

SoCARE study. Is the post-resuscitation trend in sodium levels associated with outcome? A substudy of the STEPCARE trial.

Hypernatremia is an independent risk factor for mortality in critically ill patients (Lindner et al., 2007; Waite et al., 2013). However, only a few studies have focused on sodium levels in out-of-hospital cardiac arrest (OHCA) patients. In one study, hypernatremia at hospital admission was independently associated with worse neurological outcomes at discharge compared to normonatremia. Furthermore, development of hypernatremia within the first 48 hours after admission was independently associated with both worse neurological and survival outcomes (Ye et al., 2024). On the other hand, both hypo- and hypernatremia upon hospital arrival were associated with a decreased likelihood of favourable neurological outcomes in patients with non-traumatic OHCA. Additionally, the probability of favourable neurological outcomes decreased with further changes in serum sodium levels beyond the normal range (Shida et al., 2022). A post hoc study using data from four randomised controlled trials showed that early hyponatremia after cardiac arrest was associated with a lower probability of a favourable functional outcome at 6-months (Lascarrou et al., 2023). In another study, hypernatremia at 24 hours showed a strong and independent association with poor long-term neurological outcomes in OHCA survivors (Cho et al., 2022). Madelaine et al. also found that natremia 24 hours after OHCA may serve as a predictor of brain death (Madelaine et al., 2021). Many confounders exist, as patients with severe brain injury are more likely to develop diabetes insipidus or to receive hyperosmotic fluids for brain edema (Tisdall et al., 2006). On the other hand, in an experimental porcine model of cardiac arrest, infusion of hypertonic sodium lactate could reduce brain injury (Annoni et al., 2023).

We hypothesize that deranged sodium balance with an increasing trend in serum sodium within the first days in the ICU may associate with unfavourable functional outcomes in OHCA patients. We further hypothesize that the association is different depending on the severity of disease and that in the MIRACLE2 score medium-risk group, increasing sodium levels during the first 48 hours may be associated with a favourable functional outcome.

Patients: Adult OHCA patients participating in the STEPCARE trial

Exposure: Sodium values during the first 48 hours of post OHCA care in the ICU

Outcomes: Mortality at 180 days. Functional outcome defined by using the mRS scale 6 months after OHCA.

We will investigate whether different trends in sodium concentration within the first two days after OHCA are associated with functional outcome at 180 days. We will analyse the trends according to three severity levels defined by the MIRACLE2 score (risk for poor functional outcome low MIRACLE2 score 1-2; intermediate MIRACLE2 score 3-4; and high MIRACLE 2 score 5).

Data requirements:

Daily (1st 48 hours):

-All values on Na, and K from all blood-gas analyses

-Cumulative intake of i.v. fluid/day

-Cumulative diuresis

-Cumulative administered sodium mmol/ day

-Cumulative administered potassium mmol/day

Was the patient treated with hypertonic saline yes/no?

MIRACLE2 score (collected in the main eCRF)

Additional data required*

The additional data is found in the routine eCRF data

Lead Investigators:

Emilia Kortesoja, Markus Skrifvars, Matti Reinikainen, Joonas Tirkkonen, Heikki Kiiski, Markus Tujunen, Johanna Hästbacka

Co-Investigators:

All STEPCARE site investigators interested in participating

Participating sites:

All STEPCARE sites, where investigators interested in participating and laboratory data and administered Na, K, and fluid data are available

Funding:

(Markus Skrifvars:) Academy of Finland, Sigrid Juselius Foundation

Government funding for university level research will be applied

How to join?

Contact: Johanna

johanna.hastbacka@tuni.fi

References

Annoni, F., Su, F., Peluso, L., Lisi, I., Caruso, E., Pischiutta, F., Gouvea Bogossian, E., Garcia, B., Njimi, H., Vincent, J.-L., Gaspard, N., Ferlini, L., Creteur, J., Zanier, E. R., & Taccone, F. S. (2023). Hypertonic sodium lactate infusion reduces vasopressor requirements and

biomarkers of brain and cardiac injury after experimental cardiac arrest. *Critical Care*, 27(1), 161. <https://doi.org/10.1186/s13054-023-04454-1>

Cho, E. J., Lee, M. S., Kwon, W. Y., Shin, J., Suh, G. J., Jung, Y. S., Song, W. J., Yeo, G., & Jo, Y. H. (2022). Hyponatremia is associated with poor long-term neurological outcomes in out-of-hospital cardiac arrest survivors. *The American Journal of Emergency Medicine*, 59, 30–36. <https://doi.org/10.1016/J.AJEM.2022.06.014>

Lascarrou, J. B., Ermel, C., Cariou, A., Laitio, T., Kirkegaard, H., Søreide, E., Grejs, A. M., Reinikainen, M., Colin, G., Taccone, F. S., Le Gouge, A., & Skrifvars, M. B. (2023). Dysnatremia at ICU admission and functional outcome of cardiac arrest: insights from four randomised controlled trials. *Critical Care*, 27(1), 472. <https://doi.org/10.1186/s13054-023-04715-z>

Lindner, G., Funk, G. C., Schwarz, C., Kneidinger, N., Kaider, A., Schneeweiss, B., Kramer, L., & Druml, W. (2007). Hyponatremia in the Critically Ill Is an Independent Risk Factor for Mortality. *American Journal of Kidney Diseases*, 50(6), 952–957. <https://doi.org/10.1053/J.AJKD.2007.08.016>

Madelaine, T., Cour, M., Roy, P., Vivien, B., Charpentier, J., Dumas, F., Deye, N., Bonnefoy, E., Gueugniaud, P. Y., Coste, J., Cariou, A., & Argaud, L. (2021). Prediction of Brain Death After Out-of-Hospital Cardiac Arrest: Development and Validation of the Brain Death After Cardiac Arrest Score. *Chest*, 160(1), 139–147. <https://doi.org/10.1016/J.CHEST.2021.01.056>

Shida, H., Matsuyama, T., Komukai, S., Irisawa, T., Yamada, T., Yoshiya, K., Park, C., Nishimura, T., Ishibe, T., Yagi, Y., Kiguchi, T., Kishimoto, M., Kim, S.-H., Hayashi, Y., Sogabe, T., Morooka, T., Sakamoto, H., Suzuki, K., Nakamura, F., ... Kitamura, T. (2022). Early prognostic impact of serum sodium level among out-of-hospital cardiac arrest patients: a nationwide multicentre observational study in Japan (the JAAM-OHCA registry). *Heart and Vessels*, 37(7), 1255–1264. <https://doi.org/10.1007/s00380-022-02020-3>

Tisdall, M., Crocker, M., Watkiss, J., & Smith, M. (2006). Disturbances of Sodium in Critically Ill Adult Neurologic Patients. *Journal of Neurosurgical Anesthesiology*, 18(1), 57–63. <https://doi.org/10.1097/01.ana.0000191280.05170.0f>

Waite, M. D., Fuhrman, S. A., Badawi, O., Zuckerman, I. H., & Franey, C. S. (2013). Intensive care unit–acquired hyponatremia is an independent predictor of increased mortality and length of stay. *Journal of Critical Care*, 28(4), 405–412. <https://doi.org/10.1016/J.JCRC.2012.11.013>

Ye, S. C., Cheung, C. C., Lauder, E., Grunau, B., Moghaddam, N., van Diepen, S., Holmes, D. T., Sekhon, M. S., Christenson, J., Tallon, J. M., & Fordyce, C. B. (2024). Association of

admission serum sodium and outcomes following out-of-hospital cardiac arrest.
American Heart Journal, 268, 29–36. <https://doi.org/10.1016/j.ahj.2023.11.011>