Temporal Pattern and Prognostic Significance of Hypokalemia in Patients Undergoing Targeted Temperature Management Following Cardiac Arrest

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Hypokalemia has been consistently reported as a common occurrence during targeted temperature management (TTM) in comatose survivors of cardiac arrest. We sought to better describe changes in serum potassium throughout the different stages of TTM and to assess for any prognostic significance. We analyzed a prospectively collected cohort of 240 patients treated with TTM following cardiac arrest at a tertiary care hospital between 2007 and 2014. The primary outcome was poor neurologic outcome at hospital discharge, defined as a Cerebral Performance Category score >2. Secondary outcomes included death and recurrent ventricular arrhythmia before hospital discharge. Multivariable logistic regression was used to assess for association of hypokalemia and hyperkalemia with the designated outcomes. During all phases of TTM, hypokalemia and hyperkalemia occurred in 207 (86%) and 77 (32%) of patients, respectively. Hypokalemia occurred in 203 (85%) patients at target temperature, and 25 (10%) patients were hyperkalemic following normothermia. In multivariable logistic regression, hypokalemia was not associated with poor neurologic outcomes or recurrent ventricular arrhythmia. Hypokalemia was associated with reduced odds of death before hospital discharge (odds ratio = 0.36, 95% confidence interval 0.13 to 0.97, p = 0.044). Hyperkalemia was not associated with poor neurologic outcomes, death, or recurrent ventricular arrhythmia. **(Am J Cardiol 2017;120:1110–1113)**

The use of targeted temperature management (TTM) in comatose survivors of cardiac arrest has become the standard of care.[1,2] TTM is conducted in a critical care setting with close hemodynamic monitoring and laboratory surveillance for metabolic derangements. Temperature-related disturbances in serum potassium, magnesium, and phosphorus levels during TTM have been previously described.[3,4] In particular, hypokalemia has been reported as a common occurrence during TTM, especially with lower target core temperatures.[5] Other risk factors of hypokalemia and its prognostic significance in comatose survivors of cardiac arrest undergoing TTM remain largely unknown. In this study, we sought to characterize changes in serum potassium through the different stages of TTM and to assess for association with neurologic outcomes, survival, and recurrent ventricular arrhythmias.

Methods

This study was conducted with the approval of the Vanderbilt University Medical Center institutional review board and in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The study population was derived from 341 consecutive comatose survivors of cardiac arrest treated with TTM between 2007 and 2014. The exclusion criteria for this study were an insufficient duration of TTM (<24 hours), suspected cardiac arrest from traumatic etiologies, and <3 serum potassium measurements during TTM. All patients were cooled externally using an active surface-cooling device, the Arctic Sun System, to maintain a core body temperature of 33°C during the maintenance phase of TTM.[6] This was followed by active rewarming at a goal rate of 0.25°C per hour. Our institution's TTM protocol recommended intravenous repletion with 40 mEq of KCl and 4 g of magnesium sulfate for serum potassium <2.8 mEq/L and magnesium <2 mg/dl, respectively.

Demographic and clinical data were collected for each patient in a prospective manner and stored in a REDCap database.[7] These variables included receipt of bystander cardiopulmonary resuscitation, time to return of spontaneous circulation (ROSC), and Cerebral Performance Category (CPC) scores at hospital discharge. Initial rhythm was assessed as either a shockable (ventricular tachycardia [VT] or ventricular fibrillation [VF]) or a nonshockable rhythm.

The normal range for serum potassium in the laboratory assay used for the cohort was 3.2 to 4.9 mEq/L. Magnesium levels are reported in mg/dl and not categorized as hypomagnesemia or hypomagnesemia. Serum potassium and magnesium levels were correlated to the stage of TTM in which the laboratory was drawn. Each patient's course of TTM was conceptualized in 5 parts: ROSC, induction, target

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The cohort described in the article was derived from the electronic health record of Vanderbilt University Medical Center.

See page 1113 for disclosure information.

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Table 1
Baseline characteristics*

Characteristic	Overall (n = 240)
Age (y)	61 (51–69)
Men	145 (60%)
In-hospital arrest	44 (18%)
Shockable rhythm	131/235 (56%)
Witnessed arrest	190 (79%)
Received bystander CPR	121 (50%)
Time to ROSC (min)	20 (15–34)
Time to initiation of TTM (min)	122 (65–240)
Time to reach target temperature (min)	165 (75–270)
Initial body temperature (°C)	36 (34.7–36.7)
T-max within 48 hours of arrest (°C)	37.6 (37.2–38.2)
T-min within 48 hours of arrest (°C)	31.9 (31.5–32.4)
Time at target temperature (h)	21 (18–24)
ST-segment elevation myocardial infarction	56/239 (23%)
Shock on admission	95 (40%)
Mechanical circulatory support device	37 (15%)

CPR = cardiopulmonary resuscitation; ROSC = return of spontaneous circulation; TTM = targeted temperature management.

* Data are presented as median (IQR) for continuous variables and number (percentage) of patients for categorical variables.

temperature, rewarming, and normothermia. The target temperature phase was defined as starting with first core temperature at or below the target and ending with the first attempt at active rewarming. Recurrent ventricular arrhythmias included VF in addition to monomorphic and polymorphic VT.

The primary outcome of this study was poor neurologic outcome at hospital discharge, defined as a CPC score >2.[8] A favorable neurologic outcome (neurologically intact survival) was defined as a CPC score of 1 or 2. Secondary outcomes included death and recurrent ventricular arrhythmia before hospital discharge.

All information was de-identified before statistical analysis in Stata Statistical Software: Release 14 (College Station, TX).[9] Descriptive statistics were calculated as the median with interquartile ranges (IQR) for continuous variables. Frequencies (percentages) are depicted for categorical variables. Multivariable logistic regression was used to assess for an association of hypokalemia and hyperkalemia with primary and secondary outcomes while adjusting for age, location of arrest, receipt of bystander cardiopulmonary resuscitation, initial rhythm, and time to ROSC. Odds ratios with 95% confidence intervals are presented. All tests were 2-tailed, and a p value ≤0.05 was considered statistically significant.

Results

Three hundred forty-one patients were treated with TTM during the study period. Nineteen patients had insufficient treatment with TTM, 8 patients had major trauma, and 74 patients had insufficient number of electrolyte checks during TTM and were therefore excluded. Baseline demographic and clinical characteristics of the remaining 240 patients are described in Table 1.

During all phases of TTM, hypokalemia and hyperkalemia occurred in 207 (86%) and 77 (32%) of patients, respectively. One-hundred and fifty-seven (65%) patients received potassium repletion and 140 (58%) patients received magnesium. A summary of electrolyte levels and repletion during TTM is provided in Table 2.

Table 2
Ranges and repletion of potassium (K) and magnesium (Mg) during targeted temperature management (TTM)*

Characteristic	Overall
Minimum Serum K (mEq/L)	2.7 (2.4–3.0)
Hypokalemia	207 (86%)
Maximum Serum K (mEq/L)	4.5 (4.0–5.1)
Hyperkalemia	77 (32%)
K repletion	157 (65%)
K repletion (mEq)	40 (0–80)
Minimum Serum Mg (mg/dL)	1.8 (1.6–2)
Maximum Serum Mg (mg/dL)	2.3 (2.0–2.7)
Mg repletion	140 (58%)
Mg repletion (g)	2 (0–4)

* Data are presented as median (IQR) for continuous variables and number (percentage) of patients for categorical variables.

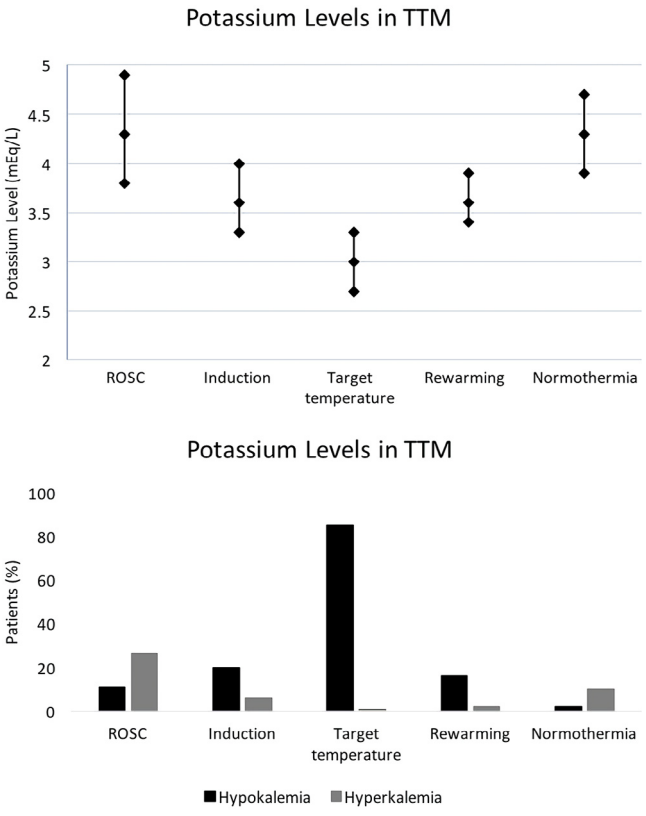

Figure 1. Variation in serum potassium during different stages of targeted temperature management (TTM).

Median serum potassium at ROSC was 4.3 mEq/L (IQR 3.8 to 4.9). At a target temperature of 33°C, median serum potassium was 3 mEq/L (IQR 2.7 to 3.3); by normothermia, median serum potassium had re-risen to 4.3 mEq/L (IQR 3.9 to 4.7). Hypokalemia was present in 203 (85%) patients at target temperature and 25 (10%) patients were hyperkalemic following normothermia (Figure 1).

One-hundred and forty-five (60%) patients had poor neurologic outcomes (CPC 3 to 5) following TTM. Distribution