ORIGINAL ARTICLE

Therapeutic hypothermia as a treatment option after out-of-hospital cardiac arrest: our experience

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ABSTRACT

Aim To examine the effects of therapeutic hypothermia on the outcome of patients with the diagnosis of out-of-hospital cardiac arrest (OHCA).

Methods The study included 76 patients who were hospitalised at the Medical Intensive Care Unit (MICU) of the Clinical Centre University of Sarajevo, with the diagnosis of out-of-hospital cardiac arrest, following the return of spontaneous circulation. Therapeutic hypothermia was performed with an average temperature of 33°C (32.3 - 34.1°C) on the patients who had coma, according to the Glasgow Coma Scale (GCS).

Results Multiple organ dysfunction syndrome (MODS) significantly affected survival (p=0.0001), as its presence reduced patients' survival by 96%. In addition, ventricular fibrillation (VF) as the presenting rhythm, also significantly affected survival (p=0.019). A degree of patient's coma, as measured by the GCS, significantly affected survival (p=0.011). For each increasing point on the GCS, the chance for survival increased twice. Moreover, other physiological factors such as the pH and the lactate serum levels significantly affected patients' survival (p=0.012 and p=0.01, respectively).

Conclusion In patients with the diagnosis of OHCA who underwent to the treatment with therapeutic hypothermia, verified VF as a presenting rhythm was a positive predictive factor for their outcome. Therefore, therapeutic hypothermia represents an option of therapeutic modality for this type of patients.

Key words: intensive care unit, treatment, ventricular fibrillation

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) presents loss of cardiac function and lack of pulse, and it is the main cause of mortality, with survival rates between 4 and 39.3% (1,2). Cardiopulmonary resuscitation (CPR) should be done as soon as possible, and hospitalization is of utmost importance (2). In late fifties of the 20th century, the therapeutic hypothermia after the cardiac arrest was first described (3). It has been shown that therapeutic hypothermia improves both neurological outcomes and survival (4-6). In 2003, the American Heart Association (AHA) and the International Liaison Committee on Resuscitation (ILCOR) recommended the use of therapeutic hypothermia after cardiac arrest (2). In 2005, a revision was made to the first recommendation and clear guidelines for its use were established as follows: unconscious adult patients with return of spontaneous circulation (ROSC) after OHCA should be cooled to 32-34 °C for 12-24 hours when initial rhythm was ventricular fibrillation (VF), patients with non-VF arrest out-of-hospital or with in-hospital arrest, hemodynamically stable patients with spontaneous mild hypothermia (>33°C) after resuscitation from cardiac arrest should not be actively rewarmed (7). Patients on which this method can be used are intubated with the treatment initiated within 6 hours after cardiac arrest (non-perfusing ventricular tachycardia (VT) or VF), patients able to maintain systolic blood pressure >90 mm Hg, with or without vasopressors after cardiopulmonary resuscitation (CPR) and patients in coma at the time of cooling (5). The aim of the treatment is to achieve the target temperature between 32 °C and 34 °C within 4 hours from the start of the cooling, while rewarming begins 24 hours after the beginning of the cooling process (7,8). Guidelines in 2015 confirmed earlier recommendation and put into focus supportive therapy and controlled rewarming (9). In the Federation of Bosnia and Herzegovina, studies of this type have not been performed.

The aim of this study was to examine the effects of therapeutic hypothermia on the outcome of patients with the diagnosis of OHCA.

PATIENTS AND METHODS

Patients and study design

This retrospective-prospective study included 76 patients who were admitted to the 7-bed Medical Intensive Care Unit, Clinical Centre, University of Sarajevo (Federation of Bosnia and Herzegovina, Bosnia and Herzegovina), during a 2-year period (January 2013-December 2015). Ethical approval was obtained from the Ethical Committee of the Clinical Centre University of Sarajevo. Legal representative were informed about the treatment and they gave the consent. The patients were admitted from the Emergency Department. The reasons for admission was the diagnosis of OHCA, following the return of spontaneous circulation (patients remained intubated and ventilated, with persistent coma after cardiac arrest).

For each patient, the following data were obtained upon admission: age, gender, the presenting rhythm (VF, asystole), time until the start of CPR, duration of CPR and time until the return of spontaneous circulation (ROSC), Glasgow Coma Scale (GCS) (method for bedside assessment of conscious level by eye opening, verbal and motor response) (10). Laboratory tests (lactate and pH serum levels) upon admission were measured, as well as and the presence of sepsis, ventilator-associated pneumonia (VAP) or multiple organ dysfunction syndrome (MODS).

Patients were divided on the basis of their outcome into two groups: survivors (patients who were discharged from the hospital), and non-survivors (patients who died during the same hospitalization).

Methods

After admission, the patients were sedated and placed on mechanical ventilation. Targeted temperature management (TTM) was started using the Arctic SunR Temperature Management System (Model 2000, Medivance Inc., Louisville, USA) with a target temperature of 33 °C which was maintained constantly for 24 hours.

All patients were resuscitated according to the advanced cardiac life support guidelines. Routine collection of data did not interfere with the patient care and treatment in any way, and statistical analyses were processed retrospectively and anonymously.

Statistical analysis

The data collected were analysed at the level of descriptive statistics by measures of central tendency (arithmetic mean and median) and measurements of variability (standard deviation,

interquartile range 25th-75th percentile). The univariate binary logistic regression examined the individual impact of independent variables on the binary dependent variable survival (survivor / non-survivor) in the medical intensive care unit. Multivariate binary regression analysis examined the influence of independent predictors (model 1), which showed a significant impact on the variable "survivor / non-survivor". The value of the model is tested by Hosmer and Lemeshow Test. All analyses were evaluated at a level of statistical significance of $p<0.05$.

RESULTS

The average age of patients was 59 ± 15.7 years, with higher prevalence of males, 55 (72%). Cardiogenic origin of OHCA was confirmed in 61 (80.3%) patients. The VF was initially detected in 47 (62%) patients, while the asystole was verified in 29 (38%) patients. The CPR was initiated after 4 (1-6) minutes of OHCA and lasted for 25 (19-33) minutes. Therapeutic hypothermia was performed with an average temperature of 33°C (32.3 - 34.1°C) to the patients who had the average value on GCS from 3 to 8. During the first 24 hours following the start of hypothermia treatment, 11 (14.5%) patients died. An overall ICU mortality was 44.7% (34 patients).

The following parameters did not significantly affect the patient's survival: age, time of the CPR onset and its duration, target temperature of therapeutic hypothermia, the occurrence of sepsis and ventilator-associated pneumonia. However, multiple organ dysfunction syndrome (MODS) had a significant effect on survival ($p=0.0001$), as its presence reduced the patients' survival by 96%. The OHCA patients with VF as their presenting rhythm had three times higher chance of survival than those who had not verified VF. Furthermore, the degree of patient's coma, as measured by the GCS significantly affected survival ($p=0.011$). For each raising point on the GCS, the chance for survival doubles. Moreover, other physiological factors, such as pH and lactate serum levels, significantly affected patients' survival ($p=0.012$, and $p=0.01$, respectively). Multivariate binary logistic regression showed statistically significant impact on the outcome. Backaer Wald method in five steps showed that MODS had the biggest effect on

survival rate, more than patient's gender, presenting rhythm and the duration of CPR (Table 1).

Male gender was a significant predictor of survival ($p=0.021$). Odds ratio for survivor was 3.5 (1.2-10) times if the patient was male, or the chance moved in the interval (CI 95%).

The VF as the presenting rhythm in OHCA patients significantly affected survival ($p=0.019$). Patients with VF as presenting rhythm were 3 (1.2-8) times more likely to survive than patients presenting with asystole (Table 1).

Table 1. The influence of independent predictors on the outcome of patients with out-of-hospital cardiac arrest in medical intensive care unit (survivor / non-survivor)*

Independent predictors- Variables	B	Wald	p	Exp (B)	95.0% C.I.for EXP(B)	
					Lower	Upper
Gender (male/female)	1.253	5.359	.021	3.500	1.212	10.109
Age (years)	-.009	.340	.560	.991	.963	1.021
Presenting rhythm (asystole/VF)	1.154	5.519	.019	3.170	1.211	8.302
Time until start of CPR (minutes)	.054	.680	.410	1.056	.928	1.201
Duration of CPR / time until ROSC (minutes)	-.043	4.900	.027	.958	.921	.995
Glasgow coma scale	.673	6.428	.011	1.960	1.165	3.298
pH	5.518	6.264	.012	249.127	3.309	1875.502
Lactate (mmol/L)	-.196	6.592	.010	.822	.708	.955
Target temperature (Co)	.064	.150	.698	1.066	.771	1.474
Sepsis (yes/no)	-.820	2.526	.112	.441	.160	1.211
MODS (yes/no)	-3.171	20.616	.0001	.042	.011	.165
VAP (yes/no)	.241	.169	.681	1.273	.403	4.016
Cerebral oedema (yes/no)	-1.378	1.367	.242	.252	.025	2.541

B, coefficient; Wald, coefficient; EXP (B), odds ratio; 95.0% CI.for EXP (B), 95% confidence interval for odds ratio; *multiple organ dysfunction syndrome (MODS) had a significant effect on survival ($p=0.0001$)

The duration of CPR impacted survival ($p=0.027$). With every passing minute of cardiopulmonary resuscitation, the chance of survival decreased by 4% (1-8%).

The extent of patients' coma, as measured by the GCS, affected survival ($p=0.011$). For each point on this scale, the chance of survival increased about 2 (1-3) times.

Lactate serum values had a significant effect on survival ($p=0.01$). For each increase in lactate serum level by 1 mmol/L, the chance of survival was reduced by 20% (5-30%).

The pH serum level impacted survival ($p=0.012$). For each increase in pH by 0.01, the chance of survival increased approximately 2 times, or in the interval of 0.03 to 18 times.

MODS significantly affected survival (p=0.0001). The present MODS in OHCA patients reduced the chance of survival by 96% (84-99%) (Table 1).

The age of the patient, presence of VAP, sepsis as well as brain oedema in our study did not show significant prediction on the OHCA patient outcome in medical intensive care unit (p>0.05). Multivariate binary logistic regression method was used to examine the influence of independent predictors on the survival of the OHCA patients in medical intensive care unit. By using Backer Wald method in 4 steps, of all the statistically significant (p<0.05) variables, the greatest impact was demonstrated for MODS (Wald coefficient=19.45), while the other three predictors had less significant influence on survival: patient gender, presenting rhythm and the duration of CPR (Wald coefficient =7.9, 6.8 and 5.7 respectively) (Table 2).

Model 1 had the values of Cox & Snell R2 = 0.513 and Nagelkerke R2 = 0.687, indicating that the set of variables in the fourth step explains between 51.3% and 68.7% variance. Further results of Hosmer and Lemeshow tests support the claim that the model is good, that is, χ2 = 3.8; p=0.872 (Table 2).

Table 2. Multivariate impact of independent predictors on the patient outcome (survivor / non-survivor) (the greatest impact was demonstrated for multiple organ dysfunction syndrome (MODS)*

Model 1	Variable	B	Wald	p	Exp(B)	95.0% C.I.for EXP(B)	
						Lower	Upper
Step 1	Gender (male/female)	2.271	6.657	.010	9.692	1.726	54.419
	Rhythm (asystole/VF)	2.148	5.786	.016	8.566	1.489	49.296
	Duration of CPR (minutes)	-.066	4.236	.040	.936	.878	.997
	GCS (1-15)	.510	1.868	.172	1.666	.801	3.464
	pH serum level	3.497	.854	.356	33.015	.020	54992.602
	Lactate serum level (mmol/L)	.075	.373	.541	1.078	.847	1.373
	MODS (yes/no)	-4.747	16.491	.0001	.009	.001	.086
Step 4	Gender (male/female)	2.433	7.990	.005	11.391	2.109	61.538
	Rhythm (asystole/VF)	2.137	6.824	.009	8.476	1.705	42.135
	Duration of CPR (min.)	-.070	5.765	.016	.932	.881	.987
	MODS (yes/no)	-4.817	19.457	.0001	.008	.001	.069

B, coefficient; Wald, coefficient; EXP (B), odds ratio; 95.0% CI.for EXP (B), 95% confidence interval for odds ratio; *p=0.0001

DISCUSSION

Sudden cardiac arrest occurs in 250,000-300,000 people in Europe every year (11). Survival in patients with out-of-hospital cardiac arrest is less than 15%, while survival with in-hospital cardiac arrest is approximately 22% (12, 13). Only 5-35% of the patients leave the hospital alive, with some degree of neurological impairment (14). In our study, during the first 24 hours, following the start of hypothermia treatment, 14.5% of patients died, while an overall mortality was 44.7%.

A cardiogenic origin was present in 61% of patients with cardiac arrest. This is comparable to the earlier reports which showed that 70% of all OHCA are due to coronary heart disease, and further 10% are caused by structural heart disease (e.g. hypertrophic cardiomyopathy), 5% to 10% are due to arrhythmic causes, in the absence of structural heart disease (15). Fifteen to 25 % of OHCA are non-cardiac in origin (16). Time from OHCA until the start of CPR was 4 minutes on average and CPR lasted for 25 minutes until ROSC. Our study is similar to earlier studies which showed that patients achieving ROSC had median total CPR duration of 18 minutes (17).

Gender was a significant predictor of survival, and male patients had 3.5 times better chance for survival. This is supported by larger studies which show that women who suffer an OHCA are less likely to have characteristics associated with survival such as arresting in a public location or an initial shockable rhythm or bystander resuscitation and have a lower rate of survival to discharge (18). Also, women are more likely to have a diagnosis of myocardial infarction missed in the Emergency Department, and are less likely to receive invasive diagnostic testing and treatments for cardiovascular diseases, such as cardiac catheterization and percutaneous coronary intervention - all of which might account for poorer outcomes and increased mortality (19). When experiencing OHCA, women are older than men, have fewer witnessed arrests, have fewer initial VF/VT rhythms and have a lower rate of bystander CPR (20). Ventricular fibrillation was initially detected in 47 (62%) patients in our study. Our results show that the respondents who have had verified VF have three times higher chance of surviving than those who have not had verified VF. Earlier studies agree with our results, as

VF and early ROSC in general were shown to be associated with better outcomes in patients with witnessed OHCA (21). Shockable rhythm conversion from initial non-shockable heart rhythms was associated with better OHCA outcomes, depending on the type of initial heart rhythm, and time of rhythm conversion (22).

The benefits of TTM have been summarized in a systematic review and meta-analysis of six randomized trials (23). According to this review, patients treated with TTM were more likely to survive than patients whose temperature was not managed with TTM. However, TTM is associated with a number of adverse effects and complications. The main adverse effects reported include shivering, seizures, bradycardia, tachyarrhythmia, pneumonia, sepsis, coagulopathy, electrolyte and metabolic disturbances (23). In our study, parameters did not significantly affect the patient's survival were the patient's age, the time of the cardiopulmonary resuscitation onset and its duration, the temperature of therapeutic hypothermia, the occurrence of sepsis and ventilator-associated pneumonia. However, multiple organ dysfunction syndrome (MODS) had a significant effect on survival, as its presence reduced patients' survival by 96%. Earlier studies also showed that MODS is a negative predictor for outcome in OHCA patients (24). Moreover, other physiological factors such as the pH and the lactate significantly affect patients' survival. Our earlier study showed that blood lactate concentration is independently associated with an increase in mortality in hospitals and it represents a statistically significant predictive marker of fatal clinical outcomes for critically ill patients. Blood lactate concentrations >2.25 mmol/L can be used by clinicians to identify patients at high mortality risk (25).

It is important to note that before our MICU was equipped with the proper cooling system, alternative cooling methods (cold IV fluids and surface cooling with ice packs, wet blankets and a cooling fan) were utilized. Only a decade ago, a minority of resuscitated patients were treated with TTM in both American and European intensive care units (26). Although in recent years there have been major improvements in the use of TTM, this practice is still not widely used in developing countries due to limited financial resources and a lack of awareness of this treatment method. A previous study showed that 15% of doctors in developing countries have used TTM in comatose survivors after cardiac arrest (27). In patients with the diagnosis of OHCA, who underwent treatment with therapeutic hypothermia, verified VF as a presenting rhythm is a positive predictive factor for their outcome.

In conclusion, therapeutic hypothermia represents an option of therapeutic modality for out-of-hospital cardiac arrest type of patients. Optimal monitoring of patients and creation of a database that would record clinical characteristics of patients who have undergone this treatment is recommended. Although a country with a modest health-care system infrastructure, Bosnia and Herzegovina was a pioneer in introducing the procedure of therapeutic hypothermia into a routine clinical practice (first therapeutic hypothermia was performed in 2009). This paper should encourage other health care professionals in intensive care units with limited resources in Bosnia and Herzegovina as well as in other countries to start using this treatment option.

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TRANSPARENCY DECLARATION

Competing interests: none to declare.

REFERENCES

1. Le Guen M, Nicolas-Robin A, Carreira S, Raux M, Leprince P, Riou B, Langeron O. Extracorporeal life support following out-of-hospital refractory cardiac arrest. Crit Care 2011; 15:R29.
2. Lee JJ, Han SJ, Kim HS, Hong KS, Choi HH, Park KT, Seo JY, Lee TH, Kim HC, Kim S, Lee SH, Hwang SM, Ha SO. Out-of-hospital cardiac arrest patients treated with cardiopulmonary resuscitation using extracorporeal membrane oxygenation: focus on survival rate and neurologic outcome. Scand J Trauma Resusc Emerg Med 2016; 24:74.
3. Maclean DA, Stevenson RS, Bata I, Green RS. Therapeutic hypothermia for out-of-hospital cardiac arrest: An analysis comparing cooled and not cooled groups at a Canadian center. J Emerg Trauma Shock 2012; 5:328–32.
4. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002; 346:557–63.

5. Polderman KH. Hypothermia and neurological outcome after cardiac arrest: State of the art. Eur J Anaesthesiol 2008; 42:23–30.

6. Gibson A, Andrews PJ. Therapeutic hypothermia, still "too cool to be true?". F1000Prime Rep 2013 5:26.

7. ECC Committee, Subcommittees and Task Forces of the American Heart Association. 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2005; 112: IV1-203.

8. Scott BD, Hogue T, Fixley MS, Adamson PB. Induced hypothermia following out-of-hospital cardiac arrest; initial experience in a community hospital. Clin Cardiol 2006 29:525-9.

9. Callaway CW, Donnino MW, Fink EL, Geocadin RG, Geocadin RG, Golan E, Kern KB, Leary M, Meurer WJ, Peberdy MA, Thompson TM, Zimmerman JL. Part 8: Post-cardiac arrest care: 2015 American Heart Association Guidelines Update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015; 132:S465-82.

10. Teasdale G, Maas A, Lecky F, Manley G, Stocchetti N, Murray G. The Glasgow Coma Scale at 40 years: standing the test of time. Lancet Neurol 2014; 13:844-54.

11. Nolan JP, Soar J, Zideman DA, Biarent D, Bossaert LL, Deakin C, Koster RW, Wyllie J, Böttiger B; ERC Guidelines Writing Group. European Resuscitation Council Guidelines for Resuscitation 2010 Section 1. Executive summary. Resuscitation 2010 81:1219-76.

12. Chan PS, McNally B, Tang F, Kellermann A, the CARES Surveillance Group. Recent trends in survival from out-of-hospital cardiac arrest in the United States. Circulation 2014; 130:1876-82.

13. Girotra S, Nallamothu BK, Spertus JA, Li Y, Krumholz HM, Chan PS; American Heart Association Get with the Guidelines–Resuscitation Investigators. Trends in survival after in-hospital cardiac arrest. N Engl J Med 2012; 367:1912-20.

14. Werling M, Thorén AB, Axelsson C, Herlitz J. Treatment and outcome in post-resuscitation care after out-of-hospital cardiac arrest when a modern therapeutic approach was introduced. Resuscitation 2007; 73:40-5

15. Centers for Disease Control and Prevention (CDC). State-specific mortality from sudden cardiac death-United States, 1999. MMWR Morb Mortal Wkly Rep 2002; 51:123-6.

16. Kuisma M, Alaspää A. Out-of-hospital cardiac arrests of non-cardiac origin. Epidemiology and outcome. Eur Heart J 1997; 18:1122-8.

17. Chokengarmwong N, Ortiz LA, Raja A, Goldstein JN, Huang F, Yeh DD. Outcome of patients receiving CPR in the ED of an urban academic hospital. Am J Emerg 2016; 34:1595-9.

18. Morrison LJ, Schmicker RH, Weisfeldt ML, Bigham BL, Berg RA, Topjian AA, Abramson BL, Atkins DL, Egan D, Sopko G, Rac VE; Resuscitation Outcomes Consortium Investigators. Effect of gender on outcome of out of hospital cardiac arrest in the Resuscitation Outcomes Consortium. Resuscitation 2016; 100:76-81.

19. Poon S, Goodman SG, Yan RT, Bugiardini R, Bierman AS, Eagle KA, Johnston N, Huynh T, Grondin FR, Schenck-Gustafsson K, Yan AT. Bridging the gender gap: Insights from a contemporary analysis of sex-related differences in the treatment and outcomes of patients with acute coronary syndromes. Am Heart J 2011; 163:66–73.

20. Safdar B, Stolz U, Stiell IG, Cone DC, Bobrow BJ, deBoehr M, Dreyer J, Maloney J, Spaite DW. Differential survival for men and women from out-of-hospital cardiac arrest varies by age: results from the OPALS study. Acad Emerg Med 2014; 21:1503-11.

21. Nadolny K, Szarpak L, Gotlib J, Panczyk M, Sterlinski M, Ladny JR, Smereka J, Galazkowski R. An analysis of the relationship between the applied medical rescue actions and the return of spontaneous circulation in adults with out-of-hospital sudden cardiac arrest. Medicine (Baltimore) 2018; 97:e11607.

22. Luo S, Zhang Y, Zhang W, Zheng R, Tao J, Xiong Y. Prognostic significance of spontaneous shockable rhythm conversion in adult out-of-hospital cardiac arrest patients with initial non-shockable heart rhythms: A systematic review and meta-analysis. Resuscitation 2017; 121:1-8.

23. Vargas M, Servillo G, Sutherasan Y, Rodríguez-González R, Brunetti I, Pelosi P. Effects of in-hospital low targeted temperature after out of hospital cardiac arrest: A systematic review with meta-analysis of randomized clinical trials. Resuscitation 2015; 91:8-18.

24. Wada T, Gando S, Ono Y, Maekawa K, Katabami K, Hayakawa M, Sawamura A. Disseminated intravascular coagulation with the fibrinolytic phenotype predicts the outcome of patients with out-of-hospital cardiac arrest. Thromb J 2016; 14:43.

25. Godinjak A, Jusufovic S, Rama A, Iglica A, Zvizdic F, Kukuljac A, Tancica I, Rozajac S. Hyperlactatemia and the importance of repeated lactate measurements in critically ill patients. Med Arch 2017; 71:404-7.

26. Abella BS, Rhee JW, Huang KN, Vanden Hoek TL, Becker LB. Induced hypothermia is underused after resuscitation from cardiac arrest: a current practice survey. Resuscitation 2005; 64:181-6.

27. Varon J, Acosta P. Therapeutic hypothermia use among health care providers in 2 developing countries. Am J Emerg Med 2008; 26:244.