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ORIGINAL ARTICLE

# Impact of a targeted temperature management quality improvement project on survival and neurologic outcomes in cardiac arrest patients

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**Abstract**

**Background:** Targeted temperature management (TTM) is recommended for postresuscitation care of patients with sudden cardiac arrest (SCA) and its implementation remains challenging. This study aimed to evaluate the newly designed Quality Improvement Project (QIP) to improve the quality of TTM and outcomes of patients with SCA.

**Methods:** Patients who experienced out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA) with return of spontaneous circulation (ROSC) and were treated in our hospital between January 2017 and December 2019 were enrolled retrospectively. All included patients received QIP intervention initiated as follows: (1) Protocols and standard operating procedures were created for TTM; (2) shared decision-making was documented; (3) job training instruction was created; and 4) lean medical management was implemented.

**Results:** Among 248 included patients, the postintervention group (n = 104) had shorter duration of ROSC to TTM than the preintervention group (n = 144) (356 vs 540 minutes, *p* = 0.042); better *survival rate (39.4% vs 27.1%, p = 0.04), and neurologic performance (25.0% vs 17.4%, p < 0.001).* After propensity score matching (PSM), patients who *received TTM (n = 48)* had better *neurologic performance than those without TTM (n = 48) (25.1% vs 18.8%, p < 0.001).* OHCA (odds ratio [OR] = 2.705, 95% CI: 1.657-4.416), age >60 (OR = 2.154, 95% CI: 1.428-3.244), female (OR = 1.404, 95% CI: 1.005-1.962), and diabetes mellitus (OR = 1.429, 95% CI: 1.019-2.005) were negative predictors of survival; while TTM (OR = 0.431, 95% CI: 0.266-0.699) and bystander cardiopulmonary resuscitation (CPR) (OR=0.589, 95% CI: 0.35-0.99) were positive predictors. Age >60 (OR= 2.292, 95% CI: 1.58-3.323) and OHCA (OR= 2.928, 95% CI: 1.858-4.616) were negative predictors of favorable neurologic outcomes; while bystander CPR (OR=0.572, 95% CI: 0.355-0.922) and TTM (OR=0.457, 95% CI: 0.296-0.705) were positive predictors.

**Conclusion:** A new QIP with defined protocols, documented shared decision-making, and medical management guidelines improves TTM execution, *duration from ROSC to TTM,* survival, and neurologic outcomes of cardiac arrest patients.

**Keywords:** Cardiopulmonary resuscitation; Out-of-hospital cardiac arrest; Quality Improvement Project; Return of spontaneous circulation; Targeted temperature management

## 1. INTRODUCTION

Sudden cardiac arrest (SCA) is a leading cause of death worldwide, and only 2% to 20% of patients survive to discharge with good neurologic outcomes.[1] The postresuscitation care of such patients includes airway and ventilation support, coronary reperfusion, hemodynamic monitoring and management, control of seizures, intensive care unit (ICU) care, and administration of inotropic agents. Targeted temperature management (TTM) has been recommended for postresuscitation care of comatose patients who had experienced preceding SCA events.[2–4]

The effects of TTM on improving the mortality and neurologic outcome mechanisms in SCA are attributed to its actions at three injury levels after SCA, including ischemic, immediate reperfusion and delayed reperfusion injuries. Although evidence is not strong and injury levels are lower than those in comatose patients with ROSC after out-of-hospital cardiac arrest (OHCA) with shockable rhythm, TTM is still recommended for patients presenting with non-shockable rhythm or in-hospital cardiac arrest (IHCA).[5]

Nevertheless, many difficulties are encountered in the execution of TTM, including that medical personnel do not have a clear concept of TTM and, until now, have not had an appropriate protocol by which to execute TTM. Furthermore, many hospital

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staff members are not cognizant of TTM clinical guidelines. In addition, the actual TTM practice remains low. One reported barrier to adoption is clinician concerns over the potential technical difficulties of TTM. Recent surveys have reported that many clinicians perceive TTM as being too technically difficult to achieve in practice, which has been identified as a major contributing factor to slowing TTM adoption.[6–8] Considering these stated difficulties associated with performing TTM, this study aimed to employ the newly designed TTM Quality Improvement Project (TTM-QIP) and evaluate its ability to improve the quality of TTM and the outcomes of patients with cardiac arrest.

## 2. METHODS

### 2.1. Study design and setting

This retrospective observational cohort study was performed at KAOHSIUNG Veterans General Hospital, a medical center in southern Taiwan. Clinical chart data were collected from consecutive patients who were treated at Kaohsiung Veterans General Hospital for cardiac arrest (including OHCA and IHCA) with ROSC after resuscitation between January 2017 and December 2019. All data were analyzed retrospectively.

### 2.2. Ethical considerations

The protocol of this study, entitled "Impact of targeted temperature management quality improvement project on survival and neurological outcome in cardiac arrest patients," was reviewed and approved by the Institutional Review Board of KAOHSIUNG Veterans General Hospital (IRB No. KSVGH21-CT12-10) on October 22, 2021. Because this was not a registered clinical trial (RCT) and patient data were analyzed retrospectively and anonymously, no registration number was needed from a national trial registration site and the IRB waived signed informed consent. All procedures in this retrospective study followed the ethical standards of the responsible committee on human experimentation at Kaohsiung Veterans General Hospital and in accord with the Helsinki Declaration of 1975. This research study was sponsored by Yun-Te Chang, MD, MPH, conducted at Kaohsiung Veterans General Hospital without funding, conflicts of interest, incentives for subjects, and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

### 2.3. Definition of ROSC and mean arterial pressure

ROSC was identified in patients with SCA through characteristic signs, including breathing, coughing, or movement. For healthcare practitioners, signs of ROSC also require evidence of a palpable pulse or measurable mean arterial blood pressure (MAP >60 mmHg) that persists for at least 20 minutes. To satisfy the definition of ROSC, MAP was checked just after ROSC and every 15 minutes regularly thereafter.[5,9]

### 2.4. Study population

The ROSC study population consisted of 248 patients who were successfully resuscitated from OHCA or IHCA and immediately admitted to the ICU. The initial rhythm was VT/VF in 25 patients and asystole or pulseless electric activity in the remaining 223. All patients with acute ST-segment elevation myocardial infarction were immediately transferred to the cardiology catheter laboratory for primary angioplasty and stenting before being admitted to the ICU. The study protocol for TTM included the combo order, charge code in the computer, and process checklist. The standard operating procedure for TTM included the choice of the proper machine for TTM, setting the work manual for TTM, and creating the operating instructions for TTM. In addition, the training program for TTM included regular TTM education and training for medical personnel, regular meetings and discussion, regular announcements of indications for TTM, simulated operations taking place at regular times, and placing TTM posters in the emergency department (ED) and intensive care unit (ICU). The flow diagram in Fig. 1 displays all elements in the study protocol.

#### *2.4.1.* Inclusion and exclusion criteria for TTM

The inclusion criteria for patients who would receive TTM were as follows (although discretion was given to the attending clinician to eventually initiate TTM): (1) OHCA and IHCA patients who presented with rhythm and sustained ROSC after cardiac arrest for >30 minutes; (2) Comatose patients with a Glasgow Coma Score of ≤8 or who were unresponsive postresuscitation; and (3) Patients who were hemodynamically stable with systolic blood pressure (BP) >90 mmHg (with or without inotropic support). The exclusion criteria for patients who would receive TTM included OHCA and IHCA patients, those who regained consciousness, organic structural brain lesion after brain computed tomography (CT) scan examination, patients with persistent hypotension despite fluid and/or vasopressor support,

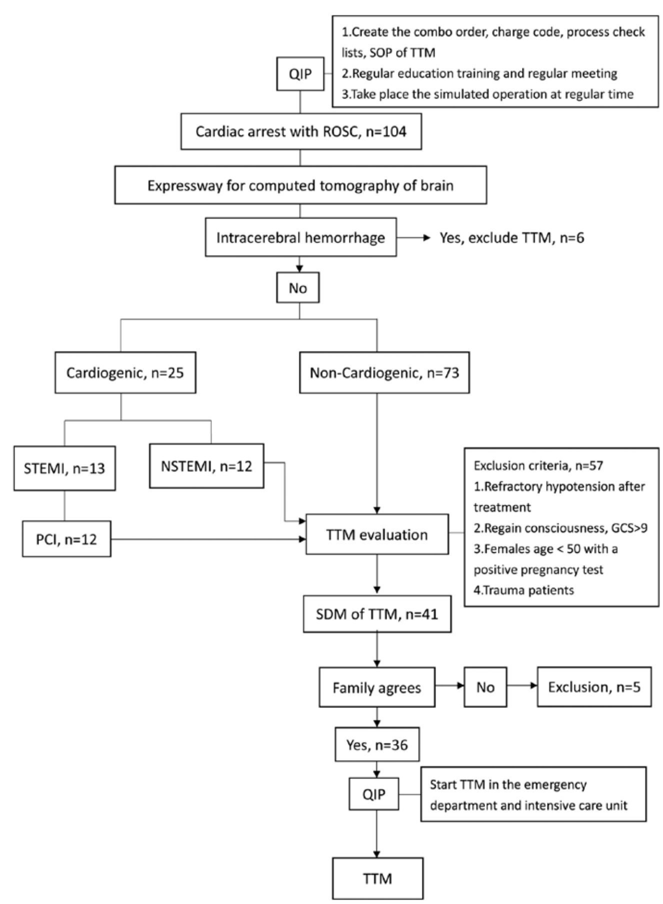


**Fig. 1** The flow diagram in Fig. 1 displays all the elements in the study protocol. The study protocol for evaluating QIP and TTM included creating the combo order, charge codes in the computer, and process checklist. The standard operating procedure for TTM included choice of the proper machine for TTM, developing the work manual for TTM, and creating operating instructions for TTM. NSTEMI = non-ST elevation myocardial infarction; QIP = Quality Improvement Project; PCI = percutaneous coronary intervention; ROSC = return of spontaneous circulation; SDM = shared decision-making; SOP = standard operating procedure; STEMI = ST elevation myocardial infarction; TTM = targeted temperature management.

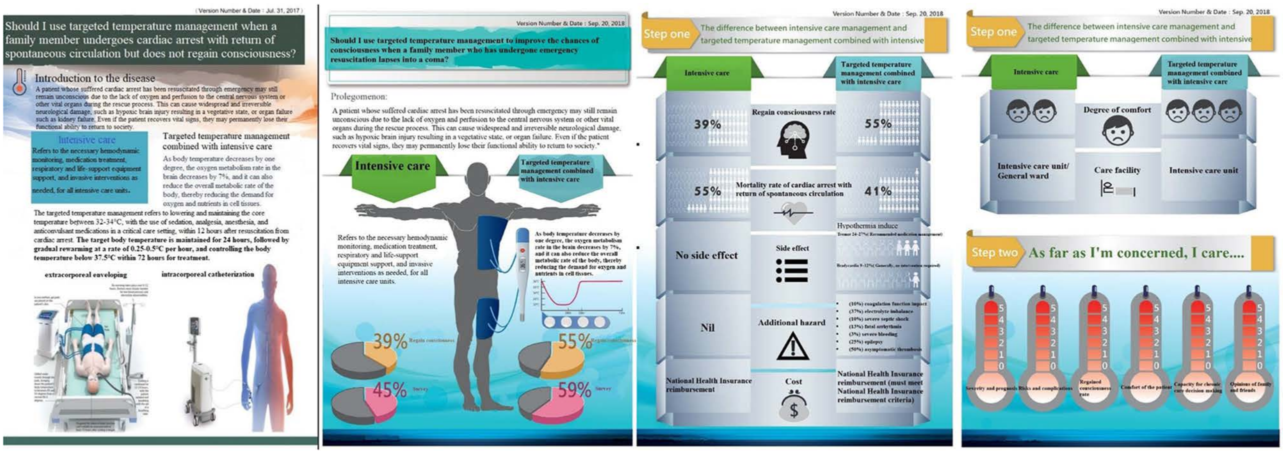


**Fig. 2** Documentation for shared decision-making. Development of documentation in TTM ensures that the decision-making process is well documented, as opposed to clinicians making decisions on behalf of family, and is gaining increasing prominence in TTM policy. TTM = targeted temperature management.

females aged <50 years with a positive pregnancy test and trauma patients. All patients were equipped with intra-arterial and central venous catheters. They were also treated with standard resuscitation (SR), which consisted of maintaining MAP at 75-80 mmHg (by using norepinephrine when necessary), $PaO_2$ at 90-100 mm Hg, $PaCO_2$ at 36-40 mmHg, and blood glucose values between 6 and 8 mmol/L. Patients with sustained hypotension and shock (systolic blood arterial pressure 90 mmHg for 60 minutes, unresponsive to volume resuscitation, and/or requiring vasopressor treatment) were equipped with a pulmonary artery catheter (Edwards Life Sciences Corporation, Irvine, CA, USA) and treated with dobutamine, aiming at mixed venous oxygen saturation 65% and arterial blood lactate 2.5 mmol/L, according to our local procedures for resuscitation after cardiocirculatory shock. Hemodynamic support was given at the discretion of the treating clinician, as described previously.[5,10,11]

#### *2.4.2.* Clinical outcomes

Clinical outcomes were defined based on the methodology of Bernard et al[5]: a favorable outcome was discharge from the hospital to home or a rehabilitation center and a poor outcome was death in the hospital or discharge to a long-term care facility or nursing home.[6]

### 2.5. TTM definition and performance

The ArcticSun machine (Medivance, Inc., Louisville, CO, USA) was used as a noninvasive method to achieve the targeted temperature. It uses a gel pad with an adhesive hydrogel that adheres to the patient's skin without requiring the removal of hair. The device operates under negative pressure and circulates water through the pads at a temperature between 4 and 42°C (39-108°F). Water is pulled through the pads, which minimizes the risk of leakage. By controlling the temperature of the water running through the gel pads, the Arctic Sun adjusts a patient's temperature.

Immediately after the decision to initiate TTM, body temperature should be measured using a probe placed in the middle of the esophagus. In the present study, 33°C was the targeted body temperature in TTM, and the cooling phase should last 24 hours. The ArcticSun machine maintained the rewarming rate at 0.15 to 0.25°C/h. The whole course during TTM, including sedation (midazolam, 0.1 mg/kg/h intravenously), analgesia (fentanyl, 1.5 g/kg/h intravenously), and paralysis (intravenous boluses of vecuronium, 0.1 mg/kg, according to nerve stimulator monitoring) must be followed in order to prevent shivering and to minimize patients' discomfort.[8]

### 2.6. Quality Improvement Project

This study initiated QIP by: (1) creating the protocols, standard operating procedure and training program for TTM. Before starting QIP, the hospital medical personnel had no concept of TTM. Thus, it was necessary to create the protocols, standard operating procedure and training courses for TTM to help medical staff members to perform TTM well; (2) developing the documentation for shared decision-making in Fig. 2. Many families of cardiac arrest patients have no awareness of TTM. Therefore, developing the documentation was intended to help family members learn about TTM and make decisions about the patients' care; (3) creating a training program to instruct medical personnel about the protocol and operating procedure. QIP is new program and most medical personnel are not yet familiar with the protocol and standard operating procedure of TTM. Thus, the training program was created to help hospital staff become familiar with TTM and the protocol and standard operating procedures; and (4) starting lean medical management. The duration from ROSC to TTM is 540 minutes. Lean medical management, which was started to decrease the period from ROSC to TTM, includes starting TTM in the ED and ICU and creating an expressway for CT. QIP was managed by the directors of the ED, the Department of Internal Medicine (IM), the head nurses of the ED, and one medical ward (MW). QIP is not evaluated directly but through evaluating the standardized application of TTM under the new QIP and the effects of TTM on the execution rates of TTM and patients' outcomes. Meetings and discussion take place every week and have a process checklist. In the meeting, every patient who was admitted as OHCA or IHCA with ROSC was discussed and the censor checklist.

### 2.7. Statistical analysis

All data analysis was done using SAS software (version 9.4; SAS Institute, Inc., Cary, NC, USA). Percentile values were used to express categorical data, which were analyzed using the Chi-square test. Logistic regression analysis was used to calculate odds ratios (ORs) and associated 95% CIs for significant variables. The distribution of continuous variables was described as mean ($\mu$) and standard deviation (mean ± SD). A $p$ value of <0.05 was considered statistical significance.

Propensity score matching (PSM) was used to analyze and determine differences between the characteristics of patients with cardiac arrest who received or do not receive TTM. PSM is a quasi-experimental method in which the researcher uses statistical techniques to construct an artificial control group by matching each treated unit with a nontreated unit of similar characteristics.

## 3. RESULTS

A total of 248 cardiac arrest patients, including OHCA and IHCA, were enrolled between January 2017 and December 2019; all patients had received resuscitation and achieved ROSC. The proportion of patients with do not resuscitate (DNR) in the preintervention group was 43.5% and in the postintervention group was 50.9%. In addition, the proportion of patients with DNR in the non-TTM group was 55.7% and 40.1% in the TTM group. No differences were found in baseline characteristics of SCA patients between the preintervention (n = 144) and postintervention groups (n = 104), including no differences in sex (male 45.8% vs 51.9%, $p$ = 0.344) and mean age of preintervention and postintervention groups (67.1 ± 15.1 vs 64.5 ± 16.1 years, $p$ = 0.205). The mean duration was 1554 ± 126 minutes. No differences were found between the two groups in comorbidities (diabetes mellitus, hypertension, coronary artery disease, dyslipidemia, heart failure, arrhythmia, chronic kidney disease, end-stage renal disease under dialysis, cerebral vascular disease, malignancy, *chronic obstructive pulmonary disease*, asthma, and liver cirrhosis) (Table 1).

No differences were found in baseline characteristics of cardiac arrest patients between survivors (n = 80) and nonsurvivor groups (n = 168), including no differences in sex (male 56.3.8% vs 54.2%, $p$ = 0.543) and mean age of survivors and nonsurvivor groups (63.9 ± 15.8 vs 67.3 ± 15.1 years, $p$ = 0.321). In addition, no differences were found between the two groups in comorbidities (diabetes mellitus, hypertension, coronary artery disease, dyslipidemia, heart failure, arrhythmia, chronic kidney disease, end-stage renal disease under dialysis, cerebral vascular disease, malignancy, chronic obstructive pulmonary disease, asthma, and liver cirrhosis) (Table 2).

No differences were found in baseline characteristics of SCA patients between groups with better neurological outcomes (n = 17) and worse neurological outcomes (n = 63), including no differences in sex (male 47.1% vs 49.2%, $p$ = 0.534) and mean age of preintervention and postintervention groups (64.7 ± 15.9 vs 67.5 ± 16.1 years, $p$ =0.310). In addition, no differences were found between the two groups in comorbidities (diabetes mellitus, hypertension, coronary artery disease, dyslipidemia, heart failure, arrhythmia, chronic kidney disease, end-stage renal disease under dialysis, cerebral vascular disease, malignancy, chronic obstructive pulmonary disease, asthma, and liver cirrhosis) (Table 3).

The postintervention group had a high TTM execution rate (34.6%) compared with that of the preintervention group (18.1%) ($p$ = 0.003), shorter ROSC duration (356 vs 540 minutes, $p$ = 0.042), higher survival to discharge (39.4% vs 27.1%, $p$ = 0.04), and favorable neurological outcomes (25.0% vs 17.4%, $p$ <0 0.001) as shown in Fig. 3. The favorable neurological outcomes represent a cerebral performance category (CPC) of 1 or 2. The CPC score is the most commonly used tool to assess cerebral performance for both research and audit purposes. The CPC of 1 means normal (good cerebral performance), and CPC of 2 means Moderate disability (disabled but independent). The definition of the survival rate to discharge is that the proportion of patients who experienced OHCA/IHCA with ROSC were still living at discharge.

### 3.1. Main outcomes

Throughout the preintervention and postintervention periods, no differences were found in baseline characteristics of cardiac arrest patients between the TTM and non-TTM groups after PSM 1:1, including OHCA/IHCA ratios, witnessed collapse, bystander CPR, defibrillation by AED, initial cardiac rhythm (ventricular fibrillation/ventricular tachycardia, asystole, pulseless electrical activity), electrical shock, sustained ROSC, heart rate at ROSC, systolic BP at ROSC, diastolic BP at ROSC, and body temperature at ROSC (Table 4), but patients in the TTM group had a higher rate of bystander CPR (77.1% vs 37.5% $p$ < 0.001) and lower Glasgow Coma Scale scores at ROSC.

The outcomes of cardiac arrest patients between the TTM (n = 48) and non-TTM groups after PSM are shown in Fig. 4A–C. The TTM group had more favorable neurological outcomes (TTM: 25.0% vs non-TTM: 18.8%, $p$ < 0.001) (Fig. 4A), higher survival rates to discharge (TTM: 41.7% vs non-TTM: 31.3%, $p$ = 0.098) in Fig. 4B, and a higher rate of improved Glasgow coma scale scores (TTM: 34.6% vs non-TTM: 25%, $p$ = 0.012)

**Table 1**

**Baseline characteristics for cardiac arrest patients between preintervention and postintervention groups**

| Variables | Preintervention (N = 144) | Postintervention (N = 104) | $p$ |
|---|---|---|---|
| Male sex no./total no. (%) | 86/144 (45.8%) | 54/104 (51.9%) | 0.344 |
| Mean age—y (μ ± SD) | 67.1 ± 15.1 | 64.5 ± 16.1 | 0.205 |
| Comorbidities no./total no. (%) | | | |
| Diabetes mellitus | 72/144 (50.0%) | 49/104 (47.1%) | 0.654 |
| Hypertension | 79/144 (54.9%) | 58/104 (55.8%) | 0.887 |
| Coronary artery disease | 26/144 (18.1%) | 19/104 (18.3%) | 0.996 |
| Dyslipidemia | 17/144 (11.8%) | 12/104 (11.5%) | 0.949 |
| Heart failure | 14/144 (9.7%) | 11/104 (10.6%) | 0.825 |
| Arrhythmia | 8/144 (5.6%) | 6/104 (5.8%) | 0.943 |
| Chronic kidney disease | 17/144 (11.8%) | 19/104 (18.3%) | 0.154 |
| End-stage renal disease under dialysis | 17/144 (11.8%) | 18/104 (17.3%) | 0.219 |
| Cerebral vascular disease | 14/144 (9.7%) | 7/104 (6.7%) | 0.404 |
| Malignancy | 17/144 (11.8%) | 16/104 (15.4%) | 0.413 |
| Chronic obstructive pulmonary disease or asthma | 5/144 (3.5%) | 5/104 (4.8%) | 0.598 |
| Liver cirrhosis | 3/144 (2.1%) | 2/104 (1.9%) | 0.929 |
| Out-of-hospital cardiac arrest | 78/144 (54.2%) | 50/104 (48.1%) | 0.344 |
| Witnessed collapse | 123/144 (85.4%) | 90/104 (86.5%) | 0.802 |
| Bystander cardiopulmonary resuscitation | 93/144 (64.6%) | 79/104 (76.0%) | 0.055 |
| Defibrillation by AED | 14/144 (9.7%) | 8/104 (7.7%) | 0.823 |
| Initial rhythm no./total no. (%) | | | 0.467 |
| Ventricular tachycardia/ Ventricular fibrillation | 16/144 (11.1%) | 9/104 (8.7%) | |
| Asystole | 102/144 (70.8%) | 70104 (67.3%) | |
| Pulseless electrical activity | 26/144 (18.1%) | 25/104 (24.0%) | |
| Electrical shock no./total no. (%) | 32/144 (22.2%) | 24/104 (23.1%) | 0.874 |
| Sustained return of spontaneous circulation (>20 min) | 141/144 (97.9%) | 103/104 (99.0%) | 0.489 |
| Glasgow Coma Scale at ROSC (μ ± SD) | 2.58 ± 1.5 | 2.29 ± 1.2 | 0.095 |
| Heart rate at ROSC (μ ± SD) | 105.5 ± 29.1 | 102.0 ± 26.9 | 0.337 |
| Systolic blood pressure at ROSC (μ ± SD) | 125.5 ± 45.4 | 125.2 ± 45.9 | 0.919 |
| Diastolic blood pressure at ROSC (μ ± SD) | 73.5 ± 29.1 | 68.9 ± 29.0 | 0.321 |
| Body temperature at ROSC (μ ± SD) | 35.5 ± 1.2 | 35.7 ± 1.3 | 0.409 |
| Treatments no./total no. (%) | | | |
| Extracorporeal membrane oxygenation | 5/144 (3.5%) | 10/104 (9.6%) | 0.016 |
| Coronary angiography | 12/144 (8.3%) | 13/104 (12.5%) | 0.160 |
| Percutaneous coronary intervention | 11/144 (7.6%) | 12/104 (11.5%) | 0.574 |

Values are expressed as mean (μ) ± standard deviation for continuous variables and numbers (%) for categorical variables.

AED = automated external defibrillator; ROSC = return of spontaneous circulation; SD = standard deviation; TTM = targeted temperature management.

**Table 2**

**Baseline characteristics for cardiac arrest patients between survivors vs nonsurvivor groups**

| Variables | Survivors (N = 80) | Nonsurvivor (N = 168) | *p* |
|---|---|---|---|
| Male sex no./total no. (%) | 45/80 (56.3%) | 91/168 (54.2%) | 0.543 |
| Mean age, y (μ ± SD) | 63.9 ± 15.8 | 67.3 ± 15.1 | 0.321 |
| Comorbidities no./total no. (%) | | | |
| Diabetes mellitus | 41/80 (51.3%) | 80/168 (47.6%) | 0.613 |
| Hypertension | 46/80 (57.5%) | 91/168 (54.2%) | 0.873 |
| Coronary artery disease | 19/80(23.8%) | 26/168 (15.5%) | 0.891 |
| Dyslipidemia | 9/80 (11.3%) | 20/168 (11.9%) | 0.913 |
| Heart failure | 7/80 (8.8%) | 22/168 (13.1%) | 0.882 |
| Arrhythmia | 5/80 (6.3%) | 7/168 (4.2%) | 0.917 |
| Chronic kidney disease | 11/80 (13.8%) | 25/168 (14.8%) | 0.257 |
| End-stage renal disease under dialysis | 9/80 (11.3%) | 26/168 (15.5%) | 0.163 |
| Cerebral vascular disease | 9/80 (11.3%) | 12/168 (7.1%) | 0.431 |
| Malignancy | 10/80 (12.5%) | 23/168 (13.7%) | 0.459 |
| Chronic obstructive pulmonary disease or asthma | 3/80 (3.8%) | 7/168 (4.2%) | 0.589 |
| Liver cirrhosis | 2/80 (2.5%) | 3/168 (1.8%) | 0.856 |
| Out-of-hospital cardiac arrest | 47/80 (58.8%) | 81/168 (48.2%) | 0.242 |
| Witnessed collapse | 73/80 (91.3%) | 140/168 (83.3%) | 0.827 |
| Bystander cardiopulmonary resuscitation | 71/80 (88.8%) | 92/168 (54.8%) | 0.041 |
| Defibrillation by AED | 8/80 (10.0%) | 14/168 (8.3%) | 0.754 |
| Initial rhythm no./total no. (%) | | | 0.518 |
| Ventricular tachycardia/ Ventricular fibrillation | 10/80 (12.5%) | 15/168 (8.9%) | |
| Asystole | 61/80 (76.3%) | 113/168 (67.3%) | |
| Pulseless electrical activity | 16/80 (20.0%) | 35/168(20.3%) | |
| Electrical shock no./total no. (%) | 19/80(23.8%) | 37/168(22.0%) | 0.897 |
| Sustained return of spontaneous circulation (>20 min) | 79/80 (98.8%) | 165/168 (98.2%) | 0.589 |
| Glasgow Coma Scale at ROSC (μ ± SD) | 2.73 ± 1.7 | 2.15 ± 1.1 | 0.063 |
| Heart rate at ROSC (μ ± SD) | 100.4 ± 25.5 | 110.9 ± 27.3 | 0.234 |
| Systolic blood pressure at ROSC (μ ± SD) | 125.6 ± 51.4 | 107.2 ± 43.1 | 0.506 |
| Diastolic blood pressure at ROSC (μ ± SD) | 76.4 ± 28.4 | 61.9 ± 24.3 | 0.401 |
| Body temperature at ROSC (μ ± SD) | 35.0 ± 1.2 | 35.7 ± 1.3 | 0.409 |

Values are expressed as mean (μ) ± standard deviation for continuous variables and numbers (%) for categorical variables.

AED = automated external defibrillator; ROSC = return of spontaneous circulation; SD = standard deviation; TTM = targeted temperature management.

(Fig. 4C). The definition of the improved Glasgow coma scale score is that the Glasgow coma scale of patients when discharged was higher than that of those who experienced OHCA/IHCA with ROSC. The survival rate and favorable neurologic outcome associated with QIP and TTM are shown in Fig. 5. The survival rate of patients receiving QIP without TTM group (QIP+TTM−) was 33.51%, while receiving QIP with TTM group (QIP+TTM+) was 44.32% and not receiving QIP nor the TTM group (QIP−TTM−) was 30.25%, and not receiving QIP but receiving the TTM group (QIP−TTM+) was 40.19%. Moreover, the favorable neurologic outcome of patients receiving QIP without the TTM− group (QIP+TTM−) was 21.93%, receiving QIP with the TTM group (QIP+TTM+) was 29.34% and not receiving QIP nor TTM group (QIP−TTM−) was 15.57%, and not receiving QIP but receiving the TTM group was 20.76% (QIP−TTM+).

Fig. 6 reports forest plots with hazard ratios based on multivariate Cox regression of survival outcomes in all cardiac arrest patients. Negative predictors of survival were: OHCA (OR = 2.705, 95% CI: 1.657-4.416), age >60 (OR = 2.154, 95% CI: 1.428-3.244), female (OR =1.404, 95% CI: 1.005-1.962), and diabetes mellitus (OR = 1.429, 95% CI: 1.019-2.005). Positive predictors for overall survival outcomes were TTM (OR = 0.431, 95% CI: 0.266-0.699) and bystander CPR (OR = 0.589, 95% CI: 0.35-0.99).

Fig. 7 shows forest plots with hazard ratios based on Cox regression of favorable neurologic outcomes in all cardiac arrest patients. Age >60 (OR = 2.292, 95% CI: 1.58-3.323) and OHCA

**Table 3**

**Baseline characteristics for cardiac arrest patients between better neurological vs worse neurological outcome**

| Variables | Better neurological outcome (N = 17) | Worse neurological outcome (N = 63) | *p* |
|---|---|---|---|
| Male sex no./total no. (%) | 8/17 (47.1%) | 31/63 (49.2%) | 0.534 |
| Mean age, y (μ ± SD) | 64.7 ± 15.9 | 67.5 ± 16.1 | 0.310 |
| Comorbidities no./total no. (%) | | | |
| Diabetes mellitus | 9/17 (52.9%) | 32/63 (50.8%) | 0.354 |
| Hypertension | 10/17 (58.8%) | 36/63 (57.1%) | 0.967 |
| Coronary artery disease | 3/17 (17.6%) | 16/63(25.4%) | 0.789 |
| Dyslipidemia | 2/17 (11.8%) | 7/63 (11.1%) | 0.932 |
| Heart failure | 2/17 (11.1%) | 5/63 (7.9%) | 0.857 |
| Arrhythmia | 1/17 (5.9%) | 4/63 (6.3%) | 0.872 |
| Chronic kidney disease | 3/17 (17.6%) | 8/63 (12.9%) | 0.216 |
| End-stage renal disease under dialysis | 2/17 (11.8%) | 7/63 (11.8%) | 0.825 |
| Cerebral vascular disease | 2/17 (11.8%) | 7/63 (11.1%) | 0.261 |
| Malignancy | 2/17 (11.8%) | 8/63 (12.7%) | 0.449 |
| Chronic obstructive pulmonary disease or asthma | 1/17 (5.9%) | 2/63 (3.2%) | 0.598 |
| Liver cirrhosis | 1/17 (5.9%) | 1/63 (1.6%) | 0.521 |
| Out-of-hospital cardiac arrest | 9/17 (52.9%) | 38/63 (60.3%) | 0.**426** |
| Witnessed collapse | 15/17 (88.2%) | 58/63 (92.1%) | 0.802 |
| Bystander cardiopulmonary resuscitation | 17/17 (100%) | 55/63 (85.7%) | 0.048 |
| Defibrillation by AED | 2/17 (9.7%) | 6/63 (7.7%) | 0.823 |
| Initial rhythm no./total no. (%) | | | 0.567 |
| Ventricular tachycardia/ Ventricular fibrillation | 2/17 (11.8%) | 8/63 (8.7%) | |
| Asystole | 12/17 (70.6%) | 49/63 (77.8%) | |
| Pulseless electrical activity | 3/17 (17.6%) | 13/63 (20.6%) | |
| Electrical shock no./total no. (%) | 4/17 (23.5%) | 15/63 (23.8%) | 0.764 |
| Sustained return of spontaneous circulation (>20 min) | 17/17 (100%) | 62/63 (98.4%) | 0.438 |
| Glasgow Coma Scale at ROSC (μ ± SD) | 3.63 ± 1.4 | 2.58 ± 1.3 | 0.105 |
| Heart rate at ROSC (μ ± SD) | 104.3 ± 22.1 | 102.2 ± 24.1 | 0.337 |
| Systolic blood pressure at ROSC (μ ± SD) | 127.5 ± 34.7 | 125.9 ± 42.6 | 0.879 |
| Diastolic blood pressure at ROSC (μ ± SD) | 78.1 ± 23.5 | 69.2 ± 26.8 | 0.370 |
| Body temperature at ROSC (μ ± SD) | 35.7 ± 1.2 | 35.0 ± 1.1 | 0.396 |
| Treatments no./total no. (%) | | | |
| Extracorporeal membrane oxygenation | 6/17 (35.3%) | 9/63 (14.2%) | 0.127 |
| Coronary angiography | 5/17 (29.4%) | 20/63 (31.7%) | 0.608 |
| Percutaneous coronary intervention | 5/17 (29.4%) | 18/63 (28.6%) | 0.774 |

Values are expressed as mean (μ) ± standard deviation for continuous variables and numbers (%) for categorical variables.

AED = automated external defibrillator; ROSC = return of spontaneous circulation; SD = standard deviation; TTM = targeted temperature management.

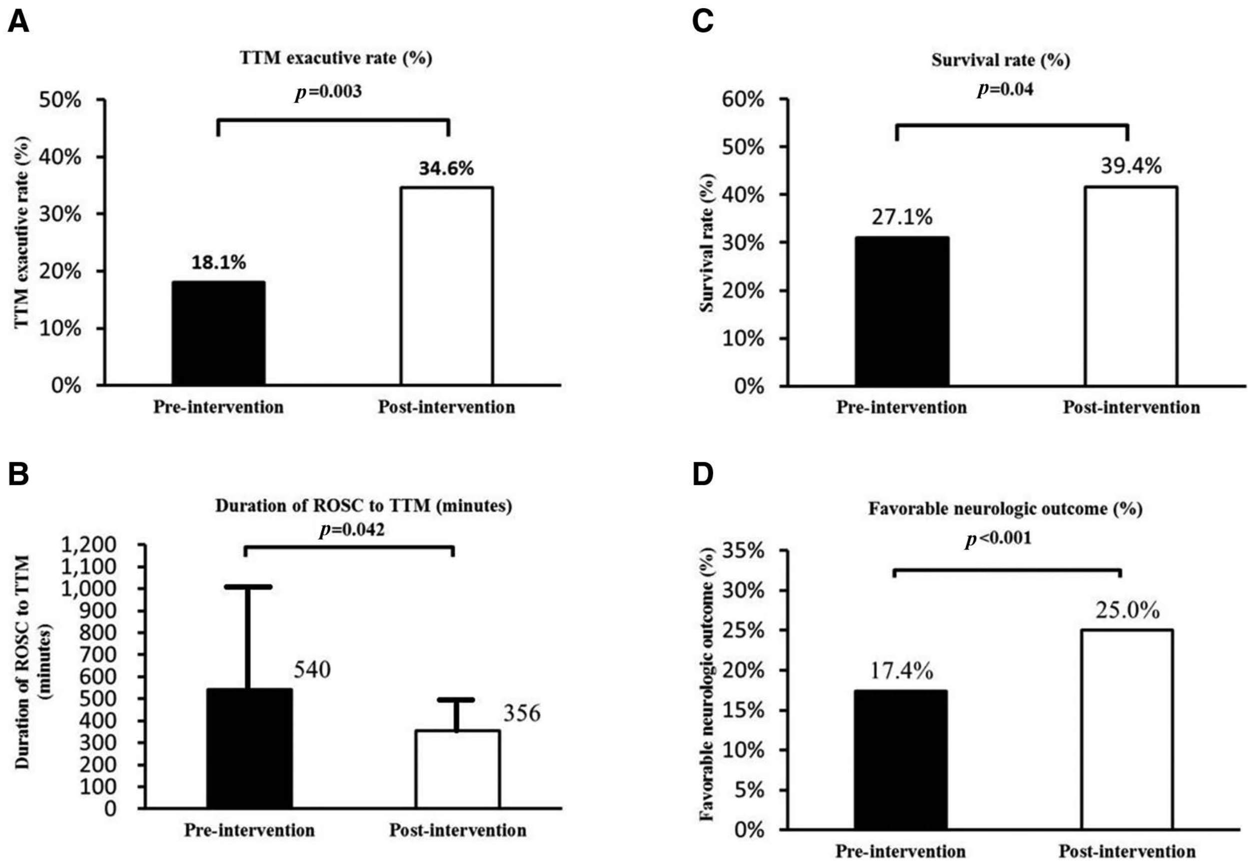


**Fig. 3** Outcomes of cardiac arrest patients between preintervention (n = 144) and postintervention (n = 104) groups. A, Postintervention group had higher TTM execution rate than the preintervention group (execution rate of preintervention: 18.1%; postintervention: 34.6%, $p = 0.003$). B, Longer duration of ROSC to TTM was observed in the preintervention group (duration of preintervention: 540 ± 438 minutes; postintervention: 356 ± 155 minutes, $p = 0.042$). C, Higher survival rate to discharge was observed in the postintervention group (survival rate of preintervention: 27.1%; postintervention: 39.4%, $p = 0.04$). D, In the preintervention group, low favorable neurologic outcomes were reported (preintervention: 17.4 %; postintervention: 25.0%, $p < 0.001$). ROSC = return of spontaneous circulation; SD = standard deviation; TTM = targeted temperature management.

(OR = 2.928, 95% CI: 1.858-4.616) were negative predictors; while bystander CPR (OR = 0.572, 95% CI: 0.355-0.922) and TTM (OR = 0.457, 95% CI: 0.296-0.705) were positive predictors for favorable neurologic outcomes.

## 4. DISCUSSION

In the present study, employing the new QIP with defined protocols, documented shared decision-making and medical management guidelines improved the execution rate of TTM and reduced the *duration from ROSC to TTM*. Providing quality-controlled TTM for OHCA and IHCA patients with ROSC demonstrated better benefits to patients, including higher favorable neurologic outcomes, better survival rates to discharge and higher rates of improved Glasgow coma scale scores. Furthermore, standardized quality improvement of TTM after employing the new QIP showed greater efficiency in achieving target temperatures than had been demonstrated previously in the largest and most efficacious randomized controlled trials.[6,12–15]

The new QIP was employed to help achieve TTM reliably in routine postresuscitation care after cardiac arrest. After using QIP, TTM in our hospital was essentially standardized, which increased the TTM execution rate, reduced the duration to ROSC (from mean 540 to mean 356 minutes in the whole study population), achieved better survival to discharge (27.1%) and more favorable neurologic outcomes than those measured previously before using the new QIP. *TTM protects neurologic function by attenuating neuronal cell death from cerebral anoxia and ischemia–reperfusion injuries via a number of proposed mechanisms that may include blunting of the cerebral proinflammatory response and decreasing the production of excitatory mediators of brain injury, decreasing the cerebral metabolic rate, and perhaps decreasing intracranial pressure.*[16–20]

Findings of the present study are similar or improved compared to those of previous *randomized controlled trials: TTM improved neurologic outcomes and reduced mortality from cardiac arrest after ROSC*. In previous studies, the survival rate to discharge was between 13% and 59%.[7,8,11–14,18] One study reported survival to discharge of 13% (3/23),[6] while the present study reported 41.7%.

Several trials targeted all patients after OHCA, regardless of the initial rhythm based on current guidelines, while other trials focused on patients after OHCA with shockable rhythms such as pulseless ventricular tachycardia and ventricular fibrillation. Among these, the outcomes of patients after OHCA due to a shockable rhythm showed significantly higher survival rates and higher favorable outcomes in the hypothermia group.[18] One study that reported relatively poor clinical outcomes compared to prior studies conjectured that this result was likely a function of patient selection. This is because randomized trials of TTM have usually employed very strict inclusion criteria to only

**Table 4**

**Baseline characteristics for cardiac arrest patients between the TTM and non-TTM groups after propensity score matching**

| Variables | Non-TTM (N = 48) | TTM (N = 48) | *p* |
|---|---|---|---|
| Male sex no./total no. (%) | 30/48 (62.5%) | 29/48 (60.4%) | 0.834 |
| Mean age, y (μ ± SD) | 62.5 ± 15.0 | 61.1 ± 12.0 | 0.611 |
| Comorbidities no./total no. (%) | | | |
| Diabetes mellitus | 25/48 (52.1%) | 23/48 (47.9%) | 0.683 |
| Hypertension | 30/48 (62.5%) | 30/48 (62.5%) | 1.0 |
| Coronary artery disease | 7/48 (14.6%) | 10/48 (20.8%) | 0.423 |
| Dyslipidemia | 7/48 (14.6%) | 9/48 (18.8%) | 0.584 |
| Heart failure | 5/48 (10.4%) | 7/48 (14.6%) | 0.537 |
| Arrhythmia | 3/48 (6.3%) | 2/48 (4.2%) | 0.646 |
| Chronic kidney disease | 9/48 (18.8%) | 10/48 (20.8%) | 0.789 |
| End-stage renal disease under dialysis | 5/48 (10.4%) | 7/48 (14.6%) | 0.537 |
| Cerebral vascular disease | 5/48 (10.4%) | 3/48 (6.3%) | 0.460 |
| Malignancy | 4/48 (8.3%) | 5/48 (10.4%) | 0.726 |
| Chronic obstructive pulmonary disease or asthma | 2/48 (4.2%) | 1/48 (2.1%) | 0.557 |
| Liver cirrhosis | 1/48 (2.1%) | 1/48 (2.1%) | 1.0 |
| Out-of-hospital cardiac arrest | 41/48 (85.4%) | 36/48 (75.0%) | 0.200 |
| Witnessed collapse | 36/48 (75.0%) | 41/48 (85.4%) | 0.200 |
| Bystander cardiopulmonary resuscitation | 18/48 (37.5%) | 37/48 (77.1%) | <0.001 |
| Defibrillation by AED | 10/48 (20.8%) | 12/48 (25.0%) | 0.197 |
| Initial rhythm | | | 0.248 |
| Ventricular tachycardia/ventricular fibrillation | 9/48 (18.8%) | 14/48 (29.2%) | |
| Asystole | 33/48 (68.8%) | 25/48 (52.1%) | |
| Pulseless electrical activity | 6/48 (12.5%) | 9/48 (18.8%) | |
| Electrical shock | 13/48 (27.1%) | 17/48 (35.4%) | 0.378 |
| Sustained return of spontaneous circulation (>20 mins) | 46/48 (95.8%) | 48/48 (100%) | 0.153 |
| Glasgow Coma Scale at ROSC (μ ± SD) | 3.29 ± 2.3 | 2.35 ± 1.1 | 0.019 |
| Heart rate at ROSC (μ ± SD) | 107.6 ± 30.1 | 100.0 ± 26.3 | 0.192 |
| Systolic blood pressure at ROSC (μ ± SD) | 118.9 ± 46.2 | 123.5 ± 46.6 | 0.613 |
| Diastolic blood pressure at ROSC (μ ± SD) | 70.0 ± 29.9 | 72.0 ± 30.4 | 0.748 |
| Body temperature at ROSC (μ ± SD) | 35.3 ± 1.4 | 36.1 ± 1.3 | 0.409 |
| Treatments | | | |
| Extracorporeal membrane oxygenation | 0/48 (0%) | 4/48 (8.3%) | <0.001 |
| Coronary angiography | 0/48 (0%) | 12/48 (25.0%) | <0.001 |
| Percutaneous coronary intervention | 0/48 (0%) | 11/48 (22.9%) | <0.001 |

Values are expressed as mean (μ) ± standard deviation for continuous variables and numbers (%) for categorical variables.

AED = automated external defibrillator; ROSC = return of spontaneous circulation; SD = standard deviation; TTM = targeted temperature management.

accrue subjects with a propensity for favorable outcomes (ie, VT/VF arrest with relatively short "downtime"), and some accrued samples with poorer prognoses at baseline (eg, the majority were with PEA and asystole arrests with no limit on length of downtime).[6]

A few previous studies examined the effectiveness of system-wide interventions to improve patients' care after OHCA. The results were comparable to those of the present study, showing the advantages of standardizing TTM protocols. Herlitz et al[13] revealed that the adjusted 1-month mortality of OHCA patients transported to the hospital varied markedly due to differences in postresuscitation treatment. Sunde et al[14] showed that after implementing a standardized postresuscitation treatment protocol, including the use of TTM among other critical care interventions, improvements were seen in in-hospital survival, favorable neurological outcomes, and one-year survival compared to historical controls. In another study, Yochum and Utley[15] followed the ED protocol and decreased the time from ROSC to initiation of cooling measures; however, the report did not include an in-depth discussion of favorable neurological outcomes.

The present study was neither an efficacy nor a clinical effectiveness trial. Rather, this was a study of the clinical feasibility of achieving target temperature with implementation of a standardized TTM via QIP. Our relatively better clinical outcomes compared to those in previous studies is likely a function of patient selection, as suggested in previous randomized trials.[6] In addition, patients in the present study who experienced OHCA and IHCA had higher rates of witnessed collapse (85.9% = 213/248) and bystander CPR (69.4% = 172/248). Also, the ethnicity of patients in the present study was Taiwanese, and studies conducted in other ethnic populations (Japanese, Indian, Chinese, and Caucasian) had different results. Further studies are needed to clarify the associations between survival outcomes and ethnicity.

Although other authors have reported effective implementation of TTM in practice,[6,12–15,19,20] results of the present study differ from those of previous reports in two important ways. First, we started TTM in the ED and achieved successful TTM and reduced the duration from ROSC to TTM. Second, the present study created an expressway for CT that helped reduce the period from ROSC to TTM.

The present study has several limitations, including the inherent limitations of retrospective observational study design, which limits the generalization of results to other populations, does not allow inferences of causality, and does not enable ruling out selection bias. The observational nature of the study does not consider that outcomes other than those stated may have influenced results for the included patients.

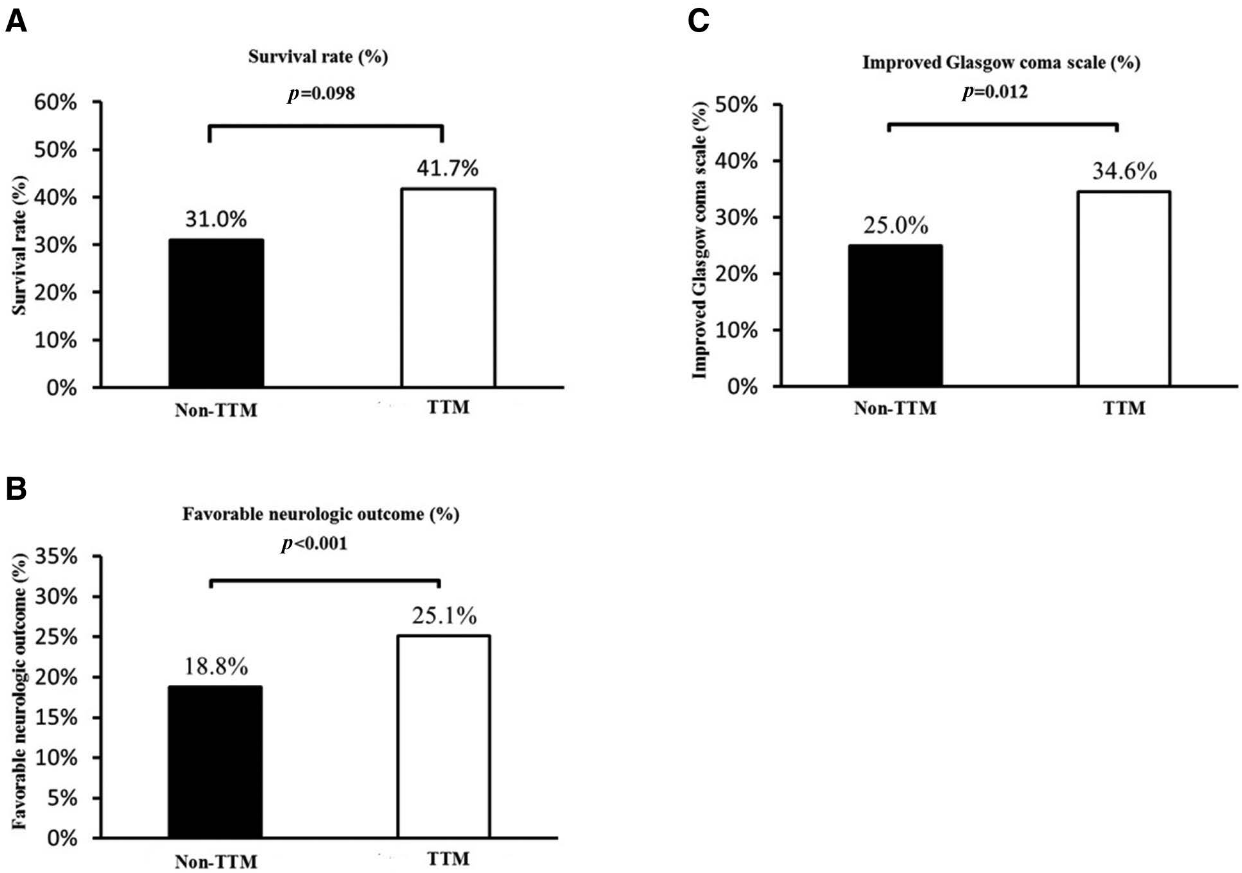


**Fig. 4** Outcomes of cardiac arrest patients between the targeted temperature management (TTM) and non-TTM groups after propensity score matching. A, TTM group (n = 48) had higher favorable neurologic outcomes (non-TTM: 18.8%; TTM: 25.0%, $p < 0.001$). B, Non-TTM group (n = 200) had poor survival rate to discharge, but without statistical significance (survival rate of non-TTM: 31.3 %; TTM: 41.7%, $p = 0.098$). C, TTM group had a higher rate of improved Glasgow coma scale scores (non-TTM: 25%; TTM: 34.6%, $p = 0.012$). TTM **=** targeted temperature management.

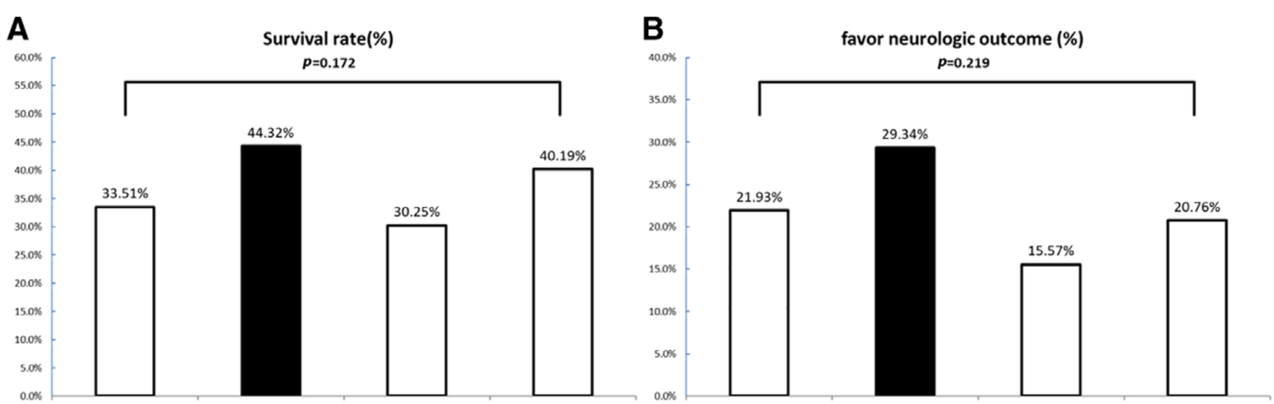


**Fig. 5** Survival rate of cardiac arrest patients between QIP+TTM−, QIP+TTM+, QIP−TTM−, and QIP−TTM+ groups. QIP+TTM+ group had higher survival rate than other groups but without statistical significance. (QIP+TTM−: 33.5%, QIP+TTM+: 44.3%, QIP−TTM−: 30.2% and QIP−TTM+: 40.1%, $p = 0.172$). receiving QIP without TTM− was 33.5%, receiving QIP with TTM was 44.3% and not receiving QIP nor TTM was 30.2%, and not receiving QIP but receiving TTM was 40.1%. QIP = Quality Improvement Project; TTM = targeted temperature management.

In conclusion, the present study has demonstrated the clinical feasibility of achieving target temperature in cardiac arrest patients by implementing a standardized TTM via QIP. The new QIP with its defined protocols, documented shared decision-making, and medical management guidelines, improves the execution rate of TTM and reduces the *duration from ROSC to TTM,* improving the survival and neurological outcomes of cardiac arrest patients.

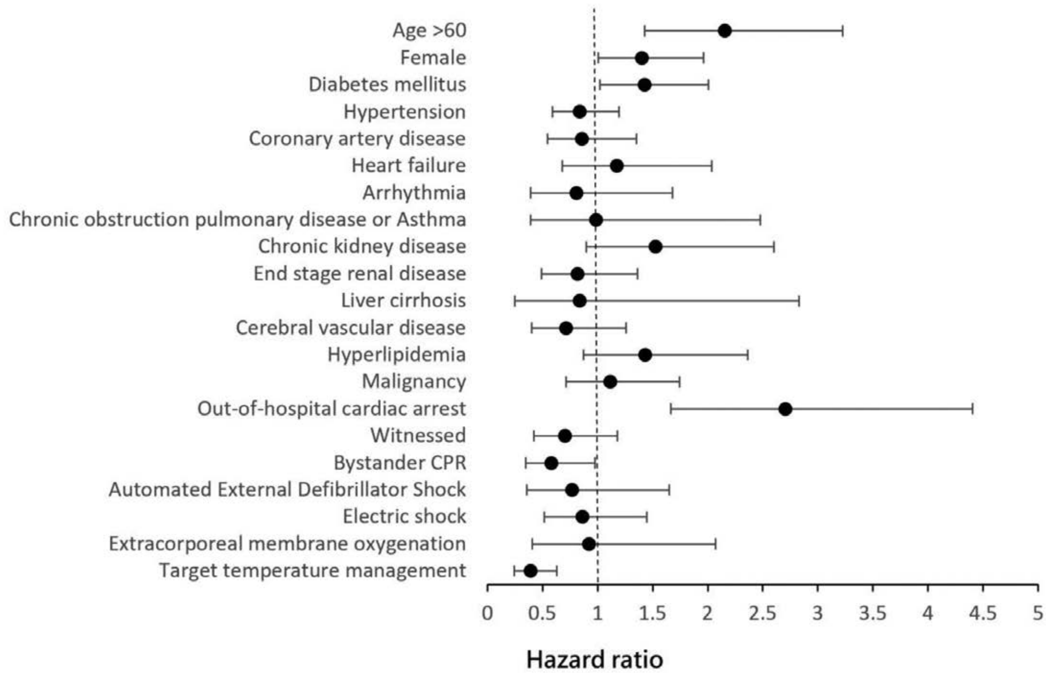


**Fig. 6** Cox regression analysis of survival outcomes in cardiac arrest patients. Total number was 248 patients and those with survival to discharge was 80. Forest plot of cardiac arrest patients. Out-of-hospital cardiac arrest (OR = 2.705, 95% CI: 1.657-4.416) and age >60 (OR = 2.154, 95% CI: 1.428-3.244) and female (OR = 1.404, 95% CI: 1.005-1.962) and diabetes mellitus (OR = 1.429, 95% CI: 1.019-2.005) were negative predictors of mortality, while target temperature management (OR = 0.431, 95% CI: 0.266-0.699) and bystander CPR (OR = 0.589, 95% CI: 0.350-0.990) were positive predictors for overall outcomes. AED = automated external defibrillator; CA = cardiac arrest; CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; OHCA = out-of-hospital cardiac arrest; OR = odds ratio.

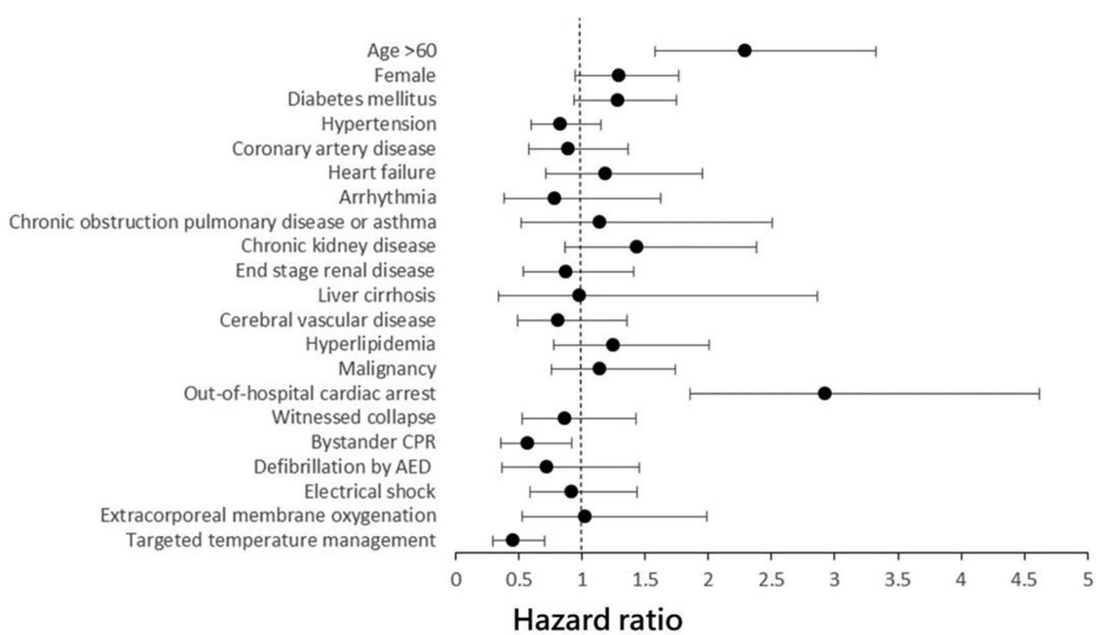


**Fig. 7** Cox regression analysis of favorable neurologic outcomes in cardiac arrest patients. Age >60 (OR = 2.292, 95% CI: 1.580-3.323) and out-of-hospital cardiac arrest (OR = 2.928, 95% CI: 1.858-4.616) were negative predictors, while bystander CPR (OR = 0.572, 95% CI: 0.355-0.922) and TTM (OR = 0.457, 95% CI: 0.296-0.705) were positive predictors for favorable neurologic outcomes. AED = automated external defibrillator; CA = cardiac arrest; CI = confidence interval; CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; OHCA = out-of-hospital cardiac arrest; OR = odds ratio; TTM = targeted temperature measurement.

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