Detection of Pulmonary Embolism During Cardiac Arrest—Ultrasonographic Findings Should Be Interpreted With Caution

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Objectives: The aim of this study was to test the hypothesis that the right ventricle is more dilated during resuscitation from cardiac arrest caused by pulmonary embolism, compared with hypoxia and primary arrhythmia.

Design: Twenty-four pigs were anesthetized and cardiac arrest was induced using three different methods. Pigs were resuscitated after 7 minutes of untreated cardiac arrest. Ultrasonographic images were obtained and the right ventricular diameter was measured.

Setting: University hospital animal laboratory.

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

Interventions: Pigs were randomly assigned to cardiac arrest induced by pulmonary embolism, hypoxia, or primary arrhythmia.

Measurements and Main Results: There was no difference at baseline. During induction of cardiac arrest, the right ventricle dilated in all groups ($p < 0.01$ for all). The primary endpoint was right ventricle diameter at the third rhythm analysis: 32 mm (95% CI, 29–36) for pulmonary embolism which was significantly larger than both hypoxia: 23 mm (95% CI, 20–27) and primary arrhythmia: 25 mm (95% CI, 22–28)—the absolute difference was 7–9 mm. Physicians with basic training in focused cardiac ultrasonography were able to detect a difference in right ventricle diameter of approximately 10 mm with a sensitivity of 79% (95% CI, 64–94) and a specificity of 68% (95% CI, 56–80).

Conclusions: The right ventricle was more dilated during resuscitation when cardiac arrest was caused by pulmonary embolism compared with hypoxia and primary arrhythmia. However, the right ventricle was dilated, irrespective of the cause of arrest, and diagnostic accuracy by physicians with basic training in focused cardiac ultrasonography was modest. These findings challenge the paradigm that right ventricular dilatation on ultrasound during cardiopulmonary resuscitation is particularly associated with pulmonary embolism. (*Crit Care Med* 2017; XX:00–00)

Key Words: anoxia; echocardiography; heart arrest; pulmonary embolism; ultrasonography

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Survival from cardiac arrest is unlikely unless a reversible cause is identified and treated (1). Identification of reversible causes is challenging, because time is limited and information obtained from a physical examination is often inadequate (2).

The current resuscitation guidelines from The American Heart Association and The European Resuscitation Council state that focused ultrasonography has potential to identify reversible causes of cardiac arrest (1, 2). However, the International Liaison Committee on Resuscitation state that it is unknown if ultrasonographic findings during cardiac arrest are interpreted correctly and identify the use of ultrasonography during resuscitation as an important knowledge gap (3).

In patients with spontaneous circulation, a dilated right ventricle (RV) is a sign of elevated pulmonary arterial pressure

(4). RV dilation can occur in patients with pulmonary embolism (PE) and is associated with worse outcome (5). This has led to a multitude of publications suggesting that the ultrasonographic finding of RV dilation during resuscitation from cardiac arrest should be interpreted as a sign of PE (6–9).

Experimental studies have demonstrated RV dilation in response to both untreated ventricular fibrillation (VF) and severe hypoxia (10, 11). However, the ultrasonographic presentation of the RV during resuscitation from different reversible causes of cardiac arrest remains to be described.

The aim of this study was to test the hypothesis that the RV is more dilated during resuscitation from cardiac arrest caused by PE, compared with hypoxia and primary arrhythmia.

MATERIALS AND METHODS

Animals and Ethics

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 (27–32 kg) were fasted over night with free access to water. Anesthesia was induced with intramuscular ketamine and midazolam and maintained with fentanyl and sevoflurane. Animals were mechanically ventilated. Details are listed in the **supplemental material** (Supplemental Digital Content 1, http://links.lww.com/CCM/C434).

Surgical Preparation and Monitoring

A perivascular ultrasonic transit time flow probe was fitted on the left common carotid artery to measure blood flow. A pulmonary artery catheter was used to measure mean pulmonary artery pressure (MPAP). Coronary perfusion pressure (CPP) was calculated as the difference between the simultaneously measured aortic and right atrial pressures during the relaxation phase (13). CPP is reported as an average of the 10 compressions preceding each rhythm analysis. An endotracheal tube was placed in the left external jugular vein to provide for injection of pulmonary emboli. Details are listed in the supplemental material (Supplemental Digital Content 1, http://links.lww.com/CCM/C434).

Experimental Protocol

The experimental protocol is shown in **Figure 1*A***. Animals were randomized into three groups:

1) PE: emboli were injected through the tube placed in the left external jugular vein every 4 minutes until cardiac arrest occurred (14). Emboli were formed from autologous venous blood, which was left to coagulate in a cylindrical silica-coated tube (BD Vacutainer; BD, Franklin Lakes, NJ) for 1 hour prior to baseline. Each embolus was 5-cm long and approximately 1 cm in diameter. The first three injections included two emboli given simultaneously; from then on, they were given one at a time.
2) Hypoxia: the tidal volume was halved every 2 minutes until the endotracheal tube was clamped after 6 minutes.
3) Primary arrhythmia: a 9-V direct current was delivered through a bipolar pacing catheter placed temporarily in the RV.

For all groups, cardiac arrest was defined as a pulse pressure below 5 mm Hg or a mean arterial pressure (MAP) below 20 mm Hg. Following 7 minutes of untreated cardiac arrest, resuscitation according to the 2010 European Resuscitation Council guidelines was commenced (15). To prevent animals from obtaining early return of spontaneous circulation (ROSC), and thereby limiting time for ultrasonographic image recording, defibrillation was not attempted before the fifth rhythm analysis. Chest compressions were performed mechanically

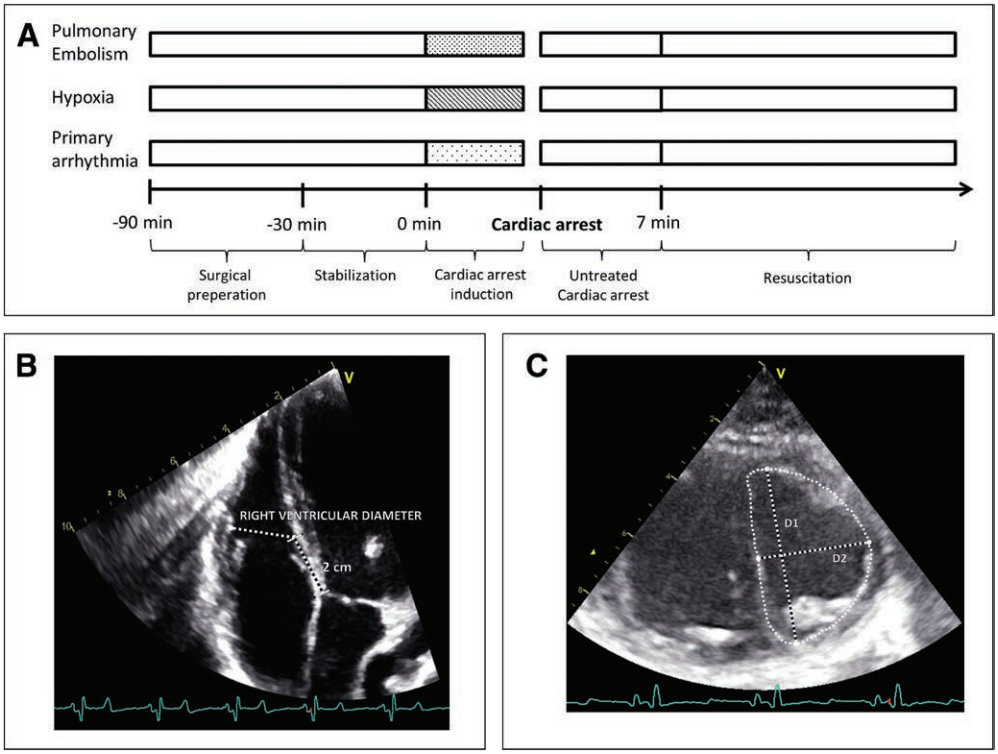

Figure 1. Experimental methods. **A**, Study protocol. **B**, Porcine subcostal five-chamber view. The right ventricular (RV) diameter was determined by: 1) defining a septal reference point by measuring 2 cm along the septum from the aorta and 2) measuring the shortest possible distance from the septal reference point to the lateral wall of the RV. **C**, Porcine parasternal short axis view. The endocardium of the left ventricle was traced and the minor axis parallel (D1) and perpendicular (D2) to the septum was measured. Eccentricity index was defined as D1/D2.

(LUCAS; Physio-Control, Redmond, WA). Ventilations were performed mechanically in volume-controlled modus with a tidal volume of 10 mL/kg, respiration rate of 10 min^{-1}, and an F_{IO_2} of 1.0. ROSC was defined as a MAP above 30 mm Hg for at least 1 minute. Animals were excluded if they achieved ROSC prior to the third rhythm analysis. If animals had not achieved ROSC before the tenth rhythm analysis, the experiment was terminated.

Cardiac Ultrasonography

Subcostal and parasternal ultrasonographic images were obtained at baseline, during induction of cardiac arrest (2-min intervals), at the onset of cardiac arrest, during untreated arrest (2-min intervals), and at each rhythm analysis (2-min intervals). A cardiac transducer was used for subcostal ultrasonography (transducer: M5sc-D; ultrasound machine: Vivid e9 with XDclear; GE Healthcare, Little Chalfont, United Kingdom). To obtain consistent high image quality, the right part of the rectus abdominis muscle and the skin above it were transected immediately caudal to the rib cage, without perforating the thoracic cavity or the peritoneum. The ultrasound probe was positioned at the anterior aspect of the right diaphragm, where the cardiac apex could be palpated. The images corresponded to a human five-chamber apical view. An acceptable image included clear visualization of the aortic valve, septum, and the RV lateral wall (**Fig. 1*B***).

Transverse images of the left ventricle, at the level of the papillary muscles, were obtained with a cardiac transducer from the left parasternal window (transducer: M4S-RS-Cardiac; ultrasonography machine: Vivid S6; GE Healthcare, Little Chalfont, United Kingdom) (**Fig. 1*C***).

Outcome Measures

The primary study endpoint was RV diameter at end diastole. After having evaluated two different methods (**Supplemental Fig. 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/C434), the following method provided the best interobserver agreement: from the septal aspect of the aortic annulus, a point 20 mm apically along the septum was determined. From this point, the shortest distance to the lateral wall of the RV was measured and defined as the RV diameter (**Fig. 1*B***).

Left ventricular end-diastolic area was determined by tracing the endocardium, including papillary muscles and trabeculations in the left ventricular cavity. The eccentricity index was calculated as previously described (16). A subset of 20 images was reanalyzed resulting in an intraobserver variability of –1 mm (95% limits of agreement, –4 to 2). Another subset of images was analyzed by author P.C., resulting in an interobserver variability of –1 mm (95% limits of agreement, –3 to 2). Image analysis was performed using EchoPAC (GE Healthcare, Little Chalfont, United Kingdom) and OsiriX (Pixmeo, Geneve, Switzerland).

Substudy–Clinical Significance

To evaluate whether a difference in RV diameter between groups was clinically relevant, we conducted a substudy to investigate if a physician would be able to differentiate different degrees of RV dilatation. Physicians with basic training in focused cardiac ultrasonography, who were either specialist anesthesiologists or in their final year of specialist training, were shown porcine ultrasound images obtained in the study. In the images, the RV diameter was either 32 ± 1 mm (corresponding to the mean value at third rhythm analysis in the PE group) or 23 ± 1 mm (corresponding to the mean value at the third rhythm analysis in the hypoxia group). The physicians were asked to rate if they found the RV on the ultrasound images to be "severely dilated" or "moderately dilated." In accordance with the Danish Act on Research Ethics Review of Health Research Projects, Act number 593 of July 14, 2011 section 14, approval from the Ethics Committee was not required for this substudy. Details are listed in the supplemental material (Supplemental Digital Content 1, http://links.lww.com/CCM/C434).

Statistical Analysis

It was predetermined to analyze the data in three phases: 1) induction phase, 2) untreated cardiac arrest phase, and 3) resuscitation phase. 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 baseline values, mean values at predetermined time points, and mean levels over time were analyzed using one-way ANOVA followed by pairwise comparisons, using Sidak corrections. Paired student *t* test was used for within group comparisons. Only data from the first to the fifth rhythm analysis were analyzed because of an uneven number of animals in each group beyond the fifth rhythm analysis due to ROSC in some animals. 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 Calculations. Based on pilot studies ($n = 6$) and ANOVA one-way power analysis, we estimated that 24 animals (eight in each group) were sufficient to detect a difference between groups at third rhythm analysis. Details are listed in the supplemental material (Supplemental Digital Content 1, http://links.lww.com/CCM/C434).

Statistical Analysis for Substudy—Clinical Significance. The ability of the clinicians to correctly identify the severely enlarged RV was quantified as sensitivity and specificity. A multilevel mixed-effects linear regression model was used to account for correlation between observations from the same ultrasound image and the same observer.

RESULTS

Overall Model

A total of 36 animals were used in the study. Three animals were excluded prior to randomization; one because of VF occurring during preparation and two because of pulmonary infections. Nine animals were excluded after randomization, all due to ROSC occurring prior to the third rhythm analysis (hypoxia, 4; PE, 5). We observed no difference in RV diameter in animals

that were included or excluded after randomization at neither baseline nor time of cardiac arrest. Overall 24 animals, eight in each group, were included in the final analysis. Time to cardiac arrest was 11 minutes 6 seconds (95% CI, 10 min 24 s to 11 min 48 s) in the PE group and 11 minutes 0 seconds (95% CI, 9 min 24 s to 12 min 30 s) in the hypoxia group. In both the PE and hypoxia group, pulseless electrical activity (PEA) was the cardiac rhythm at the time of cardiac arrest in all animals.

Ultrasonography

RV Diameter. Results concerning RV diameter are shown in **Figure 2** and **Tables 1** and **2**. There was no difference in RV diameter at baseline ($p = 0.34$). RV diameter increased during the induction phase in both the PE and hypoxia group ($p < 0.001$). At the time of cardiac arrest, RV diameter was larger in the PE group than in the hypoxia group ($p = 0.002$). Induction of primary arrhythmia caused an immediate increase in the RV diameter compared with baseline ($p = 0.007$). During untreated arrest, RV diameter means were parallel in the PE and hypoxia group, with a higher mean level in the PE group ($p = 0.01$) (Fig. 2). During resuscitation, RV mean diameter was parallel for all groups, with a higher mean level in the PE group than in both the hypoxia and primary arrhythmia group ($p < 0.001$). At the third rhythm analysis during resuscitation, the RV diameter was significantly larger in the PE group compared with both the hypoxia ($p = 0.001$) and primary arrhythmia group ($p = 0.005$). The absolute difference between the means was $\text{difference}_{(\text{PE} - \text{primary arrhythmia})} = 8$ mm (95% CI, 3–12) and $\text{difference}_{(\text{PE} - \text{hypoxia})} = 9$ mm (95% CI, 4–14).

Eccentricity Index and Left Ventricular Area. The end-diastolic eccentricity index increased during induction of cardiac arrest in both the PE and hypoxia group (Table 1). At third rhythm analysis, there was no significant difference between the groups ($p = 0.054$) (Table 2).

Left ventricular end-diastolic area decreased during induction of cardiac arrest in both the PE ($p < 0.001$) and hypoxia group ($p < 0.001$) (Table 1). At the third rhythm analysis, no difference existed between the groups ($p = 0.32$) (Table 2).

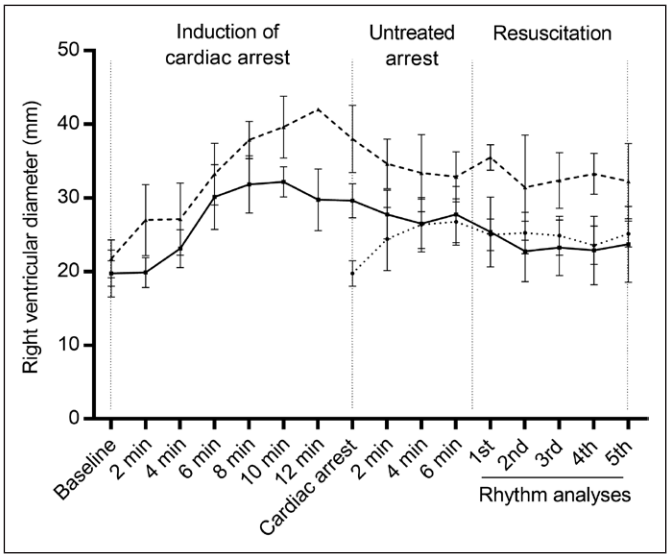

Figure 2. Mean values of the right ventricular diameter. Error bars indicate 95% CIs.

Arterial Blood Gas Values and Hemodynamics During Resuscitation. End-tidal expiratory Co_2 ($Etco_2$) was lower in the PE group than in the hypoxia and primary arrhythmia group at the third rhythm analysis ($p < 0.001$). $Paco_2$ was higher in the PE group than in the two other groups at third rhythm analysis ($p < 0.02$) (**Table 3**). Data regarding carotid blood flow and CPP during resuscitation are shown in **Table 2**, and data regarding MAP, MPAP, and carotid blood flow during induction of cardiac arrest are shown in **Supplemental Table 1** (Supplemental Digital Content 2, http://links.lww.com/CCM/C435).

ROSC. Among animals included in the final analysis, ROSC was achieved in zero of eight in the PE group, two of eight in the hypoxia group, and seven of eight in the primary arrhythmia group. Among the nine animals excluded from the final analysis because of early ROSC, eight achieved ROSC after the start of resuscitation but before the third rhythm analysis. A post hoc analysis including these animals was performed to investigate differences in RV diameter following ROSC. Ten minutes after ROSC, the median RV diameter was 30 mm (interquartile range [IQR], 28–33) for PE and 18 mm (IQR, 17–21) for hypoxia.

Results From Substudy—Clinical Significance. Twenty-two physicians were eligible for inclusion. Eighteen were included, and four did not complete the substudy because of clinical duties. The physicians tested could identify the severely dilated RV with a sensitivity of 79% (95% CI, 64–94) and a specificity of 68% (95% CI, 56–80).

Relationship Between RV Diameter and Volume. In a substudy, including four animals, there was a highly significant positive relationship between RV diameter evaluated by ultrasound and RV volume evaluated by CT. Details are listed in the supplemental material (Supplemental Digital Content 1, http://links.lww.com/CCM/C434).

DISCUSSION

In a porcine model of cardiac arrest caused by PE, hypoxia, and primary arrhythmia, the RV was dilated during resuscitation in all groups when compared with baseline. The RV was more dilated during resuscitation when cardiac arrest was caused by PE when compared with hypoxia and primary arrhythmia, but discrimination between a severely dilated and moderately dilated RV by clinicians with basic training in focused cardiac ultrasonography was modest.

Several clinical protocols and case reports on focused cardiac ultrasonography during resuscitation suggest that RV dilation should be interpreted as a sign of PE (6–9). Our study demonstrates that RV dilation is present during resuscitation, not only when cardiac arrest is caused by PE but also hypoxia and primary arrhythmia.

Although RV dilation occurs in all our experimental groups during resuscitation, the RV diameter was statistically larger in the PE group. We found that clinicians, with basic focused

TABLE 1. Ultrasonographic Parameters During Induction of Cardiac Arrest–Means (95% CIs)

Outcome Measure	Baseline	2 min	4 min	6 min	8 min	10 min	12 min	Cardiac Arrest
Right ventricular diameter, mm								
Primary arrhythmia	20 (18–22)	–	–	–	–	–	–	–
Hypoxia	20 (17–23)	20 (18–22)	23 (21–26)	30 (26–35)	32 (28–36)	32 (30–34)	30 (26–34)	30 (27–32)[a]
PE	22 (19–24)	27 (22–32)	27 (22–32)	33 (29–37)	38 (35–40)	40 (36–44)	42 (–)	38 (33–43)[b]
End-diastolic eccentricity index								
Primary arrhythmia	1.0 (1.0–1.1)	–	–	–	–	–	–	–
Hypoxia	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.6 (1.1–2.1)	2.1 (1.5–2.7)	2.2 (1.5–2.9)	1.7 (1.3–2.2)	1.5 (0.6–2.5)	1.8 (1.4–2.2)[a]
PE	1.1 (1.0–1.2)	1.5 (1.1–1.9)	1.9 (0.8–2.9)	2.0 (1.3–2.6)	2.5 (1.9–3.1)	3.0 (2.6–3.4)	3.3 (–)	2.8 (2.2–3.5)[b]
Left ventricular end-diastolic area, cm^2								
Primary arrhythmia	14 (12–16)	–	–	–	–	–	–	–
Hypoxia	12 (11–13)	12 (10–15)	9 (6–11)	7 (3–10)	6 (4–8)	8 (6–10)	9 (3–14)	8 (5–11)[a]
PE	12 (11–14)	9 (5–13)	8 (5–11)	8 (5–11)	5 (3–6)	3 (2–4)	3 (–)	4 (3–5)[c]

PE = pulmonary embolism.
[a]Groups differ significantly at the time of cardiac arrest.
[b]Significant difference in mean levels.
[c]Significant time/group interaction (analysis of variance).

cardiac ultrasonography training, could differentiate an RV dilation corresponding to that of the PE group from RV dilation corresponding to the hypoxia group with a sensitivity of 79% and a specificity of 68%. Ultrasound images were presented on a laptop in an office setting and the ability to detect a difference would most likely be lower in a clinical setting. In addition, the difference in RV dilation in a human cardiac arrest population could be less pronounced due to a larger baseline variation (17). Even if differences in RV dilation reported here could be applied to a human population, the utility of cardiac ultrasonography for diagnosing PE is unclear, as other conditions not included in this study could cause a similar RV dilation. Apart from their standardized basic training, the clinician's level of expertise in focused cardiac ultrasonography was varied. This may reflect the "real world" situation.

A high pre-test probability would increase the positive predictive value of focused cardiac ultrasonography. However, clinical and biochemical characteristics of patients with PE are nonspecific (18), and very little is known about clinicians' ability to identify reversible causes of cardiac arrest based on patient history (19).

The post hoc analysis of data from animals excluded from the main analysis due to early ROSC implies that the RV may be more dilated following cardiac arrest caused by PE than by hypoxia. This finding may serve as a hypothesis for future studies.

In the present study, significantly reduced Et_{CO_2} levels during resuscitation were observed when cardiac arrest was caused by PE compared with hypoxia and primary arrhythmia. Conversely, Pa_{CO_2} was significantly higher when cardiac arrest was caused by PE, indicating that Co_2 was produced, but not exhaled due to perfusion-ventilation mismatch. A retrospective study by Heradstveit et al (20) showed a lower Et_{CO_2} in patients with cardiac arrest caused by PE irrespective of outcome. These results may suggest that Et_{CO_2} levels and maybe arterial/venous Co_2 levels could improve discrimination between different reversible causes. This should be investigated in a future study.

Septal shift is considered a sign of acute increase in pulmonary pressure that could indicate the presence of PE in patients with spontaneous circulation (21). We quantified this by measuring the left ventricular eccentricity index. At the onset of cardiac

TABLE 2. Ultrasonographic Parameters During Cardiac Arrest–Means (95% CIs)

	Untreated Cardiac Arrest			Resuscitation				
Outcome Measure	2 min	4 min	6 min	First Rhythm Analysis	Second Rhythm Analysis	Third Rhythm Analysis	Fourth Rhythm Analysis	Fifth Rhythm Analysis
Right ventricular diameter, mm								
Primary arrhythmia	25 (21–29)	27 (23–30)	27 (24–30)	25 (23–27)	25 (22–28)	**25 (22–28)**	24 (21–26)	25 (23–27)
Hypoxia	28 (24–31)	27 (23–30)	28 (24–32)	25 (21–30)	23 (19–27)	**23 (20–27)**	23 (18–28)	24 (19–28)
PE	35 (24–31)	33 (28–39)	33 (30–36)[a]	36 (34–37)	32 (26–38)	**32 (29–36)**[b]	33 (31–36)	32 (27–37)[c]
End-diastolic eccentricity index								
Primary arrhythmia	1.4 (1.2–1.6)	1.3 (1.1–1.6)	1.4 (1.3–1.6)[d]	1.2 (1.0–1.3)	1.1 (1.0–1.3)	**1.1 (1.0–1.3)**	1.4 (1.2–1.6)	1.3 (1.1–1.6)[e]
Hypoxia	1.6 (1.3–1.8)	1.4 (1.2–1.5)	1.3 (1.2–1.4)	1.3 (1.1–1.5)	1.2 (1.0–1.3)	**1.2 (1.1–1.4)**	1.6 (1.3–1.8)	1.4 (1.2–1.5)
PE	2.4 (2.0–2.8)	2.0 (1.6–2.5)	1.7 (1.4–2.0)[f]	1.9 (1.6–2.2)	1.6 (1.0–2.2)	**1.5 (1.1–1.9)**	1.5 (1.2–1.7)	1.2 (1.0–1.4)[g]
Left ventricular end-diastolic area, cm^2								
Primary arrhythmia	11 (8–13)	10 (8–12)	11 (9–13)[d]	8 (6–10)	8 (6–10)	**8 (6–9)**	9 (6–11)	8 (5–10)[g]
Hypoxia	9 (7–11)	10 (8–11)	11 (10–13)[f]	10 (8–11)	8 (6–11)	**6 (3–9)**	5 (2–8)	5 (2–9)
PE	5 (4–7)	7 (5–10)	9 (7–10)[f]	7 (5–8)	6 (6–11)	**8 (7–9)**	7 (6–9)	8 (7–10)
Coronary perfusion pressure, mm Hg								
Primary arrhythmia	–	–	–	30 (21–38)	27 (16–38)	**26 (13–38)**	36 (19–52)	24 (14–34)
Hypoxia	–	–	–	23 (14–32)	17 (9–25)	**15 (9–21)**	14 (9–19)	12 (7–17)
PE	–	–	–	21 (4–39)	26 (13–40)	**12 (6–19)**	16 (5–27)	12 (7–17)
Carotid blood flow, mL/min								
Primary arrhythmia	3 (2–4)	2 (0–4)	1 (0–2)	73 (44–103)	83 (58–107)	**79 (36–122)**	77 (45–108)	69 (42–97)
Hypoxia	2 (−2 to 6)	0 (−1 to 1)	−1 (−2 to 1)	40 (22–58)	36 (17–55)	**42 (29–56)**	33 (11–55)	35 (21–49)
PE	4 (−3 to 10)	1 (−1 to 3)	−1 (−2 to 1)	58 (15–102)	64 (23–106)	**53 (15–90)**	42 (18–66)	47 (22–71)

PE = pulmonary embolism.
[a]Significantly higher mean level during untreated cardiac arrest.
[b]Group differs significantly from the other groups at this time point.
[c]Significantly higher mean level during resuscitation.
[d]Significant time/group interaction (analysis of variance) during untreated cardiac arrest.
[e]Significant time/group interaction (analysis of variance) during resuscitation.
[f]Significant within group time interaction (analysis of variance) during untreated cardiac arrest.
[g]Significant within group time interaction (analysis of variance) during resuscitation.
Boldface values indicate values are from the time of the primary endpoint (third rhythm analysis).

TABLE 3. Arterial Blood Gas Values During Resuscitation–Means (95% CIs)

Outcome Measure	Baseline	Onset of Cardiac Arrest	First Rhythm Analysis	Third Rhythm Analysis	Fifth Rhythm Analysis
pH					
Primary arrhythmia	7.43 (7.40–7.46)	–	7.29 (7.24–7.33)	7.27 (7.23–7.31)[a]	7.21 (7.18–7.23)[b,c]
Hypoxia	7.42 (7.39–7.45)	7.16 (7.11–7.20)[d]	7.13 (7.08–7.18)	7.11 (7.06–7.17)	7.08 (6.96–7.19)
PE	7.41 (7.37–7.45)	7.19 (7.15–7.22)[d]	7.13 (7.02–7.23)	7.03 (6.98–7.08)	6.96 (6.94–6.99)[c]
Pao_2, kPa					
Primary arrhythmia	21.0 (18.1–23.9)	–	16.7 (8.1–25.3)	27.6 (18.5–36.7)[e]	17.3 (8.1–26.5)[f]
Hypoxia	19.5 (16.9–22.2)	1.0 (0.7–1.3)[d]	10.1 (5.2–15.1)	11.5 (6.6–16.4)	14.8 (1.3–28.2)
PE	19.5 (17.5–21.6)	3.7 (3.02–4.29)[a,d]	7.7 (5.7–9.8)	6.6 (4.7–8.5)	6.8 (4.8–8.9)[f]
$Paco_2$, kPa					
Primary arrhythmia	5.8 (5.6–5.9)	–	7.6 (6.7–8.5)	6.6 (5.8–7.4)[a]	7.2 (6.6–7.8)[f]
Hypoxia	5.9 (5.6–6.3)	11.7 (10.5–12.9)[d]	9.8 (8.8–10.9)	8.7 (7.4–10.0)	7.9 (5.5–10.4)
PE	6.1 (5.6–6.6)	9.4 (8.3–10.49)[a,d]	10.1 (8.2–12.0)	11.5 (9.9–13.1)	12.0 (10.7–13.2)[c]
End-tidal expiratory Co_2, kPa					
Primary arrhythmia	5.4 (5.0–5.7)	–	5.3 (4.6–6.0)	4.8 (4.1–5.6)	4.2 (2.9–5.4)
Hypoxia	5.5 (5.2–5.8)	–	5.2 (4.0–6.4)	4.6 (3.9–5.3)	3.5 (2.3–4.7)
PE	5.7 (5.2–6.3)	–	3.5 (2.2–4.7)	2.5 1.6–3.4)[e]	2.6 (1.8–3.3)[g]

kPa = kilopascal, PE = pulmonary embolism.
[a]All groups differ significantly at this time point.
[b]All groups differ significantly in mean levels during resuscitation.
[c]Significant within group time interaction (analysis of variance).
[d]Significantly different from baseline.
[e]This group differs significantly from the two other groups, at this time point.
[f]Significant time/group interaction (analysis of variance).
[g]Group differs significantly from the two others in mean level.

arrest, the eccentricity index was higher in the PE group, but during both untreated cardiac arrest and resuscitation, the eccentricity index in the PE group decreased toward the level of the two other groups. Thus, septal shift or D-shaping of the left ventricle could be a less sensitive sign of PE as resuscitation progresses.

A few studies have attempted to correlate ultrasonographic findings during resuscitation to a verified cause of cardiac arrest (22–24). These studies all report on transesophageal echocardiography (TEE). In one sample of 25 patients with PEA, 14 had a significantly enlarged RV, but PE could only be confirmed in nine cases by either direct visualization with TEE or autopsy (22). In another sample of patients, TEE correctly identified the causes of cardiac arrest in nine of 10 cases (23). Finally, in a study by Van der Wouw et al (24), six of 48 patients were diagnosed with PE during resuscitation, based on dilation of the RV and poor filling of the left ventricle. The diagnosis could be confirmed by autopsy in two patients and was rejected in one patient.

Our study has several limitations. We used healthy adolescent pigs which limit the clinical translation as patients in cardiac arrest are typically older and with multiple comorbidities. It was not possible to blind the ultrasonographer to the cause of cardiac arrest. However, image acquisition was standardized, and experimental group and time of arrest acquisition were blinded during analysis. The animals were anesthetized during the induction phase and given analgesia during the entire experiment. This may have reduced the stress response normally associated with cardiac arrest and thus influenced our results. Another limitation was the use of the primary arrhythmia as controls, because most cardiac arrests are caused by myocardial infarction.

CONCLUSION

In a porcine model of cardiac arrest caused by PE, hypoxia, or primary arrhythmia, the RV was more dilated when cardiac arrest was caused by PE. However, the RV was dilated during resuscitation, irrespective of the cause of arrest, and detection of a dilated RV by clinicians with basic training in cardiac ultrasonography was modest. These findings challenge the

paradigm that a dilated RV during resuscitation is particularly associated with PE and suggests that the ultrasonographic findings of RV dilation during cardiac arrest should be interpreted with caution.

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