ABSTRACT

Background: Patients admitted to the hospital after successful resuscitation from sudden cardiac death (SCD) are treated with therapeutic hypothermia (TH) to facilitate brain preservation. The prognostic significance of J (Osborn) waves (JOW) in the 12 leads electrocardiogram in this setting has not been elucidated as yet.

Objectives: To ascertain retrospectively the prognostic significance of JOW recorded during TH in SCD survivors.

Methods: The study comprised 55 consecutive patients who underwent TH. All patients achieved a core temperature of 33°C at the time of electrocardiogram analysis. We compared 33 patients with JOW to 22 patients without JOW. The endpoints were in-hospital, long-term all-cause mortality, and irreversible anoxic brain injury (IABI).

Results: Patients with JOW compared to patients without JOW were younger (55.1 ± 11.6 vs. 64.5 ± 11.7 years, respectively, P < 0.006), with a lower incidence of hypertension (52% vs. 86%, P < 0.007), diabetes mellitus (15% vs. 50%, P < 0.005), and congestive heart failure (15% vs. 45%, P < 0.013). In-hospital and long-term mortality were significantly higher in patients without JOW (86% vs. 21%, 91% vs. 24%, respectively, P < 0.000001). Among patients without JOW who survived hospitalization, 66.7% presented with IABI versus 7.7% of the patients with JOW (P < 0.0001). In multivariate analysis, the absence of JOW was a significant predictor for poor prognosis.

Conclusions: The absence of J (Osborn) waves on electrocardiograms obtained during TH is associated with poor prognosis among SCD survivors.

KEY WORDS: J wave, Osborn wave, out-of-hospital cardiac arrest (OHCA), prognostic value, therapeutic hypothermia
outcomes of patients with JOW (33) to patients without JOW (22). The primary endpoints were in-hospital and long-term all-cause mortality, and the secondary endpoints were IABI and composite long-term mortality and IABI. The IABI was defined as an absence of neurological recovery during the follow-up period. The mean follow-up was 35.7 ± 20.9 months and the median follow-up was 34 months.

STATISTICAL METHODS
Categorical variables were compared by chi square, Fisher’s exact test as applicable. Continuous variables were compared by t-test or ANOVA as appropriate. Multivariate analysis of a model constructed from all clinically and univariate significant baseline variables, to predict study endpoint according to the treatment group. Survival plot was constructed by the Kaplan-Meier method. Survival by group was compared by the log-rank method. Two-sided P value < 0.05 was considered significant. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 21 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS
Our study population consisted of 55 patients (mean age 58.6 ± 12.5 years; 22% female). The patients with JOW compared to patients without JOW were younger (55.1 ± 11.6 years vs. 64.5 ± 11.7 years, P < 0.006) with a lower incidence of a history of hypertension (52% vs. 86%, P < 0.007), diabetes mellitus (15% vs. 50%, P < 0.005), congestive heart failure (15% vs. 45%, P < 0.013), and hyperlipidemia (67% vs. 91%, P = 0.038). There was lower incidence of angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARB) therapy. There were no significant differences in other baseline characteristics [Table 1].

The electrocardiogram before initiating TH did not show JOW in any patient. JOW was found in 33 patients (60%) of our study population. The electrocardiogram after complete rewarming following TH did not show JOW in any patient. There were no differences between the groups in QTc measured on the electrocardiogram obtained during TH (0.519 ± 0.049 seconds in patients without JOW vs. 0.521 ± 0.054 sec-
onds in patients with JOW, P = 0.63). The mean measured amplitudes of JOW were: Jo 0.145 ± 0.098 mV, Jp 0.238 ± 0.099 mV, and Jt 0.045 ± 0.054 mV. The mean duration of JOW was 31.52 ± 5.71 msec. The mean ratio between the tallest Jp to the R wave amplitude at the same lead was 0.302 ± 0.139.

There were no differences in the groups with and without JOW in the following characteristics: rate of witnessed cardiac arrest, time before resuscitation was started, and time to return to circulation. In 85% of the patients, the primary cause of OHCA was ventricular tachyarrhythmia without differences in the groups. At the presentation to the hospital, 67% of the patients had manifestations of acute myocardial infarction, 22% were in cardiogenic shock and 14.5% were treated with intra-aortic balloon pump. On admission after successful resuscitation blood pH was significantly lower in patients without JOW (7.13 ± 0.15 vs. 7.21 ± 0.12, P < 0.023) with a higher serum creatinine (1.42 ± 0.68 vs. 1.07 ± 0.33 mg/dl, P < 0.0353). Patients without JOW had a significantly higher incidence of acute renal failure (82% vs. 15%, P < 0.00001) [Table 2].

On admission, 45 patients (82%) underwent immediate coronary angiography, primary percutaneous coronary intervention was performed in 53% of these patients. There were failures to open the infarct related artery in four patients (13.8%). Intra-aortic balloon pump was inserted in 14.5% of the cases. There were no significant differences between the groups in variables related to coronary disease or coronary interventions. The in-hospital left ventricular ejection fraction was 41.8 ± 13.5%. No patient was sent to open heart surgery. Primary percutaneous coronary intervention had no influence on patient's survival.

No patient had in-hospital ventricular fibrillation (VF). In hospital atrial fibrillation was reported in 21 (59%) patients: 13 (38%) were without JOW and 8 (24%) were with JOW (P < 0.0085).

### Table 1. Patients baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total patient population (55)</th>
<th>With JOW (33)</th>
<th>Without JOW (22)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
<td>58.6 ± 12.5</td>
<td>55.1 ± 11.6</td>
<td>64.5 ± 11.7</td>
<td>0.0058</td>
</tr>
<tr>
<td>Gender: Females, n (%)</td>
<td>12 (22)</td>
<td>7 (21)</td>
<td>5 (23)</td>
<td>ns</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>36 (65)</td>
<td>17 (51.5)</td>
<td>19 (86.4)</td>
<td>0.0078</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>16 (29)</td>
<td>5 (15.2)</td>
<td>11 (50)</td>
<td>0.0053</td>
</tr>
<tr>
<td>Chronic renal failure, n (%)</td>
<td>5 (9)</td>
<td>1 (3)</td>
<td>4 (18.2)</td>
<td>ns</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>42 (76)</td>
<td>22 (66.7)</td>
<td>20 (90.1)</td>
<td>0.0382</td>
</tr>
<tr>
<td>Obesity (n, %)</td>
<td>25 (45)</td>
<td>12 (36)</td>
<td>13 (59)</td>
<td>ns</td>
</tr>
<tr>
<td>Coronary artery disease, n (%)</td>
<td>23 (42)</td>
<td>13 (39)</td>
<td>10 (45)</td>
<td>ns</td>
</tr>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>15 (27)</td>
<td>5 (15.2)</td>
<td>10 (45.5)</td>
<td>0.0135</td>
</tr>
<tr>
<td>Prehospital left ventricular ejection fraction (%)</td>
<td>57.4 ± 13.2</td>
<td>59.4 ± 12.7</td>
<td>54.3 ± 13.0</td>
<td>ns</td>
</tr>
<tr>
<td>Ischemic dilated cardiomyopathy, n (%)</td>
<td>10 (18)</td>
<td>4 (12)</td>
<td>6 (27)</td>
<td>ns</td>
</tr>
<tr>
<td>Non-ischemic dilated cardiomyopathy, n (%)</td>
<td>6 (11)</td>
<td>5 (15)</td>
<td>1 (5)</td>
<td>ns</td>
</tr>
<tr>
<td>Old cerebrovascular accident, n (%)</td>
<td>9 (16)</td>
<td>4 (12)</td>
<td>5 (23)</td>
<td>ns</td>
</tr>
<tr>
<td>Cigarette smoking, n (%)</td>
<td>39 (71)</td>
<td>25 (76)</td>
<td>14 (64)</td>
<td>ns</td>
</tr>
<tr>
<td>Peripheral vascular disease, n (%)</td>
<td>6 (11)</td>
<td>3 (9)</td>
<td>3 (14)</td>
<td>ns</td>
</tr>
<tr>
<td>Valvular disease, n (%)</td>
<td>8 (15)</td>
<td>5 (15)</td>
<td>3 (14)</td>
<td>ns</td>
</tr>
<tr>
<td>Chronic lung disease, n (%)</td>
<td>9 (16)</td>
<td>6 (18)</td>
<td>3 (14)</td>
<td>ns</td>
</tr>
<tr>
<td>Previous anemia, n (%)</td>
<td>12 (22)</td>
<td>6 (18)</td>
<td>6 (27)</td>
<td>ns</td>
</tr>
<tr>
<td>Family history of sudden cardiac death, n (%)</td>
<td>5 (9)</td>
<td>4 (12)</td>
<td>1 (5)</td>
<td>ns</td>
</tr>
<tr>
<td>ACE inhibitors/ARBs use, n (%)</td>
<td>24 (44)</td>
<td>10 (30.3)</td>
<td>14 (63.6)</td>
<td>0.0146</td>
</tr>
</tbody>
</table>

ACE = angiotensin converting enzyme, ARB = angiotensin II receptor blocker, ns = non-significant
In hospital infections were reported in 34 patients (62%), 9 patients (16%) underwent tracheostomy, duration of hospitalization was 17.5 ± 18 days without differences between the groups.

Cardioverter defibrillator was implanted in 9 (27%) patients with JOW and in no patients without JOW (P < 0.00675).

In-hospital and long-term mortality were significantly higher in patients without JOW than in patients with JOW: 19 patients (86%) vs. 7 patients (21%) and 20 patients (91%) vs. 8 patients (24%), respectively, P < 0.00001 [Figure 2].

Interbeat interval was reported in 2 of 3 patients (66.7%) without JOW who survived and in 2 of 24 patients (7.7%) with JOW (P < 0.0001).

All baseline variables with significant differences between the groups in univariate analysis were included into the step-wise Cox regression model. In multivariate analysis, only old age, absence of JOW, and acute renal failure were found to be strongly associated with poor outcome. The absence of JOW had 2.9 times, 95% confidence interval (95% CI) 1.13–7.41, P < 0.0268. The median age on admission had 1.04 times, 95% CI 1.01–1.07, P < 0.0254 and acute renal failure on admission had 4.85 times, 95% CI 1.94–12.13, P < 0.0007 higher risk for death or IABI compared to patients with JOW.

**DISCUSSION**

In this study the absence of JOW during TH was associated with a worse prognosis in OHCA survivors.

The JOW is a positive deflection with a dome or hump configuration occurring at the J point (QRS-ST junction) on the surface electrocardiogram [4]. It is usually most prominent in the inferior and/or lateral leads [5]. An expert consensus report that focused on the terminology of early repolarization [3] recommended that the peak of an end QRS notch and/or the onset of an end QRS slur be designated as Jp and Jp should exceed 0.1 P9LQ•FRQWLJXRXVLQIHULRUDQGRUODWHUDOOHDGVRIDVWDQGDUG

12-lead electrocardiogram for ER to be present. It was further recommended that the start of the end QRS notch or J wave be designated as Jo and the termination as Jt. With a core temperature approaching 30–33°C, the incidence of observed J waves was 50–80% [3,5,6]. Other much less frequent conditions that have been reported to cause Osborn waves are hypercalcemia [7], brain injury [8], subarachnoid hemorrhage [9], over-sedation [10], vasospastic angina [11], myocardial ischemia [12], and idiopathic ventricular fibrillation [13,14]. Fleming and Muir [15] confirmed the association of Osborn waves with ventricular fibrillation in hypothermic patients. The occurrence of ventricular fibrillation seems to be related to the augmentation of the J waves. Yan and Antzelevitch [16] showed a highly significant correlation between the amplitude of the epicardial transmembrane action potential notch (in contrast to the endocardial ventricular action potential) and the amplitude of Osborn waves during hypothermia.

Previous studies have shown that JOW in normothermic patients is associated with increased mortality, especially tachyar-
rhythmic death [17]. Deep hypothermia causes elevation of the J point in surface electrocardiogram, which is explained by dispersion of action potentials between epicardial and endocardial myocardium provoked by changes in transmembrane channels’ currents during ventricular repolarization. In accidental hypothermia, the presence of JOW increased in inverse proportion to the temperature. Although mortality was high, the association between JOW and arrhythmic death in accidental hypothermia was not established [5,18].

The prognostic value of JOW during TH in OHCA survivors remains controversial. Rolfast et al. [19] reported that TH-induced Osborn waves are not associated with unfavorable short-term outcomes. In their cohort, during TH, JOW occurred in only 30% of the patients, and JOW during cooling were significantly more prevalent in the patients with ST elevation myocardial infarction (STEMI) than in patients without STEMI. Recently published work by Harhash and co-authors [2] demonstrated an increase in mortality among patients after OHCA when JOW was present on electrocardiogram both prior to and during TH. In contrast to our work, JOW was recognized on baseline electrocardiogram tracings in 20% and idiopathic VF was the etiology of OHCA in 18.6%. These findings correlate with the results of Williams et al. [20], which demonstrated that early repolarisation during TH was more common among survivors with idiopathic ventricular fibrillation than with ventricular fibrillation associated with coronary artery disease.

Importantly, there was another group of patients with significantly increased mortality that was not emphasized by Harhash et al. [2]: the patients without JOW at baseline and during TH (very similar to our cohort), which perfectly matches our results.

It should be noted that patients from our cohort without JOW were significantly older than patients with JOW, with a higher incidence of hypertension, diabetes mellitus, hyperlipidemia, and congestive heart failure, with lower pH, higher creatinine level and higher incidence of acute renal and liver failure on admission. The patients without JOW were more

![Kaplan-Meier survival curve](image-url)
likely to develop atrial fibrillation during the hospitalization and the main reason for death was multi-organ failure, shock, and coma. In the intensive care unit setting no patient died due to recurrent tachyarrhythmia. Thus, explanation for our results could be that patients who are at higher risk for death and IABI had more frequent multi-organ failure and deeper myocardial injury, which prevents the appearance of JOW on electrocardiogram tracings.

Negative JOW was found as an independent and highly significant predictor for poor prognosis, and during our clinical evaluation, especially in high risk patients were treated by hypothermia after OHCA.

Which factor has the greatest influence of transmembrane electrolyte currents in such conditions is to be seen in further studies.

LIMITATIONS
The study was retrospective and thus some data for analysis were not available. Specifically information regarding pre-hospital details regarding the cardiopulmonary resuscitation were insufficient and were not considered. The number of patients in our study was low and subset analysis could have been influenced by the limited power of the study. Other factors, we did not consider, may have influenced patient outcome.

CONCLUSIONS
In patient undergoing TH post OHCA, the absence of JOW during TH is associated with a worse outcome compared with patients in whom JOW appears throughout the hypothermia period. The pathophysiology of this phenomenon needs to be investigated in future trials.

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