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# Long-Term Outcome of Severe Metabolic Acidemia in ICU Patients, a BICAR-ICU Trial Post Hoc Analysis

**OBJECTIVES:** Long-term prognosis of ICU survivors is a major issue. Severe acidemia upon ICU admission is associated with very high short-term mortality. Since the long-term prognosis of these patients is unknown, we aimed to determine the long-term health-related quality of life and survival of these patients.

**DESIGN:** Post hoc analysis of a multicenter, randomized, controlled trial.

**SETTING:** Twenty-six French ICUs.

**PATIENTS:** Day 28 critically ill survivors admitted with severe acidemia and enrolled in the BICAR-ICU trial.

**INTERVENTION:** Sodium bicarbonate versus no sodium bicarbonate infusion according to the randomization group.

**MEASUREMENTS AND MAIN RESULTS:** The primary outcome was health-related quality of life (HRQoL) measured with the 36-item Short Form Health Survey and the EuroQol 5-D questionnaires. Secondary outcomes were mortality, end-stage renal disease treated with renal replacement therapy or renal transplantation, place of residence, professional status, and ICU readmission. HRQoL was reduced with no significant difference between the two groups. HRQoL was reduced particularly in the role-physical health domain ( $64/100 \pm 41$  in the control group and  $49/100 \pm 43$  in the bicarbonate group,  $p = 0.28$ ), but it was conserved in the emotional domains ( $96/100 \pm 19$  in the control group and  $86/100 \pm 34$  in the bicarbonate group,  $p = 0.44$ ). Forty percent of the survivors described moderate to severe problems walking, and half of the survivors described moderate to severe problems dealing with usual activities. Moderate to severe anxiety or depression symptoms were present in one third of the survivors. Compared with the French general population, HRQoL was decreased in the survivors mostly in the physical domains. The 5-year overall survival rate was 30% with no significant difference between groups.

**CONCLUSIONS:** Long-term HRQoL was decreased in both the control and the sodium bicarbonate groups of the BICAR-ICU trial and was lower than the general population, especially in the physical domains.

**KEY WORDS:** acidemia; health-related quality of life; long-term outcome studies; metabolic acidosis; sodium bicarbonate

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The frequency of metabolic acidemia, a common condition in critically ill patients, ranges from 14% to 64% and is associated with a mortality rate as high as 57%, above all when the pH remains lower than 7.20 (1). Very low pH, responsible for an acidotic cellular environment, is associated with organ dysfunction, including decreased myocardial contractility and cardiac output, hypotension, and impairment in glucose regulation and in the immune response (2–4). Severe acidemia is indeed a major sign of severity in critically ill patients (1, 5, 6). Recently, the BICAR-ICU trial compared sodium



**Question:** What is the survival and long-term health-related quality of life of severe acidemia patients whether they were treated with sodium bicarbonate or not?

**Findings:** At 3 years, the survival rate was 30%. The quality of life was reduced, especially in the role-physical health domain with no significant difference between patients treated or not with sodium bicarbonate. Moderate to severe anxiety or depression symptoms were present in one third of the survivors.

**Meanings:** Long-term health-related quality of life was decreased in both the control and the sodium bicarbonate groups of the BICAR-ICU trial.

bicarbonate infusion versus placebo treatment in critically ill patients with severe metabolic acidemia with pH equal to or lower than 7.20 (6). Despite a lack of benefit in the population as a whole, the infusion of sodium bicarbonate in the preplanned stratum of patients with moderate to severe acute kidney injury (AKI) resulted in fewer deaths by day 28 (7).

Although ICU survivors maintain lower health-related quality of life (HRQoL) than the general population (8, 9), there are no studies examining HRQoL and the long-term prognosis of patients with severe metabolic acidemia. BICAR-ICU trial survivors therefore represent a privileged population to analyze the long-term characteristics of severe metabolic acidemia. We hypothesized that HRQoL in this high-risk population would be inferior to the general population. We aimed to evaluate quality of life in ICU survivors admitted with severe metabolic acidemia and to determine whether sodium bicarbonate infusion would be associated with long-term quality of life and long-term prognosis.

## METHODS

### Study Design

We conducted a post hoc analysis of the BICAR-ICU trial on quality of life and prognosis of the BICAR-ICU trial survivors (6). The BICAR-ICU trial was a French

multicenter, open-label, randomized, controlled, phase 3 trial whose aim was to evaluate whether sodium bicarbonate infusion would improve clinical outcome at 28 days in critically ill patients with severe metabolic acidemia. The study protocol of BICAR-ICU and the statistical analysis plan were approved for all centers by a central ethics committee (Comité de Protection des Personnes Sud-Est IV, Montpellier, France; EudraCT, number 2014-000245-73). Furthermore, our post hoc analysis was approved by the institutional review board at Montpellier University Hospital (IRB-MTP\_2020\_05\_202000462). Data were analyzed anonymously. Clinical investigations were conducted in accordance with both French law and the 2008 Declaration of Helsinki.

### Patients From the BICAR-ICU Trial

From May 5, 2015, to May 7, 2017, 394 critically ill patients admitted within 48 hours to the participating ICUs with severe acidemia ( $\text{pH} \leq 7.20$ ,  $\text{Paco}_2 \leq 45$  mm Hg and sodium bicarbonate concentration  $\leq 20$  mmol/L) and with a total Sequential Organ Failure Assessment score of 4 or more or an arterial lactate concentration of 2 mmol/L or more were included in the BICAR-ICU trial. Eligible patients were randomly assigned to receive either sodium bicarbonate infusion (bicarbonate group) or no sodium bicarbonate infusion (control group).

### Outcomes

The primary outcome for this post hoc analysis was HRQoL. From April 4, 2020, to October 26, 2020, we performed an evaluation of HRQoL by using the Medical Outcomes Study 36-item Short Form Health Survey (SF-36) and the EuroQol 5-D (EQ-5D) (**Supplemental Digital Content 1**, <http://links.lww.com/CCM/H218>; and **Supplemental Digital Content 2**, <http://links.lww.com/CCM/H219>). SF-36 derives a total score from eight different domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and -mental health. The score in each domain ranges from 0 to 100, 100 representing the best score with a five-point difference considered to be clinically significant in adequacy with previous intensive care studies (10–12). Patients were compared between BICAR-ICU groups and, as a secondary endpoint, with the French general

population (13). EQ-5D comprises two measures. First, a self-reported description of health problems according to a 5D classification: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain is evaluated through a question with five responses: no problems, slight problems, moderate problems, severe problems, or extreme problems. Second, the patients self-rated their health status using a visual analogue scale graduated from 0 (worst health status) to 100 (best health status) (14). SF-36 and EQ-5D are both standardized tools validated in France with high validity in critically ill patients that can be assessed by telephone interview. Furthermore, the mean score of general population in each domain of the SF-36 is reported in the French user manual and was used in the present post hoc study (15, 16).

To assess HRQoL, patients were contacted by telephone or e-mail to request their consent to participate. If the patient did not respond, we attempted to contact him through his general practitioner or his trusted person. If there was no general practitioner and no trusted person, we consulted the open-source French public death register. If the patient's situation was still unknown on October 26, 2020, he was considered lost to follow-up.

Secondary outcomes also included mortality, end-stage renal disease treated with renal replacement therapy or renal transplantation, place of residence, professional status, and ICU readmission. Mortality was censored on October 26, 2020. As the precise chronic kidney disease stage could not be ascertained by telephone interviews, we gathered data concerning the current need for renal replacement therapy via dialysis or transplantation.

The assessor was trained by applying the French SF-36 user guide and the EQ-5D questionnaire via simulation-based situations. Questionnaires were performed by telephone interview, and data concerning secondary outcomes were collected.

## Statistical Analysis

Baseline characteristics in each study group were expressed as numbers and percentages for categorical variables and as means and SD or medians and interquartile range for continuous variables, as appropriate. Qualitative variables were compared using the chi-square test or Fisher test, as appropriate.

The different domains of the SF-36 score were compared using the Mann-Whitney *U* test according to the group of treatment. For comparisons of EQ-5D, we used a Fisher test.

Survival time was presented with a Kaplan-Meier curve and compared with a log-rank test. For these analyses, data of patients who were lost to follow-up were censored at 28-day survival. All tests were two-sided, and *p* values less than 0.05 were considered statistically significant. Statistical analyses were performed using SAS software (SAS Enterprise Version 8.2; SAS Institute, Cary, NC).

## RESULTS

### Population and Characteristics

From May 5, 2015, to May 7, 2017, 389 critically ill patients with severe metabolic acidemia were included in the intention-to-treat analysis of BICAR-ICU (194 and 195 patients in the control group and in the bicarbonate group, respectively). One hundred ninety-one patients were deceased by day 28 after randomization (BICAR-ICU patient and BICAR-ICU survivor characteristics are respectively presented in **Supplemental Digital Content 3**, <http://links.lww.com/CCM/H220>; and **Supplemental Digital Content 4**, <http://links.lww.com/CCM/H221>). Baseline characteristics of BICAR-ICU survivors from control and intervention groups were not significantly different. Of these 198 BICAR-ICU survivors, 42 were lost to follow-up, and 82 died. Seventy-four patients were alive at the time of the present study. Among them, 12 patients did not answer the HRQoL questionnaire (9 due to cognitive impairment, 2 declined, and 1 due to language barrier). Thus, 62 patients were included in the HRQoL assessment (30 patients in the control group and 32 patients in the bicarbonate group, respectively) (**Supplemental Fig. 1**, <http://links.lww.com/CCM/H245>; legend, <http://links.lww.com/CCM/H246>).

Long-term survivors with HRQoL assessment (*n* = 62) from the control group and from the bicarbonate group did not differ in age, sex, initial Simple Acute Physiology Score, or comorbidities. Long-term survivors from the bicarbonate group had more moderate to severe AKI at admission (15 [47%] in the bicarbonate group and 7 [23%] in the control group) and were more likely to have required mechanical ventilation (29 [91%] in the bicarbonate group and 24

**TABLE 1.****Baseline Characteristics and Outcome at ICU Discharge in Long-Term Survivors With Health-Related Quality of Life Assessment**

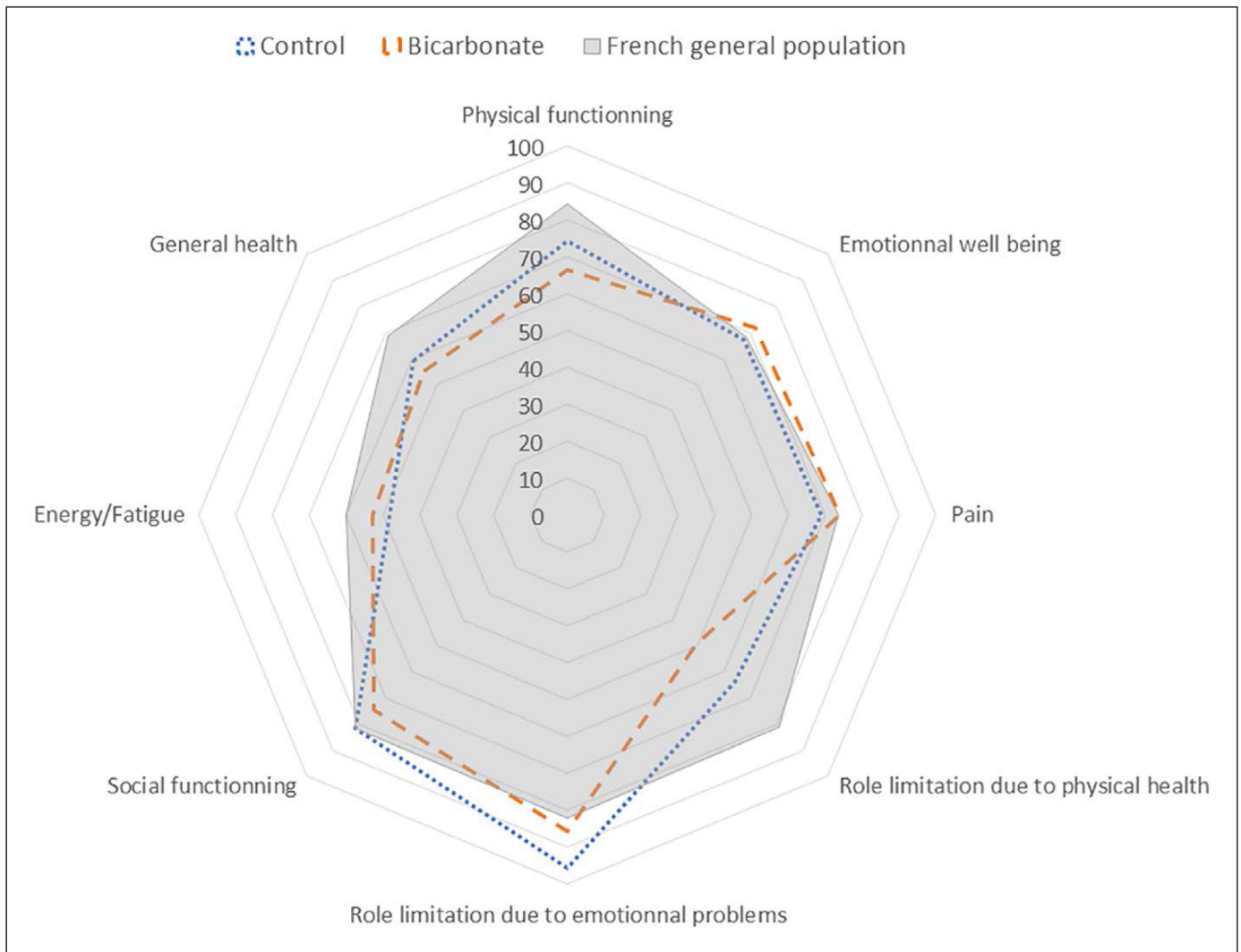
Characteristics at ICU Admission	Control Group (N = 30)	Bicarbonate Group (N = 32)
Age, yr	56 (± 12)	54 (± 15)
Gender, male, n (%)	20 (66)	21 (66)
Body mass index (kg/m <sup>2</sup> )	28 (± 8)	26 (± 4)
Simplified Acute Physiology Score II, median (interquartile range)	50 (42–64)	52 (46–60)
Pre-existing conditions, n (%)		
Smoker	13 (43)	11 (34)
Alcohol abuse	8 (27)	8 (25)
Chronic heart failure	2 (7)	0 (0)
Diabetes mellitus	3 (10)	4 (12)
Hypertension	10 (33)	13 (41)
Ischemic heart disease	3 (10)	2 (6)
Chronic renal insufficiency	4 (13)	2 (6)
Chronic respiratory insufficiency	1 (3)	1 (3)
Cirrhosis	3 (10)	3 (9)
Severe liver insufficiency	4 (13)	3 (9)
Chronic obstructive pulmonary disease	3 (10)	3 (9)
Immunocompromised patient <sup>a</sup>	4 (13)	5 (15)
McCabe class, n (%)		
No severe condition	17 (66)	22 (69)
Fatal at 5 yr	11 (37)	8 (25)
Fatal at 1 yr	2 (7)	2 (6)
Acute Kidney Injury Network stage, n (%)		
AKI 0–1	23 (77)	17 (53)
AKI 2–3	7 (23)	15 (47)
Total Sequential Organ Failure Assessment score at enrollment, median (interquartile range)	9 (7–11)	9 (7–11)
Invasive mechanical ventilation, n (%)	24 (80)	29 (91)
Vasopressor, n (%)	25 (83)	30 (94)
Characteristics at discharge from ICU		
Length of ICU stay, d, median (interquartile range)	9 (4–18)	11 (5–27)
Use of renal replacement therapy during ICU stay, n (%)	10 (33)	11 (34)
Duration of renal replacement therapy during ICU stay, d, median (interquartile range)	4 (2–6)	5 (4–12)
Dependence on dialysis at ICU-discharge, n (%)	3 (10)	3 (9)
Duration of invasive mechanical ventilation, d, median (interquartile range)	3 (2–8)	5 (2–9)
Duration of vasopressor therapy, d, median (interquartile range)	3 (2–4)	4 (3–5)
ICU-acquired infections, n (%)	8 (27)	9 (28)

AKI = acute kidney injury.

The Simplified Acute Physiology Score II is based on 17 variables; score ranges from 0 to 163, with higher scores indicating more severe disease.

<sup>a</sup>Defined as > 1 mg/kg per day prednisone for 30 d or more, HIV infection, biotherapy, or ongoing chemotherapy. Acute Kidney Injury Network (AKIN) stage = stage 1 is serum creatinine increase ≥ 26.5 μmol/L, increase to 1.5–2.0 times from baseline, or urine output < 0.5 mL/kg per hour for 6 hr; stage 2 is serum creatinine increase > 2.0–3.0 times from baseline or urine output < 0.5 mL/kg per hour for 12 hr; stage 3 is serum creatinine increase > 3.0 times from baseline or serum creatinine ≥ 4.0 mg/dL (≥ 354 μmol/L) with an acute increase ≥ 44 μmol/L, the need for renal replacement therapy, or urine output < 0.3 mL/kg per hour for 12 hr. AKIN zero means no kidney injury.





**Figure 1.** Study 36-Item Short Form Health Survey (SF-36) radar chart comparing the bicarbonate group and the control group with the French general population 5 yr after the BICAR-ICU trial. High score indicates better quality of life.

[80%] in the control group). At ICU discharge, three of 30 patients (10%) from the control group and three of 32 patients (9%) from the bicarbonate group were dialysis-dependent (**Table 1**). Regarding baseline characteristics, there was no difference between lost to follow-up patients and patients with HRQoL assessment (**Supplemental Digital Content 5**, <http://links.lww.com/CCM/H222>).

### Primary Outcomes

Regarding long-term HRQoL, there was no difference between the control group and the bicarbonate group in SF-36 and EQ-5D scores. Survivors from both groups experience and largely described diminished general health, chronic fatigue, and energy loss as well

as poor emotional well-being (**Fig. 1**). The mean SF-36 scores in emotional well-being ( $67 \pm 24$  in the control group and  $72 \pm 24$  in the bicarbonate group;  $p = 0.46$ ), pain ( $69 \pm 31$  in the control group and  $74 \pm 33$  in the bicarbonate group;  $p = 0.38$ ), and social functioning ( $82 \pm 22$  in the control group and  $75 \pm 32$  in the bicarbonate group;  $p = 0.66$ ) were not different between the two groups (Fig. 1).

Using EQ-5D, 49 patients (79%) reported no difficulty to self-care (23 [77%] in the control group and 26 [81%] in the bicarbonate group;  $p = 0.31$ ). A total of 24 of 62 patients (39%) reported moderate to severe impaired mobility (10 [33%] in the control group and 14 [44%] in the bicarbonate group), and 30 [48%] reported moderate to severe difficulty with usual activities (13 [43%] in the control group and 17 [53%] in the

**TABLE 2.**  
**Quality of Life Outcome Measures**

EuroQoL 5-D	Control (N = 30)	Bicarbonate (N = 32)	p
Mobility problems, n (%)			0.12
None	19 (63)	12 (37)	
Slight	1 (3)	6 (19)	
Moderate	4 (13)	7 (22)	
Severe	6 (20)	6 (19)	
Unable	0 (0)	1 (3)	
Personal care problems, n (%)			0.31
None	23 (77)	26 (81)	
Slight	5 (17)	2 (6)	
Moderate	1 (3)	3 (9)	
Severe	0 (0)	1 (3)	
Unable	1 (3)	0 (0)	
Pain/discomfort, n (%)			0.24
None	10 (33)	18 (56)	
Slight	7 (23)	2 (6)	
Moderate	7 (23)	6 (19)	
Severe	5 (17)	4 (13)	
Unable	1 (3)	2 (6)	
Usual activities problems, n (%)			0.42
None	14 (47)	10 (31)	
Slight	3 (10)	5 (16)	
Moderate	7 (23)	11 (34)	
Severe	6 (20)	6 (19)	
Unable	0 (0)	0 (0)	
Anxiety/depression, n (%)			0.30
None	14 (47)	17 (53)	
Slight	7 (23)	3 (9)	
Moderate	4 (13)	3 (6)	
Severe	5 (17)	8 (25)	
Unable	0 (0)	2 (6)	

bicarbonate group). A total of 31 of 62 patients (50%) reported at least slight Anxiety/Depression (14 [47%] in the control group and 17 [53%] in the bicarbonate group) (Table 2) (Supplemental Digital Content 6, <http://links.lww.com/CCM/H223>).

### Secondary Outcome

Patients in the control group had a higher mean score in role limitation due to emotional problems compared

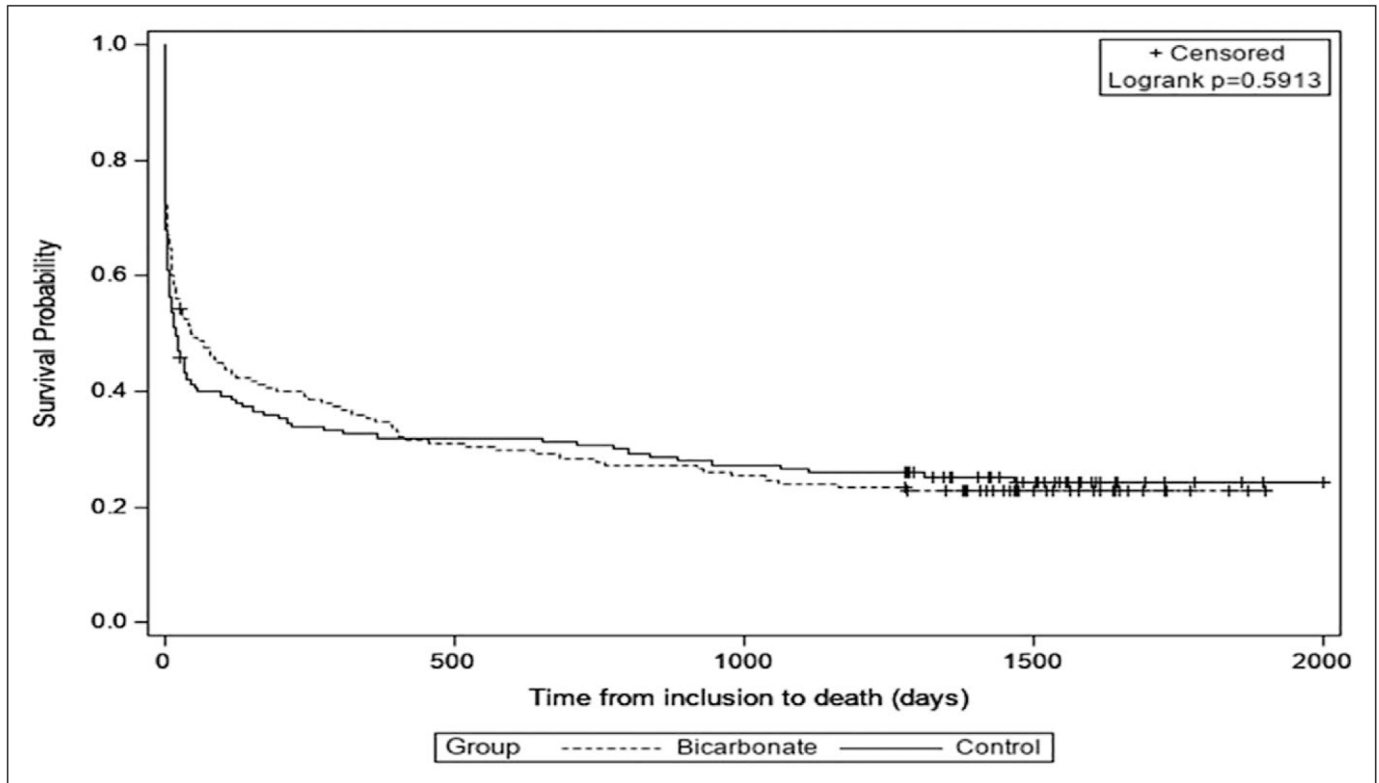
with the French general population, but there was no significant difference between the BICAR-ICU groups (96 ± 19 in the control group and 86 ± 34 in the bicarbonate group;  $p = 0.44$ ). For physical functioning, energy/fatigue, general health, and role limitation due to physical health mean scores were lower than in the general population, particularly in role limitation due to the physical health domain (64 ± 41 in the control group and 49 ± 43 in the bicarbonate group;  $p = 0.28$ ) (Fig. 1).

Overall mortality since enrollment in the BICAR-ICU trial was 70% (273 in 389 patients). Secondary outcomes were not statistically different between the two groups. At the evaluation date, mortality among BICAR-ICU trial survivors was not significantly different (33/90 [37%] in the control group and 49/108 [45%] in the bicarbonate group = 0.32). Twenty in the control group (22%) and 22 in the bicarbonate group (20%) were lost to follow-up, respectively ( $p = 0.75$ ), corresponding to 11% of the total population included in the BICAR-ICU trial. Five-year survival analysis showed no significant difference between the two groups (Fig. 2). In the subgroup of patients with AKIN stage 2 or 3 at admission, mortality did not differ significantly between the two groups (72 [80%] in the control group and 67 [73%] in the bicarbonate group;  $p = 0.07$ ) (Supplemental Digital Content 7, <http://links.lww.com/CCM/H224>). In addition, nine of 62 survivors (14%) changed careers, and 50 of 62 (80%) were able to return home. There was no difference between the two groups ( $p = 0.85$  and  $p = 0.42$  for the professional status and place of living, respectively). Four of 30 survivors (13%) in the control group and one of 32 survivors (3%) in the bicarbonate group needed a kidney transplantation or were on dialysis with no significant difference ( $p = 0.19$ ). Concerning the need for ICU readmission, four of 32 patients (12%) in the bicarbonate group and two of 30 patients (7%) in the control group needed ICU readmission, again with no a significant difference between groups (Table 3).

### DISCUSSION

This study reported the HRQoL and 5-year survival of critically ill patients with severe acidemia at ICU admission. The overall 5-year survival rate was 30% with no statistically significant difference between the control and the bicarbonate groups. Many patients reported problems with usual activities and mobility, but





**Figure 2.** Time to death after inclusion in the BICAR-ICU trial. Survival time was censored at 28 d for lost to follow-up patients. Survival was 29% in both the control group and the bicarbonate group. *Tick marks* indicate censored data.

**TABLE 3.**

**Secondary Endpoints (Quality of Life and Survival Outcome Measures) in Long-Term Survivors With Health-Related Quality of Life Assessment**

Secondary Outcome Measures	Control (N = 30)	Bicarbonate (N = 32)	p
Median time from inclusion to health-related quality of life assessment, mo, median (interquartile range)	50 (44–53)	50 (47–53)	0.69
Transplanted or dialyzed end-stage renal disease, n (%)	4 (13)	1 (3)	0.19
Professional status, n (%)			0.85
Same occupation	3 (10)	3 (9)	
Change of career	4 (13)	5 (16)	
Invalidity	8 (27)	11 (34)	
Unemployed	0 (0)	1 (3)	
Retired	15 (50)	12 (38)	
Place of living, n (%)			0.42
Personal	26 (87)	24 (75)	
Personal with home caregiver	4 (13)	7 (22)	
Health-care facility	0 (0)	0 (0)	
Living facility	0 (0)	1 (3)	
New admission in ICU unit, n (%)			0.67
No	28 (93)	28 (87)	
Yes	2 (7)	4 (12)	

quality of life at 3 years did not differ between the two groups.

In the physical domains, HRQoL was moderately reduced compared with the general population. Many patients reported problems with usual activities and mobility. In the emotional domain, the HRQoL was conserved.

In critically ill patients, compromised quality of life is related to a spectrum of impairment of physical, social, emotional, and neurocognitive functions. Many patients experience a loss in terms of quality of life after critical illness (9, 17). Although there are many studies on acid-base abnormalities in ICU patients, few specific studies focusing on severe metabolic acidemia have been conducted, and to our knowledge, the present study is unique in focusing on long-term HRQoL in this population treated or not with sodium bicarbonate as part of a randomized clinical trial.

As a secondary endpoint, we report reduced long-term HRQoL in physical domains compared with the general population, which was consistent with other studies. Indeed, ICU survivors have reduced long-term HRQoL in sepsis (8, 11), cardiac arrest (18), trauma (19, 20), and in other conditions such as acute respiratory distress syndrome (ARDS) (21, 22).

We observed a slight reduction of HRQoL in physical domains, with the lowest scores in the energy/fatigue domains, physical functioning, and role limitations due to physical health domains of the SF-36. We reported the same results with a more marked physical decrease in physical domains than in psychologic and social domains in studies focusing on ARDS (10, 21), sepsis (8, 11, 23), and trauma (19, 20). The reasons why the patients in the present cohort had lower physical scores than in the general population remain unclear. We can hypothesize by analogy with studies carried out on sepsis and ARDS that this observation results from the combination of muscle loss, cognitive impairment, and psychologic issues (21, 24–27). In a recent study, Boede et al (28) showed an association between depression symptoms, chronic pain, and posttraumatic stress in the year following ICU discharge in sepsis survivors (29). This could suggest that a long-term reduction of depression symptoms compared with the general population may be linked to a resolution of chronic pain and greater acceptance of disability after several years.

## Comparison With Previous Studies Concerning Mortality

Acidemia is a well-known predictor for ICU mortality (5, 30, 31), yet it remains unclear whether increased mortality in patients with severe acidemia reflects the severity of the pathology causing acidemia or whether acidemia per se contributes to mortality (32, 33).

Although there are many studies on acid-base abnormalities in ICU patients, studies specifically focusing on severe metabolic acidemia are rare. Although previous studies have shown an ICU mortality rate of 50–70% with hyperlactatemia as an independent risk factor for mortality (1, 6, 33), this is the first study to focus on long-term outcome in this high-risk population.

Previous studies have shown that the 5-year mortality rate (average 32–47%) among ICU survivors is higher than in the general population (34–38). However, these studies include all critical care patients pooled together; hence, mortality is probably lower than in our cohort due to the high number of patients with very severe acidemia. Previous studies focusing on septic shock survivors have reported an overall 5-year mortality rate of 61–83% (32, 39), which is a similar survival rate. In our population, we reported a similar survival rate (half of our patients were admitted for septic shock).

Poorer long-term prognosis is associated with older age, multiple comorbidity, and peak number of organ failures, and these factors continue to exert an effect on long-term survival (37).

These data support the assumption that severe acidemia is an important criterion for severity assessment in recently admitted ICU patients.

## Impact of Rehabilitation

To our knowledge, there are no data available concerning the outcome of rehabilitation in patients admitted in ICU with severe metabolic acidemia. However, considering the poor prognosis of this population, strategies to prevent poor long-term HRQoL should be considered. In similar populations, such as patients admitted for sepsis in ICU, rehabilitation strategies have been studied. In ICU management, studies have shown an improvement in delirium-free days, coma, and faster recovery of walking capacities with the “ABCDEF” bundle (Assess, Prevent, and Manage Pain [A], Both Spontaneous Awakening Trials and Spontaneous Breathing Trials [B], Choice of analgesia and sedation

[C], Delirium: Assess, Prevent, and Manage [D], Early mobility and Exercise [E], and Family engagement and empowerment [F]) (**Supplemental Digital Content 8**, <http://links.lww.com/CCM/H225>). Post-ICU management has also been studied with rehabilitation strategies, including ICU follow-up clinics and self-management strategies, but with mixed results requiring further exploration (40, 41).

Social support has shown a decrease in posttraumatic stress disorder symptoms (25). Given the wide variability in types of exercise and measurements of recovery, further studies are warranted to identify patients who could benefit from the latter, and which types of exercise could yield the best results (17).

### Limitations

First, HRQoL was not assessed before ICU admission. Therefore, we could not assess the difference between HRQoL before the ICU stay and long-term HRQoL. However, it has been shown that patients admitted in ICU have a lower HRQoL than the general population and that a posteriori evaluation of HRQoL before ICU admission may be misestimated (23, 42). Second, a significant proportion of the BICAR-ICU trial survivors (22%) were lost to follow-up. Indeed, patients who were unable to answer the HRQoL questionnaires due to cognitive disorders may have been lost to follow-up, and the latter may be among the most affected in terms of HRQoL. Third, due to the use of telephone assessment, we could not precisely collect the stages of chronic kidney disease, and further investigations are required to assess long-term renal function in these patients. Finally, our study was a transversal post hoc study, so we could not observe the progression of HRQoL in these patients. A longitudinal study of HRQoL in these patients could be of interest, particularly in patients with stage 2 or 3 AKIN, who seem to benefit the most from bicarbonate infusion.

### Implications of This Study

This study highlights the significant impact on the survival and quality of life of diseases complicated by severe acidemia. Sodium bicarbonate did not have an impact on long-term quality of life or survival. Severe acidemia should be considered by physicians not only as an important factor of short-term mortality but also as a major factor of long-term mortality and decreased quality of life. The reasons for the long-term disability

of these patients remain to be clarified as well as the relevance of referring them to ICU follow-up clinics.

## CONCLUSIONS

In the present post hoc analysis of the BICAR-ICU trial, the 5-year survival rate was 30%. Among the survivors, there were no significant differences between the control and the sodium bicarbonate groups for any outcome. As the impact of rehabilitation in this high-risk population remains unknown, further investigations to evaluate standardized post-ICU rehabilitation strategies are warranted.

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*Drs. Bendiab and Garnier contributed equally to the article.*

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