American Journal of Emergency Medicine 37 (2019) 1917–1921

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

Factors associated with the provision of targeted temperature management: A balanced factorial experiment

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ARTICLE INFO

Article history:
Received 27 July 2018
Received in revised form 9 January 2019
Accepted 11 January 2019

Keywords:
Out-of-hospital cardiac arrest
Demographic
Targeted temperature management
Game
Experimental

ABSTRACT

Aim: This study examined the influence of patient attributes and provider or organizational factors on the decision to apply targeted temperature management (TTM) to resuscitated out-of-hospital cardiac arrest (OHCA) patients.
Methods: A balanced factorial experiment was conducted among emergency medicine physicians (EMPs). Sixteen OHCA patient scenarios with balanced factors were presented. The balancing factors were dichotomous categories of patient age (45 ± 2 vs. 70 ± 2 years), patient sex (men vs. women), socioeconomic status (SES; higher vs. lower), and guardian attitudes (positive vs. reluctant) regarding TTM. Information on participant and organizational characteristics was collected. The outcome variable was a score (0–100) based on responses to questions that indicated how likely the participants were to apply TTM.
Results: Seventy-five EMPs completed the experiment. The median score for the likelihood of TTM application was 85 (interquartile range, 70–95). Scores differed significantly for patient age (90% vs. 80%, $p = 0.001$), SES (90% vs. 80%, $p = 0.001$), and guardian attitude regarding TTM (90% vs. 70%, $p = 0.001$). The likelihood of TTM application was associated with EMP experience with TTM (more or <50 times) (90% vs. 80%, $p = 0.001$). EMPs working in hospitals with commercial TTM devices or operating protocols were more likely to use TTM than those working in hospitals without TTM devices or protocols (88 vs. 80 and 90 vs. 80; $p = 0.001$, respectively).
Conclusion: Patient demographics and provider and organizational factors significantly affected the decision to apply TTM.

1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a major health problem. The annual incidence in North America is estimated to be above 350,000 cases [1,2]. Although much effort has been made to improve the survival of OHCA patients, a recent meta-analysis reported that the aggregate survival rate of OHCA (7.6%) has not significantly changed in almost three decades [3].

Targeted temperature management (TTM) is a crucial form of postresuscitation care that improves neurologic recovery in OHCA patients [4-6]. However, disparities in the provision of TTM according to nonclinical factors, such as sex or socioeconomic status (SES), have been reported [7,8] and are a barrier to improving the outcomes of OHCA patients. These nonclinical factors can be categorized as a) patient attributes (race/ethnicity, age, and sex); b) provider characteristics (age/clinical experience, sex, specialty); and c) organizational influences (geographic location, the presence of clinical guidelines, etc.). A precise understanding of the sources of variations has important implications for future educational, clinical, and policy-level interventions [9,10].

Previous studies on the diagnosis of cardiovascular disease or diabetes mellitus have reported balanced factorial experiments that used scenarios to examine the association between a diagnosis or test application and nonclinical factors [11,12]. We applied this experimental method to the use of TTM among resuscitated OHCA patients by using a balanced factorial experiment.

This study was designed to estimate the relative influence of patient, provider, and organizational factors on physician decision-making regarding the use of TTM for successfully resuscitated OHCA patients. We hypothesized that there would be no associations or interactions between the decision to apply TTM and any patient, provider, or organizational factors.

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https://doi.org/10.1016/j.ajem.2019.01.013
0735-6757/

2. Methods

2.1. Design overview

We designed a balanced factorial experiment that permitted the estimation of unconfounded main effects and interactions for each of the following factors: the patient's age, sex, and SES and guardians' attitudes regarding TTM. Sixteen versions of the scenarios were presented using text and images that represented OHCA circumstances and resuscitation processes and systematically varied the patient's sex, age (45 ± 2 vs. 70 ± 2 years), and SES (higher vs. lower) and the guardians' attitude toward TTM (positive vs. reluctant).

2.2. Experimental subjects and data collection

We sent e-mails to emergency medicine physicians (EMPs) from February 20 to March 19, 2018. The e-mail included an introduction to this study and the link to the web survey pages. Informed consent was obtained through previous participation in a web survey. The eligibility criteria for participation were (1) board-certified EMPs in the Republic of Korea (Korea) (2) EMPs with experience in the application of TTM to OHCA patients. To assess experience levels, we asked the following question: "As the person in charge of a clinical situation, have you ever decided to use TTM for an OHCA patient?" We excluded respondents who did not complete the experiment.

After reading each scenario, the participants responded to questions regarding the application of TTM to the patient. The participants assigned a number indicating their level of certainty on a scale of 0–100, with 0 indicating no certainty and 100 indicating complete certainty. All 16 scenarios were presented to the participants. To prevent the effects of autocorrelation, the order of presentation was randomized.

We also collected information on the participants' demographics, yearly duration of clinical experience as an EMP, number of OHCA patients treated and patients who received TTM in the preceding year, and experience with TTM methods. The TTM methods were categorized as (1) external conventional cooling (ECC), such as ice water, fans, and simple blankets; (2) external device cooling (EDC) using a pad with a cooling device; (3) intravascular cooling using cold saline (IVC-saline); and (4) intravascular cooling using an intravascular cooling catheter (IVC-cath). Participants could give multiple responses regarding the TTM method categories (they were asked to choose all of the given TTM method categories with which they had clinical experience). Information regarding the organizational characteristics of the participants' hospitals, including the presence of a TTM device or operating protocols, was also collected.

We repeatedly requested participation in the experiment via e-mail and social network services until the final sample size was achieved. The participants were given modest stipends (KW 10,000₩).

The study protocol was approved by the Institutional Review Board of Myongji Hospital (2018-01-019).

2.3. Experimental scenarios

Clinical validity was established through a process involving EMPs and a pilot test. We conducted an extensive background literature search and reviews of international guidelines and OHCA cases. A script that included both verbal and nonverbal directions was developed with experienced, clinically active advisors. A master script was developed to ensure that the script and image presentations were both clinically accurate and typical of how a patient would present during an emergency department (ED) visit.

Table 1
Patient demographics and characteristics of out-of-hospital cardiac arrest patients embedded in the clinical scenarios.

Category	Contents
Sex	
Male	
Female	
Age	
Young	45 ± 2 years
Old	70 ± 2 years
Socioeconomic status	
High	Famous actor or actress, lawyer, doctor, pharmacist, golfer, wealthy neighborhood resident, etc.
Low	Laborer, informal employee, waitress, housekeeper, a person living alone, poor neighborhood resident, etc.
Clinical information	
Witnessed status	Yes
Bystander CPR	Yes
Initial ECG rhythm	Various (VF, PEA etc.)
Mode of transportation	EMS
Defibrillation	Yes (place of defibrillation was various, pre-hospital or in-hospital)
Total collapse to ROSC time interval	20–25 min (pre-hospital time interval was various)
Mental status after ROSC	Coma
Guardian attitude	
Positive	Please do everything you can.
Reluctant	I do not want the patient to receive any painful treatment.

CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; VF, ventricular fibrillation; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation.

The script was designed to include the key evidence that would lead physicians to decide to apply TTM (Table 1). In all scenarios, we presented OHCA patients who were witnessed having cardiac arrests, had received bystander cardiopulmonary resuscitation (CPR) and were transported by emergency medical services (EMS). The total CPR time for each case was similar. The actor/actress who played the EMP in these scenarios stated that the cause of OHCA was strongly suspected to be of cardiac origin. The conditions of patients in the postresuscitation state were coma and hemodynamic stability. The script did not deliberately attempt to divert the participants' attention by including indications for TTM, and no pre-existing comorbidities were presented.

2.4. Statistical analysis

We performed an unbalanced analysis of variance (ANOVA) using the 'proc GLM' statement in SAS as the primary analytical method. The balanced factorial design allowed the unconfounded estimation of all main effects and two-way interactions using ANOVA.

Our sample size of 64 physicians provided 80% power to detect an absolute difference of 30% in the means in the analyses of the main effects of physician or patient characteristics. We calculated the sample size regardless of multiple comparisons. In light of the multiple tests administered, we facilitated interpretation by presenting actual *p*-values, unadjusted for multiple testing, to allow readers to choose their preferred level of significance. We used SAS v.9.1 (SAS Institute, Inc., Cary, NC) to conduct these analyses.

3. Results

A total of 82 EMPs completed the experiment. We excluded 7 EMPs because of lack of experience with the decision to perform

Table 2
Participant responses regarding the certainty of the decision to apply targeted temperature management (TTM) according to patient attributes.

		Certainty of application for TTM		
		Median (%)	Interquartile range	*p*-Value
Sex				
	Male	80	(60–99)	0.68
	Female	84.5	(60–99)	
Age group				
	Young	90	(50–95)	0.001
	Old	80	(70–100)	
Socioeconomic status				
	High	90	(70–100)	0.001
	Low	80	(50–95)	
Attitude toward to TTM				
	Positive	90	(80–100)	0.001
	Reluctant	70	(41–90)	

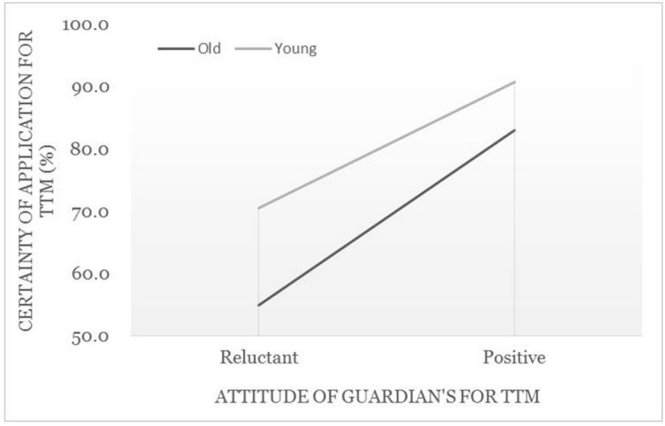

Fig. 1. Interaction plot of the certainty of application of targeted temperature management (TTM) between patient age and guardian attitude regarding TTM (estimate −7.8, 95% CI −13.3 to −2.3).TTM, targeted temperature management.

TTM. The final analysis included 75 EMPs. Female EMPs comprised 32% of the study population.

The EMPs' responses regarding their certainty of applying TTM differed significantly in relation to patient age (young vs. old: 90% vs. 80%, $p = 0.001$) and SES (higher vs. lower; 90% vs. 80%, $p = 0.001$), and guardians' attitude regarding TTM (positive vs. reluctant; 90% vs. 70%, $p = 0.001$). Patient sex did not affect the EMPs' responses (male vs. female; 80% vs. 84.5%, $p = 0.68$) (Table 2).

There was a significant interaction between patient age and guardians' attitude regarding TTM (estimate −7.8, 95% confidence interval [CI] −13.3 to −2.3). When the guardians had a reluctant attitude toward TTM, patient age had a greater effect on the EMPs' responses regarding the application of TTM (Fig. 1). The significance of this interaction persisted after adjusting for the EMPs' TTM experience and organizational characteristics (estimate −8.3, 95% CI −13.9 to −2.7). There were no significant interactions between patient sex and SES and other patient attributes.

A total of 34.6% of the participants reported experience with >50 cases of TTM. Almost all of the participants (94.7%) responded that they had experience with EDC and had worked with commercial TTM devices such as EDC or IVC-cath. (84%). Two-thirds (66.7%) of the participants worked at hospitals with TTM protocols (Table 3).

Table 3 shows the certainty regarding TTM application according to EMP and organizational characteristics. EMPs who had experienced >50 cases of TTM indicated a higher certainty of TTM use (90% vs. 80%, $p = 0.001$). EMPs with experience with device-free TTM methods (ECC and IVC-saline) indicated higher certainty of TTM use (86.5% vs. 80.0%, $p = 0.001$). EMP sex, age and duration of clinical experience were not associated with the certainty of TTM application. EMPs working in hospitals with commercial TTM devices or operating protocols indicated a higher likelihood of TTM use than those working in hospitals without TTM devices or protocols (88% vs. 80% and 90% vs. 80%; $p = 0.0001$, respectively).

4. Discussion

In this experiment, we found evidence that nonclinical factors, such as patient demographics, providers' experience with TTM, and organizational environment, affected the decision to apply TTM. The participants responded less positively to the use of TTM in patients who were older, had a low SES, and whose guardians had a reluctant attitude toward postresuscitation care. EMPs working in hospitals with commercial TTM devices or operating protocols indicated higher certainty regarding TTM use.

We used a rigorous experimental design to ensure the internal validity of the results. The factorial design removed the potential bias regarding patient sex, age, and SES. In the pilot test, advisory panels evaluated the scenarios according to the presented OHCA patients' sex, age group, SES, and guardians' attitude and classified them into two levels. Scenarios that were considered ambiguous and could not be classified into either of the two levels were revised. The final classification of the experimental factors in the scenarios was confirmed through feedback. The advisory panels also evaluated whether the clinical information included in each scenario was similar and assessed whether enough information was available to form a decision regarding the application of TTM.

The effects of patient factors in this experiment were particularly interesting. Guardian attitude, not surprisingly, was the most influential factor in the decision to apply TTM. When the guardians had a reluctant attitude toward postresuscitation care, the EMPs were less likely to apply TTM for old patients than for young patients. OHCA in older patients is associated with significantly lower survival [13]. However, several recent studies have reported that the majority of older survivors are discharged with a favorable neurological outcome [13,14]. Another patient attribute assessed in the present study was sex. Several studies have reported sex disparities in the provision of TTM to OHCA patients [8,15,16]. In this study, the EMPs' certainties regarding the use of TTM did not differ according to the patient's sex. Controversy exists regarding whether sex disparities in the use of TTM found in previous studies were the result of gender inequality or the accumulation of various vulnerability factors in women. Female OHCA patients are more likely to be older, have more comorbidities and have lower SES

Table 3
Certainty of application of targeted temperature management by physician and organization characteristics for patients with successfully resuscitated out-of-hospital cardiac arrest.

		Participants		Certainty of application for TTM		
		n	(%)	Median	IQR	*p*-Value
Sex						
Male		51	68.0	87	(60–99)	0.42
Female		24	32.0	80.5	(60–99)	
Age group (years)						
30s		29	38.7	81	(60–99)	0.31
40s		42	56.0	83.5	(60–99)	
50s		4	5.3			
Clinical experience with EMP						
<10 years		45	60.0	85	(60–100)	0.27
>11 years		30	40.0	81	(60–98)	
Experience with TTM (cases)						
<10		12	16.0	80	(51–95)	0.001
11–50		37	49.3			
51–100		10	13.3	90	(70–100)	
>101		16	21.3			
Experience with TTM methods						
Device-free methods	ECC	47	62.7	86.5	(65.5–100)	0.001
	IVC-saline	46	61.3			
Commercial devices	EDC	71	94.7	80	(50–95)	
	IVC-cath	31	41.3			
Work with commercialized TTM devices						
No		12	16.0	80	(50–99)	0.001
Yes		63	84.0	88	(62.5–99)	
Work with TTM protocols						
No		22	29.3	80	(50–95.5)	0.001
Unknown		3	4.0			
Yes		50	66.7	90	(66–100)	

TTM, targeted temperature management; IQR, interquartile range; EMP, emergency physician; ECC, external conventional cooling such as ice water, fans, and simple blankets; EDC, external device cooling using a pad with cooling device; IVC-saline, intravascular cooling using cold saline; IVC-cath, intravascular cooling using an intravascular cooling catheter.

than male OHCA patients. Finally, the present study also assessed EMPs' responses according to patient SES. The reasons for disparities according to SES are likely multifactorial. Differences in the provision of postresuscitation care according to SES have been reported in a publicly financed health care system [17]. The higher frailty burden in lower-SES populations requires further study. Provider bias regarding the provision of care according to SES may be a burden in low-SES populations.

In the present study, EMPs who had experience with device-free TTM methods indicated high certainty regarding TTM use. A recent study reported that the cooling methods used for TTM were not associated with significant differences in neurological recovery among OHCA patients [18,19]. It is interesting to note that EMPs with "experience with device-free TTM" were more certain in their decisions, as were EMPs who worked in "hospitals with commercial TTM devices." These two findings seem to be at odds with each other; however, they can be explained in part by the context of the Korean medical insurance system. In Korea, the use of commercial TTM devices for OHCA patients is not covered by national health insurance. The use of commercial TTM devices for OHCA patients is expensive but could reduce the workload of providers. In contrast, a separate fee is not charged for device-free TTM. This seems to attenuate the economic barrier against TTM application. When a device-free TTM method is used, EMPs may be burdened with more frequent monitoring to maintain the target temperature and meticulous observation for complications.

The use of a protocol might relieve providers' psychological burden and reduce the risk of a biased decision. In a study of critical care provision for septic shock patients, one successful strategy was the standardization of acute care by using checklists to eliminate implicit biases [20]. The implementation of TTM protocols has yielded positive patient outcomes [21].

5. Limitations

We used a rigorous experimental design to ensure the internal validity of the results. The factorial design removed potential bias regarding patient sex, age, and SES. A previous study randomly sampled participants to minimize bias according to sex, age, etc.; however, we could not randomly sample participants because we did not have access to a database with information on EMPs' sex or age. The median age and proportion of female EMPs in this experiment were similar to those of EMPs in Korea [22].

Previous sizable studies have used video vignettes with professional actors/actresses to present re-enactments of real situations encountered in practice [11,12]. The situations presented in previous studies almost always took place in outpatient clinics, and only one actor/actress was filmed in the patient role. In this study, several health care providers with various positions participated in OHCA resuscitation. Because we aimed to evaluate the influence of guardian attitude, additional actors/actresses were needed to act as guardians. It is a challenge to film such complex scenarios, and our budget and research time were limited. Rather than using video vignettes, we presented images representative of patient demographics, SES, and resuscitation situations.

We measured the likelihood of TTM application via a web-based survey and self-coding. A previous study conducted face-to-face interviews to ensure the independence of the responses [11,12]. However, it is difficult to completely ensure the independence of responses in web-based surveys. We asked the participants to decide independently rather than discussing their responses with others. An additional limitation of web-based surveys is the possibility that a single person will respond multiple times. Because the participants responded anonymously, it was impossible to systematically prohibit them from participating more than once. We

instructed the participants to participate only once in the survey. Because completing the survey took a considerable amount of time (>30 min), we believed that few EMPs would have participated multiple times. Finally, we used a self-reported 0–100 scale to assess the certainty of the decision. The self-reported 0–100 scale has been used in previous studies [9-12]; however, we are not sure whether the scoring of certainty is predictive of real-world clinical decisions. Scoring should be validated with respect to TTM application in OHCA patients.

6. Conclusion

The decision to apply TTM is significantly influenced by non-clinical factors, such as patient attributes and provider and organizational factors.

Funding sources

This research was supported by the faculty grant of Myongji Hospital, Republic of Korea (Grant ID 1701-05-05).

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