Article Appraisal

Article: Prediction and risk stratification of survival in accidental hypothermia requiring extracorporeal life support: An individual patient data meta-analysis

Date of Journal Club: June 19, 2018

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Background and Study Objective(s):

In the US, 400-1500 patients die annually from hypothermia. For patients with hypothermic out-of-hospital cardiac arrest, extracorporeal life support (ECLS) is associated with a 10-50% improvement in survival over the baseline rate of 10-37% with a NNT of 2-5. While ECLS is increasingly available in North America, it is not often available in the rural and remote sites where hypothermic OHCA occurs, and there is significant variation among sites for transfer of patients for ECLS. Early identification of OHCA patients who may benefit from ECLS is challenging, and a key differentiation is patients with primary hypothermia who had OHCA, as opposed to those with a primary OHCA that became hypothermic. A reliable prognostication tool to aid in this scenario has been lacking. The goal of this meta-analysis was to combine currently available data into a robust, patient-level analysis to identify factors independently associated with survival with good neurological outcome in patients treated with ECLS for hypothermic cardiac arrest, and if possible, develop a scoring tool for prognostication.

Study Design:

A meta-analysis that included patient-level, rather than aggregate, data from each study to facilitate standardization across papers. Studies reporting the use of ECLS for treatment of accidental hypothermia were included – observational or randomized cohort studies or case reports. Exclusion criteria were non-human subjects, non-English language, or topic reviews. Asphyxia was considered a proxy for hypoxia; for example, avalanche burial with no air pocket or water submersion. Neurological outcomes were dichotomized into favourable and unfavourable according to 3 different scores – Cerebral Performance Category, Glasgow Outcome Scale, and Pediatric Overall Performance Category, or according to description if the study did not use a score. Univariate predictors of favourable neurologic outcomes were calculated, and a mixed-effects multi-level logistic regression was used to develop a model to predict favourable outcomes in this cohort.

Results:

Forty-four retrospective cohort studies and 40 individual case descriptions were included; 77 had individual data and seven aggregate data, for a total of 658 patients. The mean survival rate of the entire cohort was 46% with 40.3% having a good neurological outcome. Univariable analysis identified variables associated with good neurological

outcomes: initial cardiac rhythm, cooling mechanism (air, water, or snow), initial pH, and lactate. Multivariate adjustment identified four independent predictors: slower ECLS rewarming rate (mean of 6 vs 7.8C / hr), lack of asphyxiation, lower serum potassium, and female gender. Since the goal was to create a predictive model of good neurologic outcomes, only pre-ECLS variables (gender, asphyxiation, potassium) were included in the model. The resultant International Accidental Hypothermia Extracorporeal Life Support (ICE) Survival Score, ranging from -3 to 15, was demonstrated to have good model predictive performance by calibration plot and Hosmer-Lemeshow test (p=77.9) and excellent discrimination as represented by the c-statistic (0.849; 95% CI: 0.823, 0.875).

Validity of Results:

The authors acknowledged all limitations. Data quality is the major issue: Firstly, publication bias is a concern since successful cases are more likely to be published. Secondly, there were no relevant randomized trials, close to half of the included articles are n-of-1 studies, and the score was developed based on case series and case reports. However, this meta-analysis of the existing data is the most rigorous approach to date. Thirdly, many studies did not report Utstein-level data, and other critical information such as time from accident to ECLS, mode of CPR, or drugs administered, were inconsistently reported. There is lack of a robust registry for hypothermia and these cases are often in rural or remote settings. Finally, the limitations of the score require careful interpretation of the history and context; for example, the tool should not be applied to a clearly hypoxia-first OHCA that becomes hypothermic.

Generalizability of Results:

The included studies involved cases in numerous countries in rural, remote, community, and urban settings. The hypothermic population potentially eligible for ECLS in BC is likely similar to that represented in the studies.

The Bottom Line:

This meta-analysis is the most rigorous analysis of the available data on the prognostication of neurologic outcome in hypothermic OHCA treated with ECLS and is appropriately done given the limitations of the currently available data. Hopefully, this paper will serve as an impetus for a robust hypothermia registry to facilitate further research and guide clinical practice and resource utilization. Clinical decision-making in severe hypothermia cases is nuanced and complex. The discussion emphasized that depending on the context, seeking expert opinion may be advisable and that calling the Emergency Physician Online Support (EPOS) physician is part of the current BC guidelines. Given the limitations of the data, the ICE Survival Score is not likely ready to be universally applied, but rather to be taken into consideration in the overall clinical context of a hypothermic OHCA.