Brief Report

# Serum Bicarbonate in Acute Heart Failure: Relationship to Treatment Strategies and Clinical Outcomes

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**ABSTRACT**

**Background:** Though commonly noted in clinical practice, it is unknown if decongestion in acute heart failure (AHF) results in increased serum bicarbonate.

**Methods and Results:** For 678 AHF patients in the DOSE-AHF, CARRESS-HF, and ROSE-AHF trials, we assessed change in bicarbonate (baseline to 72–96 hours) according to decongestion strategy, and the relationship between bicarbonate change and protocol-defined decongestion. Median baseline bicarbonate was 28 mEq/L. Patients with baseline bicarbonate ≥28 mEq/L had lower ejection fraction, worse renal function and higher N-terminal pro–B-type natriuretic peptide than those with baseline bicarbonate <28 mEq/L. There were no differences in bicarbonate change between treatment groups in DOSE-AHF or ROSE-AHF (all $P > .1$). In CARRESS-HF, bicarbonate increased with pharmacologic care but decreased with ultrafiltration (median +3.3 vs −0.9 mEq/L, respectively; $P < .001$). Bicarbonate change was not associated with successful decongestion ($P > .2$ for all trials).

**Conclusions:** In AHF, serum bicarbonate is most commonly elevated in patients with more severe heart failure. Despite being used in clinical practice as an indicator for decongestion, change in serum bicarbonate was not associated with significant decongestion. (*J Cardiac Fail 2016;22:738–742*)

**Key Words:** Heart failure, Edema, Diuretics.

Acute heart failure (AHF) is common, and treatment decisions are often based on an assessment of a combination of clinical conditions and laboratory measures.[1] Many clinicians view increasing serum bicarbonate levels as a sign of volume contraction and use it as a marker of decongestion.[2] However, empirical evidence to support this practice is lacking. With the use of data from 3 AHF trials, we sought to describe the characteristics of patients hospitalized for AHF according to serum bicarbonate levels at baseline and follow-up for different treatment strategies, and to describe the association between serum bicarbonate and decongestion.

## Methods

### Data Source and Study Population

This analysis was performed with the use of data from 3 National Heart, Lung, and Blood Institute–sponsored Heart Failure Network trials: Diuretic Optimization Strategy Evaluation in Acute Heart Failure (DOSE-AHF), Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF), and Renal Optimization Strategies Evaluation in Acute Heart Failure (ROSE-AHF). The design and primary results of these trials have been published previously.[3–8]

All study participants provided written informed consent. The studies were approved by protocol review and data safety monitoring committees as well as each participating site's Institutional Review Board.

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Manuscript received August 10, 2015; revised manuscript received December 22, 2015; revised manuscript accepted January 7, 2016.

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Funding Sources: DOSE-AHF, CARRESS-HF, and ROSE-AHF were funded by the National Heart, Lung, and Blood Institute. Dr Cooper is supported by grant T32HL069749-11A1 from the National Institute of Health. The content of this paper is the responsibility solely of the authors and does not necessarily represent the official views of the National Institutes of Health.

See page 742 for disclosure information.

1071-9164/$ - see front matter



http://dx.doi.org/10.1016/j.cardfail.2016.01.007

Patients enrolled in the DOSE-AHF, CARRESS-HF, and ROSE-AHF trials were included in the present study population if they had had a serum bicarbonate level measured at baseline and follow-up at 72 hours or 96 hours.

### Statistical Analyses

Baseline characteristics were compared between patients with a baseline serum bicarbonate level above and below the median with the use of the use of the Wilcoxon rank sum test for continuous variables and the Pearson chi-square test for categorical variables. Baseline characteristics were described with the use of medians and 25th–75th percentiles for continuous variables and frequencies and proportions for categorical variables.

Linear regression was used to estimate the serum bicarbonate change differences across decongestion strategies within each trial. The models were adjusted for baseline serum bicarbonate. For analyses pooling all trials, an indicator variable for trial was also included. Complete decongestion was defined per study protocol as jugular venous distention <8 cm, trace or no peripheral edema, and no orthopnea.[4,6]

Spearman correlations were used to assess the associations between the change in serum bicarbonate and the following: change in weight, change in renal function, and change in N-terminal pro–B-type natriuretic peptide (NT-proBNP).

## Results

Of 835 unique patients in the DOSE-AHF, CARRESS-HF, and ROSE-AHF trials, 678 patients had a serum bicarbonate level measured at baseline and at follow-up (72 or 96 hours): 225 in DOSE-AHF, 309 in ROSE-AHF, and 144 in CARRESS-HF. Patients with baseline serum bicarbonate above the median (≥28 mEq/L) were significantly more likely to have a reduced ejection fraction, and at baseline they had lower serum sodium and higher blood urea nitrogen, creatinine, and NT-proBNP (Table 1).

No difference could be detected in the change in serum bicarbonate between bolus versus infusion ($P = .40$) or low-dose versus high-dose diuretics ($P = .10$) in DOSE-AHF, or between dopamine versus nesiritide versus placebo ($P = .37$) in ROSE-AHF (Table 2). In CARRESS-HF, subjects randomized to stepped pharmacologic care showed an increase in serum bicarbonate from baseline to 96 hours compared with those on ultrafiltration (change +3.3 mEq/L vs –0.9 mEq/L; $P < .001$).

**Table 1.** Baseline Characteristics by Baseline Median Serum Bicarbonate Level

| Variable | Serum Bicarbonate <28 mEq/L (n = 362) | Serum Bicarbonate ≥28 mEq/L (n = 316) | *P* Value* |
|---|---|---|---|
| Characteristics | | | |
| Age, y | 68.5 (61.0–78.0) | 68.5 (58.0–78.0) | .46 |
| Sex, male | 279 (77.1%) | 223 (70.6%) | .05 |
| Race, white | 291 (80.4%) | 208 (65.8%) | <.001 |
| Ejection fraction, % | 33.6 (28.2–40.0) | 30.4 (25.7–36.0) | <.001 |
| Preserved ejection fraction | 121 (33.7%) | 80 (25.6%) | .03 |
| Heart failure hospitalization in past year | 262 (73.6%) | 217 (69.1%) | .20 |
| Medical history | | | |
| Ischemia as cause of heart failure | 222 (61.3%) | 174 (55.1%) | .10 |
| Atrial fibrillation/flutter | 221 (61.0%) | 155 (49.1%) | .002 |
| Diabetes | 218 (60.2%) | 172 (54.4%) | .13 |
| Chronic obstructive pulmonary disease | 103 (28.5%) | 77 (24.4%) | .23 |
| Medications before hospitalization | | | |
| Beta-blockers | 292 (80.7%) | 266 (84.2%) | .23 |
| Aldosterone antagonist | 902 (24.9%) | 83 (26.3%) | .68 |
| Furosemide equivalent dose, mg/d | 120.0 (80.0–160.0) | 80.0 (80.0–160.0) | .002 |
| Baseline evaluation | | | |
| Weight, lb | 216.9 (185.4–267.4) | 196.2 (168.0–241.8) | <.001 |
| Systolic blood pressure, mm Hg | 114.0 (103.0–126.0) | 116.0 (104.0–127.0) | .36 |
| Heart rate, beats/min | 75.0 (67.0–84.0) | 76.5 (66.5–87.5) | .18 |
| Jugular venous pressure ≥8 cm | 330 (95.7%) | 284 (93.4%) | .21 |
| Orthopnea | 317 (91.1%) | 276 (92.3%) | .58 |
| New York Heart Association functional class | | | .77 |
| I | 1 (0.3%) | 0 (0.0%) | |
| II | 8 (2.4%) | 9 (3.0%) | |
| III | 217 (64.8%) | 191 (64.1%) | |
| IV | 109 (32.5%) | 98 (32.9%) | |
| Sodium, mg/L | 139.0 (136.0–141.0) | 138.0 (135.0–140.0) | .001 |
| Blood urea nitrogen, mg/dL | 36.5 (26.0–51.0) | 40.0 (27.0–59.0) | .05 |
| Creatinine, mg/dL | 1.6 (1.2–2.0) | 1.7 (1.3–2.3) | <.001 |
| NT-pro BNP, pg/mL | 3929 (1999–8493) | 6230 (2886–12,200) | <.001 |
| eGFR | 43.2 (34.1–55.9) | 38.7 (28.2–53.6) | .001 |

Data are presented as n (%) or median (25th–75th percentiles). NT-proBNP, N-terminal pro–B-type natriuretic peptide; eGFR, estimated glomerular filtration rate.

*$P$ values were obtained with the use of Wilcoxon rank-sum test for continuous variables and Pearson chi-square test for categorical variables.