

**Critical Review Form  
Therapy**

Kawano T, Grunau B, Scheuermeyer FX, Gibo K, Dick W, Fordyce CB, Dorian P, Stenstrom R, Straight R, Christenson J. Prehospital sodium bicarbonate use could worsen long term survival with favorable neurological recovery among patients with out-of-hospital cardiac arrest. Resuscitation. 2017 Oct;119:63-69.

**Objectives:** "to investigate the association between prehospital SB [sodium bicarbonate] use and both survival and favorable neurological recovery to hospital discharge among non-traumatic OHCA [out-of-hospital cardiac arrest] patients. In addition, we further intended to assess the effect of SB on those with a prolonged attempt at resuscitation." (p. 64)

**Methods:** This was a secondary analysis of data collected prospectively for the Resuscitation Outcomes Consortium (ROC). Adult patients (18 years or older) with OHCA treated by EMS in four major metropolitan areas of British Columbia between December 2005 and March 2016 were screened for enrollment. Patients were excluded if they were not treated by ALS units, if they had DNR orders, or if they were declared dead at the scene. Data were collected from paramedic and dispatch records as part of the ROC registry. Neurologic outcome data was only collected during enrollment for 5 particular clinical trials; in those cases, these outcomes were evaluated by trained research assistance using standardized forms.

The primary outcome of interest was survival to hospital discharge; the secondary outcome was survival to hospital discharge, defined as a modified Rankin Scale (mRS) of 0 to 3. Outcomes were assessed using unadjusted data, as well using multivariable logistic regression to control for multiple confounders. Subgroup analyses were also conducted based on total dose of epinephrine and length of resuscitation to determine the effect of SB on those with shorter or longer lengths of resuscitation.

Among 15601 nontraumatic OHCA patients treated during the study period, 13865 met inclusion criteria. Of these, 5165 received sodium bicarbonate. The median age in the bicarbonate and no bicarbonate groups was 65 and 68, respectively, and 71.4% and 66.7% were male.

Guide		Comments
I.	Are the results valid?	
A.	Did experimental and control groups begin the study with a similar prognosis?	
1.	Were patients randomized?	No. This was a retrospective review of prospectively collected data. Despite the use of multivariable logistic regression and <a href="#">propensity matching</a> to balance the two groups, the study is at high risk of <a href="#">selection bias</a> .

2.	Was allocation concealed? In other words, was it possible to subvert the randomization process to ensure that a patient would be “randomized” to a particular group?	N/A. Patients were not randomized
3.	Were patients analyzed in the groups to which they were randomized?	N/A. Patients were not randomized. They were, however, analyzed based on whether or not they received sodium bicarbonate by EMS.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No. Patients in the SB group were less likely to be in a shockable rhythm (19.8% vs. 29.9%), were less likely to have an EMS-witnessed arrest (9.3% vs. 13.4%), received significantly more doses of epinephrine (median 6.0 vs. 2.0), and had significantly longer length of resuscitation (median 30.0 vs. 17.0 minutes). Overall, patients in the SB group appeared to have a worse prognosis at baseline.
<b>B.</b>	<b>Did experimental and control groups retain a similar prognosis after the study started?</b>	
1.	Were patients aware of group allocation?	No. Patients were in cardiac arrest and hence would not be aware of any treatment administered.
2.	Were clinicians aware of group allocation?	Yes. This was not a randomized trial and hence blinding was not attempted or possible. Bicarbonate administration decisions were made at the paramedics, and the decision to administer bicarbonate was likely, in itself, a significant prognostic indicator ( <a href="#">selection bias</a> ). Specifically, local guidelines recommended SB administration for "prolonged" cardiac arrest.
3.	Were outcome assessors aware of group allocation?	No. Data for this study was collected prospectively as part of a large registry of OHCA patients. Primary outcome data came directly from the registry; neurologic outcomes were only collected during enrollment for other clinical trials. While outcome assessors were not specifically blinded to SB administration, they also would not have been aware that SB administration would later be assessed.
4.	Was follow-up complete?	Yes. Outcome data was available for all included participants.
<b>II.</b>	<b>What are the results ?</b>	
1.	How large was the treatment effect?	<ul style="list-style-type: none"> <li>After multivariable logistic regression, SB administration was associated with decreased survival to hospital discharge (AOR 0.48, 95% CI 0.35-0.65) and decreased survival with a favorable</li> </ul>

		<p>neurologic outcome (AOR 0.61, 95% CI 0.43-0.86).</p> <ul style="list-style-type: none"> <li>• Among patients whose total median epinephrine dose was <math>\leq 4.0</math> mg, SB was associated with a decreased rate of favorable neurologic outcomes (AOR 0.57, 95% CI 0.37-0.88); among those with a median epinephrine dose <math>&gt; 4.0</math> mg, there was no significant difference in rates of favorable neurologic outcomes between the SB and no SB groups (AOR 0.77, 95% CI 0.41-1.45).</li> <li>• Among patients whose length of resuscitation was <math>&gt;22.6</math> minutes, SB was associated with a decreased rate of favorable neurologic outcomes (AOR 0.33, 95% CI 0.16-0.66); among those whose resuscitation lasted less than 22.6 minutes, there was no significant difference in rates of favorable neurologic outcomes between the SB and no SB groups (AOR 0.73, 95% CI 0.49-1.09).</li> <li>• There were 5638 patients selected for propensity score matching. After adjustment, patients receiving SB had an OR for survival to discharge of 0.63 (95% CI 0.46–0.87).</li> </ul>
2.	How precise was the estimate of the treatment effect?	See above.
<b>III.</b>	<b>How can I apply the results to patient care?</b>	
1.	Were the study patients similar to my patient?	Yes. This study included patients suffering OHCA in a Canadian EMS system; only patients transported by ALS units (who would received similar care to that provided in in our system) were included.
2.	Were all clinically important outcomes considered?	Mostly yes. While discharge from the hospital with a favorable neurologic outcome is likely adequate, the <a href="#">Research Working Group of the American Heart Association Emergency Cardiovascular Care Committee</a> has recommended that large trials designed to have a major impact should use longer-term endpoints at least 90 days out coupled with some neurological and quality-of-life assessment.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. Unfortunately, this study was severely limited by selection bias, as evidenced by the significant baseline differences between those who did and those who did not receive SB. Specifically, patients who were given SB had significantly longer resuscitation times, were given significantly more epinephrine, and were less likely to be in a shockable rhythm; overall, the prognosis was much worse for those patients given SB, which likely accounts for

		much of the difference in outcomes observed (even after adjustment for known confounders).
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**Limitations:**

1. While this study drew from a large, prospective registry, only patients included in certain research studies had neurologic outcomes measured.
2. This was a retrospective, observational study at high risk of [selection bias](#). Despite the use of multivariable logistic regression analysis and [propensity matching](#) to control for several known confounders, there remains the risk of imbalance of unknown [confounders](#).
3. The study measured only short-term outcomes (out to hospital discharge). The [Research Working Group of the American Heart Association Emergency Cardiovascular Care Committee](#) has recommended that large trials designed to have a major impact should use longer-term endpoints at least 90 days out coupled with some neurological and quality-of-life assessment.

**Bottom Line:**

This retrospective review of data collected in a prospective registry found no difference in survival to hospital discharge or discharge with a favorable neurologic outcome among patients who received sodium bicarbonate for OHCA and those who did not receive sodium bicarbonate. When looking at patients with prolonged cardiac arrest (> 22.6 minutes), patients receiving sodium bicarbonate were less likely to survive with good neurologic outcome (AOR 0.33, 95% CI 0.16-0.66).