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ORIGINAL ARTICLE

Impact of Targeted Temperature Management on ED Patients with Drug Overdose–Related Cardiac Arrest

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Abstract

Introduction Drug overdose is the leading cause of non-traumatic out-of-hospital cardiac arrest (OHCA) among young adults. This study investigates whether targeted temperature management (TTM) improves hospital survival from presumed overdose-related cardiac arrest.

Methods Retrospective chart review of consecutive cardiac arrests presenting to an urban tertiary care hospital ED from 2011 to 2015. ED patients with cardiac arrest were included if ≤ 50 years old, and excluded if there was a non-overdose etiology (e.g., trauma, ST-elevation myocardial infarction, subarachnoid hemorrhage). The main intervention was TTM, carried out with a combination of the Arctic Sun device and refrigerated crystalloid/antipyretics (goal temperature 33–36 °C). The primary outcome was survival to hospital discharge; neurologically intact survival was the secondary outcome.

Results Of 923 patients with cardiac arrest, 802 (86.9%) met exclusion criteria, leaving 121 patients for final analysis. There were 29 patients in the TTM group (24.0%) vs 92 patients in the non-TTM group (76.0%). Eleven patients (9.1%) survived to hospital discharge. TTM was associated with increased odds of survival to hospital discharge (OR 11.3, 95% CI 2.8–46.3, $p < 0.001$), which increased substantially when palliative outcomes were excluded from the cohort (OR 117.3, 95% CI 17.0–808.4, $p < 0.001$). Despite achieving statistical significance (OR 1.1, 95% CI 1.0–1.3), TTM had no clinically significant effect on neurologically intact survival.

Conclusions TTM was associated with improved survival in ED patients with presumed drug overdose–related cardiac arrest. The impact of TTM on neurologically intact survival among these patients requires further study.

Keywords Toxicology · Cardiac arrest · Targeted temperature management

Introduction

As of 2016, there are more than 350,000 out-of-hospital cardiac arrests (OHCAs) occurring in the USA every year, with an estimated 10.6% survival rate to hospital discharge among adults [1–5]. Drug overdose is a rapidly worsening public health crisis in the USA, with recent data showing that the age-adjusted rate of overdose-related deaths has increased by 5.5% per year [6]. Drug overdose is the leading cause of non-traumatic OHCAs among young adults [7]. From 2000 to 2015, more than half a million people died from drug overdose, and overdose rates are highest among people aged 25–54 years [8, 9]. In 2015, drug-related deaths killed more people than HIV at its peak [10, 11]. Recent data indicates that drug overdose-related deaths only continue to increase, with opiates and prescription drug abuse being a major contributor [6].

Data from this study were previously presented at the following meetings:
1. American College of Medical Toxicology (ACMT) Annual Scientific Meeting, March 2017 in San Juan, Puerto Rico.
2. European Association of Poisons Centres and Clinical Toxicologists (EAPCCT), May 2017 Congress in Basel, Switzerland.

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Therapeutic hypothermia/targeted temperature management (TTM) has been shown to improve neurologic function and survival among patients with OHCAs [12]. By lowering core body temperature, TTM may reduce the inflammatory response associated with post-cardiac arrest syndrome [13] and may have beneficial effects related to slowed metabolism. However, in the setting of drug overdose, slowed metabolism may have detrimental effects related to prolongation of drug toxicity. Specifically, TTM may potentially worsen outcomes in drug-related cardiac arrest due to effects on Cytochrome P450s [14], or by increased QTC prolongation and dysrhythmia generation [15]. In addition, TTM has been linked with several potential adverse events, which include metabolic abnormalities, seizures, coagulopathies, and dysrhythmias [16]. Another potential issue is that TTM is indicated in those with decreased level of consciousness after ROSC. However, drug overdose patients may be altered or comatose from intoxication from sedative-hypnotics than directly due to cardiac arrest**.** For these reasons, the role of TTM in the resuscitation of drug overdose–related OHCA is unclear.

The goal of this study was to determine the effect of TTM on hospital survival among presumed drug overdose–related cardiac arrests. Based on the plausibility of TTM to potentially worsen drug toxicity, we hypothesized that TTM may have inadvertently worsened neurologic outcome and increased the mortality rate of this patient population.

Methods

The study was a retrospective chart review of consecutive cardiac arrests presenting to a 557-bed public hospital based in a large metropolitan center. The study population included all cardiac arrests from January 2011 to October 2015. The study protocol was approved by the institutional review board for research with waiver of consent.

Presumed overdose-related cardiac arrests were defined by this study as those $\leq$ 50 years old without a clear alternate etiology, using assumptions based on prior large populational cohort data from Australia that examined etiologies of cardiac arrest among young adults [7]. Deaths from cardiac arrests were abstracted based on ICD-9 and ICD-10 codes. Patients were excluded from the study population if they were greater than 50 years old, because populational cohort data demonstrate that the minority of cardiac arrests in this demographic are overdose-related [17]. Additionally, patients were excluded if they had an alternate etiology that was determined by adjudication from a panel that constituted a board-certified medical toxicologist, a board-certified intensivist, and a board-certified emergency physician. Prevalence of specific drug overdoses in the study's catchment area is quite diverse and has been previously described [18]. Inclusion based on only toxicology results was not performed because toxicology testing is rarely performed in our cardiac arrest population, which would have biased the study toward non-inclusion of potential drug-related cardiac arrests. Alternate etiologies were defined to be any of the following: (1) traumatic, (2) respiratory (clear aspiration events not related to substance abuse), (3) primary cardiovascular (pre-hospital ECG notable for ST segment elevation myocardial infarction [STEMI], or a coronary catheterization report notable for significant coronary artery disease), (4) metabolic, (5) subarachnoid hemorrhage, (6) sepsis, (7) environmental, (8) oncologic, or (9) sudden infant death syndrome. Deaths related to aspiration or environmental factors from a presumed drug-induced cause (e.g., the chart included historical evidence of substance abuse) were included as a presumed overdose-related arrest.

Targeted temperature management was the primary intervention studied. TTM was carried out with a combination of the Arctic Sun device and refrigerated crystalloid/antipyretics maintained for 24 hours (goal temperature 33–36 °C). Shivering and sedation protocols were used to help reach goal temperature—these included a combination of buspirone, opiates, anesthetics (propofol/ketamine/dexmedetomidine), or paralytics. TTM was applied for post-cardiac arrest patients at the clinical discretion of the primary team based on the following institutional criteria: post-cardiac arrest (any rhythm as cause of the arrest was eligible), ROSC < 30 minutes from EMS/code team arrival, time now < 6 hours from ROSC, comatose patient. Patients were excluded from TTM if they had a DNR, MOLST, poor baseline status, terminal disease, unwitnessed asystole as the initial rhythm, or the following relative contraindications: age $\geq$ 80 years old, cryoglobulinemia, severe sepsis/septic shock or active hemorrhage as the cause of the arrest.

Before April 2014, the protocol cooled patients to a goal temperature of 33 °C; after April 2014, the new goal temperature was set to 36 °C based on new clinical trial data [19]. The intervention was determined to be received if the chart had specific mention of some type of temperature management (using the methods described before) being instituted after ROSC. Due to the limitations of retrospective chart review, it was impossible to ascertain clear inpatient data on how many patients met goal temperature within a 24-hour period; therefore, we assumed all patients met goal temperature for the purposes of this analysis.

Data elements were collected from the medical chart at the study hospital between 2011 and 2015 utilizing a single abstractor, use of data abstraction tools, and consensus agreement in cases when data was felt to be unclear by the single abstractor. Data were abstracted by author SK, a PGY2 resident in emergency medicine at the time of abstraction. Electronic medical record data was abstracted from the Allscripts (New York, NY) ED medical record; inpatient electronic data was

abstracted from the Quadramed system (Herndon, VA). Variables included demographic characteristics (age, gender, ethnicity), serum/urine toxicologic data, advanced cardiovascular life support (ACLS) medications (both EMS and ED, including the use of 20% fat emulsion therapy), the presenting rhythm, whether the arrest was an OHCA, whether the patient had ROSC at any point, whether the patient received TTM, ED survival, if the patient received a cardiac catheterization, final disposition (defined below), and palliative decisions (defined as patients that were palliatively extubated, made do-not-resuscitate, or were transferred to a hospice facility). The initial presenting rhythm used was the first Emergency Medical Systems (EMS) rhythm. If the EMS rhythm was not documented, then the initial ED rhythm was used. Missing measurements were excluded from the final analysis.

Our primary outcome was survival to hospital discharge**.** The secondary outcome of neurologically intact survival was defined according to the specific disposition location, based on prior literature [13], and further defined to include (1) home, (2) rehab/long-term care (LTC) facility, (3) transfer to outside hospital/facility (generally performed for patients that required diagnostic testing not available at the study hospital), or (4) transfer to hospice care facility. Neurologically intact survival was defined as disposition location 1 or 2 above. Disposition location 3 (i.e., transfer to an outside hospital) was not included as a secondary outcome because we did not have information on the final outcomes in these cases. Data on the primary and secondary outcomes were reported for the overall cohort, and also after June 2014 (while the protocol change was instituted in April 2014, June 2014 was chosen to account for protocol implementation).

Pre-planned subgroup analyses were performed in order to account for patient population heterogeneity and thus possible differential performance of TTM based on differing presentations. Thus, associations between TTM and the primary/secondary outcomes were performed in the following subgroups: patients with OHCA only, and only patients who eventually achieved ROSC. In addition, associations between TTM and the primary/secondary outcomes were determined based on the initial presenting rhythm of cardiac arrest (e.g., ventricular rhythm, asystole, or pulseless electrical activity [PEA]). Ventricular rhythms were defined as either ventricular fibrillation or ventricular tachycardia.

Categorical variables were analyzed with chi-squared testing and Fisher's exact test. Odds ratios (OR) were calculated with a 95% confidence interval (CI). Assuming a baseline 25% TTM performance rate and 10% overall survival, we calculated the need to analyze 100 total patients in order to have > 80% power to detect a threefold difference in survival between groups, with 5% alpha. Computer analysis was performed using SPSS version 22 software (IBM, New York).

Results

Patient Enrollment and Demographics Of 923 patients with cardiac arrest, 802 (86.9%) were excluded from the study, leaving 121 patients for final analysis (see Fig. 1). Seven hundred twenty-eight patients (78.9%) were excluded because they were > 50 years old. Please refer to Fig. 1 for the specific exclusions. There are 29 patients in the TTM group (24.0%) vs 92 patients in the non-TTM group (76.0%). Among the TTM group, the median age was 41 years old, 69% of the sample was male, and 41.4% were White. Among the non-TTM group, the median age was 41.5 years, 76.1% of the sample was male, and 13% were White. Serum toxicologic data was available for 62.1% of the TTM group and 5.4% of the non-TTM group; in either case, alcohol was the most common toxin (17.2% and 1.1% respectively). Urine toxicologic data was available for 41.4% of the TTM group and 3.3% of the non-TTM group; benzodiazepines were the most common drug class with positive screens (24.1% and 2.2%). Asystole was the most common initial rhythm in either group (TTM 34.5%, non-TTM 62%); ventricular dysrhythmias were noted in 31% of the TTM group and 16.3% of the non-TTM group. Patient demographics, arrest data, and toxicologic data are summarized in Tables 1 and 2.

ACLS Medication Administration ED and EMS epinephrine was the most commonly administered medication among all groups (e.g., among patients that obtained ROSC vs those that did not obtain ROSC). Twenty percent fat emulsion was used in four cases of cardiac arrest, none of which achieved ROSC. Other data regarding ACLS and ED pharmacologic interventions are summarized in Table 3**.**

Main Analysis Among the overall cohort, 11 patients (9.1%) survived to hospital discharge. TTM was associated with improved survival to hospital discharge (OR 11.3, 95% CI 2.8–46.3, $p < 0.001$). TTM was associated with 14% higher odds of neurologically intact survival (OR 1.14, 95% CI 1.0–1.3, $p < 0.01$). The effect of TTM on survival to hospital discharge and neurologically intact survival is summarized in Tables 4 and 5.

Subgroup Analysis Among patients that received TTM, there was a 42% increased odds of any survival after June 2014, but this was underpowered to show significance ($p = 1.0$). There was also a 4.25-fold increased odds of neurologically intact survival after June 2014, but this was also underpowered to show significance ($p = 0.23$). Among OHCAs, TTM was associated with a significantly improved chance to survive to hospital discharge (OR 13.5, 95% CI 2.6–69.8, $p < 0.001$). We were not adequately powered to perform to analysis of the in-hospital cardiac arrest subgroup. Excluding palliative

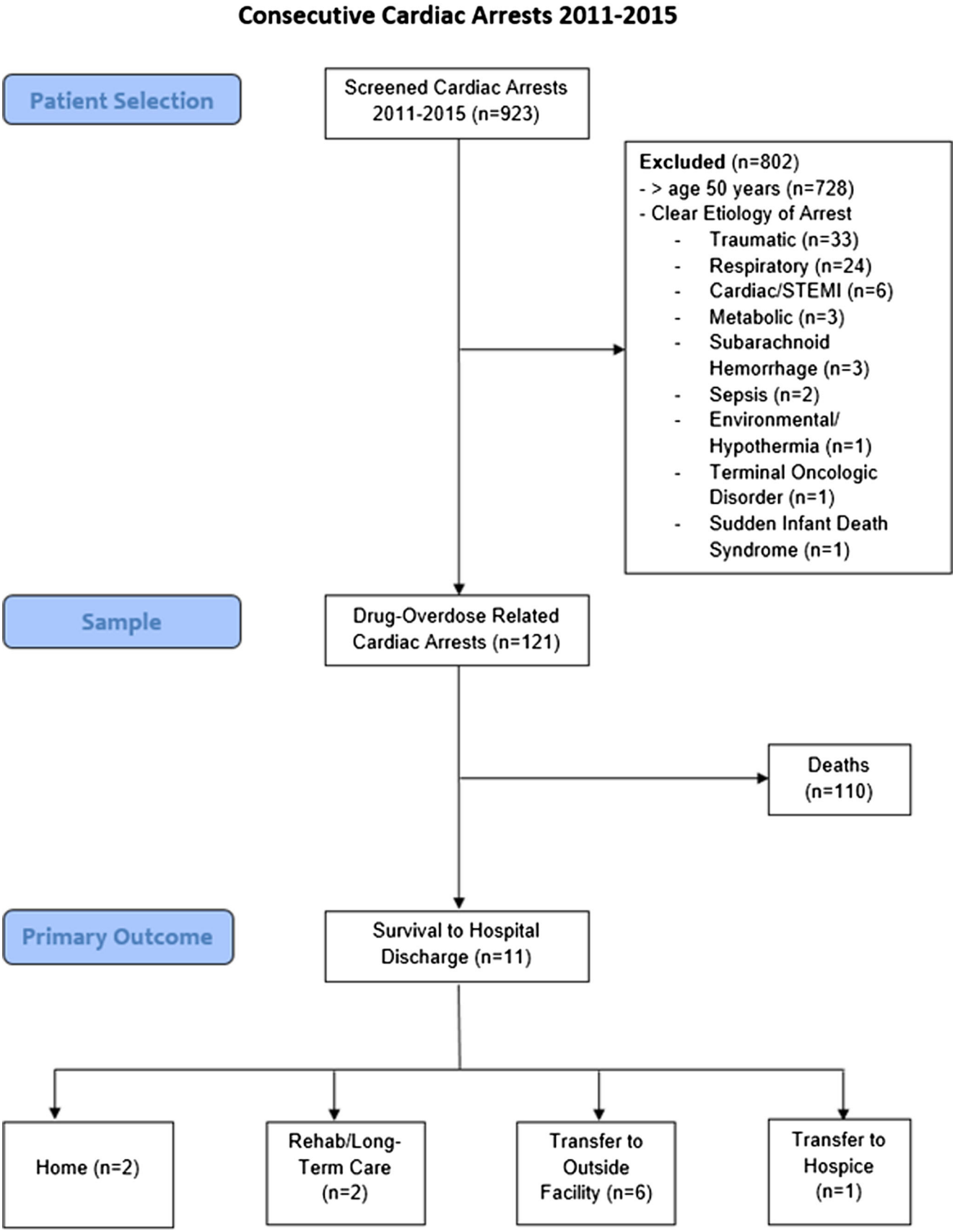

Fig. 1 Consecutive cardiac arrests 2011–2015. STEMI ST segment elevation myocardial infarction

Table 1 Patient demographics and arrest data

	TTM group ($n = 29$), n (%)	Non-TTM group ($n = 92$) n (%)
Demographics		
Median Age, years	41 (0.5–50)	41.5 (0.25–50)
Gender, male	20 (69.0)	70 (76.1)
Race		
White	12 (41.4)	12 (13.0)
African American	2 (6.9)	15 (16.3)
Asian	4 (13.8)	19 (20.6)
Hispanic	3 (10.3)	11 (12.0)
Other	8 (27.6)	33 (35.9)
Data unavailable	0	2 (2.2)
Arrest data		
OHCA	28 (96.6)	83 (90.2)
ROSC at any point	29 (100)	18 (19.6)
Survival to hospital discharge	8 (27.6)	3 (3.3)
Presenting rhythm		
Ventricular rhythm	9 (31)	15 (16.3)
PEA	7 (24.1)	15 (16.3)
Asystole	10 (34.5)	57 (62.0)

outcomes from the overall cohort, TTM was associated with significantly higher odds of survival to hospital discharge (OR 117.3, 95% CI 17.0–808.4, $p < 0.001$). Among only patients that achieved ROSC, TTM had no significant effect on survival to hospital discharge (OR 1.9, 95% CI 0.4–8.4, $p = 0.4$). TTM did not have a significant effect on neurologically intact survival among any subgroup. Subgroup analyses are summarized in Tables 4 and 5.

Rhythm Analysis Among patients that presented with ventricular rhythms, TTM was linked to a significantly improved chance to survive to hospital discharge (OR 8.1, 95% CI 1.1–59.2, $p < 0.03$). TTM had no significant effect on survival among patients that presented in pulseless electrical activity (OR 2.3, 95% CI 0.1–43.8, $p = 1.0$) or asystole (OR 1.1, 95% CI 0.9–1.4, $p = 0.15$). The rhythm analysis is summarized in Table 4.

Table 2 Toxicologic data for the TTM vs non-TTM group

Toxicologic data	TTM group ($n = 29$), n (%)	Non-TTM group ($n = 92$) n (%)
Serum toxicologic data	18 (62.1)	5 (5.4)
Positive alcohol screen	5 (17.2)	1 (1.1)
Positive salicylate screen	1 (3.4)	0
Positive acetaminophen screen	2 (6.9)	0
Urine toxicologic data	12 (41.4)	3 (3.3)
Positive benzodiazepine screen	7 (24.1)	2 (2.2)
Positive cocaine screen	2 (6.9)	0
Positive opiate screen	5 (17.2)	1 (1.1)

Table 3 EMS and ED ACLS Pharmacologic Interventions by Subgroup

ACLS medication	ROSC, survived to hospital discharge ($n = 11$), n (%)	Attained ROSC but expired ($n = 36$), n (%)	Never attained ROSC ($n = 74$), n (%)
EMS interventions			
Epinephrine	6 (54.5)	31 (86.1)	55 (74.3)
Vasopressin	5 (45.4)	27 (75)	44 (59.5)
Calcium	3 (27.3)	2 (5.6)	4 (5.4)
Bicarbonate	3 (27.3)	3 (8.3)	13 (17.6)
Atropine	2 (18.2)	7 (19.4)	4 (5.4)
Magnesium	0	2 (5.6)	1 (1.3)
Amiodarone	2 (18.2)	5 (13.9)	8 (10.8)
D50	2 (18.2)	20 (55.6)	40 (54)
Naloxone	1 (9.1)	7 (19.4)	5 (6.8)
ED interventions			
Epinephrine	2 (18.2)	28 (77.8)	63 (85.1)
Vasopressin	0	1 (2.8)	2 (2.7)
Calcium	0	24 (66.7)	40 (54.0)
Bicarbonate	2 (18.2)	26 (72.2)	47 (63.5)
Atropine	1 (9.1)	9 (25)	8 (10.8)
Magnesium	0	2 (5.6)	7 (9.5)
Amiodarone	1 (9.1)	7 (19.4)	6 (8.1)
D50	1 (9.1)	3 (8.3)	20 (27.0)
Naloxone	0	1 (2.8)	4 (5.4)
20% fat emulsion	0	0	4 (5.4)

Discussion

The main finding of this study is that TTM was associated with significantly improved survival among the entire cohort and among OHCAs. Additionally, TTM was associated with a survival benefit among patients that presented in a ventricular rhythm. TTM was associated with 14% higher odds of neurologically intact survival among the full cohort. Given that the initial study hypothesis was that TTM would increase mortality in this patient population, these are surprising findings.

These results are consistent with prior work that showed that TTM reduced mortality with arrests with a presenting rhythm of ventricular fibrillation [12]. The prior literature is unclear on the efficacy of TTM in patients presenting in asystole or PEA, as most studies are limited by small samples [20–22]. While the present study is underpowered to make a definitive conclusion, there was not a benefit of TTM in patients presenting in PEA or asystole, consistent with the results of one large French registry [21]. TTM has been linked to

Table 4 Effect of TTM on survival to hospital discharge (overall/subgroup/rhythm analysis)

Analysis	TTM applied	Death, *n* (%)	Survived to hospital discharge, *n* (%)	OR for survival	95% CI	*p* value
Overall	No TTM	89 (80.9)	3 (27.2)	11.3	2.8–46.3	< 0.001
	Received TTM	21 (19.1)	8 (72.7)			
Subgroup analyses						
TTM subgroup	TTM before June 2014	17 (80.9)	6 (75)	1.42	0.2–9.8	1.0*
	TTM after June 2014	4 (19.0)	2 (25)			
OHCA	No TTM	81 (79.4)	2 (22.2)	13.5	2.6–69.8	< 0.001
	Received TTM	21 (20.6)	7 (77.8)			
Overall (palliative deaths/hospice excluded)	No TTM	88 (96.7)	2 (20)	117.3	17.0–808.4	< 0.001
	Received TTM	3 (3.3)	8 (80)			
ROSC	No TTM	15 (41.7)	3 (27.3)	1.9	0.4–8.4	0.4
	Received TTM	21 (58.3)	8 (72.7)			
Rhythm analyses						
Ventricular rhythms	No TTM	13 (76.5)	2 (28.6)	8.1	1.1–59.2	< 0.03
	Received TTM	4 (23.5)	5 (71.4)			
PEA	No TTM	14 (70)	1 (50)	2.3	0.1–43.8	1*
	Received TTM	6 (30)	1 (50)			
Asystole	No TTM	57 (86.4)	0 (0)	1.1	0.9–1.4	0.15*
	Received TTM	9 (13.6)	1 (100)			

*Fisher's exact test

decreased mortality 6 months after cardiac arrest in some patients presenting in ventricular fibrillation [12], but the present study was unable to confirm or refute this finding due to lack of follow-up.

The present study extends the current literature by reporting the effect of TTM on a cohort of presumed drug overdose–related cardiac arrests. As drug-associated cardiac arrests tend to feature younger subjects [2, 3, 23], this study population was based on assumptions from larger populational cohorts by examining cardiac arrests ≤ 50 years and excluding cases that had clearly defined alternative etiologies. In addition, TTM had the strongest association with survival among patients that presented with a ventricular rhythm, concordant with other data [12].

This study is the largest database to examine the role of TTM in this patient population. Our study had a very heterogeneous population, the majority of whom received epinephrine and vasopressin as part of resuscitative efforts. Interestingly, 0/4 patients that were given 20% fat emulsion attained ROSC. Toxicological data, the presence of ethanol, and the presence of illicit drugs was much higher in our TTM group. This may represent a confounder in outcome. Further study is therefore necessary. Other studies exist on the efficacy of TTM among patients with a drug-related etiology of cardiac

Table 5 Effect of TTM on neurologically intact survival (overall/subgroup analysis)

Analysis	TTM applied	No NIS, *n* (%)	NIS, *n* (%)	OR for NIS	95% CI	*p* value
Overall	No TTM	90 (81.1)	0	1.1	1.0–1.3	< 0.01*
	Received TTM	21 (18.9)	4 (100)			
Subgroup analyses						
TTM subgroup	TTM before June 2014	17 (80.9)	2 (50)	4.25	0.4–40.0	0.23*
	TTM after June 2014	4 (19.0)	2 (50)			
OHCA	No TTM	81 (79.4)	0	1.1	1.0–1.2	0.05*
	Received TTM	21 (20.6)	2 (100)			
Overall (palliative deaths/hospice excluded)	No TTM	88 (96.7)	0	2	0.9–4.4	< 0.001*
	Received TTM	3 (3.3)	3 (100)			
ROSC	No TTM	16 (43.2)	0	1.1	1.0–1.3	0.26*
	Received TTM	21 (56.8)	3 (100)			

*Fisher's exact test

NIS neurologically intact survival (defined as discharge to home or long-term care facility)

arrest. A 2016 study noted no significant differences among survival and good neurologic outcome among toxin-related cardiac arrests vs non-toxin-related arrests [4]. In this study, every cardiac arrest patient received TTM, and 48 patients were determined to suffer a toxin-related arrest. This study reported a higher survival rate among its toxin-related cardiac arrest group (42%) compared to other studies, who calculated survival to range from 4.5–19% [2, 3, 24]. The authors hypothesize that their increased survival rate may have been due to the effect of TTM, and their clinical pathway which excluded patients with severe terminal illness and refractory shock from receiving TTM.

Besides this, another study from Korea examined the effect of TTM on OHCAs caused by ingestions (most commonly pesticides)—among 24 patients that received TTM, 11 (46%) survived to discharge and 5 (21%) had good neurologic function at the time of discharge [5]. A recent study in the USA examined the effects of TTM among confirmed drug-associated cardiac arrests, but was underpowered to make conclusions on this population [2]. The present study provides the largest dataset to date in support of the use of TTM following presumed drug overdose–related cardiac arrest.

Neurologically intact survival in the present study was rare, occurring in just 4 patients. While TTM was associated with 14% significantly higher odds of neurologically intact survival, the clinical significance of this is unclear. The impact of TTM on neurologically intact survival among these patients requires further study. Future work should further examine the effect of specific temperature goals on survival among patients with drug-associated arrests. TTM slows metabolism and will decrease drug metabolism by cytochrome P450s [25], thereby increasing concentrations of specific drugs such as fentanyl [26]. Future work should examine whether hypothermia to 33 °C or avoidance of normothermia will improve the outcomes in these patients, as overly hypothermic settings may exacerbate drug toxicity due to effects on the cardiac conducting system. Therefore, larger studies in the future are warranted to allow us to determine the general effect of TTM among survival and neurologically intact outcome based on different classes of poisonings (e.g., opioids vs. sympathomimetics vs. channel blockers).

Our study had several limitations which require consideration. Due to relatively small N, only one chart abstractor was utilized; even though the single abstractor did not have knowledge of the final data analysis at the time of abstraction, it is important to acknowledge the potential bias of single abstractor . In rare cases where data were missing or difficult to interpret, disagreements were resolved with group discussion and agreement among all co-investigators. A pilot abstraction phase was not deemed necessary because the data were straightforward. We did not address inter-rater reliability because of the use of a single abstractor; instead, a consensus process was used in the rare cases where data were felt to be unclear by the single abstractor.

Our study is also limited because we did not have documentation of patients who met goal temperatures within 24 hours. The definition of presumed overdose-related cardiac arrest, while based on large populational data [7], may have overestimated the true prevalence. In addition, the primary outcome data is limited by the final patient disposition in several instances. For example, several of the patients that survived required transfer to another hospital after stabilization; however, they were excluded from the secondary analysis because it was not possible to determine the final outcome of these patients. Autopsy verification was not available for the majority of patients. This was a limitation for the classification of overdose. However autopsy data does not necessarily correlate with medical toxicologist cause of death [27].

Due to limitations of research approval with waiver of consent, we are unable to report on 3- or 6-month mortality; this should be evaluated in future studies. Demographically, the study catchment area is located in the most racially diverse neighborhood in the USA according to the 2010 US Census Bureau [28]. Both the TTM and non-TTM group were noted to have significant racial differences—it is unclear how race impacted the application of TTM. Racial markers may be a confounder or a marker of socioeconomic differences in the study. This was not assessed and is a limitation of our study. Finally, our conclusions are limited by this being a single-site study.

Conclusions

Targeted temperature management (TTM) was significantly associated with improved survival among patients with presumed drug overdose–related cardiac arrest. TTM was associated with a survival benefit in the OHCA subgroup, and performed best for patients with initial ventricular rhythms. The present study provides the largest sampling to date in support of the use of TTM following presumed drug overdose–related cardiac arrest. The impact of TTM on neurologically intact survival among these patients requires further study.

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Author Contributions AFM, CMM, and SB conceived the research questions and study design. AFM supervised the conduct of the study and the data collection. SK reviewed charts and performed data abstraction. AFM provided statistical advice on study design and performed statistical analyses on the data. SK drafted the manuscript, and all authors contributed significantly to its revision. AFM takes responsibility for the paper as a whole.

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Compliance with Ethical Standards

Conflict of Interest None.

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