ACTA MEDICA LITUANICA. 2019. Vol. 26. No. 3. P. 159–166

Electrocardiographic changes during therapeutic hypothermia: observational data from a single centre

Dovilė Jančauskaitė[1*],

Robertas Samalavičius[2],

Sigita Glaveckaitė[3, 4],

Palmyra Semėnienė[3, 4],

Pranas Šerpytis[3, 4, 5]

[1] *Faculty of Medicine,*
Vilnius University,
Vilnius, Lithuania

[2] *Centre of Anaesthesia,*
Intensive Care and Pain Management,
Vilnius University Hospital
Santaros klinikos,
Vilnius, Lithuania

[3] *Clinic of Cardiovascular Diseases,*
Faculty of Medicine,
Vilnius University,
Vilnius, Lithuania

[4] *Centre of Cardiology and Angiology,*
Vilnius University Hospital
Santaros klinikos,
Vilnius, Lithuania

[5] *Emergency Medicine Centre,*
Vilnius University Hospital
Santaros klinikos,
Vilnius, Lithuania

Background. Therapeutic hypothermia is recommended to reduce the risk of hypoxic brain damage and improve short-term survival after cardiac arrest. It also temporarily affects the cardiac conduction system. The aim of this study was to evaluate electrocardiographic changes during therapeutic hypothermia and their impact on the outcome.

Materials and methods. This retrospective analysis involved 26 patients who underwent therapeutic hypothermia after cardiac arrest in Vilnius University Hospital Santaros Klinikos from 2011 to 2015.

Results. During cooling, a significant reduction in the heart rate ($p = 0.013$), shortening of QRS complex duration ($p = 0.041$), and prolongation of the QTc interval ($p < 0.001$) were observed. During the cooling period, five patients had subtle Osborn waves, which disappeared after rewarming. The association between electrocardiographic changes during cooling and unfavourable neurological outcome or in-hospital mortality was non-significant.

Conclusions. Therapeutic hypothermia after cardiac arrest causes reversible electrocardiographic changes that do not increase the risk of in-hospital mortality or unfavourable neurological outcomes.

Keywords: therapeutic hypothermia, electrocardiography, Osborn wave, unfavourable neurological outcome, in-hospital mortality

* Correspondence to: Dovilė Jančauskaitė, Faculty of Medicine, Vilnius University, M. K. Čiurlionio 21, Vilnius 03101, Lithuania.
Email: dovile.jancauskaite@gmail.com

INTRODUCTION

The risk of neurological damage remains high even after successful restoration of spontaneous circulation (1, 2). Many studies have shown that hypothermia significantly reduces the risk of hypoxic brain damage, affects cardiac conduction, and has a positive effect on short-term survival (3–5). Therapeutic hypothermia is strongly recommended to prevent brain damage after cardiac arrest (2). Furthermore, it causes specific electrocardiographic (ECG) changes including sinus bradycardia and prolongation of the PR interval, QRS complex, and QTc interval (6, 7). In several studies, a reduction in body temperature has been associated with Osborn waves (1, 6, 7). The aim of this study was to evaluate ECG changes during therapeutic hypothermia and their impact on the outcome.

MATERIALS AND METHODS

This retrospective analysis of patients who suffered cardiac arrest and underwent therapeutic hypothermia after successful restoration of spontaneous circulation was performed in Vilnius University Hospital Santaros Klinikos. The study was approved by the local ethics committee (Vilnius University Hospital Santaros Klinikos, No. EK–55). From January 2011 to August 2015, therapeutic hypothermia was performed on 39 individuals. Patients were included in the study if three ECGs (before, during, and after therapeutic hypothermia) were available, although the patients with a pacemaker rhythm before cooling were excluded. The final evaluation included 26 patients, and 157 ECGs were analysed.

During therapeutic hypothermia, patients were cooled to 33 ± 1°C, hypothermia was maintained for 24 hours, then the patients were gradually rewarmed over a period of 12 hours. An extracorporeal heat exchanger was used for inducing and maintaining therapeutic hypothermia. The circuit consisted of two dialysis catheters placed in the femoral (for drainage) and internal jugular veins (for reinfusion of cooled blood), a centrifugal pump (Biopump BP-80, Medtronic Biomedicus, Minneapolis, Minn), an external heat exchanger (CSC 14, Sorin Group, Italy), and 1/4 inch PVC tubing. Intravenous propofol was used for sedation. Patients were treated by intensive cardiac care physicians while the cooling system was supervised by perfusionists. Before, during, and after therapeutic hypothermia, 12-lead ECGs were collected and analysed.

The cause of cardiac arrest, initial and post-hospitalisation rhythms, ECG parameters, electrolyte abnormalities (K^+, Na^+ and Ca^{2+}), unfavourable neurological outcomes (moderate to severe neurologic deficits, Glasgow Coma Scale ≤12), and in-hospital mortality were analysed. The ECG parameters analysed included the heart rate, duration of PR, QTc intervals, QRS complex, atrial fibrillation, and Osborn waves. Statistical analyses were performed using MS Excel and SPSS software packages. Numerical variables were compared by *t*-test, and categorical variables were compared by chi-square test or Fisher's exact test if the expected cell count was <5. Categorical data are presented as absolute numbers (*n*) and percentages (%). Numerical data are presented as the mean and standard deviation (SD). For all tests, a *p*-value less than 0.05 was considered significant.

RESULTS

The mean age of the studied patients was 56 ± 12 years, 20 (77%) of whom were males. Nineteen (73%) patients experienced an out-of-hospital cardiac arrest. The most common cause of cardiac arrest was myocardial infarction ($n = 21$, 81%), with 12 (46%) patients suffering myocardial infarction with ST segment elevation. The most common initial heart rhythm upon first medical contact was ventricular fibrillation, which was present in 20 (77%) patients. On admission to the hospital, the sinus rhythm was registered in 24 (92%) patients and atrial fibrillation in two (8%) patients. The characteristics of the patients in this study are presented in Table 1.

A total of 157 ECGs were analysed for changes during therapeutic hypothermia. These changes are presented in Table 2.

During cooling, a statistically significant reduction in the heart rate (93 ± 22 vs. 82 ± 21 bpm, $p = 0.013$), shortening of QRS complex duration (109 ± 20 vs. 102 ± 19 ms, $p = 0.041$), and prolongation of the QTc interval (481 ± 29 vs. 518 ± 30 ms, $p < 0.001$) were observed (Figs. 1–3).

Table 1. Characteristics of the study patients ($N = 26$)

Age (years)	56 ± 12
Male	20 (77%)
Cardiac arrest in the hospital	
No	19 (73%)
Diagnosis	
Myocardial infarction	21 (81%)
With ST segment elevation	12 (46%)
Without ST segment elevation	9 (35%)
Pulmonary embolism	1 (4%)
Ischemic stroke	1 (4%)
Life-threatening arrhythmias	3 (12%)
Initial rhythm	
Ventricular fibrillation	20 (77%)
Asystole	3 (12.5%)
No data	3 (12.5%)
Rhythm after arrival at the hospital	
Sinus rhythm	24 (92%)
Atrial fibrillation	2 (8%)
Interventions	
Coronary angiography	25 (96%)
Primary stenting	17 (65%)

Table 2. Changes in ECG and arrhythmias before, during, and after therapeutic hypothermia

	Before TH	During TH	After TH
Heart rate (bpm)	93 ± 22	82 ± 21	107 ± 26
PR interval (ms)	176 ± 25	173 ± 20	152 ± 35
QRS duration (ms)	109 ± 20	102 ± 19	104 ± 23
QTc interval (ms)	481 ± 29	518 ± 30	470 ± 46
Atrial fibrillation (*n*)	2	2	4
Osborn wave (*n*)	0	5	0

TH, therapeutic hypothermia; *n*, number of patients.

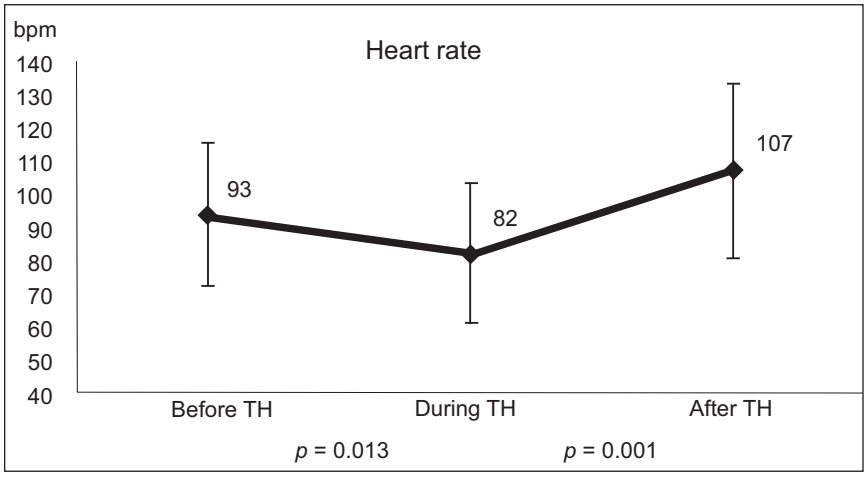

Fig. 1. Heart rate changes during therapeutic hypothermia

TH – therapeutic hypothermia.

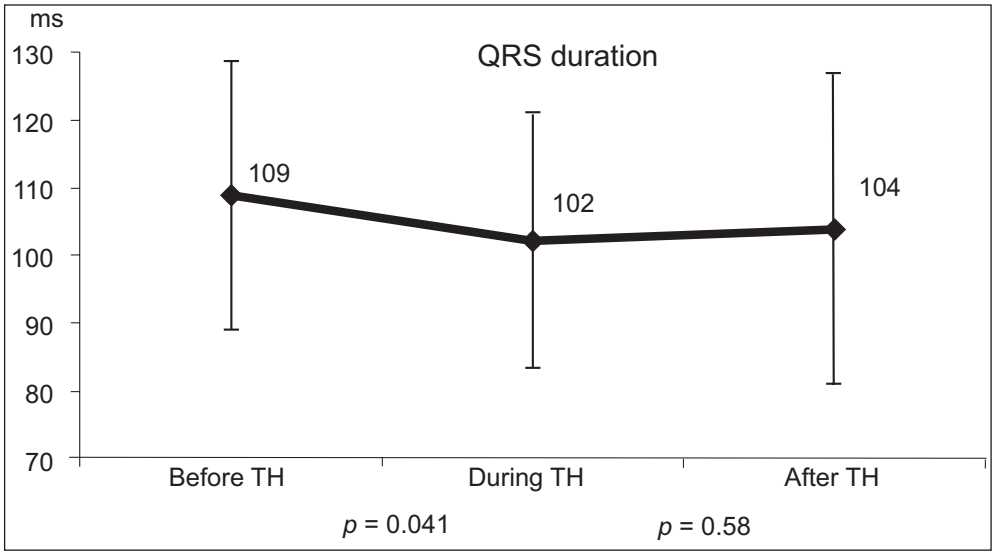

Fig. 2. Changes in QRS duration during therapeutic hypothermia

TH – therapeutic hypothermia. QRS duration measured in milliseconds.

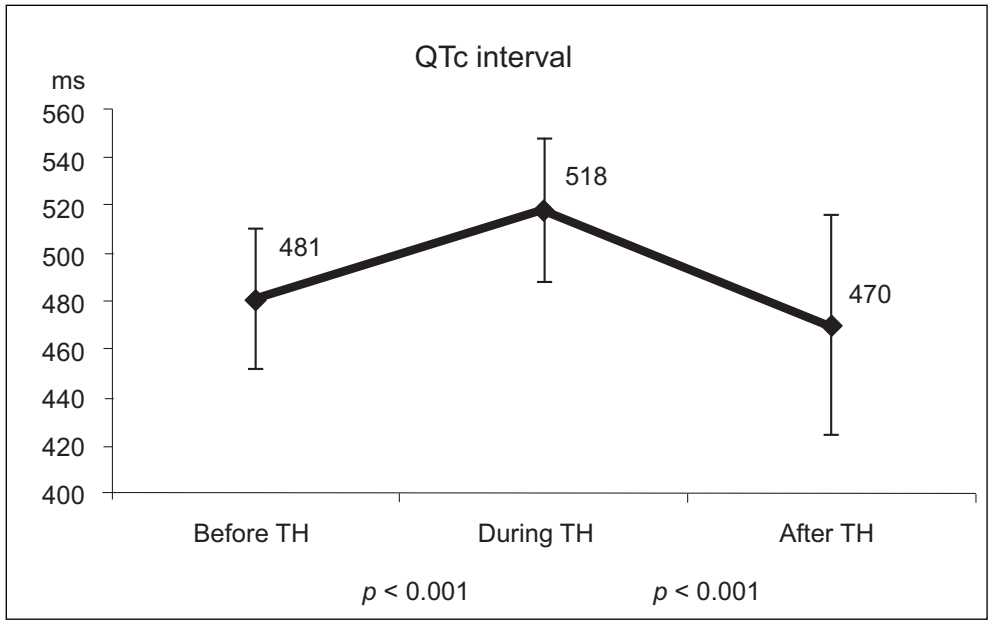

Fig. 3. Changes in QTc interval during therapeutic hypothermia

TH – therapeutic hypothermia. QTc interval measured in milliseconds.

There was no statistical difference in PR interval duration before or during therapeutic hypothermia, but the duration of the PR interval was significantly reduced after therapeutic hypothermia (173 ± 20 vs. 152 ± 35 ms, $p < 0.01$). No new episodes of arrhythmia were observed during cooling, except in two patients who already had atrial fibrillation prior cooling. After rewarming, three patients had new-onset atrial fibrillation and one patient had returned to the sinus rhythm. Three patients had a heart rhythm <60 bpm during cooling. One patient required temporary pacing because of conduction abnormalities after therapeutic hypothermia. No life-threatening arrhythmias (ventricular tachycardia or ventricular fibrillation) were observed. Moreover, five patients had subtle Osborn waves while hypothermic, which disappeared during rewarming (Fig. 4).

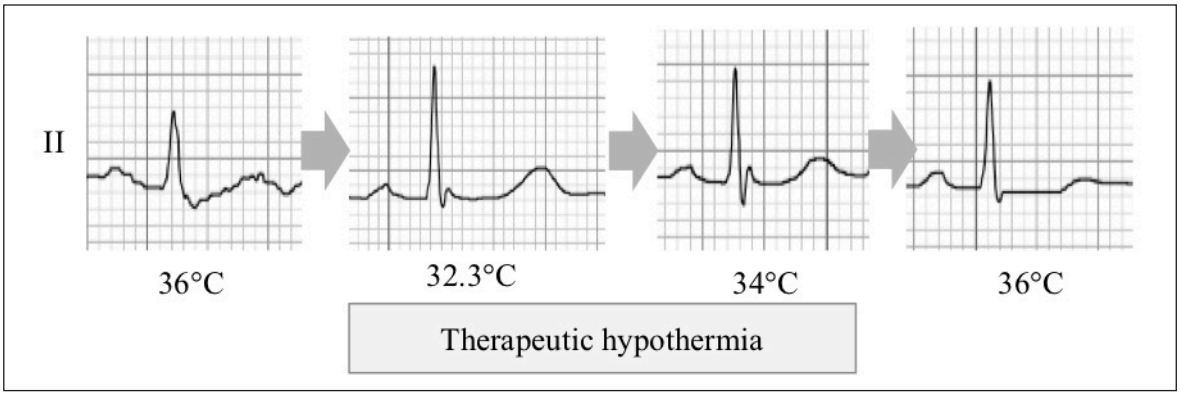

Fig. 4. Osborn wave during therapeutic hypothermia in the ECG of one patient (II standard derivation)

The changes in ECG during cooling were not found to be significantly associated with electrolyte concentration during hospitalisation, an unfavourable neurological outcome, or in-hospital mortality (Tables 3 and 4).

A favourable neurological outcome after rewarming was observed in 11 (42.3%) patients. Twelve (46.2%) patients died during the hospitalisation period.

DISCUSSION

The typical ECG patterns in therapeutic hypothermia are sinus bradycardia, atrial fibrillation,

Table 3. Change in ECG parameters and their impact on unfavourable neurological outcomes

Change in ECG parameters (before – during TH)	Favourable neurological outcome	Mean ± SD	*p*-value
Δ **in** HR (bpm)	Yes	6.5 ± 18.9	0.349
	No	14.4 ± 22.4	
Δ **in** PR interval (ms)	Yes	0.6 ± 23.0	0.673
	No	4.6 ± 24.5	
Δ **in** QRS duration (ms)	Yes	6.2 ± 14.2	0.752
	No	8.5 ± 20.3	
Δ **in** QTc interval (ms)	Yes	–39.4 ± 25.2	0.631
	No	–34.5 ± 25.5	

ECG, electrocardiographic; TH, therapeutic hypothermia; SD, standard deviation; HR, heart rate.

Table 4. Change in ECG parameters and their impact on in-hospital mortality

Change in ECG parameters (before – during TH)	In-hospital mortality	Mean ± SD	*p*-value
Δ in HR (bpm)	Yes	18.3 ± 21.4	0.105
	No	4.9 ± 19.1	
Δ in PR interval (ms)	Yes	–0.6 ± 23.0	0.497
	No	5.9 ± 24.3	
Δ in QRS duration (ms)	Yes	8.0 ± 14.0	0.897
	No	7.1 ± 20.9	
Δ in QTc interval (ms)	Yes	–38.7 ± 23,6	0.696
	No	–34.7 ± 26.9	

ECG, electrocardiographic; TH, therapeutic hypothermia; SD, standard deviation; HR, heart rate.

prolongation of PR and QTc intervals, prolongation of QRS complex, presence of Osborn waves, atrial fibrillation, and ventricular fibrillation (6, 7). These ECG changes are dependent on the core body temperature. It is recommended to maintain a constant target core temperature between 32°C and 36°C for patients for whom temperature control is used (2).

Bradycardia is the most common bradyarrhythmia during hypothermia (8). Mild therapeutic hypothermia was found to reduce heart rate in our and other studies (1, 9–11); however, a rate <60 bpm was only observed in three patients. Souza et al. found a significant correlation between core body temperature and the heart rate, whereby lower temperatures were associated with more intense bradycardia (12). Decreased body temperature leads to a slowing down of metabolic and cardiovascular processes. This leads to a decreased conduction velocity, which can cause bradycardia, heart block, and prolongation of QT interval (11). Hypothermia reduces the diastolic depolarisation rate of the sinoatrial node P cells while also decreases resting potential, as well as prolongs the action potential and refractory period (slowing repolarisation) (6, 13).

Studies have shown that the PR interval is prolonged during therapeutic hypothermia (10, 11), but this is not statistically significant in all cases (1, 9). In our study, no significant difference in the PR interval was found before and during cooling, but the duration of the PR interval significantly reduced after therapeutic hypothermia.

There are no consistent data on changes in the QRS complex during therapeutic hypothermia. According to the results of a study by Salinas et al., the duration of the QRS complex was prolonged during cooling (9), which is in contrast with the results of our and other studies in which it was found to be shortened (1, 10, 11).

The QT interval reflects the entire electric ventricular systole, including processes of depolarisation and repolarisation. It has been suggested that it is more likely that hypothermia prolongs the ventricular repolarisation phase rather than the depolarisation phase (14). This is because greater changes are observed in the QTc interval than in the QRS complex. A secondary cause of the prolonged QT/QTc interval is J wave formation and the slowdown of ventricular repolarisation (6). It is likely that hypothermia has a protective effect on myocardial cell membranes; therefore, the short-term change in the QT interval is not sufficient to cause arrhythmias or lead to an unfavourable outcome (11). Several studies have reported significant prolongation of the QTc interval during cooling (1, 9–11, 15). Thus, ECG should be carefully monitored during therapeutic hypothermia in patients with long QT syndrome (9).

Studies have shown that the Osborn wave frequency ranges from 2% to 3% during therapeutic hypothermia (32–34°C) (1, 11). Osborn waves (J waves) are observed in 80% of patients with a core body temperature below 30°C (6) and 100% of those with a temperature below 28°C [16]. The first time a J wave was described in detail was by John J. Osborn in 1953 [17], and they have since then been referred to as Osborn waves. He experimentally induced hypothermia in dogs and examined the effect of hypothermia on respiratory and cardiac functions. Osborn waves are the most specific ECG change during hypothermia, but these are not pathognomonic.

Atrial fibrillation most frequently occurs in moderate hypothermia (50–60% of cases) before the body temperature falls below 29°C (6). During therapeutic hypothermia, no new episodes of atrial fibrillation were observed (Table 2). Ventricular fibrillation is most frequently observed when the core body temperature reaches 28°C (6).

Therapeutic hypothermia has a low proarrhythmic potential despite significant prolongation of the PR and QTs intervals in patients after cardiac arrest. According to previous studies, a high frequency of ventricular tachyarrhythmias are observed in patients with a body temperature <32°C; however, therapeutic hypothermia is safe to use in patients after cardiac arrest when the temperature is between 32°C and 34°C (10, 18). Therefore, the prevalence of arrhythmia probably depends on the body temperature during cooling. Therapeutic hypothermia could be used on many patients after cardiac arrest without an increased risk of arrhythmias, despite significant changes in ECG (10).

Mild hypothermia might have an impact on coagulation and increase the risk of bleeding, although this has not yet been confirmed by clinical studies (2). According to several studies,

3.7–4.8% of patients experience bleeding complications and 4.6% experience severe cardiogenic shock during hypothermia (10, 19). In our study, three (11.5%) patients had bleeding complications during therapeutic hypothermia. The reason for the higher frequency of bleeding complications may be the high percentage of patients (88%) requiring treatment with anticoagulants and/or antiplatelet drugs due to acute coronary syndrome.

The ECG changes observed during hypothermia were not associated with increased in-hospital mortality or an increased risk of unfavourable neurological outcomes. Twelve (46.2%) patients died during hospitalisation. These data are very similar to the findings of a retrospective study by Lam et al. (11), which reported an in-hospital mortality of around 45% (45 out of 101 patients died). Prolongation of the QTc interval during therapeutic hypothermia was not associated with increased in-hospital mortality (11). However, according to a study by Stær-Jensen et al., bradycardia during therapeutic hypothermia was associated with a good neurological outcome, indicating that bradycardia should not be aggressively treated during cooling (20).

CONCLUSIONS

According to the findings of our study, therapeutic hypothermia led to a reduction in the heart rate, shortening of the QRS complex duration, and prolongation of the QTc interval. These electrocardiographic changes during cooling were not associated with unfavourable neurological outcomes or in-hospital mortality.

CONFLICT OF INTEREST

None declared.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Received 13 October 2019
Accepted 12 November 2019

References

1. Rolfast CL, Lust EJ, de Cock CC. Electrocardiographic changes in therapeutic hypothermia. Crit Care. 2012; 16(3): R100.
2. Nolan JP, Soar J, Cariou A, Cronberg T, Moulaert VRM, Deakin CD, et al. European Resuscitation Council and European Society of Intensive Care Medicine Guidelines for Post-resuscitation Care 2015: Section 5 of the European Resuscitation Council Guidelines for Resuscitation 2015. Resuscitation. 2015; 95: 202–22.
3. Tiainen M, Poutiainen E, Kovala T, Takkunen O, Häppölä O, Roine RO. Cognitive and neurophysiological outcome of cardiac arrest survivors treated with therapeutic hypothermia. Stroke J Cereb Circ. 2007; 38(8): 2303–8.
4. Kim F, Olsufka M, Longstreth WT, Maynard C, Carlbom D, Deem S, et al. Pilot randomized clinical trial of prehospital induction of mild hypothermia in out-of-hospital cardiac arrest patients with a rapid infusion of 4 degrees C normal saline. Circulation. 2007; 115(24): 3064–70.
5. Kämäräinen A, Virkkunen I, Tenhunen J, Yli-Hankala A, Silfvast T. Prehospital induction of therapeutic hypothermia during CPR: a pilot study. Resuscitation. 2008; 76(3): 360–3.
6. Darocha T, Sobczyk D, Kosiński S, Jarosz A, Gałązkowski R, Nycz K, Drwiła R. Electrocardiographic changes caused by severe accidental hypothermia. J Cardiothorac Vasc Anesth. 2015; 29(6)e83–6.
7. Doshi HH, Giudici MC. The EKG in hypothermia and hyperthermia. J Electrocardiol. 2015; 48(2): 203–9.
8. Omar HR, El-Khabiry E, Mangar D, Camporesi EM. The effect of various stages of hypothermia on the ECG. Cardiovasc Endocrinol. 2016; 5(1): 28–32.
9. Salinas P, Lopez-de-Sa E, Pena-Conde L, Viana-Tejedor A, Rey-Blas JR, Armada E, et al. Electrocardiographic changes during induced therapeutic hypothermia in comatose survivors after cardiac arrest. World J Cardiol 2015 Jul. 26; 7(7): 423–30.
10. Lebiedz P, Meiners J, Samol A, Wasmer K, Reinecke H, Waltenberger J, et al. Electrocardiographic changes during therapeutic hypothermia. Resuscitation. 2012; 83(5): 602–6.
11. Lam DH, Dhingra R, Conley SM, Kono AT. Therapeutic hypothermia-induced electrocardiographic

changes and relations to in-hospital mortality. Clin Cardiol. 2014; 37(2): 97–102.
12. de Souza D, Riera ARP, Bombig MT, Francisco YA, Brollo L, Filho BL, et al. Electrocardiographic changes by accidental hypothermia in an urban and a tropical region. J Electrocardiol. 2007; 40(1): 47–52.
13. Polderman KH. Mechanisms of action, physiological effects, and complications of hypothermia. Crit Care Med. 2009; 37(7 Suppl): S186–202. Cited in PubMed; PMID: 19535947.
14. Zimmerman F. Tachycardia and bradycardia in the ICU. In: ACCP Critical Care Medicine Board Review: 21st Edition 2012. American College of Chest Physicians. 2012. p. 123–34.
15. Khan JN, Prasad N, Glancy JM. QTc prolongation during therapeutic hypothermia: are we giving it the attention it deserves? Europace. 2010; 12(2): 266–70.
16. Higuchi S, Takahashi T, Kabeya Y, Hasegawa T, Nakagawa S, Mitamura H. J waves in accidental hypothermia. Circ J. 2014; 78(1): 128–34.
17. Osborn JJ. Experimental hypothermia; respiratory and blood pH changes in relation to cardiac function. Am J Physiol. 1953; 175(3): 389–98.
18. Piktel JS, Jeyaraj D, Said TH, Rosenbaum DS, Wilson LD. Enhanced dispersion of repolarization explains increased arrhythmogenesis in severe versus therapeutic hypothermia. Circ Arrhythm Electrophysiol. 2011; 4(1): 79–86.
19. de Bourmont S, Demory D, Durand-Gasselin J, Donati SY, Arnal J-M, Corno G, et al. Efficiency and safety of a noninvasive therapeutic hypothermia protocol in cardiac arrest. Eur J Emerg. 2015; 22(1): 29–34.
20. Stær-Jensen H, Sunde K, Olasveengen TM, Jacobsen D, Drægni T, Nakstad ER, et al. Bradycardia during therapeutic hypothermia is associated with good neurologic outcome in comatose survivors of out-of-hospital cardiac arrest. Crit Care Med. 2014; 42(11): 2401–8.

Dovilė Jančauskaitė, Robertas Samalavičius, Sigita Glaveckaitė, Palmyra Semėnienė, Pranas Šerpytis

ELEKTROKARDIOGRAFINIAI POKYČIAI TAIKANT TERAPINĘ HIPOTERMIJĄ: VIENO GYDYMO CENTRO STEBĖJIMO DUOMENYS

Santrauka

Įvadas. Terapinė hipotermija rekomenduojama siekiant sumažinti hipoksinio smegenų pažeidimo riziką ir pagerinti išgyvenamumą sustojus širdžiai. Hipotermija laikinai paveikia širdies laidžiąją sistemą. Tyrimo tikslas – nustatyti elektrokardiografinius pokyčius taikant terapinę hipotermiją ir įvertinti jos įtaką gydymo taktikoms.

Metodai. Atlikta retrospektyvinė 26 pacientų, kuriems Vilniaus universiteto ligoninės Santaros klinikose 2011–2015 m. taikyta terapinė hipotermija sustojus širdies darbui, atvejų analizė.

Rezultatai. Šaldymo metu stebėtas reikšmingas širdies dažnio retėjimas (p = 0,013), QRS komplekso trukmės trumpėjimas (p = 0,041) ir QTc intervalo ilgėjimas (p < 0,001). Penkiems pacientams stebėtos nežymios Osborno bangos, kurios išnyko šildant. Reikšmingo ryšio tarp elektrokardiografinių pakitimų, nepalankių neurologinių išeičių ar hospitalinio mirštamumo nepastebėta.

Išvados. Terapinė hipotermija sustojus širdžiai sukelia grįžtamus elektrokardiografinius pakitimus, kurie nedidina hospitalinio mirštamumo ar nepalankių neurologinių išeičių rizikos.

Raktažodžiai: terapinė hipotermija, elektrokardiografija, nepalankios neurologinės išeitys, hospitalinis mirštamumas