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Clinical paper

Osborn waves following out-of-hospital cardiac arrest—Effect of level of temperature management and risk of arrhythmia and death☆

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ABSTRACT

Background: The Osborn or J-wave, an upright deflection of the J-point on the electrocardiogram (ECG), is often observed during severe hypothermia. A possible relation between Osborn waves (OW) and increased risk of ventricular arrhythmia has been reported. We sought to determine whether the level of targeted temperature management (TTM) following out-of-hospital cardiac arrest (OHCA) affects the prevalence of OW and to assess the associations between OW and risk of ventricular arrhythmia and death.

Methods and results: The present study is part of the TTM-trial ECG-substudy (including OHCA-patients randomized to TTM at 33 °C vs. 36 °C from 24 of 36 sites). Serial 12-lead ECGs from 680 (94%) patients were analysed and stratified by OW at predefined time-points (0, 4, 28, 36, 72-h after admission).

On admission, the overall prevalence of OW was 16%, increasing to 32% at target temperature, with higher prevalence in the 33 °C-group (40% vs. 23%, $p < 0.0001$). No difference in prevalence was found between the 33 °C- and 36 °C-groups on admission (18% vs. 14%, $p = .11$) or after rewarming (13% vs. 10%, $p = .44$). OW were not associated with increased risk of ventricular arrhythmia (Odds ratio = 0.78 (0.51–1.20), $p = .26$), but associated with significantly lower 180-day mortality as compared to no OW (38% vs. 52%, $p_{log\text{-}rank} = 0.001$) in univariable analyses only.

Conclusion: OW are frequent during TTM, particularly in patients treated with 33 °C. OW are not associated with increased risk of ventricular arrhythmia, and may be considered a benign physiological phenomenon, associated with lower mortality in univariable analyses.

INTRODUCTION

Mild hypothermia in the form of targeted temperature management (TTM) between 32° and 36 °C remains a guideline supported treatment modality for attenuation of neurological injury following out-of-hospital cardiac arrest (OHCA) [1,2]. The treatment is generally considered safe [3], however a subset of OHCA-patients is affected by potentially life-threatening arrhythmias during post-cardiac arrest care and TTM [4].

Studies on accidental hypothermia and the effects of TTM in both animals and humans have contributed with knowledge of the pathophysiological and physiological processes during cooling [5]. Lowering of the core temperature affects the body in various ways; especially cardiac electrophysiology is affected with distinct changes in the electrocardiogram (ECG) [6], e.g. lowering of the heart rate, prolongation of PR, QRS and QT intervals, and presence of Osborn waves (OW) (Fig. 1) [7]. Case reports of severe accidental hypothermia below 30 °C have reported occurrence of arrhythmia including malignant ventricular tachycardia (VT) and fibrillation (VF) [8], potentially leading to fatal outcome.

Markers of patients at risk of arrhythmia during TTM could be useful in providing basis for individualized post-cardiac arrest care. Tomaszewski was the first to report hypothermia-induced ECG changes in 1938 [9]. He observed an upright deflection of the J-point (terminal part of the QRS complex) in an accidentally hypothermic patient. Osborn later confirmed this hypothermia-triggered change in dogs [10], as

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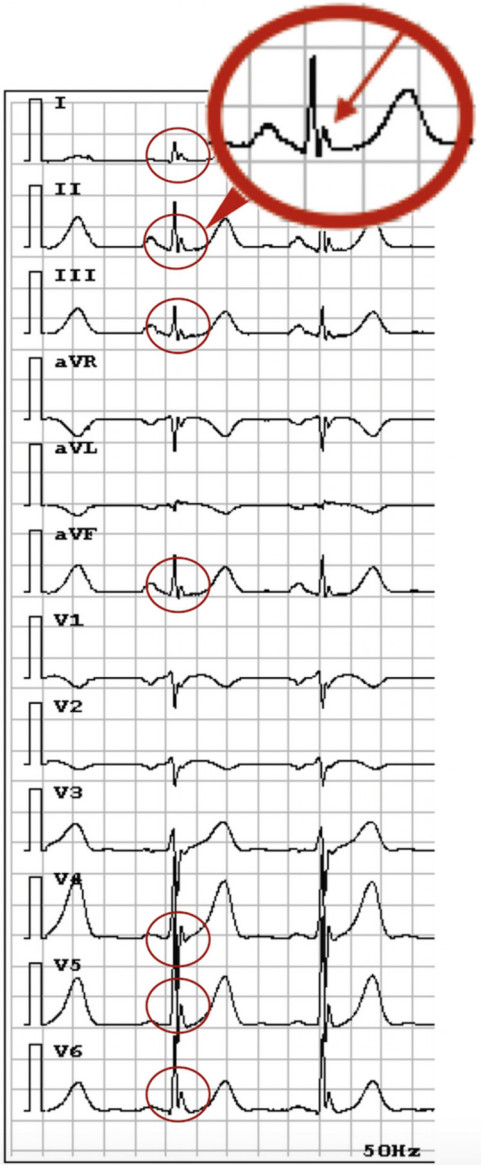

Fig. 1. Infero-lateral Osborn waves (red circles) during targeted temperature management following out-of-hospital cardiac arrest. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

a distinct deflection progressively seen by lower core temperature and reversible by rewarming. Recent case reports in cardiac arrest patients have suggested a possible relation between OW and an increased risk of ventricular arrhythmia [11], while a smaller observational study has failed to confirm this association [12].

We sought to assess the effect of two levels of TTM on the prevalence of OW following OHCA. Furthermore, we assessed the associations between OW and risk of ventricular arrhythmia and death.

METHODS

The present study is part of the multicenter-ECG and single-center Holter sub-study of the TTM-trial [13]. The main trial included adult comatose patients resuscitated after OHCA (N = 939) from a presumed cardiac cause with return of spontaneous circulation (ROSC) for at least 20 min (regardless of initial rhythm). Patients were enrolled and randomized in a 1:1 fashion to a 36-h TTM protocol aimed at either 33 °C or 36 °C. The main trial showed no difference in outcome between the two temperature groups [13]. Patients were included as fast as possible but within 240 min from sustained ROSC. A complete list of inclusion and exclusion criteria has been published previously [13].

Twenty-four out of 36 sites participated in the ECG sub-study, with 726 eligible patients. The present sub-study included 680 (94%) patients with at least one 12-lead ECG after admission (Fig. S1). In addition, a subgroup of 113 patients admitted at the cardiac intensive care units (ICU) at Copenhagen University Hospital (Rigshospitalet) was continuously Holter-monitored during TTM.

TTM was controlled by automated feedback devices and intravascular or surface cooling were used with similar frequencies between the groups. The target temperature (TT) was reached as fast as possible. After 28 h rewarming to 37 °C was commenced with a maximum increase of 0.5 °C/hour. Post-cardiac arrest care including mandatory sedation, intubation and mechanical ventilation were carried out through the specified intervention period of 36 h.

The serial 12-lead ECGs after OHCA were obtained at fixed time points: ECG_1–on admission to the hospital, ECG_2–at the allocated TT, ECG_3–24 h after induction of TTM, ECG_4–36 h after induction (at normothermia after rewarming) and ECG_5–72 h after induction. Trained assessors, blinded for temperature group and outcome, manually analysed available ECGs. Obtained ECGs were stratified by OW vs. no OW at any given time-point, with an OW defined as an upright deflection of the J-point compared to the isoelectric baseline (Fig. 1). We chose a pragmatic approached including all upright deflections at the J-point including QRS end-slurs, irrespective of lead location and amplitude height. Right bundle branch block (RBBB)/R wave – S wave – R wave (RSR) configuration in lead V1-V2 was not considered an OW. In three ECGs, however, it was judged that the changes could represent both OW and RBBB. Interobserver agreement with regards to presence of OW was assessed in 30 randomly selected patients, with observers blinded to temperature group and previous assessment, with very good agreement (total of 113 ECGs assessed with a Cohen's kappa coefficient = 0.81).

Demographics and prehospital data concerning the circumstances of the OHCA were collected according to the Utstein guidelines [14].

Ethics

The main study protocol was approved by Ethics Committees in all participating countries. Written informed consent was obtained or waived, either from included patients after regaining consciousness or as proxy consent from the patients' relatives (next of kin), the latter either alone or combined with the patients' general practitioner's consent in accordance with national legislation. The TTM-trial complied with the Declaration of Helsinki and was registered at ClinicalTrials.gov (Identifier: NCT01020916).

Statistical analysis

Baseline characteristics were presented and stratified by OW during TTM at any given time, including sub-stratification by TT. Categorical variables were presented by proportions (%) and differences tested by χ^2-test. Continuous normally distributed variables were presented by mean ± standard deviation (SD) and tested by *t*-test. Non-normally distributed variables were presented with median and the 25–75 percentile range and compared by Wilcoxon rank sum test. To assess the interaction between presence of OW and allocated TT over time, a repeated measure model (generalized linear model) was used and the fixed type 3 effects reported (SAS Genmod).

For assessment of 6 months survival between the groups, we used Kaplan-Meier survival curves and log-rank tests. Uni- and multivariable proportional hazards Cox-regressions were used to assess the associations between OW at any time point and 6 months mortality. Logistic regression was used to assess the association between OW and unfavourable neurological outcome after 6 months. Neurological