolic Acidosis in This Patient?

Mr Y presents with severe metabolic acidemia, with arterial pH of < 7.20 and a markedly reduced plasma HCO_3^- concentration. Although we present the acid-base assessment using a HCO_3^--centered framework, an equivalent interpretation can be reached using the Stewart approach, which quantitatively provides the diagnosis of decreased strong ion difference metabolic acidemia in this patient.

TABLE 1] Arterial Blood Gas and Laboratory Findings on Admission

Parameter	Value
pH	7.19
P_{CO_2}, mm Hg	30
P_{O_2}, mm Hg	70
HCO_3^-, mM	12
Base excess, mM	−14.5
Lactate, mM	3
Sodium (Na^+), mM	138
Potassium (K^+), mM	5.2
Chloride (Cl^-), mM	103
Blood urea nitrogen, mM (mg/dL)	38.9 (109)
Creatinine, mM (mg/dL)	507 (5.73)
Glucose, mM (mg/dL)	11.1 (200)
Total calcium, mM (mg/dL)	1.98 (7.9)
Ionized calcium, mM	0.97
Phosphate, mM (mg/dL)	3.8 (11.8)
Magnesium, mM (mg/dL)	0.79 (1.9)
Total protein, g/L (g/dL)	46 (4.6)
Albumin, g/L (g/dL)	27 (2.7)

HCO_3^- = bicarbonate.

The corrected anion gap was:

$$\text{Corrected anion gap} * = Na^+ - Cl^- - HCO_3^- + [(40 - \text{albumin}) \times 0.25] = 138 - 103 - 12 + [(40 - 37) \times 0.25] = 138 - 103 - 12 + 0.75 = 23 \text{ mM}.$$

(*Corrected anion gap formula if albumin is expressed as grams per deciliter: Corrected anion gap* = $Na^+ - Cl^- - HCO_3^- + [(4 - \text{albumin}) \times 2.5]$).

This elevated corrected anion gap (> 12 mM) likely was attributable to acute kidney injury (AKI) in the context of septic shock, with a lactic acidosis (lactate, 3 mM). As part of evaluation of high-anion gap acidemia, venous β-hydroxybutyrate level or urine ketones were measured and showed negative findings, excluding ketoacidosis.

According to Winter's formula, the expected respiratory compensation was: $P_{CO_2} = (1.5 \times HCO_3^-) + 8 = (1.5 \times 12) + 8 = 26$ mm Hg.[13] The measured P_{CO_2} of 30 mm Hg falls within the accepted range of variability (by up to 5 mm Hg[14]), indicating the absence of a major superimposed respiratory acid-base disorder.

To characterize the acid-base disturbance further, the change in gap minus the change in HCO_3^- was calculated, taking into account the context of lactic acidosis.[15] The value did not suggest an additional nonanion gap metabolic acidosis, supporting the presence of a single predominant metabolic process:

$$0.6 \times \Delta AG - \Delta HCO_3^- = 0.6 \times (23 - 10) - (25 - 12) = 7.8 - 13 = -5 \text{ mM}.$$

Taken together, this phenotyping identifies a severe high-anion gap metabolic acidemia associated with AKI and shock. In this context, and given the potential physiologic consequences of a persistently low pH, we consider IV sodium HCO_3^- to increase blood pH while definitive treatment of the underlying cause is ongoing.

Why Do We Consider Using Buffers?

The physiological effects of metabolic acidosis have been investigated largely through in vitro studies and small animal models. Therefore, caution is required when extrapolating these findings to clinical practice. Nevertheless, severe metabolic acidemia is associated with widespread cardiovascular, neurologic, immune, and metabolic disturbances that might be mitigated partially by buffer administration (Table 2).

Lower blood pH is associated with impaired myocardial contractility and reduced cardiac output, together with arterial vasodilation contributing to hypotension.[16] When pH falls to approximately < 7.10 to 7.20, these effects become more pronounced. Moreover, acidemia blunts the inotropic and vasoconstrictive responses to catecholamines and increases the risk of ventricular arrhythmias, further compromising hemodynamic stability.[8,16]

Neurologically, acute acidemia often is associated with altered mental status, including confusion and lethargy. Oxygen delivery also is affected by acidemia. Initially, acidemia induces a rightward shift of the oxyhemoglobin dissociation curve (the Bohr effect), which facilitates oxygen unloading, but within 12 to 24 hours, this effect may be counterbalanced by reductions in 2,3-diphosphoglycerate, resulting in a relative leftward shift of the dissociation curve and increased hemoglobin-oxygen affinity.[17] The net effect on tissue oxygen delivery depends on both the severity and duration of the acidemia.[8,18]

From a metabolic perspective, acidemia interferes with insulin signaling[19] and cellular energy production, in part through inhibition of key glycolytic enzymes such as phosphofructokinase. Acidosis also modulates immune function by stimulating macrophage cytokine production and suppressing lymphocyte function, leading to enhanced systemic inflammation and weakened host defense, potentially increasing susceptibility to infections.[20]

From a practical standpoint, these considerations suggest that in critically ill patients with severe metabolic acidemia, when accompanied by shock and AKI, simply tolerating a profoundly low pH may expose patients to clinically relevant physiologic harm. In conjunction with addressing the underlying cause, we consider IV sodium HCO_3^- as a reasonable strategy to correct the severe metabolic acidemia, rather than withholding buffer therapy altogether.

TABLE 2] Buffering Delivery Across Various Sodium HCO_3^- Protocols and Renal Replacement Settings

Therapy	Volume Infused, mL	Buffering Delivery (Theoretical)	Buffering Delivery (70-kg Patient)
Isotonic HCO_3^- (150 mEq/L)	1,000	150 m	150 mEq (total)
Half-isotonic HCO_3^- (75 mEq/L)	1,000	75 mEq	75 mEq (total)
Hypertonic 4.2% (500 mEq/L)	1,000	500 mEq	500 mEq (total)
Hypertonic 8.4% (1,000 mEq/L)	100	100 mEq	100 mEq (total)
Continuous RRT (HCO_3^- concentration, 34 mEq/L; replacement, 20 mL/kg/h)	0	0.68 mEq/kg/h	47.6 mEq/h
Prolonged intermittent RRT (HCO_3^- concentration, 40 mEq/L; dialysate, 200 mL/min)	0	480 mEq/h	480 mEq/h
Intermittent hemodialysis (HCO_3^- concentration, 40 mEq/L; dialysate, 800 mL/min)	0	1,920 mEq/h	1,920 mEq/h

Note that buffering delivery and changes in plasma HCO_3^- are distinct, because the alteration in HCO_3^- levels is influenced by factors such as distribution volume, conversion of HCO_3^- to CO_2, transmembrane distribution, HCO_3^- loss in effluent, and proton generation. HCO_3^- = bicarbonate; RRT = renal replacement therapy.

When Should We Consider RRT?

In addition to treating the underlying cause of metabolic acidemia, 2 main therapeutic strategies are available to increase blood pH in critically ill patients: IV sodium HCO_3^- and RRT. RRT, by design, provides HCO_3^- through the dialysate solution or replacement fluid while addressing electrolyte disturbances, uremia, and fluid overload. Established indications for initiating RRT in the ICU include severe hyperkalemia, symptomatic hypercalcemia, uremic complications, refractory pulmonary edema, ingestion of dialyzable toxin, and severe metabolic acidemia refractory to medical therapy.[21-23]

The correction of acidemia with RRT depends on the method. Intermittent hemodialysis achieves rapid pH correction via high-efficiency diffusion over short sessions, whereas continuous RRT offers slower, continuous correction through convection, diffusion, or both. Prolonged intermittent RRT is an intermediate approach. Across all methods, the rate and extent of pH correction are determined by intensity[24] and the HCO_3^- concentration of the dialysate or replacement fluid. HCO_3^--buffered solutions are preferred in critically ill patients because of better cardiovascular tolerance and more predictable control of acid-base balance. Although HCO_3^- concentrations of 30 to 35 mM are used commonly and are considered safe, these recommendations largely are derived from observational data and expert consensus.[25]

Intermittent hemodialysis achieves rapid acidosis correction through diffusion-based HCO_3^- transfer during 3- to 6-hour sessions using high dialysate (500-800 mL/min) and blood flow rates (200-250 mL/min using a line and up to 500 mL/min if using a fistula).[21,26] The dialysate is produced online by mixing treated water with electrolytes, typically containing HCO_3^- concentrations of 30 to 35 mM. This rapid correction is particularly effective for life-threatening acid-base disturbances.

However, the speed of correction carries risks. Rapid pH normalization, particularly with intermittent hemodialysis, may be associated with adverse effects,[26] including intradialytic alkalosis and osmotic disequilibrium, particularly in patients with severe or chronic acidemia.[21,26] Conversely, continuous renal replacement therapy and prolonged intermittent methods provide gradual, continuous pH correction while requiring prolonged vascular access and anticoagulation.

We suggest starting using continuous renal replacement therapy (or low-flow low-dose prolonged intermittent kidney replacement therapy if available) in hemodynamically unstable patients with a dose from 25 to 30 mL/kg/h. In hemodynamically stable patients, we suggest using intermittent hemodialysis with a moderate flow (200-300 mL/min) and dialysate rate (200-300 mL/min) with a HCO_3^- buffer concentration of 15 to 20 mM more than the patient's plasma HCO_3^- concentration, not exceeding 35 mM, and reassessing every 2 to 4 hours at the beginning of the therapy.

Table 2 compares the buffering delivery in various sodium HCO_3^- scheme and renal replacement settings. Buffering delivery and plasma HCO_3^- change are different because blood HCO_3^- levels will be dependent on the distribution volume, HCO_3^- conversion to CO_2, distribution across cells membrane, HCO_3^- loss in effluent, and proton generation.

It should be noted that RRT carries important risks. It requires central venous access and may lead to a range of complications: hemodynamic instability (eg, volume shifts, hypotension), arrhythmias, electrolytes imbalances, hypothermia, altered drug pharmacokinetics, nutrient losses, vascular access-related complications, and both regional and systemic anticoagulation-associated risks such as bleeding or thrombosis.[21,26-30] These risks must be weighed against the expected benefits, particularly when metabolic derangement is the primary indication. In major RCTs comparing early vs delayed RRT initiation in critically ill patients with moderate to severe AKI, early initiation did not improve clinical outcomes. Notably, all trials included a pH threshold of 7.15 to 7.20 among criteria for RRT initiation, although no evidence-supported threshold exists for the optimal pH trigger for RRT.[26,28-30]

The Sodium Bicarbonate Therapy for Patients With Severe Metabolic Acidaemia in the Intensive Care Unit (BICAR-ICU) trial was an open-label, multiple-center RCT that evaluated the impact of 4.2% IV sodium HCO_3^- in critically ill patients with severe metabolic acidemia across 26 French ICUs.[4] IV sodium HCO_3^- infusion targeting the arterial pH of > 7.30 did not affect the primary composite outcome significantly (all-cause mortality at day 28, the presence of at least 1 organ failure at day 7, or both) in the overall population, but was associated with a reduction in both

the primary outcome and 28-day mortality in a prespecified subgroup of patients with moderate to severe AKI. Similarly, in the BICAR-ICU 2 trial targeting severe metabolic acidemia and moderate to severe AKI, sodium HCO_3^- therapy did not reduce 90-day mortality, but was associated with less use of RRT without an increase in adverse events. Although RRT initiation criteria were standardized in both RCTs, the open-label design, as in many RCTs performed in the ICU, left room for potential bias in the decision to initiate RRT. These trials underscore the safety of hypertonic sodium HCO_3^- infusion in critically ill patients and suggest its potential to delay or obviate the need for RRT in certain patients. Two additional RCTs currently are underway. The ongoing Multicentre Evaluation of Sodium Bicarbonate in Acute Kidney Injury in Critical Care (MOSAICC)[11] and Sodium Bicarbonate for Metabolic Acidosis in the ICU (SODa-BIC)[12] trials are investigating further HCO_3^- therapy in critically ill patients with moderate or severe metabolic acidemia.[31,32]

In the clinical practice, RRT therefore is not considered and automatic response to severe metabolic acidemia. Rather, IV sodium HCO_3^- may serve as a safe temporizing measure for patients with severe metabolic acidosis and moderate to severe AKI while definitive treatment is undertaken, with RRT reserved for patients with acidemia that remains refractory or in whom other indications emerge.

What Precautions Should We Take When We Administer Sodium HCO_3^-?

IV sodium HCO_3^- administration is associated with several important physiologic effects that warrant careful observation. First, sodium HCO_3^- infusion inevitably results in fluid and sodium loading, which may be problematic in patients with impaired cardiac function or limited volume tolerance, particularly when higher doses are administered. Second, sodium HCO_3^- can alter electrolyte balance, most notably by reducing ionized calcium concentration. Ionized hypocalcemia is among the most clinically significant adverse effects of HCO_3^- therapy and has been reported consistently in both experimental and clinical settings.[7,8,33] The reduction in ionized calcium may result in a combination of increased binding affinity to albumin in the setting of alkalemia and direct chelation of calcium by HCO_3^-. Ionized calcium plays a critical role in vascular tone and myocardial contractility[7]; further reduction in bioavailable calcium may exacerbate[32] hemodynamic instability in patients who already are compromised physiologically. In this context, correction of hypocalcemia should be considered when administering sodium HCO_3^-.

Overcorrection of acidemia may result in rebound alkalemia, particularly in patients with transient acid-base disturbances. A systematic review of 12 studies examining the biochemical effects of IV sodium HCO_3^- in acute metabolic acidosis reported consistent increases in arterial pH, serum HCO_3^-, base excess, serum sodium, and P_{CO_2} during the administration of sodium HCO_3^-.[34,35] The SODa-BIC pilot randomized trial showed that overcorrection did not occur when sodium HCO_3^- was given as a continuous infusion, along with dose adjustments guided by arterial blood gas measurements.[31] Table 3 summarizes randomized clinical studies that have examined sodium HCO_3^- in patients with metabolic acidemia, excluding studies focused on diabetic ketoacidosis.[4,9,29,31,36-39]

Concerns also have been raised regarding the production of CO_2 and its potential to worsen intracellular acidosis. In theoretical terms, HCO_3^- buffering produces CO_2, which readily diffuses across cell membranes and may combine with intracellular water to form carbonic acid. Experimental and in vitro studies demonstrated transient decreases in intracellular pH after HCO_3^- exposure.[40-44] However, data from human healthy volunteers suggested that these changes were modest,[41] and the clinical relevance of intracellular acidification in critically ill patients remains uncertain.

When Sodium HCO_3^- May Be Inappropriate or Harmful

Life-threatening electrolytes disturbances with associated kidney failure require urgent initiation of RRT. In such scenarios, sodium HCO_3^- infusion may offer only brief physiologic stabilization while RRT is being arranged (Fig 1).[23] Sodium HCO_3^- also may worsen hypoxemia in patients with severe pulmonary edema and anuria because of fluid and sodium loading. Risk-benefit balance then must be assessed carefully, especially in nonintubated patients; in addition, hypokalemia should be corrected before any administration of sodium HCO_3^-.

Specific clinical contexts where the risk-benefit balance is less favorable include the following:

- Diabetic ketoacidosis: Sodium HCO_3^- has been proposed to mitigate severe acidemia and potentially

TABLE 3] Summary of Randomized Studies on $NaHCO_3$ Administration in Metabolic Acidosis (Excluding Diabetic Ketoacidosis Studies)

Study	Design	No. of Patients	Mechanical Ventilation	$NaHCO_3$ Administration	Primary Outcome	Key Secondary Outcomes
Cooper et al[31] (1990)	Lactic acidosis crossover vs hypertonic saline	14	14 (100%)	0.9 M of 2 mM/kg for 15 min	No improvement in hemodynamics	↑ pH ↑ $Paco_2$ ↓ ionized calcium
Mathieu et al[36] (1991)	Lactic acidosis crossover vs hypertonic saline	10	10 (100%)	0.7 M of 1 mM/kg for 30 min	No improvement in hemodynamics	↑ pH ↑ $Paco_2$ ↓ ionized calcium
Mark et al[37] (1993)	Mild MA (intraoperative) vs saline	40	40 (100%)	0.86 M, base deficit × 0.2 × BW for 30 s	Decrease in cardiac output by 8% and in oxygen consumption by 11% with sodium HCO_3^-	↑ pH ↑ $Paco_2$
Leung et al[38] (1994)	Mild MA (intraoperative) vs Carbicarb	36	18 (100%)	1 M, base deficit × 0.3 × BW for 30 s	Rapid correction of pH and base deficit	Systemic use of lactate increased with c Carbicarb
Hoste et al[39] (2005)	Mild MA vs THAM	18	7 (70%)	1 M, base deficit × 0.3 × BW for 60 min	Increased pH and HCO_3^- in both groups	↑ sodium ↓ potassium
Serpa Neto et al[29] (2023), SODa-BIC pilot	Moderate MA (pH ≤ 7.30) vs no sodium HCO_3^-	30	24 (80%)	600 mEq $NaHCO_3$-, 100 mL/h up to 5 h to target pH > 7.30	Feasibility and No. of hours alive and free of vasopressors at day 7	HCO_3^- group: 132 h (median; IQR, 86-139 h) alive and free of vasopressors vs 97 h (median; IQR, 69-132 h) in the control group
Jaber et al[4] (2018), BICARICU 1 trial	Severe MA (pH ≤ 7.20, HCO_3^- ≤ 20) vs no sodium HCO_3^-	389	324 (83%)	4.2% $NaHCO_3$, 125-250 mL bolus, titrated up to 28 d	Primary composite (28-d mortality plus organ failure at day 7): no overall difference	In AKI subgroup: higher survival, less RRT, faster pH correction
Jung et al[9] (2025), BICARICU 2 trial	Severe MA (pH < 7.20, HCO_3^- < 20) vs no sodium HCO_3^-	629	472 (75%)	4.2% $NaHCO_3$, titrated to pH ≥ 7.30 up to 28 d	Primary: 90-d mortality: no overall difference	Less RRT, 50% less frequent bloodstream infection

AKI = acute kidney injury; BICAR-ICU = Sodium Bicarbonate Therapy for Patients With Severe Metabolic Acidaemia in the Intensive Care Unit; BW = body weight; HCO_3^- = bicarbonate; IQR = interquartile range; MA = metabolic acidosis; $NaHCO_3$ = sodium bicarbonate; RRT = renal replacement therapy; SODa-BIC = Sodium Bicarbonate for Metabolic Acidosis in the ICU; THAM = Tris hydroxymethyl aminomethane.

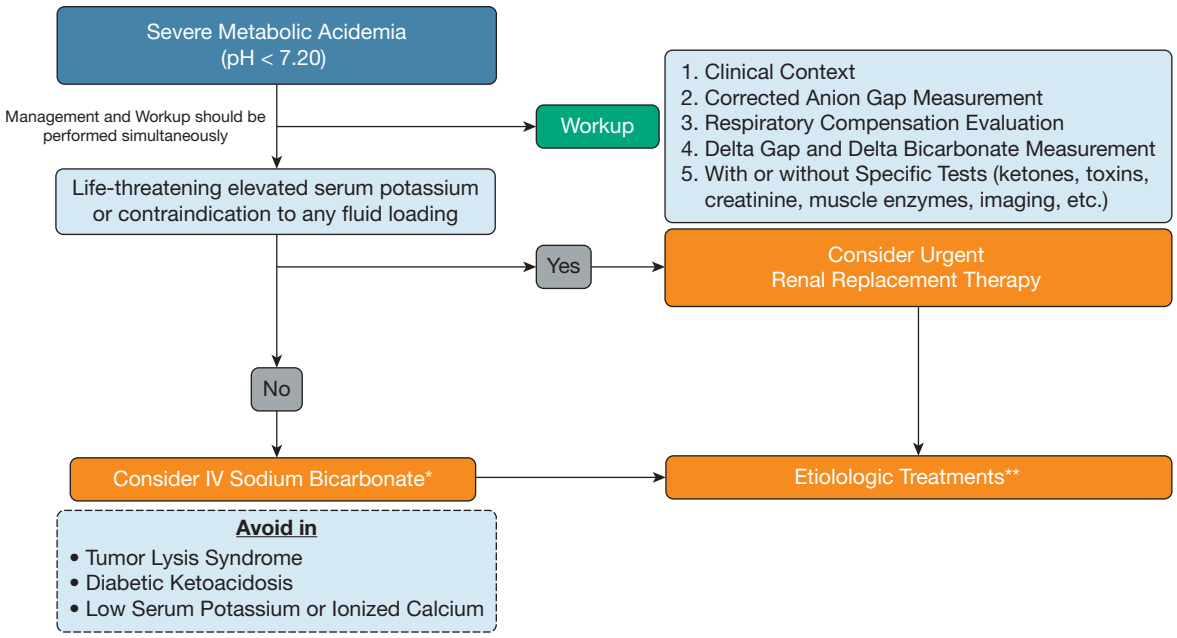

Figure 1 – *Flow diagram showing the authors' process for treating a critically ill patient with severe metabolic acidemia.* [a]*The optimal dose and duration of sodium bicarbonate infusion remain unestablished. In the Sodium Bicarbonate Therapy for Patients With Severe Metabolic Acidaemia in the Intensive Care Unit (BICAR-ICU) 1 and BICAR-ICU 2 trials, 125 to 250 mL of 4.2% sodium bicarbonate was administered over 60 to 120 minutes, corresponding to 250 to 500 mEq.*[3,4] *Other studies have proposed using a lower dose, such as 60 mEq/h as a continuous infusion in 5% dextrose.*[32] [b]*Etiologic treatments may include renal replacement therapy (extracorporeal removal of dialysable toxins, fulminant cell lysis, refractory severe metabolic acidosis, pulmonary edema, uremic syndrome, persistent anuria); fomepizole (alcohol poisoning); N-acetylcysteine (acetaminophen poisoning); insulin (diabetic ketoacidosis); thiamine, glucose, and hydration (nondiabetic ketoacidosis); rasburicase (tumor lysis syndrome); and shock resuscitation and etiologic treatment of shock (lactic acidosis).*

improve insulin responsiveness in diabetic ketoacidosis. Although approximately 30% of intensivists report administering sodium HCO_3^- at low pH thresholds,[42] a 2011 systematic review concluded that HCO_3^- therapy does not shorten the duration of acidosis, ketosis, or hyperglycemia significantly and is associated with a higher risk of hypokalemia, which potentially can worsen cardiac and neuromuscular complications.[43,44]

- Tumor lysis syndrome with AKI: Alkalinizing the urine with sodium HCO_3^- historically has been used to increase uric acid solubility and to facilitate its excretion. However, this practice may lead to precipitation of calcium phosphate crystals in renal tubules, particularly in the context of hyperphosphatemia. With the availability of uricase agents such as rasburicase, sodium HCO_3^- is no longer recommended in the management of tumor lysis syndrome complicated by AKI.[45]
- Low ionized calcium: Situations like massive transfusion, acute pancreatitis, rhabdomyolysis, tumor lysis syndrome, malnutrition, and deficiencies in parathyroid hormone or vitamin D are common causes of hypocalcemia. In these cases, sodium HCO_3^- may reduce ionized calcium further by increasing calcium binding to albumin and promoting calcium carbonate formation. IV calcium supplementation should be administered before any infusion of sodium HCO_3^-.

Other non-CO_2-producing buffers, such as Tris hydroxymethyl aminomethane, have been described, but are used rarely in contemporary clinical practice.

Should We Manipulate Minute Ventilation in Patients With Severe Metabolic Acidemia Who Are Receiving Invasive Mechanical Ventilation?

Current evidence does not determine conclusively whether increasing minute ventilation is advantageous or detrimental for mechanically ventilated patients experiencing severe metabolic acidosis. Contemporary clinical practice prioritizes lung-protective ventilation, because excessive minute ventilation inevitably elevates mechanical power, a parameter associated with mortality. Although augmenting minute ventilation can assist in limiting further declines in arterial pH, this strategy must be balanced against the risks of ventilator-induced lung injury and hemodynamic compromise. In our practice, we do not aim to normalize pH through aggressive ventilatory manipulation.

For patients who require intubation in the setting of severe metabolic acidemia, particular attention should be paid to the transition from spontaneous to controlled ventilation. Immediately after intubation, we aim to approximate the patient's preintubation P_{CO_2} levels by aligning the initial ventilator settings with the patient's preintubation respiratory pattern. This typically requires matching the preintubation respiratory rate and using tidal volumes of 8 to 10 mL/kg of predicted body weight for an initial short period to mitigate the risk of abrupt rises in Pa_{CO_2} and further pH decline. Subsequently, ventilator settings are tailored with close attention to mechanical power or its principal components (respiratory rate, tidal volume, driving pressure) that may change with minute ventilation. In this context, ventilatory support is used as an adjunct to, rather than a substitute for, other interventions.

How We Use Sodium HCO_3^- in Patients With Metabolic Acidosis at the Bedside

In the patient whose case we present herein, severe metabolic acidemia (pH, 7.19; HCO_3^-, 12 mM; base excess, –14 mM) occurred in the setting of septic shock and AKI without evidence of diabetic ketoacidosis or tumor lysis syndrome. In this context, we considered sodium HCO_3^- as a temporizing strategy to raise blood pH while definitive treatment of the underlying cause was being undertaken. From a Stewart approach perspective, the acid-base disturbance in this patient was characterized by a reduced strong ion difference, which provides a physiologic rationale for administering sodium HCO_3^-, a solution with a large strong ion difference, to increase plasma strong ion difference and thereby raise arterial pH (Fig 1). In our practice, sodium HCO_3^- administration should be preceded by correction of electrolyte abnormalities that may exacerbate hemodynamic instability, particularly hypokalemia and low ionized calcium. In the patient presented herein, this was not necessary.

The metabolic acidemia in this patient was not the result of gastrointestinal HCO_3^- loss. In such instances, we do not use isotonic sodium HCO_3^-. Instead, given a low pH and ongoing shock status, we use hypertonic sodium HCO_3^-. Specifically, we may administer 250 mL of 4.2% sodium HCO_3^- (premade or equivalent) over 60 minutes, with close monitoring of arterial blood gases, electrolytes, and hemodynamics. If acidemia persists, a second 250-mL infusion may be administered, aiming to raise arterial pH approximately 7.30, rather than to normalize pH. Consistent with the BICAR-ICU and BICAR-ICU 2 trials, the total dose generally is limited to a maximum of 1,000 mL (4.2%) within 24 hours. The response to sodium HCO_3^- should be reassessed frequently, and RRT is considered if acidemia remains refractory, because the metabolic acidosis was complicated by severe AKI.

Conclusions

In the case of a patient whose such as the one presented herein, we would infuse sodium HCO_3^- to raise and maintain the arterial pH of > 7.30, which mitigates the physiologic consequences of metabolic acidemia. In this context, sodium HCO_3^- is used as a temporizing strategy while definitive treatment of the underlying cause, such as antibiotics, source control, and hemodynamic management, is undertaken, with the aim of delaying or potentially avoiding RRT. This approach reflects our practice in selected critically ill patients with severe metabolic acidemia and AKI in whom metabolic derangement alone does not mandate immediate RRT.

Funding/Support

M. F. has been funded through grants provided by the Montpellier Université d'Excellence Young Investigators PhD Award 2022, the Societe de Reanimation de Langue Française, and the Fulbright France Foundation.

Financial/Nonfinancial Disclosures

The authors have reported to *CHEST* the following: S. J. reports receiving consulting fees from Drager, Medtronic, Mindray, Fresenius, Baxter, and Fisher & Paykel. None declared (B. J., M. F., T. F., J. A. K.).

Acknowledgments

Role of sponsors: The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

References

1. Jung B, Rimmele T, Le Goff C, et al. Severe metabolic or mixed acidemia on intensive care unit admission: incidence, prognosis and administration of buffer therapy. A prospective, multiple-center study. *Crit Care*. 2011;15(5):R238.
2. Jung B, Martinez M, Claessens Y-E, et al. Diagnosis and management of metabolic acidosis: guidelines from a French expert panel. *Ann Intens Care*. 2019;9(1):92.
3. Jung B, Huguet H, Molinari N, Jaber S. Sodium bicarbonate for the treatment of severe metabolic acidosis with moderate or severe acute kidney injury in the critically ill: protocol for a randomised clinical trial (BICARICU-2). *BMJ Open*. 2023;13(8):e073487.
4. Jaber S, Paugam C, Futier E, et al. Sodium bicarbonate therapy for patients with severe metabolic acidaemia in the intensive care unit

(BICAR-ICU): a multicentre, open-label, randomised controlled, phase 3 trial. *Lancet*. 2018;392(10141):31-40.

5. Kurtz I, Kraut J, Ornekian V, Nguyen MK. Acid-base analysis: a critique of the Stewart and bicarbonate-centered approaches. *AJP Ren Physiol*. 2008;294(5):F1009-F1031.
6. Mochizuki K, Fujii T, Paul E, Anstey M, Pilcher DV, Bellomo R. Early metabolic acidosis in critically ill patients: a binational multicentre study. *Crit Care Resusc*. 2021;23(1):67-75.
7. Kimmoun A, Ducrocq N, Sennoun N, et al. Efficient extra- and intracellular alkalinization improves cardiovascular functions in severe lactic acidosis induced by hemorrhagic shock. *Anesthesiology*. 2014;120(4):926-934.
8. Kraut JA, Madias NE. Treatment of acute metabolic acidosis: a pathophysiologic approach. *Nat Rev Nephrol*. 2012;8(10):589-601.
9. Jung B, Jabaudon M, De Jong A, et al. Sodium bicarbonate for severe metabolic acidemia and acute kidney injury: the BICARICU-2 randomized clinical trial. *JAMA*. 2025;334(22):2000-2010.
10. Blank SP, Blank RM, Laupland KB, et al. Sodium bicarbonate administration for metabolic acidosis in the intensive care unit: a target trial emulation. *Intensive Care Med*. 2025;51(6):1-9.
11. Multicentre evaluation of sodium bicarbonate in acute kidney injury in critical care (MOSAICC). International Standard Randomised Controlled Trial identifier: ISRCTN14027629. Updated October 24, 2025. https://www.isrctn.com/ISRCTN14027629
12. Sodium bicarbonate for metabolic acidosis in the ICU (SODa-BIC). ClinicalTrials.gov identifier: NCT05697770. Updated March 27, 2026. http://clinicaltrials.gov/ct2/show/NCT05697770
13. Engel K, Dell RB, Rahill WJ, Denning CR, Winters RW. Quantitative displacement of acid-base equilibrium in chronic respiratory acidosis. *J Appl Physiol*. 1968;24(3):288-295.
14. Adrogué HJ, Madias NE. Secondary responses to altered acid-base status: the rules of engagement. *J Am Soc Nephrol*. 2010;21(6):920-923.
15. Berend K, Vries APJ de. Physiological approach to assessment of acid–base disturbances. *N Engl J Med*. 2014;371(15):1434-1445.
16. Rodríguez-Villar S, Kraut JA, Arévalo-Serrano J, et al. Systemic acidemia impairs cardiac function in critically Ill patients. *EClinicalMedicine*. 2021;37:100956.
17. Ibrahim E el, din S, McLellan SA, Walsh TS. Red blood cell 2,3-diphosphoglycerate concentration and in vivo P50 during early critical illness. *Crit Care Med*. 2005;33(10):2247-2252.
18. Kraut JA, Madias NE. Lactic acidosis. *N Engl J Med*. 2014;371(24):2309-2319.
19. Reaich D, Graham KA, Channon SM, et al. Insulin-mediated changes in PD and glucose uptake after correction of acidosis in humans with CRF. *Am J Physiol*. 1995;268(1 pt 1):E121-E126.
20. Kellum JA, Song M, Li J. Science review: extracellular acidosis and the immune response: clinical and physiologic implications. *Crit Care*. 2004;8(5):331-336.
21. Ostermann M, Bagshaw SM, Lumlertgul N, Wald R. Indications for and timing of initiation of KRT. *Clin J Am Soc Nephrol*. 2023;18(1):113-120.
22. Ostermann M, Basu RK, Mehta RL. Acute kidney injury. *Intensive Care Med*. 2023;49(2):219-222.
23. Mullins ME, Kraut JA. The role of the nephrologist in management of poisoning and intoxication: core curriculum 2022. *Am J Kidney Dis*. 2022;79(6):877-889.
24. Yagi K, Fujii T, Kageyama A, Takagi T, Ikeda J, Uezono S. The effects of early-phase, low- or standard-intensity continuous renal replacement therapy on acid-base control and clinical outcomes: an observational study. *Blood Purif*. 2024;53(9):716-724.
25. Wald R, Gaudry S, da Costa BR, et al. Initiation of continuous renal replacement therapy versus intermittent hemodialysis in critically ill patients with severe acute kidney injury: a secondary analysis of STARRT-AKI trial. *Intensive Care Med*. 2023;49(11):1305-1316.
26. Gaudry S, Hajage D, Schortgen F, et al. Initiation strategies for renal-replacement therapy in the intensive care unit. *N Engl J Med*. 2016;375(2):122-133.
27. Kovvuru K, Velez JCQ. Complications associated with continuous renal replacement therapy. *Semin Dial*. 2021;34(6):489-494.
28. The STARRT-AKI Investigators. Timing of initiation of renal-replacement therapy in acute kidney injury. *N Engl J Med*. 2020;383(3):240-251.
29. Barbar SD, Clere-Jehl R, Bourredjem A, et al. Timing of renal-replacement therapy in patients with acute kidney injury and sepsis. *N Engl J Med*. 2018;379(15):1431-1442.
30. Gaudry S, Hajage D, Martin-Lefevre L, et al. Comparison of two delayed strategies for renal replacement therapy initiation for severe acute kidney injury (AKIKI 2): a multicentre, open-label, randomised, controlled trial. *Lancet*. 2021;397(10281):1293-1300.
31. Serpa Neto A, Fujii T, McNamara M, et al. Sodium bicarbonate for metabolic acidosis in the ICU: results of a pilot randomized double-blind clinical trial. *Crit Care Med*. 2023;51(11):e221-e233.
32. Serpa Neto A, McNamara M, Cooper J, et al. Protocol summary and statistical analysis plan for the sodium bicarbonate for metabolic acidosis in the intensive care unit (SODa-BIC) trial. *Crit Care Resusc*. 2025;27(2):100108.
33. Cooper DJ, Walley KR, Wiggs BR, Russell JA. Bicarbonate does not improve hemodynamics in critically ill patients who have lactic acidosis. A prospective, controlled clinical study. *Ann Intern Med*. 1990;112(7):492-498.
34. Fujii T, Udy A, Licari E, Romero L, Bellomo R. Sodium bicarbonate therapy for critically ill patients with metabolic acidosis: a scoping and a systematic review. *J Crit Care*. 2019;51:184-191.
35. Yagi K, Fujii T. Management of acute metabolic acidosis in the ICU: sodium bicarbonate and renal replacement therapy. *Crit Care*. 2021;25(1):314.
36. Mathieu D, Neviere R, Billard V, Fleyfel M, Wattel F. Effects of bicarbonate therapy on hemodynamics and tissue oxygenation in patients with lactic acidosis: a prospective, controlled clinical study. *Crit Care Med*. 1991;19(11):1352-1356.
37. Mark NH, Leung JM, Arieff AI, Mangano DT. Safety of low-dose intraoperative bicarbonate therapy: a prospective, double-blind, randomized study. The study of perioperative ischemia (SPI) research group. *Crit Care Med*. 1993;21(5):659-665.
38. Leung JM, Landow L, Franks M, et al. Safety and efficacy of intravenous Carbicarb in patients undergoing surgery: comparison with sodium bicarbonate in the treatment of mild metabolic acidosis. SPI research group. Study of perioperative ischemia. *Crit Care Med*. 1994;22(10):1540-1549.
39. Hoste EA, Colpaert K, Vanholder RC, et al. Sodium bicarbonate versus THAM in ICU patients with mild metabolic acidosis. *J Nephrol*. 2005;18(3):303-307.
40. Ritter JM, Doktor HS, Benjamin N. Paradoxical effect of bicarbonate on cytoplasmic pH. *Lancet*. 1990;335(8700):1243-1246.
41. Nakashima K, Yamashita T, Kashiwagi S, Nakayama N, Kitahara T, Ito H. The effect of sodium bicarbonate on CBF and intracellular pH in man: stable Xe-CT and 31P-MRS. *Acta Neurol Scand Suppl*. 1996;166:96-98.
42. Jozwiak M, Hayes MM, Canet E, et al. Management of diabetic keto-acidosis in adult patients admitted to intensive care unit: an ESICM-endorsed international survey. *Crit Care*. 2024;28(1):408.
43. Dhatariya KK. the Joint British Diabetes Societies for Inpatient Care. The management of diabetic ketoacidosis in adults—an updated guideline from the Joint British Diabetes Society for Inpatient Care. *Diabet Med*. 2022;39(6):e14788.
44. Duhon B, Attridge RL, Franco-Martinez AC, Maxwell PR, Hughes DW. Intravenous sodium bicarbonate therapy in severely acidotic diabetic ketoacidosis. *Ann Pharmacother*. 2013;47(7-8):970-975.
45. Howard SC, Jones DP, Pui C-H. The tumor lysis syndrome. *N Engl J Med*. 2011;364(19):1844-1854.