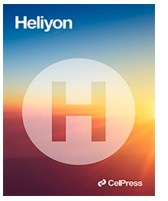
Heliyon 11 (2025) e41743

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Effectiveness of advanced cardiovascular life support in hyperkalemic cardiac arrest: A randomized experimental study in pigs

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ARTICLE INFO

Keywords:
Heart arrest
Cardiopulmonary resuscitation
Perfusion
Hyperkalemia

ABSTRACT

Current treatment recommendations for hyperkalemic cardiac arrest focus exclusively on the addition of antihyperkalemic therapies and are otherwise identical to those for cardiac arrest caused by non-hyperkalemic etiologies. We were unable to find any studies that specifically examine the hemodynamic effects of cardiopulmonary resuscitation in hyperkalemic cardiac arrest compared to cardiac arrest from non-hyperkalemic etiologies. We hypothesized that myocardial ischemic contracture would be less severe in hyperkalemic cardiac arrest compared with ventricular fibrillation cardiac arrest, resulting in higher cerebral perfusion pressure, brain tissue oxygen tension, and coronary perfusion pressure during cardiopulmonary resuscitation. Twenty-two pigs randomly underwent either electrically induced ventricular fibrillation arrest or hyperkalemic arrest induced by potassium infusion. Hemodynamic, echocardiographic, and brain tissue oxygen tension measurements were obtained during advanced cardiovascular life support and compared using linear mixed-effects models. Two animals developed massive hemothorax associated with cardiopulmonary resuscitation and were excluded from further analysis. The remaining 20 animals had no internal organ injury due to cardiopulmonary resuscitation and were included in the study. Left ventricular wall thickness was significantly lower in the hyperkalemic arrest group than in the ventricular fibrillation arrest group (group effect, $P = 0.019$). The decrease in end-diastolic volume over time was significantly less pronounced in the hyperkalemic arrest group (group-time interaction, $P = 0.010$). Coronary perfusion pressure (group effect, $P = 0.041$) and cerebral perfusion pressure (group effect, $P = 0.020$) were significantly lower in the hyperkalemic arrest group. Although not significant, brain tissue oxygen tension was

Abbreviations: ACLS, advanced cardiovascular life support; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; CoPP, coronary perfusion pressure; CePP, cerebral perfusion pressure; CSF, cerebrospinal fluid; $PbtO_2$, brain tissue oxygen tension; LV, left ventricular; EDV, end-diastolic volume; SD, standard deviation; CI, confidence interval; ATP, adenosine triphosphate; ROSC, return of spontaneous circulation.

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https://doi.org/10.1016/j.heliyon.2025.e41743
Received 3 August 2024; Received in revised form 27 December 2024; Accepted 6 January 2025
Available online 9 January 2025

also lower in the hyperkalemic arrest group. In conclusion, the left ventricular wall thickness was smaller, and the decrease in end-diastolic volume over time was less pronounced in the hyperkalemic arrest group. However, perfusion pressure was poorer, and cerebral oxygenation was not better in the hyperkalemic arrest group.

1. Introduction

Sudden cardiac arrest presents a significant challenge to modern medicine, attributable not only to its high incidence but also to its catastrophic consequences [1,2]. More than 350,000 out-of-hospital cardiac arrests occur in the United States annually, with survival rates of only approximately 10 % [2]. Hyperkalemic cardiac arrest, a cardiac arrest attributable to hyperkalemia, accounts for approximately 10 % of in-hospital cardiac arrests in adults and may account for a more significant proportion of in-hospital cardiac arrests in patients with impaired renal function [3–5].

Current resuscitation guidelines recommend incorporating antihyperkalemic treatments into standard advanced cardiovascular life support (ACLS) to treat hyperkalemic cardiac arrest [6,7]. However, the hemodynamic effectiveness of standard ACLS in hyperkalemic cardiac arrest may differ from that in cardiac arrest caused by non-hyperkalemic etiologies. The use of hyperkalemic solutions to induce flaccid diastolic arrest for cardiac surgery is well-established [8,9]. Myocardial ischemic contracture, which reduces the hemodynamic effectiveness of cardiopulmonary resuscitation (CPR) [10,11], may therefore be attenuated in hyperkalemic cardiac arrest. This attenuation could potentially lead to enhanced hemodynamic effectiveness of CPR in hyperkalemic cardiac arrest compared to cardiac arrest due to non-hyperkalemic etiologies. Understanding the hemodynamic effectiveness of CPR in hyperkalemic cardiac arrest relative to cardiac arrest due to non-hyperkalemic etiologies may aid in identifying an optimal resuscitation strategy for hyperkalemic cardiac arrest. However, we were unable to locate any studies examining the hemodynamic effects of CPR in hyperkalemic cardiac arrest compared to cardiac arrest due to non-hyperkalemic etiologies.

In the present study, we compared hemodynamic, echocardiographic, and cerebral oxygenation measurements between ventricular fibrillation (VF) and hyperkalemic cardiac arrest in pigs to determine the effectiveness of ACLS in hyperkalemic cardiac arrest relative to VF cardiac arrest. We hypothesized that myocardial ischemic contracture would be less severe in hyperkalemic cardiac arrest than in VF cardiac arrest, resulting in greater coronary perfusion pressure (CoPP) and cerebral perfusion pressure (CePP) and better cerebral oxygenation during CPR.

2. Methods

A total of 22 healthy Yorkshire/Landrace cross pigs, with an average weight of 22.5 (22.1–23.2) kg were used in this prospective experimental study. This study was approved by the Animal Care and Use Committee of Chonnam National University Hospital (CNUH IACUC-23025) and adhered to the National Institutes of Health Guide for the Care and Use of Laboratory Animals. All surgical procedures were conducted under sevoflurane anesthesia, and all efforts was made to minimize animal distress.

2.1. Preparation

The animals were acclimated for 7 days prior to the experiments. Following initial sedation with an intramuscular injection comprising xylazine (2.2 mg/kg) and ketamine (20 mg/kg), they were anesthetized with inhaled sevoflurane (5 %), intubated, and ventilated with a nitrous oxide/oxygen mixture (7:3). Sevoflurane anesthesia was maintained throughout the preparation period and adjusted to prevent signs of distress (withdrawal reflex and increased heart rate or blood pressure). Rectal temperature and end-tidal carbon dioxide were continuously monitored, and normothermia (37–38 °C) and normocarbia (35–45 mmHg) were maintained throughout the preparation period. Rectal temperature and end-tidal carbon dioxide were monitored, and normothermia (37–38 °C) and normocarbia (35–45 mmHg) were maintained throughout the preparation period. The right femoral artery was catheterized using a 7-F catheter for blood sampling and arterial pressure monitoring, and the right external jugular vein was catheterized using an additional 7-F catheter for right atrial pressure monitoring and fluid administration (0.9 % sodium chloride solution, 5 mL/kg/h). Once the animals were placed in the prone position, the L2 spinous process was exposed through a skin incision and subsequently removed. Following L2 laminectomy, a 5-F catheter was inserted into the subarachnoid space and advanced to the mid-thoracic level to measure cerebrospinal fluid (CSF) pressure. CSF pressure measured via lumbar puncture has demonstrated a close correlation with intracranial pressure [12]. A cranial burr hole was created in the right parietal bone after the scalp incision. An optical oxygen sensor (PM-PSt7; PreSens-Precision Sensing GmbH, Regensburg, Germany) was inserted through the dura and positioned with the tip in contact with the cerebral cortex to measure brain tissue oxygen tension (PbtO2). Following the placement of the oxygen sensor, the animals were placed in the supine position. A subcutaneous pocket extending 4–5 cm under the xiphoid process and sternum was created through a 2 cm skin incision below the xiphoid process. A transesophageal echocardiography probe (UST-5293-5; Hitachi Aloka Medical Ltd., Tokyo, Japan) was introduced through the subcutaneous pocket for echocardiographic left ventricular (LV) measurements, and the probe was manipulated to obtain an adequate long-axis view of the LV. We have effectively employed this technique to visualize the LV during CPR [13–15].

2.2. Experimental protocol

Fig. 1 illustrates the experimental timeline of the present study. Once baseline measurements were obtained, the animals were randomized to either the hyperkalemic or VF arrest group based on the information in a sealed envelope. Hyperkalemic arrest was induced utilizing a potassium administration protocol by Aagaard et al. [16]. Hyperkalemia was induced via intravenous infusion of potassium chloride at a rate of 2.8 mmol/kg/h for 30 min, followed by infusion at 2.2 mmol/kg/h for an additional 15 min. Immediately following this, cardiac arrest was induced by a bolus injection of 0.3 mmol/kg potassium chloride. Animals in the VF arrest group received an intravenous infusion of an equal volume of 0.9 % sodium chloride solution over 45 min, after which VF was induced by delivering a 60-Hz (30 mA) alternating current stimulus via a pacing catheter inserted close to the right ventricle through the subcutaneous pocket for echocardiographic measurement. In both groups, mechanical ventilation and sevoflurane anesthesia were discontinued immediately following the cardiac arrest induction. After 7 min of untreated cardiac arrest, CPR was initiated with a mechanical CPR device (Life-Stat Michigan Instruments, Grand Rapids, MI, USA). The CPR device was set to compress the sternum to 20 % of the anteroposterior chest diameter at a rate of 100 compressions/min. During CPR, manual ventilations were provided with high-flow oxygen (15 L/min) at a rate of 10 ventilations/min. Epinephrine (0.02 mg/kg) was administered intravenously 3 min after starting CPR and then repeated every 3 min thereafter. CPR was paused for 10 s every 2 min to simulate a 10-s pause in chest compressions for rhythm analysis in clinical CPR. Electrical defibrillation was not attempted because we intended to observe the progression of myocardial ischemic contractures and subsequent changes in the CoPP, CePP, and $PbtO_2$ during CPR. CPR was continued until the completion of the experiment, which was 22 min after cardiac arrest induction. Because the animals were in cardiac arrest following the experiment, no further euthanasia procedures were necessary for the present study. At the completion of each experiment, an autopsy was routinely performed to identify CPR-related internal organ injuries, such as pneumothorax, hemothorax, and hemoperitoneum, which could affect the hemodynamic data.

2.3. Measurements

The primary outcomes were the CoPP and myocardial ischemic contracture, with the latter measured by LV wall thickness. The secondary outcomes included the end-diastolic volume (EDV), CePP, $PbtO_2$, and potassium concentration. Arterial pressure, right atrial pressure, and CSF pressure were continuously monitored and sampled at baseline and 1 min intervals during CPR. CoPP was determined as the difference between arterial end-diastolic pressure and right atrial end-diastolic pressure, while CePP was determined as the difference between mean arterial pressure and CSF pressure. An experienced researcher (Y.H.J.) obtained echocardiograms at baseline and 1-min intervals during CPR. The researcher performing the echocardiographic measurements could not be blinded to the group allocations because, unlike in hyperkalemic arrest, rapid fluttering movements of the LV were observed in VF arrest. The LV wall thickness and EDV during CPR were assessed using the LV long-axis view at a frame representing the maximal LV chamber dimension during the relaxation phase of chest compressions. The LV wall thickness was measured at the mid-ventricular lateral walls, and the EDV was calculated using Simpson's method. The optical oxygen sensor was connected to an oxygen meter (OXY-1 ST; PreSens-Precision Sensing GmbH) for the $PbtO_2$ measurements. The $PbtO_2$ data were transferred to a personal computer and sampled at baseline and 1 s intervals during CPR. Arterial blood gases (GEM Premier 3000; Instrumentation Laboratory Company, Lexington, MA, USA) and serum potassium levels (Unicel DXC 800, Beckman Coulter, Fullerton, CA, USA) were assessed from blood samples collected from the arterial catheter at baseline, immediately before cardiac arrest induction, and at 16 and 22 min after cardiac arrest induction.

2.4. Statistical analysis

The sample size for this study was calculated in advance based on LV wall thickness data (mean ± standard deviation [SD], 10.0 ± 3.8 mm; variance, 14.8 mm) from a pilot study. In the pilot study, the LV wall thicknesses were 12.6 ± 3.7 mm and 7.3 ± 1.3 mm in the

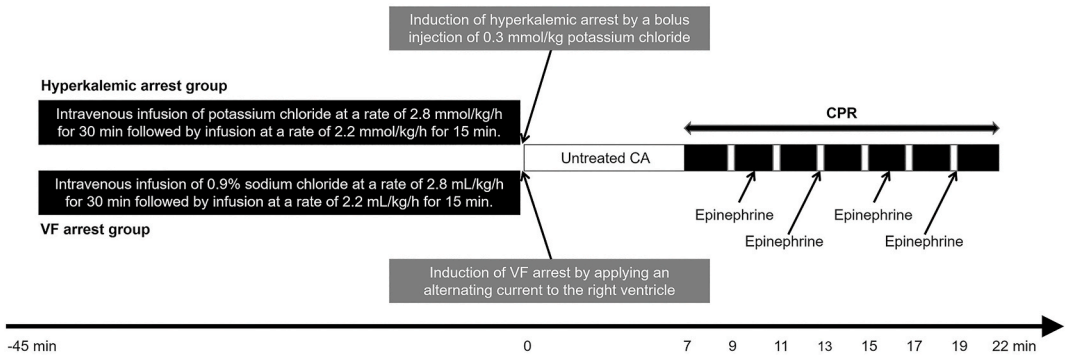

Fig. 1. Experimental timeline. Electrical defibrillation was not attempted during CPR because we intended to observe the progression of myocardial ischemic contracture and subsequent changes in coronary perfusion pressure, cerebral perfusion pressure, and cerebral oxygenation during CPR. CPR, cardiopulmonary resuscitation; CA, cardiac arrest; VF, ventricular fibrillation.

VF and hyperkalemic arrest groups, respectively, and the calculated within-group variance in the LV wall thickness was 7.62. It was determined that 10 animals per group would be needed to achieve 80 % power at a 5 % significance level ($\alpha = 0.05$). To mitigate any effects of data loss, a total of 22 animals were included in the study. The data were analyzed using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) and T&F program version 4.0 (YooJin BioSoft, Goyang, Korea). Normally distributed continuous data were reported as the means ± SDs and compared using the independent two-sample *t*-test. In contrast, non-normally distributed continuous data were reported as medians with interquartile ranges and compared using the Wilcoxon rank-sum test. The group effect, time effect, and group-time interaction in serially obtained measurements were determined after controlling for random effects arising from the repeated measurements using linear mixed-effects models. In cases where the inclusion of group-time interaction in a linear mixed-effects model resulted in severe multicollinearity, group-time interaction was excluded from the model. The level of statistical significance was set at two-tailed $P < 0.05$. The level of statistical significance was set at two-tailed $P < 0.05$.

3. Results

Of the 22 animals used in this study, two animals (one each from the hyperkalemic arrest group and the VF arrest group) were found to have a massive hemothorax associated with CPR during autopsy and were excluded from further analysis. In the remaining 20 animals, no internal organ injury due to CPR was found, and these animals were included in the analysis. Baseline measurements did not differ between the VF and hyperkalemic arrest groups (Table 1). Table 2 presents the arterial blood gases and potassium levels measured immediately before cardiac arrest induction and during CPR. In the hyperkalemic arrest group, the 45-min continuous intravenous infusion of potassium chloride resulted in severe hyperkalemia (9.7 ± 0.9 mmol/L). After the bolus injection of 0.3 mmol/kg potassium chloride, all animals in the hyperkalemic arrest group developed cardiac arrest with a non-shockable rhythm that rapidly transitioned from sine waves to asystole.

During CPR, potassium levels were significantly higher in the hyperkalemic arrest group than in the VF arrest group (group effect, $P < 0.001$; coefficient [95 % confidence interval {CI}], 5.827 [4.361–7.292]). However, the two groups had no significant differences in pH, $PaCO_2$, or PaO_2. The LV wall thickness, EDV, CoPP, CePP, and $PbtO_2$ during CPR are shown in Fig. 2. The LV wall thickness was significantly lower in the hyperkalemic arrest group than in the VF arrest group (group effect, $P = 0.019$; coefficient [95 % CI], −1.264 [−2.238 to −0.289]). Although no significant group effect was observed concerning the EDV, the decrease in EDV over time was significantly less pronounced in the hyperkalemic arrest group than in the VF arrest group (group-time interaction, $P = 0.010$; coefficient [95 % CI], 0.584 [0.178–0.989]). CoPP (group effect, $P = 0.041$; coefficient [95 % CI], −7.778 [−14.136 to −1.421]) and CePP (group effect, $P = 0.020$; coefficient [95 % CI], −7.182 [−12.860 to −1.503]) were significantly lower in the hyperkalemic arrest group than in the VF arrest group. No significant group effect or group-time interaction was observed for $PbtO_2$.

4. Discussion

This is the first study comparing hemodynamic, echocardiographic, and cerebral oxygenation measurements obtained during ACLS between hyperkalemic and VF cardiac arrest. In the present study, myocardial ischemic contracture was less severe in the hyperkalemic arrest group: the LV wall thickness was significantly lower, and the EDV, although not significantly different, was greater in

Table 1
Pre-arrest baseline characteristics.

Variable	VF arrest (N = 10)	Hyperkalemic arrest (N = 10)	*P* value*
Weight (kg)	22.3 (21.5–23.4)	22.6 (22.3–23.1)	0.820
Systolic arterial pressure (mmHg)	113 (109–121)	120 (105–121)	0.594
Diastolic arterial pressure (mmHg)	72 ± 9	74 ± 13	0.621
Mean arterial pressure (mmHg)	89 ± 9	91 ± 10	0.684
Systolic right atrial pressure (mmHg)	10 ± 2	10 ± 1	0.638
Diastolic right atrial pressure (mmHg)	6 ± 1	6 ± 1	0.213
Mean right atrial pressure (mmHg)	8 (6–9)	9 (8–9)	0.285
Heart rate (beats/min)	91 ± 12	88 ± 14	0.589
Rectal temperature (°C)	37.7 ± 0.5	37.3 ± 0.5	0.119
Arterial pH	7.55 ± 0.05	7.55 ± 0.03	0.957
$PaCO_2$ (mmHg)	39 ± 2	41 ± 4	0.111
PaO_2 (mmHg)	130 ± 26	141 ± 27	0.381
Lactate (mmol/L)	1.2 ± 0.9	0.9 ± 0.2	0.286
Potassium (mmol/L)	3.9 ± 0.2	3.8 ± 0.2	0.410
LV wall thickness (mm)	4 (4–4)	4 (4–5)	0.492
EDV (mL)	39 ± 12	36 ± 8	0.551
CSF pressure (mmHg)	9 ± 2	9 ± 2	0.686
$PbtO_2$ (mmHg)	52.8 ± 14.9	48.2 ± 10.5	0.428

Note: The data are presented as the means ± standard deviations or medians with interquartile ranges. The LV wall thickness and chamber area were measured at end-diastole.
**P* values were computed using the independent two-sample T test or Wilcoxon rank-sum test for differences between the VF and hyperkalemic arrest groups. VF, ventricular fibrillation; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; LV, left ventricular; EDV, end-diastolic volume; CSF, cerebrospinal fluid; $PbtO_2$, brain tissue oxygen tension.

Table 2
pH, $PaCO_2$, PaO_2, and potassium levels immediately before cardiac arrest induction and during cardiopulmonary resuscitation.

	Immediately before cardiac arrest induction	16 min after cardiac arrest induction	22 min after cardiac arrest induction	*P* value*
pH				Group, 0.543; Time, <0.001
VF arrest (N = 10)	7.54 ± 0.04	7.20 ± 0.13	7.07 ± 0.14	
Hyperkalemic arrest (N = 10)	7.55 ± 0.05	7.15 ± 0.18	7.04 ± 0.17	
$PaCO_2$ (mmHg)				Group, 0.456; Time, 0.002
VF arrest (N = 10)	38 ± 1	54 ± 15	67 ± 23	
Hyperkalemic arrest (N = 10)	35 ± 4†	61 ± 21	73 ± 25	
PaO_2 (mmHg)				Group, 0.093; Time, 0.046
VF arrest (N = 10)	116 ± 16	77 ± 44	64 ± 54	
Hyperkalemic arrest (N = 10)	110 ± 20	49 ± 18	40 ± 13	
Potassium (mmol/L)				Group, <0.001; Time 0.791;
VF arrest (N = 10)	3.7 ± 0.3	7.6 ± 1.7	7.7 ± 2.7	Group-time, 0.559
Hyperkalemic arrest (N = 10)	9.7 ± 0.9†	12.7 ± 2.7†	12.6 ± 3.4†	

Note: The data are presented as the means ± standard deviations.
**P* values were derived from linear mixed-effects models. Only the 16- and 22-min data were included in the linear mixed-effects models.
†$P < 0.05$ versus VF arrest by independent two-sample *t*-test. VF, ventricular fibrillation; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen.

the hyperkalemic arrest group. The decrease in EDV over time was significantly less pronounced in the hyperkalemic arrest group than in the VF arrest group. However, contrary to our hypothesis, CoPP and CePP were lower in the hyperkalemic arrest group compared to the VF arrest group. Although not significant, $PbtO_2$ was also lower in the hyperkalemic arrest group.

Myocardial ischemic contracture, a progressive thickening of the LV wall following ischemia, arises from severe adenosine triphosphate (ATP) depletion and often occurs during cardiac arrest [17,18]. This leads to a progressive reduction in the LV chamber volume, which, in turn, reduces the stroke volume produced by chest compressions [10,11]. The attenuation of myocardial ischemic contracture in the hyperkalemic arrest group is consistent with a study by Digerness et al. [19]. In a study using isolated rat hearts [19], Digerness et al. reported that reperfusion with potassium delayed the onset of myocardial ischemic contracture. We did not determine the mechanism underlying the attenuation of myocardial ischemic contracture in the hyperkalemic arrest group, but it might be identical to the mechanism by which hyperkalemic cardioplegia induces a flaccid diastolic state. An increase in the extracellular potassium concentration induced by hyperkalemic cardioplegia shifts the resting membrane potential further from the threshold for sodium channel activation, which is responsible for the rapid upstroke of the cardiac action potential (phase 0) [20]. This shift blocks the conduction of the cardiac action potential, leading to a flaccid diastolic state.

Attenuation of myocardial ischemic contracture should improve the hemodynamic effectiveness of CPR by maintaining larger LV volumes during the relaxation phase of chest compressions. Several interventions that attenuate myocardial ischemic contracture have been shown to improve hemodynamic effectiveness of CPR and, thereby, facilitate successful resuscitation [14,21]. However, in the present study, the CoPP and CePP in the hyperkalemic arrest group were lower than in the VF arrest group despite the attenuation of myocardial ischemic contracture. Although not significant, $PbtO_2$ was also lower in the hyperkalemic arrest group. Both the CoPP and CePP are primarily determined by arterial pressure. CePP is the driving force for cerebral blood flow, a major determinant of cerebral oxygen delivery. The lower CoPP and CePP in the hyperkalemic arrest group might be attributable to potassium-induced vasodilation. Hyperkalemia can cause relaxation of vascular smooth muscle by activating the sodium-potassium pump and the inward rectifier potassium channels [22–24]. In the hyperkalemic arrest group, the pressor effect of epinephrine might have been significantly attenuated due to the hyperkalemia-induced vasodilation.

Asystole is the end-stage cardiac arrest rhythm that typically occurs after prolonged VF or pulseless electrical activity, when myocardial ATP is severely depleted, and the electrical activity of the heart ceases. It is generally more associated with failure to achieve ROSC than VF [25], but this may not be the case for asystole in the hyperkalemic arrest group of this study. Myocardial oxygen consumption is lower in potassium-induced asystole compared to VF [26,27], leading to slower ATP depletion in potassium-induced asystole. The slower rate of ATP depletion observed in potassium-induced asystole may be beneficial in achieving ROSC. Based on these studies [26,27], hyperkalemic cardiac arrest may be easier to resuscitate than VF cardiac arrest. The outcomes of hyperkalemic cardiac arrest have not been systematically investigated, but a survival rate of 3.7 % was reported in a study of patients with in-hospital cardiac arrest accompanied by severe hyperkalemia [3]. Although direct comparisons between survival rates cannot be made, this is much lower than the reported survival rate for undifferentiated cardiac arrest (20%–26 %) [28]. The dismal outcome of hyperkalemic cardiac arrest may be attributable to the lower perfusion pressure in the hyperkalemic arrest group observed in the present study.

Achieving the return of spontaneous circulation (ROSC) from cardiac arrest depends on the CoPP [29,30]. In the hyperkalemic

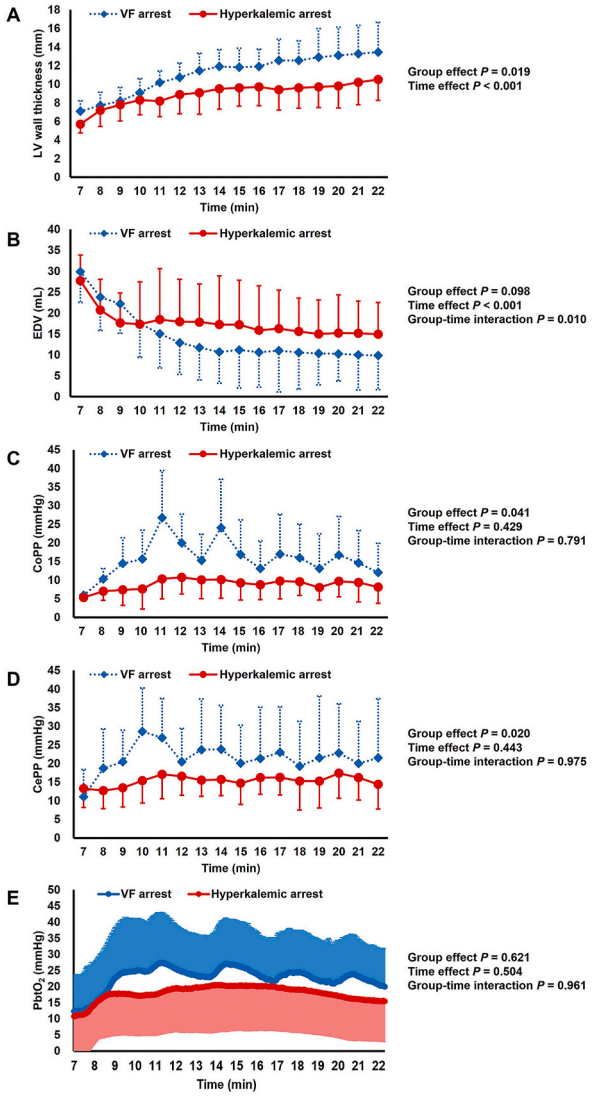

Fig. 2. LV wall thickness (A), EDV (B), CoPP (C), CePP (D), and PbtO2 (E) during cardiopulmonary resuscitation. The data are presented as the means ± SDs. P values were derived from linear mixed-effects models. VF, ventricular fibrillation; LV, left ventricular; EDV, end-diastolic volume; CoPP, coronary perfusion pressure; CePP, cerebral perfusion pressure; PbtO2, brain tissue oxygen tension.

arrest group, the CoPP was well below the threshold needed to achieve ROSC [31]. Therefore, vasopressor drug therapy with greater vasoconstriction action may have been necessary to raise the CoPP to the level necessary for ROSC in the hyperkalemic arrest group. While epinephrine increases CoPP and myocardial blood flow during CPR and facilitates ROSC [32,33], it may have adverse effects on the brain [34–36]. Several studies suggest that the α1-adrenergic agonist action of epinephrine may compromise cerebral microcirculation following ROSC, increasing the risk of cerebral tissue hypoxia and subsequent cerebral injury [34,35]. In the largest randomized clinical trial of epinephrine versus saline placebo for adult out-of-hospital cardiac arrest to date [36], the epinephrine group showed higher ROSC and 30-day survival rates. However, this group also had significantly more survivors with severe neurologic impairment compared to the saline placebo group, resulting in no significant difference in favorable neurologic outcomes between the two groups. The β-adrenergic agonist action of epinephrine increases myocardial oxygen consumption, contributing to post-resuscitation myocardial dysfunction [37,38]. These harmful adrenergic side effects of epinephrine may be exacerbated when higher doses of epinephrine are administered, potentially offsetting the survival benefit from the improved perfusion pressure achieved with higher doses of epinephrine during CPR. Further studies are needed to identify the optimal vasopressor therapy for the treatment of hyperkalemic cardiac arrest.

With the widespread use of point-of-care blood gas analyzers, potassium levels can be quickly determined during clinical CPR. The serum potassium concentration increases during CPR due to the release of potassium from cells secondary to the failure of energy-dependent cellular membrane pumps [39–41]. Acidosis, a common occurrence in cardiac arrest, can also cause a potassium shift from intracellular to extracellular space, thereby increasing plasma potassium levels. In a study including 22 adult cardiac arrest

patients without preexisting renal disease [40]. Martin et al. reported that 32 % of patients had potassium concentrations greater than 6 mEq/L. Antihyperkalemic treatments, including calcium and sodium bicarbonate, may be deleterious in VF cardiac arrest [42–45]. The upper limit of serum potassium, which serves as a threshold for diagnosing hyperkalemic cardiac arrest and initiating antihyperkalemic treatment during CPR, is unknown, but a potassium level of 6.5 mEq/L is often considered the upper limit [46]. In the present study, serum potassium concentrations during CPR showed hyperkalemia even in the VF arrest group (7.8 ± 2.2 mEq/L). Twelve (60.0 %) of 20 blood samples obtained during CPR in the VF arrest group had potassium concentrations greater than 6.5 mEq/L. Although potassium concentrations in the VF arrest group were significantly lower than those in the hyperkalemic arrest group, there was considerable overlap in the potassium concentrations between the two groups. The diagnosis of cardiac arrest due to hyperkalemia should not be based solely on blood potassium levels but should also consider pH and presence of precipitating factors for hyperkalemia, such as chronic kidney disease.

Our study had several limitations. First, our study was conducted using anesthetized young pigs. Therefore, our results may not be generalizable to human patients with cardiac arrest. Second, hyperkalemic arrest was induced by exogenous potassium administration, which might not adequately reflect hyperkalemic cardiac arrest observed in clinical practice. Third, we used a single potassium administration protocol to induce hyperkalemic arrest. However, the physiological effects of hyperkalemia might vary depending on potassium levels. Fourth, the animals in the VF and hyperkalemic arrest groups did not receive defibrillation or antihyperkalemic treatments, respectively. Previous studies comparing defibrillation-first and CPR-first strategies in a pig model of VF cardiac arrest reported no difference in CPP between the two approaches [47,48]. In a study evaluating the efficacy of calcium chloride and sodium bicarbonate on ROSC in a pig model of hyperkalemic cardiac arrest [49], neither calcium nor sodium bicarbonate had an effect on CPP. Based on these studies [47–49], it is unlikely that the addition of these treatments to ACLS would have influenced CPP. Fifth, only the electrically induced VF model was used to represent cardiac arrest with non-hyperkalemic etiologies. The findings from this study may not be applicable to cardiac arrest with other non-hyperkalemic etiologies, such as ischemia-induced VF arrest or asphyxial arrest. Sixth, we did not assess resuscitation outcomes, including ROSC and survival. Further research is needed to determine whether lower perfusion pressure in the hyperkalemic arrest group directly contributes to worse resuscitation outcomes. Seventh, this study was powered to detect a difference in the LV wall thickness and thus might be underpowered to detect differences in other outcomes, including EDV and PbtO2.

5. Conclusion

In the present study, which compared hemodynamic, echocardiographic, and cerebral oxygenation measurements obtained during ACLS between hyperkalemic and VF cardiac arrest in pigs, the LV wall thickness was smaller, and the decrease in EDV over time was less pronounced in the hyperkalemic arrest group. However, perfusion pressure was poorer in the hyperkalemic arrest group, and cerebral oxygenation was not better. Further studies are needed to determine the optimal vasopressor therapy for hyperkalemic cardiac arrest.

CRediT authorship contribution statement

Najmiddin Mamadjonov: Writing – original draft, Methodology, Investigation. **Wan Young Heo:** Investigation. **Kyung Woon Jeung:** Writing – original draft, Resources, Methodology, Funding acquisition, Conceptualization. **Yong Hun Jung:** Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Funding acquisition. **Hyoung Youn Lee:** Resources, Methodology, Investigation. **Seok Jin Ryu:** Formal analysis. **Byung Kook Lee:** Formal analysis. **Yong Soo Cho:** Formal analysis. **Tag Heo:** Supervision.

Ethics statement

This study was approved by the Animal Care and Use Committee of Chonnam National University Hospital (CNUH IACUC-23025) and conducted in compliance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

Data availability statement

The data and materials used in this study are available from the corresponding author upon reasonable request.

Funding

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) [grant number, NRF-2020R1A2C1013332] and a research fund from Chonnam National University [grant number, 2024-0447].

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Yong Hun Jung reports financial support was provided by National Research Foundation of Korea. Kyung Woon Jeung reports financial support was provided by Chonnam National University. If there are other authors, they declare that they have no known

competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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