The Right Ventricle Is Dilated During Resuscitation From Cardiac Arrest Caused by Hypovolemia: A Porcine Ultrasound Study

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Objectives: Dilation of the right ventricle during cardiac arrest and resuscitation may be inherent to cardiac arrest rather than being associated with certain causes of arrest such as pulmonary embolism. This study aimed to compare right ventricle diameter during resuscitation from cardiac arrest caused by hypovolemia, hyperkalemia, or primary arrhythmia (i.e., ventricular fibrillation).

Design: Thirty pigs were anesthetized and then randomized to cardiac arrest induced by three diffrent methods. Seven minutes of untreated arrest was followed by resuscitation. Cardiac ultrasonographic images were obtained during induction of cardiac arrest, untreated cardiac arrest, and resuscitation. The right ventricle diameter was measured. Primary endpoint was the right ventricular diameter at the third rhythm analysis.

Setting: University hospital animal laboratory.

Subjects: Female crossbred Landrace/Yorkshire/Duroc pigs (27–32 kg).

Interventions: Pigs were randomly assigned to cardiac arrest caused by either hypovolemia, hyperkalemia, or primary arrhythmia.

Measurements and Main Results: At the third rhythm analysis during resuscitation, the right ventricle diameter was 32 mm (95% CI, 29–35) in the hypovolemia group, 29 mm (95% CI, 26–32) in the hyperkalemia group, and 25 mm (95% CI, 22–28) in the primary arrhythmia group. This was larger than baseline for all groups ($p = 0.03$). When comparing groups at the third rhythm analysis, the right ventricle was larger for hypovolemia than for primary arrhythmia ($p < 0.001$).

Conclusions: The right ventricle was dilated during resuscitation from cardiac arrest caused by hypovolemia, hyperkalemia, and primary arrhythmia. These findings indicate that right ventricle dilation may be inherent to cardiac arrest, rather than being associated with certain causes of arrest. This contradicts a widespread clinical assumption that in hypovolemic cardiac arrest, the ventricles are collapsed rather than dilated. (*Crit Care Med* 2017; XX:00–00)

Key Words: arrhythmias, cardiac; echocardiography; heart arrest; hyperkalemia; hypovolemia; ultrasonography

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Identifying a reversible cause of cardiac arrest during resuscitation increases the chance of survival (1). Resuscitation and cardiac ultrasonography guideline stipulate that ultrasonography has the potential to detect such causes (2–4). However, no studies have compared transthoracic cardiac ultrasonographic findings during resuscitation with a verified cause of cardiac arrest.

Based on data from patients with spontaneous circulation, resuscitation guidelines suggest that when pulmonary embolism is the cause of cardiac arrest, the right ventricle (RV) may be dilated (5). However, in porcine models, RV dilation has also been demonstrated in response to untreated ventricular fibrillation (VF) (6, 7). Further, we have demonstrated that RV dilation persists throughout resuscitation from cardiac arrest caused by VF, hypoxia, and pulmonary embolism (8).

Severe hypovolemia causes a reduction in RV diameter in patients with spontaneous circulation (9, 10). However, whether this reduction persists during cardiac arrest and

resuscitation is unknown. Furthermore, hyperkalemia may cause RV dilation by arresting the heart in diastole (11).

Hence, the aim of the current study was to compare RV diameter during resuscitation from cardiac arrest caused by hypovolemia, hyperkalemia, or primary arrhythmia.

MATERIALS AND METHODS

Animals

The study was approved by the Danish National Committee on Animal Research Ethics (2012-15-2934-00450) and conducted in accordance with the Principles of Laboratory Animal Care (12). Female crossbred Landrace/Yorkshire/Duroc pigs (27.3–31.2 kg) were fasted overnight with free access to water. Refer to **supplemental text** (Supplemental Digital Content 1, http://links.lww.com/CCM/C634) for details.

Anesthesia and Ventilation

Anesthesia was induced with intramuscular ketamine (6.25 mg/kg) and midazolam (0.625 mg/kg) and maintained with sevoflurane at a minimum alveolar concentration of 1–1.2 and fentanyl 15 μg/kg/h. The animals were intubated and volume-controlled ventilated. During preparation, the ventilation rate was adjusted to maintain a $Paco_2$ ranging from 41 to 45 mm Hg. Core temperature was maintained at approximately 38°C at baseline. Saline 0.9% supplemented with glucose (15 mg/mL) (to prevent hypoglycemia) was continuously infused (10 mL/kg/h) during the entire experiment. Refer supplemental text (Supplemental Digital Content 1, http://links.lww.com/CCM/C634) for details.

Surgical Preparation and Monitoring

A perivascular flow probe was fitted around the left carotid artery to measure blood flow. Vascular sheaths were placed in the femoral arteries and right external jugular vein. Pressure catheters were placed in the proximal aorta and the right atrium via the left femoral artery and the right external jugular vein. Coronary perfusion pressure (CPP) was calculated as the difference between the simultaneously measured aortic and right atrial pressures at the end of each relaxation phase (13). The CPP is reported as an average of the 10 measurements preceding each rhythm analysis. Mean pulmonary artery pressure (MPAP) was measured using a pulmonary artery flotation catheter inserted through the external jugular vein. Refer to supplemental text (Supplemental Digital Content 1, http://links.lww.com/CCM/C634) for details.

Experimental Protocol

Baseline measurements were performed 30 minutes after the end of surgical preparation. The animals were randomized into three groups of 10 (**Fig. 1*A***). Cardiac arrest was defined as a mean arterial pressure (MAP) less than 20 mm Hg or a pulse pressure less than 5 mm Hg sustained for 1 minute.

Cardiac arrest was induced as follows:

Hypovolemia: animals were bled at a rate of 1.7 mL/kg/min for the first 7 minutes followed by 0.9 mL/kg/min. This biphasic approach results in a more physiological response than exsanguination at a fixed rate (14). When the MAP was less than 20 mm Hg or pulse pressure was less than 5 mm Hg, ventilation was discontinued until resuscitation was commenced, as respiration is the first vital sign to cease when hypovolemia progresses from shock to cardiac arrest (15). If the blood pressure criteria for cardiac arrest were not sustained for 1 minute, blood withdrawal was continued until cardiac arrest.

Hyperkalemia: potassium chloride (1 mmol/mL) was continuously infused peripherally at a rate of 2.8 mL/kg/h for 30 minutes followed by a rate of 2.2 mL/kg/h for 15 minutes. Cardiac arrest was then induced by injecting a potassium chloride bolus (0.3 mmol/kg) through the distal end of the pulmonary artery flotation catheter. Refer to **supplemental pilot study** (Supplemental Digital Content 2, http://links.lww.com/CCM/C635) for details on development of this model.

Primary arrhythmia: a 9-V direct current was delivered through a bipolar pacing catheter placed temporarily in the RV.

Following 7 minutes of untreated cardiac arrest, advanced life support, per the 2010 European Resuscitation Council guidelines, was commenced with the exception that defibrillations were omitted to prevent animals from obtaining return of spontaneous circulation (ROSC). Chest compressions were performed using a mechanical device (LUCAS; Physio-Control/Jolife, Lund, Sweden). Ventilations were performed mechanically in a volume-controlled setting: tidal volume 10 mL/kg, respiration rate 10/min, and FIO_2 1.0. ROSC was defined as an MAP greater than 30 mm Hg for at least 1 minute. The experiment proceeded until the end of the fifth rhythm analysis.

Cardiac Ultrasonography

Subcostal and parasternal ultrasonographic images were obtained at baseline, during induction of cardiac arrest (5-min intervals), at the onset of cardiac arrest, during untreated arrest (2-min intervals), and at each rhythm analysis during resuscitation (2-min intervals).

For both subcostal and parasternal ultrasonography, a phased array transducer was used (transducer: M4S-RS-Cardiac; ultrasonography machine: Vivid S6; GE Healthcare, Little Chalfont, United Kingdom).

To obtain consistently high image quality in the subcostal window, the right part of the rectus abdominis muscle was transected immediately caudal to the rib cage, without perforating the diaphragm or peritoneum (16). The ultrasound probe was positioned at the anterior aspect of the right diaphragm, where the impetus of the cardiac apex could be palpated. The images obtained corresponded to a human five-chamber apical view. Acceptable images included clear visualization of the aortic valve, septum, and the lateral wall of the RV (**Fig. 1*B***). From the left parasternal window, transverse images of the left ventricle (LV), at the level of the papillary muscles, were obtained (**Fig. 1*C***). For consistency, one operator obtained all subcostal images, whereas another operator obtained all parasternal images.

Outcome Measures

The primary endpoint was the RV diameter at end-diastole from the subcostal view at the third rhythm analysis. The RV

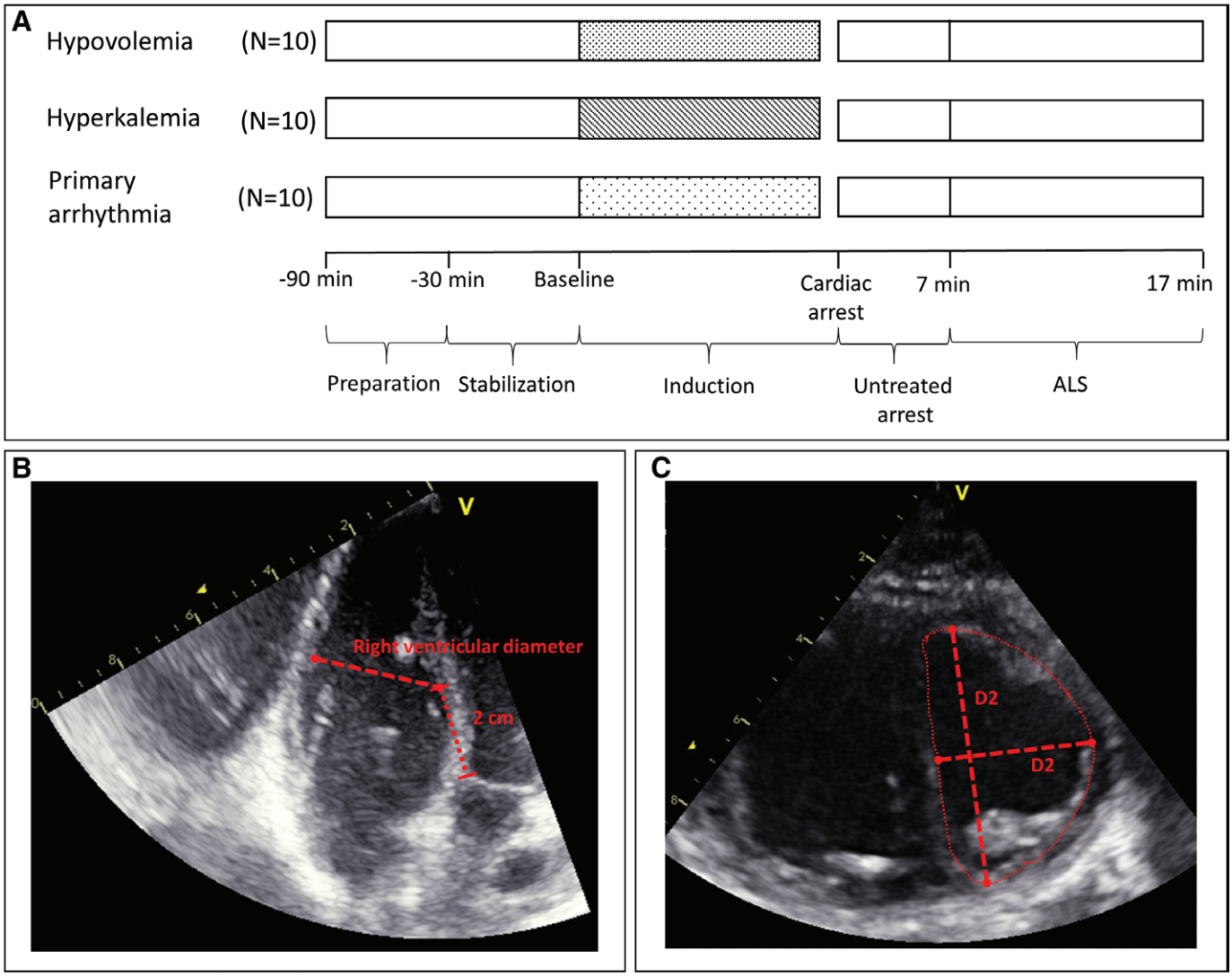

Figure 1. Experimental methods. **A**, Timeline of the experimental protocol, advanced life support (ALS). **B**, Method for measuring right ventricular diameter. In a five-chamber view, we measured 2 cm along the septum, starting at the septal aspect of the aortic valve. From this point, we measured the shortest possible distance to the lateral wall of the right ventricle. **C**, Method for measuring left ventricular area. In left parasternal short-axis images, we traced the endocardium of the left ventricle and measured the minor axis parallel (D1) and perpendicular (D2) to the septum. Papillary muscles were considered part of the left ventricular lumen.

diameter was determined by measuring 20 mm apically along the septum from the septal aspect of the aortic valve. From this point on the septum, the shortest possible distance to the free wall of the RV was measured and defined as the RV diameter (Fig. 1*B*). We have previously validated the correlation of RV diameter with RV volume (8). Ultrasound images were analyzed by the first author, who was blinded to both experimental group and time point in the study protocol. A random subset of 20 subcostal images was reanalyzed, resulting in an intraobserver variability of –0.4 mm (95% limits of agreement, –2.4 to 1.7). Refer to **Supplemental Figure 1** (Supplemental Digital Content 3, http://links.lww.com/CCM/C636; **legend,** Supplemental Digital Content 1, http://links.lww.com/CCM/C634) for a Bland-Altman plot.

From the parasternal window, LV end-diastolic area was determined by tracing the endocardium, including papillary muscles and trabeculations in the LV cavity. The eccentricity index was calculated as described previously (17). A subset of 20 parasternal images was reanalyzed resulting in an intraobserver variability of –0.2 cm^2 (95% limits of agreement, –3.4 to 3.0). Refer to Supplemental Figure 1 (Supplemental Digital Content 3, http://links.lww.com/CCM/C636; legend, Supplemental Digital Content 1, http://links.lww.com/CCM/C634) for a Bland-Altman plot.

Statistical Analysis

As predetermined, the repeated measurements data were analyzed in three phases: 1) cardiac arrest induction phase, 2) untreated cardiac arrest phase, and 3) resuscitation phase. During the cardiac arrest induction phase, image acquisition was increasingly difficult as more blood was withdrawn in the hypovolemia group. After 30 minutes of withdrawing blood,

the heart could be visualized only in three pigs. For this reason, analyses concerning the cardiac arrest induction phase only included the time points from baseline to 30 minutes. Repeated measurements analyses of variance (ANOVA) were used to analyze data for time-dependent within-group differences and between-group differences for continuous variables measured over time. Differences in mean values at predetermined time points and mean levels over time were analyzed using one-way ANOVA followed by pairwise comparisons, using Sidak corrections. During the cardiac arrest induction phase, comparisons were performed only between the hypovolemia and hyperkalemia groups because cardiac arrest was induced momentarily in the primary arrhythmia group. Paired *t* tests were used for within-group comparisons and Student *t* tests were used for group comparisons at predetermined time points, when only two groups were compared. The analyses were performed using Stata/IC 13 (StataCorp LP, Collage Station, TX). *p* Value of less than 0.05 was considered significant.

Sample Size Calculation

Based on pilot studies and data from a previous study, a one-way ANOVA sample size estimation was performed, estimating that 30 pigs (10 in each group) were sufficient to detect a difference in RV diameter between groups at the third rhythm analysis. Refer supplemental text (Supplemental Digital Content 1, http://links.lww.com/CCM/C634) for details.

RESULTS

Overall Model

In total, 32 pigs were used in the study. Two pigs were excluded, one from the hypovolemia group due to a technical issue with the ventilator and the other from the hyperkalemia group because of accidental administration of calcium chloride. Overall, 30 pigs were included in the final analyses.

In the hypovolemia group, ventilation was stopped after 46 minutes 15 seconds (95% CI, 41 min 25 s to 51 min 4 s), and cardiac arrest occurred after 54 minutes 28 seconds (95% CI, 49 min 36 s to 59 min 19 s). Blood was withdrawn after the ventilation was stopped in all pigs. The total amount of blood withdrawn was 1,579 mL (95% CI, 1,458–1,700), corresponding to 70% (95% CI, 64–75) of the estimated total blood volume (18).

Time to cardiac arrest was 45 minutes for nine of 10 pigs in the hyperkalemia group, as defined by the protocol. In one pig, cardiac arrest occurred 36 minutes and 41 seconds into the cardiac arrest induction phase with a potassium of 9.1 mmol/L, whereas potassium in the remaining nine pigs after 45 minutes was 9.4 mmol/L (95% CI, 8.7–10.0).

Ultrasonography

Right Ventricular Diameter. At baseline, there was no difference in RV diameter ($p = 0.69$) (**Fig. 2*A***). During cardiac arrest induction, the RV diameter decreased in the hypovolemia group ($p > 0.001$ for change over time) and increased in the hyperkalemia group ($p = 0.02$ for change over time). During the period of untreated cardiac arrest, RV diameters in the three groups were parallel ($p = 0.98$) with no difference in mean levels ($p = 0.48$). At the third rhythm analysis (primary endpoint), the mean RV diameter was 32 mm in the hypovolemia group (95% CI, 29–35), 29 mm in the hyperkalemia group (95% CI, 26–32), and 25 mm in the primary arrhythmia group (95% CI, 22–28). The RV diameter in the hypovolemia group was significantly larger than in the primary arrhythmia group ($p = 0.008$), whereas no difference was found between hyperkalemia and hypovolemia ($p = 0.36$) or hyperkalemia and primary arrhythmia groups ($p = 0.24$). At

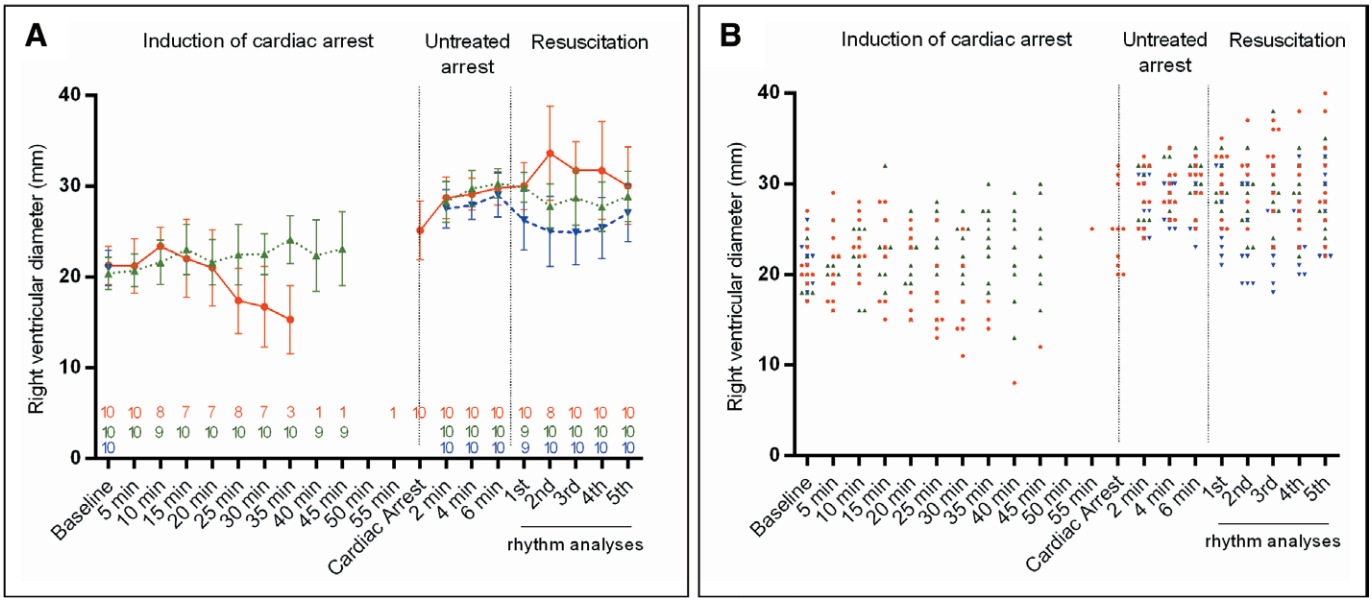

Figure 2. Right ventricular diameter during cardiac arrest induction, untreated cardiac arrest, and resuscitation. *Red circles* represent the hypovolemia group. *Green triangles* represent the hyperkalemia group. *Blue triangles* represent the primary arrhythmia group. **A**, Means and 95% CI intervals. Ten pigs were included in each group. Numbers represent the number of images successfully obtained at each time point. Mean values with error bars are only plotted for time points containing three or more measurements. **B**, Scatter plot showing each right ventricular diameter measurement performed in the study.

the third rhythm analysis, the RV diameter was larger than at baseline in all three groups. The difference from baseline was 10 mm (95% CI, 7–14; $p < 0.001$) in the hypovolemia group, 8 mm (95% CI, 5–11; $p < 0.001$) in the hyperkalemia group, and 4 mm (95% CI, 0–8; $p < 0.03$) in the primary arrhythmia group. Refer to **Supplemental Figure 2** (Supplemental Digital Content 4, http://links.lww.com/CCM/C637; legend, Supplemental Digital Content 1, http://links.lww.com/CCM/C634) for RV values for the individual pigs.

LV End-Diastolic Area. At the third rhythm analysis, the LV area was smaller compared with baseline for all groups ($p > 0.004$), and it was also observed to be smaller in the hypovolemia group than in both the hyperkalemia ($p = 0.01$) and primary arrhythmia ($p = 0.04$) groups (**Fig. 3*A***).

Arterial Blood Gasses and Hemodynamics. There was no difference between groups at the third rhythm analysis regarding Pao_2 ($p = 0.43$) or pH ($p = 0.84$). At the third rhythm analysis, $Paco_2$ was lower in the hypovolemia group than in the other two groups ($p = 0.003$), whereas lactate was higher ($p < 0.001$) (**Table 1**). Carotid blood flow was significantly lower in the hypovolemia group than in the hyperkalemia and primary arrhythmia group at the third rhythm analysis ($p < 0.001$) (**Table 2**). Right atrial pressure was significantly lower in the hypovolemia group than in the other two groups at the third rhythm analysis ($p < 0.001$). Refer to **Supplemental Table 1** (Supplemental Digital Content 1, http://links.lww.com/CCM/C634) for data concerning MAP, MPAP, and carotid blood flow during induction of cardiac arrest.

DISCUSSION

The RV was dilated during resuscitation from cardiac arrest caused by hypovolemia, hyperkalemia, or primary arrhythmia. The RV was significantly more dilated during resuscitation when cardiac arrest was caused by hypovolemia than when the arrest was caused by primary arrhythmia. The LV cross-sectional area was significantly smaller during resuscitation when cardiac arrest was caused by hypovolemia, when compared with both hyperkalemia and primary arrhythmia.

The RV dilation seen in all groups may be explained by pooling of blood on the venous side of the systemic circulation as the heart fails to maintain a pressure gradient between the arteries and veins. When pressures equilibrate, a relative volume expansion will occur in the more compliant venous vasculature (19). This phenomenon has been demonstrated previously in porcine models of untreated VF (6, 7). Similarly, in a recent porcine study, we demonstrated RV dilation during both untreated cardiac arrest and resuscitation, when cardiac arrest was caused by pulmonary embolism, hypoxia, or primary arrhythmia (8).

Based on overall reduction in blood volume in the hypovolemic animals, less blood should theoretically be pooled on the venous side of the systemic circulation, resulting in a smaller RV diameter than in euvolemic animals. Indeed, the present study demonstrates that the RV diameter is reduced when the animals are subjected to severe hypovolemia if spontaneous circulation is still present (9). However, contradictory to our beliefs, an increase in RV diameter was present throughout resuscitation in the hypovolemic pigs. In fact, the RV was significantly larger in the hypovolemia group than in the primary arrhythmia group, but the absolute difference in their means was small, and the scatter plot reveals a considerable overlap between all groups (**Fig. 2*B***).

A possible explanation for the surprising finding of RV dilation during resuscitation from cardiac arrest caused by hypovolemia is pulmonary vasoconstriction. Both hypoxia and

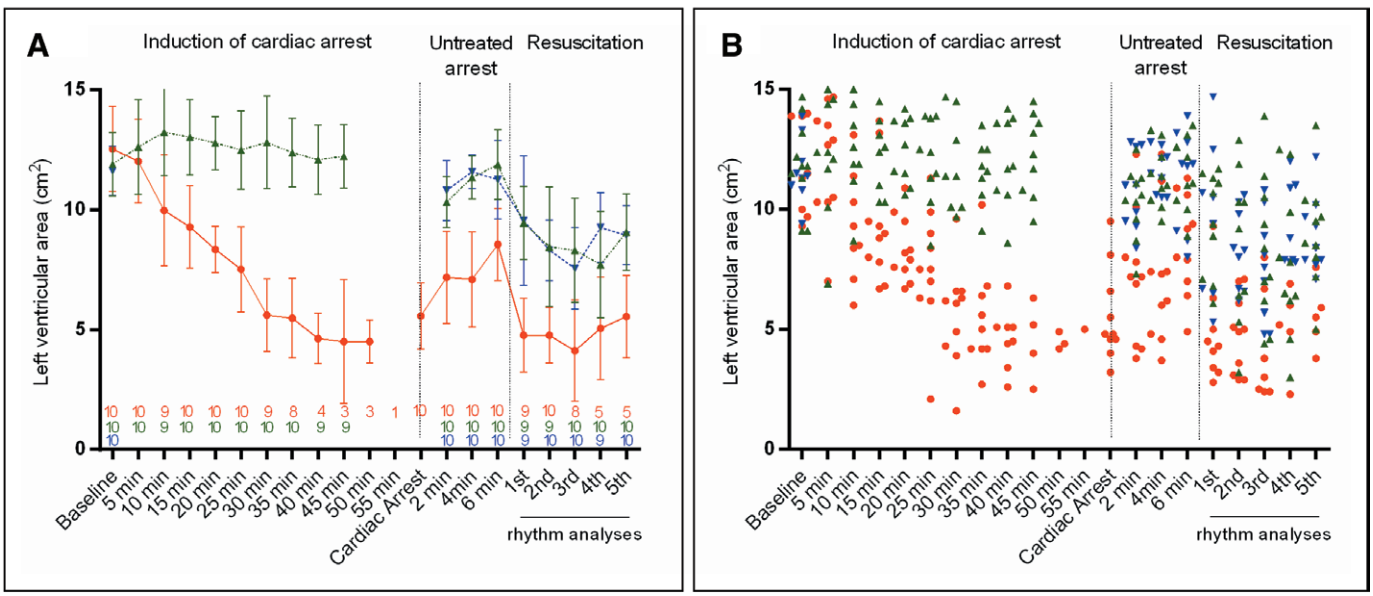

Figure 3. Left ventricular area during cardiac arrest induction, untreated cardiac arrest, and resuscitation. *Red circles* represent the hypovolemia group. *Green triangles* represent the hyperkalemia group. *Blue triangles* represent the primary arrhythmia group. **A**, Means and 95% CI intervals. Ten pigs were included in each group. Numbers represent the number of images successfully obtained at each time point. Mean values with error bars are only plotted for time points containing three or more measurements. **B**, Scatter plot showing each left ventricular area measurement performed in the study.

TABLE 1. Arterial Blood Gas Samples During Induction of Cardiac Arrest and Resuscitation

	Induction of Cardiac Arrest					Resuscitation		
Variables	Baseline	15 Min	30 Min	45 Min	Cardiac Arrest	First	Third	Fifth
pH								
Hypovolemia	7.41 (7.40–7.42)	7.42 (7.40–7.44)	7.41 (7.39–7.43)	7.39 (7.30–7.48)	6.94 (6.87–7.00)	7.08 (6.91–7.24)	7.24 (6.97–7.51)	7.06 (6.80–7.32)
Hyperkalemia	7.41 (7.39–7.44)	7.41 (7.39–7.44)	7.41 (7.39–7.44)	7.42 (7.38–7.47)	–	7.32 (7.27–7.36)	7.28 (7.22–7.35)	7.22 (7.15–7.30)[a]
Primary arrhythmia	7.42 (7.40–7.44)	–	–	–	–	7.33 (7.27–7.40)	7.26 (7.22–7.30)	7.22 (7.18–7.26)[b]
Hemoglobin (mmol/L)								
Hypovolemia	5.2 (4.9–5.6)	5.1 (4.8–5.4)	4.9 (4.7–5.1)	5.2 (4.4–6.1)	5.6 (5.3–5.9)	4.9 (4.5–5.4)	4.1 (3.3–4.9)[c]	3.8 (3.6–4.1)[a,b]
Hyperkalemia	5.4 (5.2–5.6)	5.4 (5.2–5.6)	5.6 (5.4–5.7)	5.8 (5.6–6.0)[d]	–	6.4 (6.1–6.7)	7.1 (6.6–7.6)	7.4 (7.2–7.6)
Primary arrhythmia	5.4 (5.2–5.6)	–	–	–	–	6.4 (6.1–6.7)	7.2 (6.9–7.4)	7.2 (6.9–7.4)
Serum potassium (mmol/L)								
Hypovolemia	3.9 (3.7–4.1)	4.2 (4.0–4.4)	4.8 (4.2–5.3)	4.4 (4.1–4.8)	7.4 (6.5–8.2)	6.0 (5.5–6.5)	6.3 (5.5–7.1)	6.5 (5.2–7.9)
Hyperkalemia	4.0 (3.8–4.1)	6.5 (6.2–6.7)	7.6 (7.2–8.1)	8.3 (7.3–9.3)[e]	–	10.7 (9.2–12.2)	10.1 (9.1–11.1)[c]	9.4 (8.7–10.0)[a]
Primary arrhythmia	4.1 (4.0–4.2)	–	–	–	–	5.6 (5.3–5.9)	6.4 (6.1–6.6)	6.1 (5.7–6.5)[a,b]
Lactate (mmol/L)								
Hypovolemia	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.6 (1.3–1.9)	1.8 (0.5–3.1)	7.8 (6.6–9.1)	7.9 (6.8–8.9)	9.5 (8.2–10.7)[c]	11.2 (9.4–12.9)[a]
Hyperkalemia	1.3 (1.1–1.4)	1.2 (1.0–1.4)	1.2 (0.9–1.4)	1.2 (0.9–1.5)	–	2.7 (2.0–3.4)	5.2 (4.6–5.8)	6.6 (6.1–7.1)[a]
Primary arrhythmia	1.2 (1.0–1.4)	–	–	–	–	3.0 (2.6–3.3)	5.2 (4.9–5.4)	6.1 (5.7–6.6)[a,b]
Pao_2 (mm Hg)								
Hypovolemia	158 (138–176)	159 (143–176)	156 (140–172)	154 (66–243)	20 (11–29)	150 (79–221)	275 (117–433)	247 (97–396)
Hyperkalemia	169 (158–180)	168 (155–181)	169 (155–183)	164 (150–171)	–	95 (30–161)	179 (87–270)	130 (44–216)[a]
Primary arrhythmia	172 (167–185)	–	–	–	–	166 (72–260)	236 (124–347)	128 (38–218)[a,b]
$Paco_2$ (mm Hg)								
Hypovolemia	44 (43–44)	42 (41–44)	42 (40–44)	42 (40–45)	110 (101–118)	50 (37–63)	28 (15–41)[c]	31 (17–44)
Hyperkalemia	44 (43–45)	44 (43–45)	44 (42–45)	43 (38–47)	–	52 (46–57)	47 (40–53)	49 (38–59)
Primary arrhythmia	43 (42–44)	–	–	–	–	50 (43–58)	50 (44–56)	51 (44–58)

[a]Significant within-group time interaction (analysis of variance) during resuscitation.
[b]Significant time/group interaction between groups during resuscitation.
[c]This group differs from the others at this time point.
[d]Significant time/group interaction between the hyperkalemia and hypovolemia groups during induction.
[e]Significant within-group time interaction (analysis of variance) during induction.
Dashes represent time points where no measurements were made.

TABLE 2. Hemodynamic Variables During Resuscitation, Means (95% CIs)

Variables	Rhythm Analyses				
	First	Second	Third[a]	Fourth	Fifth
Carotid blood flow (mL/min)					
Hypovolemia	7 (2–12)	3 (1–6)	5 (2–8)[b]	4 (2–7)	5 (1–9)[c]
Hyperkalemia	47 (29–65)	52 (30–73)	49 (30–67)	38 (24–51)	33 (14–52)
Primary arrhythmia	44 (26–62)	65 (45–85)	67 (47–87)	42 (19–65)	44 (25–63)[d]
Coronary perfusion pressure (mm Hg)					
Hypovolemia	10 (5–15)	10 (5–15)	11 (6–16)[e]	12 (6–18)	12 (6–18)[c]
Hyperkalemia	16 (12–20)	18 (11–26)	14 (9–19)	19 (13–25)	11 (4–18)[d]
Primary arrhythmia	27 (20–34)	23 (18–27)	22 (17–27)	33 (25–40)	21 (15–26)[d]
Right atrial pressure (mm Hg)					
Hypovolemia	7 (5–8)	7 (5–8)	7 (5–9)[b]	7 (5–9)	11 (7–14)[c,d]
Hyperkalemia	15 (11–19)	16 (13–19)	18 (16–20)	19 (14–23)	16 (10–22)
Primary arrhythmia	14 (12–16)	15 (13–16)	17 (15–19)	15 (13–17)	13 (10–15)

[a]Time of the primary endpoint.
[b]Group differs significantly from the other groups at this time point.
[c]Significant time/group interaction (analysis of variance).
[d]Significant within-group time interaction (analysis of variance).
[e]Hypovolemia differs significantly from primary arrhythmia.

hypercapnia can cause pulmonary vasoconstriction (20, 21). In the present study, the hypovolemia group endured a longer period without ventilation and was more hypoxic and hypercapnic at the onset of cardiac arrest than the other two groups. However, hypoxic pulmonary hypertension resolves rapidly when normoxia is restored (22). Importantly, all animals in this study were ventilated equally during resuscitation, resulting in similar Pa_{O_2} and pH levels across groups, whereas Pa_{CO_2} levels were actually lower in the hypovolemia group.

The similarities in cardiovascular anatomy and physiology (including intracardiac and vascular pressures) between humans and pigs render this species useful for investigating hemodynamic variables (23, 24). The pig model is regarded as the most clinically relevant animal model for clinical translation of new therapies (25, 26).

It has been proposed that cardiac arrest should be considered a continuum of hemodynamic instability, meaning that ultrasonographic findings in hemodynamically unstable patients with spontaneous circulation can be extrapolated to those in cardiac arrest (27–30). However, the lack of spontaneous circulation and performance of chest compressions may alter ultrasonographic findings (31). For instance, in spontaneous circulation, large hemodynamically significant pulmonary embolism can cause RV dilation and severe hypovolemia can cause a reduction in the RV diameter (9, 32). Indeed, this study demonstrated a reduction in both the RV diameter and LV cross-sectional area in severe hypovolemia during spontaneous circulation. However, the RV was dilated beyond baseline levels throughout resuscitation in all groups, demonstrating that evaluating the RV may not be useful for differentiating these causes of cardiac arrest.

In a prior study, we demonstrated RV dilation during resuscitation when cardiac arrest was caused by pulmonary embolism, hypoxia, and primary arrhythmia (8). Overall, it seems that RV dilation may be expected during resuscitation, irrespective of the cause of cardiac arrest. Although these findings need clinical confirmation, they do merit attention from clinicians who assume that RV dilation is associated with pulmonary embolism and a small RV is associated with hypovolemia during resuscitation. Until clinical studies comparing cardiac ultrasound findings during resuscitation with a verified cause of cardiac arrest have been carried out, RV dilation during resuscitation should be interpreted cautiously.

The limitations of this study include the use of healthy adolescent pigs. This limits generalizability to a human cardiac arrest population, which is typically older and with multiple comorbidities. However, the animal model enabled us to study the isolated effect of different causes of cardiac arrest. The animals were anesthetized during the cardiac arrest induction phase and given analgesia during the entire experiment. This is likely to have reduced the stress response normally associated with cardiac arrest and may have influenced our results. Resection of the right rectus abdominis muscle could theoretically have altered abdominal pressure and thus hemodynamics in pigs during resuscitation.

CONCLUSION

The RV was dilated during resuscitation from cardiac arrest caused by hypovolemia, hyperkalemia, and primary arrhythmia. These findings indicate that RV dilation may be inherent to cardiac arrest, rather than being associated with certain

causes of arrest. From the clinical point of view, RV dilation in hypovolemic cardiac arrest is especially interesting, as this finding contradicts a widespread clinical assumption that in hypovolemic cardiac arrest ventricles are collapsed, rather than dilated.

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