Osmangazi Tıp Dergisi
Osmangazi Journal of Medicine 2021

Research Article / Araştırma Makalesi

Targeted Temperature Management in Postcardiac Arrest Syndrome: A Single-Center Experience with 47 Patients

Postkardiyak Arrest Sendromunda Hedeflenen Sıcaklık Yönetimi: Tek Merkez Deneyimi

[1]Havva Kocayigit, [2]Gurkan Demir, [3]Kezban Ozmen Suner, [2]Ali Fuat Erdem

[1]Sakarya University Education and Research Hospital, Department of Anestesiology and Reanimation, Sakarya, Turkey

[2] Sakarya University Faculty of Medicine, Department of Anestesiology and Reanimation, Sakarya, Turkey

[3] Sakarya University Education and Research Hospital, Department of Intensive Care, Sakarya, Turkey

Abstract

Our aim in this study is to retrospectively analyze the results of Targeted Temperature Management (TTM) treatment in our intensive care unit. Following the ethics committee's approval, the demographic data, cardiac arrest history, the follow-up process, and the final status of patients who were applied TTM in Sakarya University Training and Research Hospital Anesthesia Intensive Care Unit between January 2017 and December 2019 were recorded. Then, the effect of these parameters on mortality was evaluated using regression analysis. Data of 47 patients who met the study criteria were analyzed. The mean age of the patients was 50 ± 16 and 14 (29.8%) patients were female. The duration of cardiopulmonary resuscitation (CPR) was 22.35 ± 16.08 minutes, 35 (74.5%) patients had a witness to arrest, 25 (53.2%) patients were arrested in the hospital, and 13 (27.7%) patients had shockable rhythm. It was determined that 60% of the patients died, 20% of them were care patients with poor neurological outcomes and 20% of them were discharged outpatient with good neurological outcomes. Age, development of acute renal failure, requiring vasopressor, high APACHE scores, and length of hospital stay were found to be independent risk factors for mortality.

Keywords: Cardiac arrest, intensive care, targeted temperature management, mortality.

Özet

Çalışmamızdaki amacımız yoğun bakım ünitemizde uygulanmış olan Hedeflenen Sıcaklık Yönetimi (HSY) tedavisinin sonuçlarını retrospektif olarak analiz etmektir. Bu amaçla etik kurul onayının ardından, Ocak 2017-Aralık 2019 tarihleri arasında Sakarya Üniversitesi Eğitim ve Araştırma Hastanesi Anestezi Yoğun Bakım Ünitesi'nde HSY uygulanan hastaların demografik verileri, kardiyopulmoner resusitasyon öyküsü, yoğun bakım takip süreci ve yoğun bakım sonlanımları incelendi. Daha sonra bu parametrelerin mortalite üzerindeki etkisi regresyon analizi kullanılarak değerlendirildi. Çalışma kriterlerini karşılayan 47 hastanın verileri analiz edildi. Hastaların yaş ortalaması 50 ± 16 olduğu ve 14 (% 29,8) hastanın kadın olduğu saptandı. CPR süresi ortalama 22.35 ± 16.08 dakika idi ve 35 (% 74.5) hastada arreste tanıklık eden birinin olduğu, 25 (% 53.2) hastanın hastane içinde arrest olduğu ve 13 (% 27.7) hastada ilk muayenede şok verilebilir ritim olduğu gözlendi. Sonuç olarak hastaların % 60'ının ex olduğu, % 20'sinin bakım hastası olarak, %20'sinin de ayaktan taburcu edildiği belirlendi. Yaş, akut böbrek yetmezliği gelişimi, gerekli vazopressör, yüksek APACHE skorları ve hastanede kalış süresi mortalite için bağımsız risk faktörleri olarak bulundu.

Anahtar Kelimeler: Kardiyak arrest, yoğun bakım, hedeflenen sıcaklık yönetimi, mortalite.

Correspondence:
Havva KOCAYİĞİT
Sakarya University Education and Research Hospital, Department of Anestesiology and Reanimation,
Sakarya, Turkey
e-mail: havvakocayigit@gmail.com

***Received* 23.12.2020 *Accepted* 05.07.2021 *Online published* 05.07.2021**

Kocayigit H, Demir G, Ozmen Suner K, Erdem AF, Targeted Temperature Management in Postcardiac Arrest Syndrome: A Single-Center Experience with 47 Patients, Osmangazi Journal of Medicine, 2021;43(6): 648-653, Doi: 10.20515/otd.846041

1. Introduction

Cardiac arrest is the cessation of blood circulation in the whole body with the cessation of heartbeats at the last moment of life. With the cessation of blood circulation, the oxygen supply to the tissues stops. With CPR, blood circulation and oxygen delivery to tissues are attempted. Inadequate oxygen delivery results in damage and cell death in all tissues such as neurons in the cerebral tissue and nephrons in the kidney. The higher the cell death, the higher the morbidity and mortality (1).

The European Resuscitation Council and the European Society of Intensive Care Medicine published a post-resuscitation guideline in March 2021. In this guide, post-resuscitation care is explained in three steps: “immediate treatment”, “diagnosis” and “optimizing recovery”. In the immediate treatment step, which is the first step of post resuscitation, temperature control is recommended when airway and circulation are provided and vital signs are stabilized. It's recommended that targeted temperature management (TTM) for adults after either OHCA or in-hospital cardiac arrest (IHCA) (with any initial rhythm) who remain unresponsive after ROSC; Maintaining a target temperature at a constant value between 32 and 36 °C for at least 24 h. and avoiding fever (>37.7 °C) for at least 72 h after ROSC in patients who remain in a coma (2).

TTM treatment is routinely applied in our clinic. Our aim in this study is to retrospectively analyze the results of TTM treatment in the last two years in our intensive care unit.

2. Materials and Method

Following the approval of the ethics committee, the data of patients who were applied TTM in the Anesthesia Intensive Care Unit of Sakarya University Training and Research Hospital between January 2017 and December 2019 were retrospectively analyzed. Inclusion criteria were defined as patients aged 18-80 years, whose spontaneous circulation returned after cardiac arrest. Patients who developed cardiac arrest after TTM treatment, who had incomplete information, and who died before TTM treatment was completed were excluded from the study.

Age, gender, disease etiology, comorbidities, and Acute Physiology, Assessment and Chronic Health Evaluation (APACHE II) score during admission to intensive care were recorded for each patient. The duration of CPR for the history of cardiac arrest, whether there was a witness during the arrest, whether the arrest was in the hospital or at home, the presence of shockable rhythm (VF, VT) when the patient was first monitored, and requiring vasopressors were analyzed in detail. During the follow-up period, developing kidney failure, the duration of hospitalization was recorded. The intensive care outcome of the patient was evaluated by dividing it into three categories: discharge, need for palliative care (as a care patient with a home ventilator), and death. Finally, the effects of these parameters on mortality were evaluated using regression analysis.

The Arctic Sun® (Medivance Corp, Louisville, Co.) device is used in our clinic for TTM treatment, and deep sedation and neuromuscular blocker drugs are applied to patients during TTM treatment. TTM treatment was applied in 3 phases as follows; 1st phase, rapid cooling within 1-3 hours with the target temperature being 33-35 0C; 2nd phase, maintaining the target temperature for the next 24 hours; 3rd phase, 0.2-0.33oC per hour until body temperature reaches 36.5-37.5 ° C heating phase to be.

Statistical analysis

Statistical analyzes were performed using the IBM SPSS Statistics 22 program. The distribution of numerical variables was evaluated by Kolmogorov Smirnov. Data for categorical variables were expressed as numbers and percentages, while continuous variables were expressed as mean ± standard deviation or median (interquartile range). Chi-square and Fisher's exact tests were used for categorical variables. A binary logistic regression test was used to evaluate the effects of independent variables on mortality. p <0.05 was considered significant.

3. Results

It was found that TTM was applied to 55 patients. It was determined that 4 patients died before completing TTM treatment, 2 patients were applied TTM to protect cerebral functions without a cardiac arrest, and 2 patients under the age of 18 (8 years) were applied TTM. Eight patients were excluded from the study, and the data of 47 patients who met the inclusion criteria were analyzed.

The mean age of the patients was 50 ± 16 and 14 (29.8%) patients were female and 33 (70.2%) patients were male. Cardiac arrests due to myocardial infarction (53.2%) were the most common etiologies that caused cardiac arrest. When the etiology of cardiac arrest was examined, it was found that 8 patients (16.1%) due to chronic obstructive pulmonary disease, 6 patients (12.8%) due to congestive heart failure, 3 patients (6.4%) in the postoperative period, and 2 patients (4.3%) due to pulmonary embolism developed. The most common comorbidities were coronary artery disease 8 (17%), hypertension 7 (14.9%), congestive heart failure 6(12.8%), and chronic obstructive pulmonary disease 5 (10.6%). The APACHE II mean score was 28.11 ± 7.92. The duration of CPR was 22.35 ± 16.08 minutes, 35 (74.5%) patients had a witness to arrest, 25 (53.2%) patients were arrested in the hospital, and 13 (27.7%) patients had a rhythm that could be shocked (Table 1).

Table 1. Demographic data of the patients

	n=47
Age (year)	50 ± 16
Gender, n(%)	
Female	14 (29.8)
Male	33 (70.2)
Etiology, n (%)	
Myocardial infarction	25 (53.2)
COPD	8 (16.1)
Congestive heart failure	6 (12.8)
Postoperative	3 (6.4)
Pulmonary embolism	2 (4.3)
Status epilepticus	1 (2.1)
Pacemaker inactivation	1 (2.1)
Stroke	1 (2.1)
Comorbidity, n (%)	
CAD	8 (17.0)
HT	7 (14.9)
CHF	6 (12.8)
COPD	5 (10.6)
DM	4 (8.5)
Stroke	4 (8.5)
Malignancy	2 (4.3)
CRF	2 (4.3)
APACHE II	28.11 ± 7.92
Duration of CPR (min)	22.35 ± 16.08
Witness of Arrestet, n (%)	
yes	35 (74.5)
no	12 (25.5)
OHCA, n(%)	22 (46.8)
İn Hospital, n(%)	25 (53.2)
shockable rhythm, n(%)	
yes	13 (27.7)
no	34 (72.3)

CAD: Coronary artery disease, HT: hypertension, CHF: Congestive heart failure, COPD: Chronic Obstructive pulmonary disease, DM: Diabetes Mellitus, CRF: chronic renal failure, APACHE Score: Acute Physiology, Assessment and Chronic Health Evaluation score.

While antiedema treatment (mannitol) was applied to all patients and amantadine treatment was applied to 9 (19.1%) patients, it was observed that 37 (78.7%) patients required vasopressor. During the intensive care follow-up period, acute renal failure developed in 13 (27.7%) patients, and the average hospital stay was recorded as 25 (8-67) days. It was found that 9 (19.1%) patients were discharged from intensive care, 9 (19.1%) patients needed palliative care, and 29 (61.6%) patients died (Table 2).

Table 2. Treatments and outcomes of the patients

	n=47
Antiedema treatment, n(%)	47 (%100)
vasopressor, n(%)	37 (%78,7)
Amantadin , n(%)	9 (%19,1)
Acute renal failure, n(%)	13 (%27,7)
Lenght of stay in ICU (day)	
Mean ± SD	40 ± 43
Median (IQR)	25 (8-67)
Outcome, n(%)	
Discharge	9 (%19,1)
Palliative service	9 (%19,1)
Exitus	29 (%61,6)

Risk factors for mortality was age [odds ratio = 1.049, 95% confidence interval = 1.061--1.228, p = 0.025], acute renal failure [odds ratio = 1.163, 95% confidence interval = 1.010--2.613, p = 0.026], requiring vasopressor [odds ratio = 0.099, 95% confidence interval = 0.012--1.797, p = 0.030], length of hospital stay [odds ratio = 0.981, 95% confidence interval = 0.959-1.003, p = 0.019] and APACHE II score [odds ratio = 1.029, 95% confidence interval = 0.048-1.166, p = 0.050] (Table 3).

Table 3. Binary logistic regression analysis of independent risk factors associated with mortality

	Odds ratio	95% confidence interval	*p*
Age	1.049	0.989-1.112	0.025*
Gender	0.771	0.086-6.949	0.817
Witness to arrest	2.707	0.248-29.523	0.414
OHCA	0.412	0.053-3.232	0.399
Shockable rhythm	1.994	0.265-15-02	0.503
Acute renal failure	0.163	0.010-2.613	0.026*
Lactate	0.962	0.790-1.172	0.703
Vasopressor	0.099	0.012-0.797	0.030*
Lenght of ICU stay	0.981	0.959-1.003	0.019*
APACHE II	1.029	0.048-1.166	0.050*

OHCA: out of hospital cardiac arrest, APACHE II: Acute Physiology and Chronic Health Evaluation II. p<0.05 was considered statistically significant.

4. Discussion

In this study, patients who underwent TTM after cardiac arrest were analyzed retrospectively in terms of demographic characteristics, CPR characteristics, and clinical outcomes. It was found that the cause of cardiac arrest was often caused by myocardial infarction, most patients needed inotropic support and mortality was approximately 60%. In addition, the age of the patient, requiring vasopressors, the arrival APACHE II score, the development of renal failure during the intensive care period, and the prolonged hospital stay were determined as risk factors for mortality.

In patients whose spontaneous circulation returns after cardiac arrest, the time that the cerebral tissue is exposed to hypoxia is important in terms of neurological damage and mortality (1,3). This hypoxia process of the cerebral tissue is followed by the waiting time for CPR, the duration of CPR administration, whether there is a witness of the arrest, and the clinical findings such as the patient's lactate level, development of acute kidney injury or requiring vasopressors. Neurological damage and mortality are tried to be decreased with TTM treatment.

TTM is first applied to the target temperature, staying at the target temperature and then warming up, and many studies in the literature have reported that TTM reduces mortality (4,5). In the FINNRESUSCI study, out-of-hospital cardiac arrests were examined and TTM was shown to reduce mortality. Similar results were reported in a review on out-of-hospital cardiac arrests [OR 0.51; 95% CI 0.40-0.64] (5).

APACHE II score is a scoring system calculated in patients admitted to intensive care. Gündeniz et al. found that the APACHE II score being 17.5 and above (the threshold value determined by ROC analysis) in determining mortality has 81.4% sensitivity and 51% specificity (6). In our study, the average APACHE score is 28, these patients have a poor general condition, more additional diseases, and high mortality rates are expected. Mortality rate was found to be 60%, and it was found to be compatible with the literature (7).

In our study, age was determined as an independent risk factor for mortality. Although there is no age limit for the application of TTM in the guidelines, similar to our findings, it has been reported that TTM does not positively affect mortality and neurological outcomes in elderly patients (8,9).

In the management of patients after cardiac arrest, it is also important to protect tissues and organs exposed to hypoxia during the arrest. Anaerobic respiration develops due to insufficient oxygen supply to tissues exposed to hypoxia and blood lactate levels increase. In the ongoing hypoxia process, organs lose their functions (10). In this respect, lactate increase, acute renal failure, and development of liver failure are indirect indicators that the hypoxia period of the patient is long. In the risk factor analysis for mortality, acute renal failure was found to be an independent risk factor.

Regarding "targeted temperature management", Çiçekçi et al. Found that there was no relationship between CPR duration and the first monitored rhythm in terms of neurological outcome (11). Although we determined the CPR time as a risk factor for mortality in our study, we think that the duration of hypoxia affects mortality. In a study published by Karcıoğlu et al. On TTM, they reported that TTM has a protective effect on glucose metabolism (12)

Although publications are reporting that the target temperature for TTM was reached with isotonic saline infusion, TTM was applied with The Arctic Sun® (Medivance Corp, Louisville, Co.) device in our study in order not to increase the fluid load (13).

This retrospective study has all limitations of retrospective studies. Due to the study design, we could not obtain the data of the door to cool time and the time to reach the targeted temperature value of patients who were applied TTM. Another limitation is that a small number of patients were included in the study.

5. Conclusion

As a result, TTM treatment was applied to 47 patients in our clinic in the last 2 years. These patients had very high APACHE scores, needed inotropes, and had poor general conditions. While 60% of the patients died, 20% of them were care patients with poor neurological outcomes and 20% of them were discharged outpatient with good neurological outcomes. Age, development of acute renal failure, need for inotropes, high APACHE scores, and length of hospital stay were found to be independent risk factors for mortality.

Ethical approval

Written permission was obtained from Sakarya University Non-interventional Clinical Research Ethics Committee (E.107426, Approval date: 26.06.2020) to conduct the study.

REFERENCES

1. Stub D, Bernard S, Duffy SJ, et al. Post Cardiac Arrest Syndrome: A Review Of Therapeutic Strategies. *Circulation*. 2011;123:1428-35.
2. Nolan JP, Sandroni C, Böttiger BW, et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. *Intensive Care Med* 2021;47, 369–421
3. İnal MA, Ural SG, Çakmak HŞ, et al. Approach to Perioperative Hypothermia by Anaesthesiology and Reanimation Specialist in Turkey: A Survey Investigation. *Turk J Anaesthesiol Reanim.* 2017 ;45:139-145.
4. Vaahersalo J, Hiltunen P, Tiainen M, et al. Therapeutic Hypothermia After Out-Of-Hospital Cardiac Arrest In Finnish Intensive Care Units: The Finnresusci Study. *Intensive Care Medicine.* 2013:39, 826–37.
5. Schenone AL, Cohen A, Patarroyo G, et al. Therapeutic Hypothermia After Cardiac Arrest: A Systematic Review/Meta-Analysis Exploring The Impact Of Expanded Criteria And Targeted Temperature. *Resuscitation.* 2016;108:102-10.
6. Gündeniz A, Tabakoğlu E, Özdemir L, et al. Solunum Yoğun Bakım Hastalarında Mortalite Oranları ve İlişkili Faktörlerin Belirlenmesi. *Toraks Dergisi* 2007;8:79-84.
7. Polderman KH. Induced Hypothermia And Fever Control For Prevention And Treatment Of Neurological İnjuries. *Lancet* 2008;371:1955-1969.
8. Granberg B , McGillis E, Solbiati M. Gruppo Di Autoformazione Metodologica (Gram), Therapeutic Induced Hypothermia Does Not Improve The Prognosis Of Out-Of-Hospital Cardiac Arrest Patients. *Intern Emerg Med.* 2014;9:677-9.
9. Hakim SM, Ammar MA, Reyad MS. (2018). Effect Of Therapeutic Hypothermia On Survival And Neurological Outcome In Adults Suffering Cardiac Arrest: A Systematic Review And Meta-Analysis. *Minerva Anestesiol.* 84, 720–730.
10. Wagner SR 4th, Lanier WL. Metabolism Of Glucose, Glycogen, And High Energy Phosphates During Complete Cerebral İschemia. A Comparison Of Normoglycemic, Chronically Hyperglycemic Diabetic, And Acutely Hyperglycemic Nondiabetic Rats. *Anesthesiology*. 1994;81:1516-26.
11. F Cicekci, AU Uca, I Kara. Study of Cerebral Performance Categories Based on Initial Rhythm and Resuscitation Time Following In-Hospital Cardiac Arrest in a State Hospital in Turkey- *Hosp Pract Res.* 2018;3:44-49
12. Karcioglu O, Topacoglu H, Dikme O. A systematic review of safety and adverse effects in the practice of therapeutic hypothermia. Am J Emerg Med. 2018 ;36:1886-94.
13. Kızılaslan D, Erdoğan C, Çiftçi B, et al. Detailed Therapeutic Hypothermia Protocol After Cardiac Arrest. *J Turk Soc Intens Care* 2019;17:231-233.