Original Article

The R-R Interval Variation as the Good Outcomes Predictor in Survivors after Cardiac Arrest with Targeted Temperature Management

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Objective: Targeted temperature management (TTM) is recommended for patients suffering a cardiac arrest after restoration of spontaneous circulation (ROSC). Heart rate variability (HRV), which reflects autonomic function, has been proposed as an outcome predictor but HRV measurement is not suitable for everyday practice. RR interval variation (RRIV), which can be measured easily at the bedside using surface electrocardiography, is a parameter indicating the integrity of the autonomic nervous system. We assessed the neurologic outcomes and predictive factors involving RRIV in cardiac arrest patients who received TTM.

Materials and Methods: We performed a retrospective, single-center, observational study to describe the neurologic outcomes of cardiac arrest patients who received TTM measured by the cerebral performance categories (CPC) scale. Clinical data was collected from medical records dated from January 2010 to June 2015. RRIV was calculated by difference between the maximum RR interval and the minimum RR interval.

Results: During the study period, 46 patients were examined; 56.5% were male. The most common cause of cardiac arrest was cardiac in origin (37%). The most common initial cardiac rhythm was asystole (52.2%). RRIV was correlated with HRV parameter by standard analysis software in the first 11 patients. In our setting, 12 patients (26.1%) displayed favorable neurologic outcomes (CPC1 or 2). RRIV ≥40 msec was associated with favorable neurologic outcomes (p = 0.046).

Conclusion: RRIV may be used as a tool for predicting neurologic outcomes. RRIV at ≥40 msec was associated with favorable neurologic outcomes.

Keywords: Targeted temperature management, Cardiac arrest, Neurologic outcomes, RR interval variation

J Med Assoc Thai 2020;103(Suppl.3): 87-94
Website: http://www.jmatonline.com

Cardiac arrest is a widespread and prominent public health problem. It is estimated that out-of-hospital cardiac arrests account for 300,000 deaths in United States and Europe each year among the adult population[1]. Up to 11% of patients with out-of-hospital cardiac arrest survive until hospital discharge, however, this depend on the initial cardiac rhythm[2]. Among survivors, 19 to 32% have poor neurologic outcomes[3,4]. Targeted temperature management (TTM) has been shown to increase the rate of favorable neurologic outcomes and reduce mortality[5,6]. TTM is recommended by standard guidelines for comatose cardiac arrested patients after restoration of spontaneous circulation (ROSC). The purposed mechanisms for this neuroprotective effect are a reduction in cerebral oxygen consumption and the manipulation of several cellular chemical and physical properties[7]. Endovascular and surface cooling methods are accepted for TTM[8]. Despite many reported cases of TTM after cardiac arrest in Thailand, few studies have evaluated neurologic outcomes and their predictors[9].

Heart rate variability (HRV), a well-known indicator of autonomic function, has been proposed as an outcome predictor after carrying out TTM[10,11]. However, the process of HRV measurement is quite sophisticated, requiring computer software tools, and is thus not suitable for predicting neurologic outcome in standard clinical practice. RR interval variation (RRIV), which can be measured easily at the bedside using surface electrocardiography, is a parameter indicating integrity of the autonomic nervous system[12]. But no studies have yet evaluated the role of RRIV in predicting neurologic outcomes in the setting of post cardiac arrest. Therefore, we assessed the neurologic outcomes and predictive factors for the outcomes involving RRIV in cardiac arrest adult patients receiving TTM at Thammasat University Hospital, Thailand.

Materials and Methods

Study design

The present study was designed as a retrospective, single-center, observational study. The protocol was

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How to cite this article: Muengtaweepongsa S, Visuttichaikit S, Jantanukul A. The R-R Interval Variation as the Good Outcomes Predictor in Survivors after Cardiac Arrest with Targeted Temperature Management. J Med Assoc Thai 2020;103(Suppl.3): 87-94.

approved by the Human Ethics Committee of Thammasat University.

Population study

We reviewed the medical records of Thammasat University Hospital to identify all patients ≥15 years of age who had suffered out-of-hospital and in-hospital cardiac arrest with restoration of spontaneous circulation and received TTM. The most common technique employed was surface cooling with ArcticSun™, as shown in Figure 1. The Thammasat University Hospital selection Criteria for TTM after cardiac arrest were: witnessing the cardiac arrest, the initial cardiac rhythm of ventricular fibrillation, pulseless ventricular tachycardia, pulseless electrical activity, or asystole, an estimated interval of less than 15 minutes from the patient's collapse to resuscitation, a resuscitation time of less than 60 minutes, a Glasgow Coma Scale of 8 or below, a systolic blood pressure of more than 90 mmHg with or without vasopressors, and an interval of less than 8 hours from restoration of spontaneous circulation to TTM.

Figure 1. TTM at 33 degrees celsius by surface cooling at Thammasat University targeted temperature nanagement excellence center.

The exclusion criteria for TTM were as follows: pregnancy, a Glasgow Coma Scale of 10 and improving, a known terminal illness, comatose state prior to cardiac arrest, prolonged hypotension (mean arterial pressure less than 60 mmHg) for more than 30 minutes after the return of spontaneous circulation, evidence of hypoxemia more than 15 minutes following the return of spontaneous circulation, or a known coagulopathy that cannot be corrected. The inclusion/exclusion criteria of Thammasat University Targeted Temperature Management Excellence Center are shown in Table 1.

The TTM protocol was divided into 3 phases: induction, sustainment, and rewarming. In the induction phase, patients were cooled to a target temperature of 33°C as quickly as possible with the use of an external cooling device. The core temperature monitoring was made with an esophageal temperature probe. The Bedside Shivering Assessment Score was recorded every 30 minutes. Shivering was initially treated by a skin counter-warming technique and intravenous administration of pethidine as needed. In the sustainment phase, the core temperature was maintained at 33°C for 24 hours from the start of cooling with no or minor fluctuation (maximum 0.2°C to 0.5°C). In the rewarming phase, patients were slowly rewarmed at the rewarming rate of 0.1°C to 0.5°C per hour. The ideal temperature curve is shown in Figure 2.

Data collection

Demographic characteristics (sex, age, occupation, underlying diseases), cause of cardiac arrest, location of the cardiac arrest, interval from the patient's collapse to resuscitation, initial cardiac rhythm, cardiopulmonary resuscitation details, duration of resuscitation, heart rate after the return of spontaneous circulation, heart rate during TTM, result of non–contrast-enhanced brain computed tomography

Table 1. Inclusion and exclusion criteria for TTM after cardiac arrest

Inclusion criteria
1) Witnessed arrest
2) Any initial rhythm, However initial rhythm VF or pulseless VT is the first priority
3) Time to ACLS was less than 15 minutes and total of ACLS time less than 60 minutes
4) GCS of 8 or below
5) SBP of >90 with or without vasopressors
6) Less than 8 hours have elapsed since return of spontaneous circulation (ROSC)
Exclusion criteria
1) Pregnancy
2) Known functional dependence
3) Down time of >30 minutes
4) ACLS preformed for >60 minutes
5) Known terminal illness
6) Comatose state prior to cardiac arrest
7) Prolonged hypotension (i.e. MAP <60 for >30 minutes)
8) Evidence of hypoxemia for >15 min following ROSC
9) Known coagulopathy that cannot be reversed

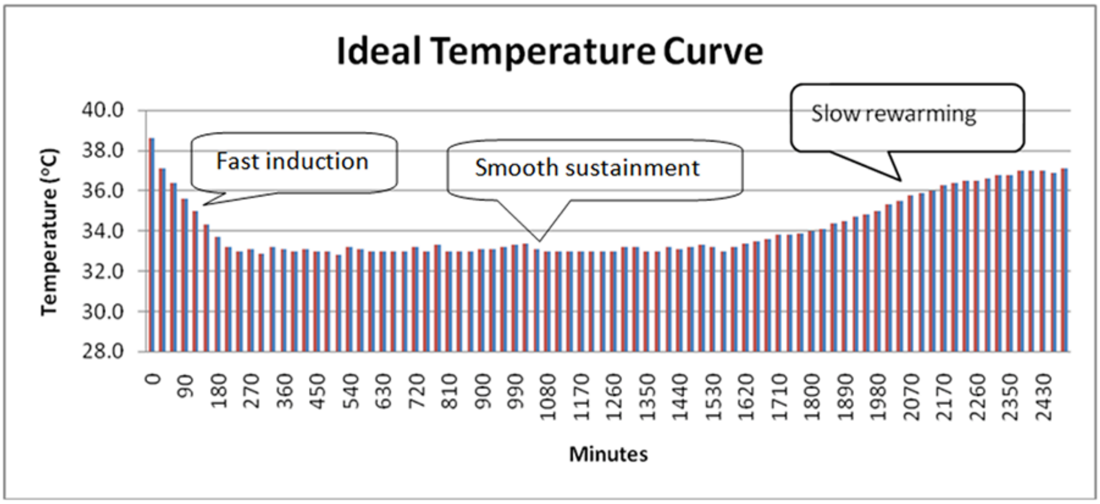

Figure 2. The ideal temperature curve for TTM.

(NECT), and neurologic outcome using the cerebral performance categories (CPC) scale of individual patients were collected from medical records dated from January 2010 to June 2015. RRIV, measured with a surface 12-lead electrocardiogram at the time the target temperature of 33°C was achieved, was calculated by the difference between the maximum RR and minimum RR intervals.

The electrocardiogram signals of 11 patients were analyzed for any correlation between RRIV methods and HRV parameter by using standard analysis software. The lead II ECG data was measured for 10 minutes and a sampling rate of 1,000 Hz was recorded using Power Lab systems and LabchartPro7 Software (AD Instruments). Next, the HRV parameters, time domain and frequency domain, were analyzed using Heart Rate Variability Analysis Software (Kubios-HRV version 2.0). A Spearman rank correlation coefficient was performed to analyze the relationship between our methods and standard analysis software.

Neurologic outcome assessment

Neurologic outcome measures were determined by a medical chart review at the time of hospital discharge with the use of CPC, a 5-category scale for measuring neurologic status after cardiac arrest[13,14].

CPC 1 (good cerebral performance): conscious, alert, able to work and lead a normal life. May have minor psychologic or neurologic deficits.

CPC 2 (moderate cerebral disability): conscious. Sufficient cerebral function for part-time work in sheltered environment or independent activities of daily life. May have hemiplegia, seizures, ataxia, dysarthria, or permanent memory or mental changes.

CPC 3 (severe cerebral disability): conscious. Dependent on others for daily support. Has at least limited cognition. This category includes a wide range of cerebral abnormalities, from patients who are ambulatory but have severe memory disturbances or dementia precluding independent existence, to those who are paralyzed and can communicate only with their eyes, as in the "locked in" syndrome.

CPC 4 (coma/vegetative state): unconscious. Unaware of surroundings, no cognition. No verbal and/or psychologic interaction with environment.

CPC 5: brain dead, circulation preserved.

CPC 1 to 2 were determined to be favorable neurologic outcomes. CPC 3 to 5 were determined to be unfavorable outcomes.

Statistical analysis

Continuous variables are reported as medians and interquartile ranges. Categorical variables are reported as counts and percentages. The Chi-square test, or Fisher's exact test, was used to compare categorical variables in the group with favorable neurologic outcome and group with unfavorable outcomes. Continuous variables between groups were compared by t-test or Mann-Whitney U test. Multivariate models were adjusted for suspected predictors of favorable neurologic outcomes. The *p*-values of less than 0.05 were considered to indicate statistical significance. IBM SPSS Statistics software version 22.0 was used to analyze the data.

Results

Patient characteristics

A total of 46 cardiac arrest patients receiving TTM were assessed; 30 (65.2%) suffered out-of-hospital cardiac arrests and 16 (34.8%) suffered in-hospital cardiac arrests. Table 2 shows the clinical characteristics of the patients. 26 patients (56.5%) were male. The most common underlying disease was diabetes mellitus (21.7%). The most common cause of cardiac arrest was cardiac in origin (37%), followed by respiratory failure (30.4%). The most frequent initial cardiac rhythm was asystolic (52.2%). RRIV was correlated with HRV parameter by standard analysis software in the first 11 patients, as shown in Table 3. At hospital discharge, 12 patients (26.1%) had favorable neurologic outcomes (CPC 1 or 2). Patients who had favorable neurologic outcomes were more likely to have underlying malignancy (p = 0.015) and unknown causes of cardiac arrest (p = 0.020). Patients with unfavorable neurologic outcomes were more likely to have had a cardiac-based cause for cardiac arrest (p = 0.017).

Variables associated with favorable neurologic outcome at hospital discharge

Table 4 shows the variables associated with neurologic outcome. In univariate analyses, patients who had favorable neurologic outcomes had significantly higher RRIV rates (p<0.001) when compared with the patients with unfavorable outcomes.

In multivariate analyses, as shown in Table 5, only RRIV of ≥40 milliseconds was significantly associated with favorable neurologic outcomes (OR 7.961, 95% CI, 1.036 to 61.182, p = 0.046).

Generalized brain edema, as revealed by brain

Table 2. Characteristics of post cardiac arrest patients receiving TTM according to neurologic outcome at hospital discharge

Characteristic	All patients (n = 46)	Favorable neurologic outcome* (n = 12)	Unfavorable neurologic outcome+ (n = 34)	p-value
Male sex (%)	26 (56.5)	6 (50)	20 (58.8)	0.596
Age (year), median (IQR)	48 (39 to 66)	42 (29.25 to 57.25)	53 (40 to 67)	0.081
Medical history, No. (%)				
Diabetes	10 (21.7)	1 (8.3)	9 (26.5)	0.190
Coronary artery disease	2 (4.3)	1 (8.3)	1 (2.9)	0.431
Asthma	3 (6.5)	1 (8.3)	2 (5.9)	0.768
Chronic obstructive pulmonary disease	1 (2.2)	0 (0)	1 (2.9)	0.548
HIV infection	1 (2.2)	0 (0)	1 (2.9)	0.548
Malignancy	2 (4.3)	2 (16.7)	0 (0)	0.015
None	18 (39.1)	5 (41.7)	13 (38.2)	0.834
Cause of cardiac arrest, No. (%)				
Cardiac	17 (37)	1 (8.3)	16 (47.1)	0.017
Respiratory failure	14 (30.4)	6 (50)	8 (23.5)	0.087
Sepsis	3 (6.5)	0 (0)	3 (8.8)	0.287
Trauma	6 (13)	2 (16.7)	4 (11.8)	0.665
Metabolic	1 (2.2)	0 (0)	1 (2.9)	0.548
Unknown	4 (8.7)	3 (25)	1 (2.9)	0.020
Others	1 (2.2)	0 (0)	1 (2.9)	0.548
Location of cardiac arrest, No. (%)				
Out of hospital	30 (65.2)	8 (66.7)	22 (64.7)	0.902
In hospital	16 (34.8)	4 (33.3)	12 (35.3)	0.902
Initial cardiac rhythm, No. (%)				
Asystole	24 (52.2)	6 (50)	18 (52.9)	0.861
PEA	10 (21.7)	1 (8.3)	9 (26.5)	0.190
VF	11 (23.9)	5 (41.7)	6 (17.6)	0.094
Pulseless VT	1 (2.2)	0 (0)	1 (2.9)	0.548

* Patients with cerebral performance categories scale 1 to 2 at hospital discharge; + Patients with cerebral performance categories scale 3 to 5 at hospital discharge

Table 3. Correlation between R-R interval and HRV parameter in 11 patients

	SDNN	pNN50	VLF	LF	HF	LF HF ratio
Spearman r*	0.688	0.184	0.610	0.789	-0.789	0.789
Number of XY pairs	11	11	11	11	11	11

* >0.05

Table 4. Clinical factors of post cardiac arrest patients receiving TTM categorized by neurologic outcome at hospital discharge

Clinical factor	All patients (n = 46)	Favorable Neurologic Outcomes (n = 12)	Unfavorable Neurologic Outcomes (n = 34)	*p*-value
Interval between collapse and resuscitation (min), median (IQR)	8.5 (5 to 20)	7.5 (5 to 13.75)	8.5 (5 to 20)	0.442
Resuscitation duration (min), median (IQR)	20 (8.75 to 32.5)	17 (2.75 to 29.5)	24 (12.25 to 34.25)	0.226
Total adrenaline dose (mg), median (IQR)	5 (2 to 10)	4.5 (1.25 to 9.25)	5.5 (2.75 to 10)	0.445
Number of defibrillation, median (IQR)	1 (0 to 4)	1 (0 to 4.75)	1 (0 to 4)	0.782
Interval between restoration of spontaneous circulation to TTM* (hr), median (IQR)	4.15 (3 to 6.55)	5.15 (3.25 to 6.75)	4 (2.94 to 6.55)	0.447
Mean heart rate during TTM (bpm), median (IQR)	86 (74.75 to 101)	82 (72.25 to 89.75)	87 (77.25 to 101.50)	0.358
Minimum heart rate during TTM (bpm), median (IQR)	70.5 (55.5 to 83.75)	65.5 (55 to 77)	72.5 (55.5 to 86.5)	0.268
Mean heart rate reduction during TTM compared with before TTM (bpm), median (IQR)	13.5 (7 to 30.5)	22.5 (13.75 to 35.25)	11.5 (3.75 to 28.5)	0.214
Time to target temperature (hr), median (IQR)	4 (2 to 5)	3 (2 to 7.25)	4 (2 to 5)	0.402
R-R interval variation (msec), median (IQR)	22 (10 to 40)	54 (22.5 to 82.5)	20 (10 to 24)	<0.001
R-R interval variation ≥40 msec, No. (%)	13 (28.3)	8 (66.7)	5 (14.7)	0.001
Generalized brain swelling, No. (%)	21 (45.7)	2 (16.7)	19 (55.9)	0.019

TTM = targeted temperature management

Table 5. Multivariate analysis of neurologic outcome predictors

Predictor	Odds ratio	95% confidence interval	*p*-value
Cause of cardiac arrest			
Cardiac	0.127	0.011 to 1.470	0.099
Unknown	11.171	0.280 to 446.121	0.200
R-R interval variation ≥40 msec	7.961	1.036 to 61.182	0.046
Generalized brain swelling	0.061	0.005 to 0.755	0.029

NECT, was significantly associated with unfavorable neurologic outcomes in both univariate (p = 0.019) and multivariate analyses (OR 0.061, 95% CI, 0.005 to 0.755, p = 0.029).

Discussion

Cerebral hypoxic-ischemic injuries occur after cardiac arrest. In addition, cerebral reperfusion injuries also occur when cerebral blood flow is restored after resuscitation[15]. TTM for comatose survivors after cardiac arrest has been proven to hold benefits for favorable neurologic outcomes and has been established as the class I recommendation in the most prominent practice guidelines, including the European Resuscitation Council and European Society of Intensive Care Medicine 2015 guidelines for post-resuscitation care and the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care[16,17]. TTM after cardiac arrest has also been successfully implemented at Thammasat University Hospital[18,19]. However, the predictors of clinical outcomes after TTM in patients with post-cardiac arrest have not been well established.

In the present study of the neurologic outcomes of TTM for post cardiac arrest patients, 26.1% of the patients had favorable neurologic outcome. According to the Multicenter Hypothermia after Cardiac Arrest Study in Europe, 55% of patients in the hypothermia group had favorable outcomes[5]. Further, in the remarkable study by Bernard et al in Australia, 49% of patients in the hypothermia group were considered to have a favorable outcome[6]. These differences in the neurologic outcomes between the studies might be explained by differences in the study population and the inclusion criteria for TTM, such as the initial cardiac rhythm. The initial cardiac rhythm in the inclusion criteria was ventricular fibrillation in the study by Bernard et al and ventricular fibrillation or nonperfusing ventricular tachycardia in the Hypothermia after Cardiac Arrest Study[5,6]. In our study, the Thammasat University Hospital criteria for TTM included all types of initial cardiac rhythms and included both out-of-hospital and in-hospital cardiac arrest patients.

The most common cause of cardiac arrest in our study was cardiac in origin and the most commonly presented cardiac rhythm was asystolic. These findings are consistent with other studies in Thailand [20-22]. Asystolic cardiac rhythm may imply a prolonged interval between onset of cardiac arrest and the start of resuscitation, resulting in prolonged cerebral hypoxic-ischemic injury. This may explain the unusually low proportion of patients with favorable neurologic outcomes in our study. Nevertheless, there are still clear benefits using TTM in post cardiac arrest patients.

Significant independent predictors of favorable neurologic outcomes at the time of hospital discharge in this study included an RRIV of $\geq$40 milliseconds during TTM. RRIV reflects high frequency variations in heart rate. In the study by Whitsel et al, RRIV indicated high internal validity and re-reading reliability as a measure of parasympathetically mediated variation in the heart rate, which is related to autonomic function[12]. This could explain the finding in our study that post-cardiac arrest patients with high RRIV, which reflects the functioning of the autonomic functions, were more likely to have favorable neurologic outcomes after TTM when compared with patients having a low RRIV. Moreover, the estimation of RRIV only requires the measurement of the smallest and largest RR intervals between normally conducted QRS complexes in a 12-leads electrocardiogram, which indicates that it may be a promising new predictor of neurologic outcomes in post cardiac arrest patients who received TTM. In the present study by Thomsen et al, sinus bradycardia during hypothermia was associated with a lower 180-day mortality rate in comatose survivors of out-of-hospital cardiac arrest[23]. Our results show that the patients with favorable neurologic outcomes had a trend toward lower mean and minimum heart rates and higher reductions of mean heart rate during TTM when compared with the patients with unfavorable outcomes, although the standards of statistical significance were not met. These differences may have been obscured due to the small sample sizes.

As expected, we found that generalized brain swelling revealed by brain NECT after cardiac arrest predicted unfavorable neurologic outcomes[24]. These independent predictions in multivariate modeling support the complementary use of brain NECT in prognosticating outcomes in post cardiac arrest patients.

We selected the CPC scale of measurement of neurologic outcomes in our study. The CPC scale has been widely used in research and quality assurance to assess neurologic outcome following cardiac arrest[14,25,26]. The study by Stiell et al shows that the CPC scale can be used to rule out good quality of life with high sensitivity and include poor quality of life with high specificity[27]. Serum Neuron Specific Enolase (NSE) is a well-known biomarker for prognosis prediction in post-cardiac arrest comatose patients[28]. However, it is currently controversial whether it is beneficial to use NSE as a single prognostigator in post-cardiac arrest patients treated with TTM[29]. NSE is not a routine test for post-cardiac arrest patients in our center. Therefore, RRIV is not compared with NSE in our study. Recent studies suggest measuring serial NSEs rather than single NSEs, as previously recommended, as a prognosis predictor in post-cardiac arrest patients undergoing TTM[30].

To the best of our knowledge, this is the first study that shows RRIV measurement as an indicator of favorable neurologic outcomes in comatose survivors of cardiac arrest.

There are, however, limitations in the present study. First, because of the retrospective nature of our study, there is a possibility that errors occurred in recording or interpreting information from medical records. Second, due to the small sample size, our study may have been insufficient for detecting meaningful differences between some expected variables, such as heart rates during TTM. Lastly, we did not investigate neurologic outcomes on long-term outpatient follow-up. Such investigation would further demonstrate the long-term effects of TTM on the neurologic outcome in post-cardiac arrest patients.

In conclusion, the proportion of comatose survivors of cardiac arrest receiving TTM with favorable neurologic outcomes at the time of hospital discharge was 26.1%. Therefore, it appears that RRIV can be used as a predictor of neurologic outcomes as an RRIV of $\geq$40 msec during TTM was associated with favorable neurologic outcomes. However, further studies are required to confirm these findings and determine the implementation of RRIV measurement in cardiac arrest patients.

What is already known on this topic?

Heart Rate Variability (HRV) is an outcome predictor in post-cardiac arrest patients treated with targeted temperature management (TTM).

What this study adds?

R-R interval variation (RRIV), which can be done at bedside and represented HRV, may be an outcome predictor in post-cardiac arrest patients treated with targeted temperature management (TTM).

Acknowledgements

This work is supported by Stroke Excellence Center, Thammasat University Hospital and Center of Excellence in Stroke from Thammasat University.

Potential conflicts of interest

The authors declare no coflicts of interest.

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การใช้ความผกผันของระยะห่างระหว่างกราฟอาร์ในคลื่นหัวใจไฟฟ้าเป็นตัวทำนายผลลัพธ์ที่ดีของการรักษาด้วยการควบคุมอุณหภูมิในผู้ป่วยหลังภาวะหัวใจหยุดเต้น

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วัตถุประสงค์: การรักษาด้วยการควบคุมอุณหภูมิเป็นการรักษาที่เป็นมาตรฐานในผู้ป่วยหลังภาวะหัวใจหยุดเต้น

วัสดุและวิธีการ: ความผกผันของอัตราการเต้นหัวใจ ซึ่งบ่งชี้ถึงการทำงานของระบบประสาทอัตโนมัติที่ปกติใช้เป็นตัวทำนายผลลัพธ์ของการรักษาในผู้ป่วยหลังภาวะหัวใจหยุดเต้นได้ แต่อุปกรณ์ที่ใช้วัดความผกผันของอัตราการเต้นหัวใจมีความยุ่งยาก ความผกผันของระยะห่างระหว่างกราฟอาร์ในคลื่นหัวใจไฟฟ้า (RRIV) ซึ่งวัดได้สะดวก สามารถทำได้ข้างเตียงผู้ป่วยโดยไม่ต้องใช้อุปกรณ์พิเศษใด ๆ อาจนำมาใช้แทนความผกผันของอัตราการเต้นหัวใจในการทำนายผลลัพธ์การรักษาในผู้ป่วยหลังภาวะหัวใจหยุดเต้นที่ได้รับการรักษาด้วยการควบคุมอุณหภูมิได้ จึงได้ทำการศึกษาย้อนหลัง นำเอาข้อมูลความผกผันของระยะห่างระหว่างกราฟอาร์ในคลื่นหัวใจไฟฟ้า ของผู้ป่วยหลังภาวะหัวใจหยุดเต้นตั้งแต่ เดือนมกราคม พ.ศ. 2553 ถึง เดือนกรกฎาคม พ.ศ. 2558 มาวิเคราะห์เชิงสถิติถึงความสัมพันธ์กับผลลัพธ์หลังการรักษาด้วยการควบคุมอุณหภูมิเมื่อผู้ป่วยได้รับการจำหน่ายออกจากโรงพยาบาล

ผลการศึกษา: พบว่าความผกผันของระยะห่างระหว่างกราฟอาร์ในคลื่นหัวใจไฟฟ้า (RRIV) ที่มากกว่าหรือเท่ากับ 40 มิลลิวินาที บ่งชี้ถึงโอกาสการมีผลลัพธ์ที่ดีหลังการรักษาในผู้ป่วยหลังภาวะหัวใจหยุดเต้นที่ได้รับการรักษาด้วยการควบคุมอุณหภูมิ

สรุป: ความผกผันของระยะห่างระหว่างกราฟอาร์ในคลื่นหัวใจไฟฟ้า (RRIV) อาจนำมาใช้ในการทำนายผลลัพธ์ทางคลินิกในผู้ป่วยหลังภาวะหัวใจหยุดเต้นที่ได้รับการรักษาด้วยการควบคุมอุณหภูมิได้ อย่างไรก็ตามยังต้องการการศึกษาทางคลินิกที่มีประสิทธิภาพเพื่อยืนยันข้อสรุปนี้