Magnetic Resonance Imaging During Untreated Ventricular Fibrillation Reveals Prompt Right Ventricular Overdistention Without Left Ventricular Volume Loss

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Background—Most out-of-hospital ventricular fibrillation (VF) is prolonged (>5 minutes), and defibrillation from prolonged VF typically results in asystole or pulseless electrical activity. Recent visual epicardial observations in an open-chest, open-pericardium model of swine VF indicate that blood flows from the high-pressure arterial system to the lower-pressure venous system during untreated VF, thereby overdistending the right ventricle and apparently decreasing left ventricular size. Therefore, inadequate left ventricular stroke volume after defibrillation from prolonged VF has been postulated as a major contributor to the development of pulseless rhythms.

Methods and Results—Ventricular dimensions were determined by MRI for 30 minutes of untreated VF in a closed-chest, closed-pericardium model in 6 swine. Within 1 minute of untreated VF, mean right ventricular volume increased by 29% but did not increase thereafter. During the first 5 minutes of untreated VF, mean left ventricular volume increased by 34%. Between 20 and 30 minutes of VF, stone heart occurred as manifested by dramatic thickening of the myocardium and concomitant substantial decreases in left ventricular volume.

Conclusions—In this closed-chest swine model of VF, substantial right ventricular volume changes occurred early and did not result in smaller left ventricular volumes. The changes in ventricular volumes before the late development of stone heart do not explain why defibrillation from brief duration VF (<5 minutes) typically results in a pulsatile rhythm with return of spontaneous circulation, whereas defibrillation from prolonged VF (5 to 15 minutes) does not. (Circulation. 2005;111:1136-1140.)

Key Words: cardiopulmonary resuscitation ■ heart arrest ■ hemodynamics ■ magnetic resonance imaging ■ ventricular fibrillation

Each year, >600 000 people in the United States and Europe are victims of sudden cardiac arrest, commonly caused by ventricular fibrillation (VF). Because the vast majority of these deaths occur out of hospitals, VF tends to be prolonged before defibrillation is available. Whereas defibrillation from brief VF (<5 minutes) typically results in return of spontaneous circulation, defibrillation from prolonged VF (5 to 15 minutes) typically results in asystole or pulseless electrical activity. Not surprisingly, outcomes from prolonged untreated VF are dismal despite successful defibrillation (ie, successful termination of fibrillation).

Recent observations by Steen and colleagues indicate that blood flows from the high-pressure arterial system to the lower-pressure venous system during a 6.5-minute period of untreated VF in swine with an open chest and open pericardium. Aortic pressure decreased abruptly during the first 30 seconds of VF and then slowly over the next 6 minutes. Moreover, right atrial pressure increased from <5 to ≈ 18 mm Hg over the first few minutes of VF and then slowly decreased to aortic pressure (≈ 10 mm Hg) after 5 to 6 minutes of VF. From direct visualization and video recording of the epicardial surface of the heart, they also noted that the right ventricle (RV) became substantially distended over the first 3 minutes of VF and apparently further distended over the next few minutes of VF. Concomitant with the RV enlargement, the left ventricle (LV) appeared to progressively decrease in size, presumably because of ventricular interdependence. Therefore, these authors and others have concluded that the poor outcomes from prolonged VF may result from inadequate LV filling during VF, leading to inadequate stroke volume and inadequate coronary blood flow immediately after fibrillation is terminated. In addition, they have
suggested that provision of chest compressions before defibrillation can pump blood from the RV to the LV, improving LV preload and thereby explaining the superiority of CPR first (chest compressions before defibrillation) over defibrillation first for prolonged VF.\textsuperscript{7–10}

Because pericardial and chest wall constraints may influence hemodynamics during untreated VF, we chose to further evaluate these issues in a more clinically relevant closed-chest model of prolonged swine VF. In addition, we evaluated LV and RV internal dimensions directly by state-of-the-art MRI methods rather than extrapolating from epicardial observations.\textsuperscript{11}

\section*{Methods}

\subsection*{Animal Preparation and Experimental Protocol}

The University of Arizona Institutional Animal Care and Use Committee approved the experimental protocol. Six female swine (27±1 kg) were subjected to masked anesthesia with isoflurane, followed by oral endotracheal intubation. They were mechanically ventilated with a rate- and volume-regulated ventilator (Narkomed 2A, North American Drager) on a mixture of room air and titrated isoflurane (\textsim1\% to 2.5\%), and the end-tidal carbon dioxide was maintained at 40±2 mm Hg.

After a surgical plane of anesthesia was obtained, introducer sheaths were placed in the right internal jugular vein and right carotid artery by cut-down technique. A high-fidelity, solid-state, micromamometer-tipped catheter (MPC-500, Millar Instruments) was advanced into the thoracic aorta for initial pressure monitoring. The animal was then moved to the MRI room and placed in an MRI scanner. After MRI measurements in normal sinus rhythm to set up the appropriate imaging planes for evaluation during VF, a pacing catheter electrode was placed temporarily into the RV, and VF was induced with 100-Hz alternating current delivered in the RV, catheter electrode was placed temporarily into the RV, and VF was confirmed by the ECG waveform. Assisted ventilation was discontinued, and the pacing wire was removed.

\subsection*{Measurements}

MRI was performed on a 1.5-T GE Signa NV-CV/i scanner (GE Medical Systems). A 4-element phased-array coil was used for signal detection. Data were acquired by a steady-state free-precession pulse sequence. Pulse sequence parameters were as follows: repetition time, 3.7 ms; echo time, 1.6 ms; α = 45°; acquisition matrix size, 224×224; field of view, 36×27 cm\textsuperscript{2}; slice thickness, 6 mm; and slice gap, 0 mm. Before fibrillation, a set of short-axis views was acquired at various phases during the cardiac cycle (20 phases) with retrospective ECG gating. A total of 16 to 19 slices were acquired, covering the heart from just beyond the LV apex through the entire LV and part of the aorta. After VF, the pulse sequence was set to acquire data at a single phase. In this manner, data through the same 16 to 19 slices were acquired in 10.5 to 12.5 seconds (acquisition time per slice, 658 ms). Data collection started immediately after the initiation of VF and continued every 30 seconds for 30 minutes. Data were transferred to a workstation for volume calculation (CMR Tools).

The endocardium of the LV and RV was manually traced, and LV and RV volumes were calculated at each time point with Simpson’s method.\textsuperscript{12} Interventricular septum thickness was measured anteriorly to avoid the papillary muscles.

\subsection*{Data Analysis}

More than 8000 individual images were analyzed. Comparisons of continuous variables such as mean ventricular volumes and interventricular septum widths were evaluated by repeated-measures ANOVA and are described as mean±SEM. Interventricular septum width during normal sinus rhythm was compared with the width during the initial VF measurement by linear regression analysis. All statistical analyses were performed with Stata 8 (Stata Corp LP) and StatView 5.0 (SAS Institute, Inc) software.

\section*{Results}

The most important findings are shown in the Table and Figure 1. Within 1 minute of untreated VF, mean RV volume rapidly increased by 29\% compared with initial VF images but did not increase thereafter (Figure 1 and the Table). During the first 5 minutes of untreated VF, mean LV volume increased by 34\% compared with the initial VF images (Figure 1 and the Table). Ventricular septum width decreased at 5 to 20 minutes of VF compared with the width when VF was initially induced (the Table). Between 20 and 30 minutes of untreated VF, mean LV volume dramatically shrank, and the mean interventricular width markedly thickened (the Table and Figures 1 and 2).

Ventricular measurements during normal sinus rhythm are included in the Table. The interventricular septal width during the initial VF measurement was closely correlated with the width in normal sinus rhythm ($y=2.36+0.72x$; $R^2=0.93$; $P<0.01$).

Figure 2 is a short-axis view of the RV and LV through the same midventricular slice over time in 1 animal, thereby providing a graphic demonstration of these changes during 30 minutes of untreated VF. The quantitative changes noted above are clearly exhibited.

\section*{Discussion}

This study establishes that RV volume can increase substantially during the first minute of untreated VF and remain relatively constant over the next 20 minutes in a closed-chest model of swine VF. Moreover, LV volumes were not diminished through interventricular interaction during the first 20 minutes of untreated VF. Instead, the LV volume also increased during untreated VF; however, the time course of LV dilation was slower than the RV dilation. In addition, the interventricular septum became thinner during those first 20
minutes of untreated VF, most likely because of stretch from increased ventricular volumes.

Our observations and the findings of Steen et al.\textsuperscript{1} are consistent with the observation of Guyton et al.\textsuperscript{13} in the 1950s that flow continues to occur after cardiac arrest until there is no pressure gradient between the arteries and veins.\textsuperscript{13} As noted earlier, Steen et al. demonstrated the time course of aortic and right atrial pressure changes during 6.5 minutes of untreated closed-chest VF in swine using fluid-filled catheters. We retrospectively reviewed aortic and right atrial pressure data measured by high-fidelity micromanometer-tipped catheters during 7 minutes of untreated closed-chest VF from a previous experiment,\textsuperscript{14} and our vascular pressure data are similar to theirs (Figure 3). These pressure changes are apparently the driving force for the abrupt increases in RV dimensions during the first minute of VF.

![Figure 1](image1.png)

**Figure 1.** A, Time course of relative RV and LV volumes during 30 minutes of untreated VF in 6 pigs. Each line represents 1 pig. All volumes were “zeroed” to respective initial VF ventricular volumes. Time 0 refers to time VF was induced. B, Time course of mean ventricular volumes (mean±SEM) during untreated VF. *Ventricular volume differs from that at time 0; \( P < 0.05 \).
The open-chest epicardial observations of Steen et al were interpreted as evidence that the LVs became progressively smaller during prolonged VF. They also noted that after defibrillation the “less-than-normal sized LVs were seen to contract...but without creating pressure in the intrathoracic aorta.” They and others have concluded that the poor outcomes from prolonged VF may result from inadequate LV filling, leading to inadequate stroke volume and inadequate coronary blood flow immediately after defibrillation.1,5,6 Our model was closed chest rather than open chest, and we directly measured ventricular volumes and myocardial thickness. Open-chest epicardial observations provide excellent visualization of the anterior RV but less clear visualization of the posterior LV. In contrast to the interpretations from the epicardial observations by Steen and colleagues in their open-chest and open-pericardium model, we did not observe any decreases in LV dimensions until the changes in ischemic contracture, “stone heart,” after 20 to 30 minutes of VF.15–19 Instead, LV volume increased during the first 5 minutes of VF, presumably as a result of flow from the higher-pressure pulmonary arteries to the lower-pressure left atrium and ventricle. The time course of LV volume increases was delayed compared with the RV changes. We speculate that this delay occurred because the LV is less compliant than the RV and because the pressure differences between the pulmonary artery and left heart are less than those between the aorta and the right heart. Our findings cannot directly address whether LV volume decreases occur during untreated VF in humans. Nevertheless, these data clearly refute their occurrence in a clinically relevant closed-chest swine model of untreated VF.

The most remarkable finding of Steen and colleagues1 was the observation that the RV distended most dramatically in the first few minutes of VF, with less apparent change in size for up to 6.5 minutes. We hypothesized that pericardial and chest wall constraints would result in substantial differences. In particular, we assumed that the RV would fill more slowly and would not enlarge as much as in the open-chest model of Steen et al. Because our ventricular volume measurements were direct and theirs were indirect, comparing our data with prompt preshock and/or postshock CPR is provided.3,4,9,10,21 Although it has been postulated that these pulseless rhythms may be due to RV overdistention and inadequate LV preload, our data argue strongly against this mechanism. Our findings establish that RV overdistention occurred during the first minute of untreated VF and that LV volumes did not decrease concomitantly with RV overdistention. Therefore, the changes in ventricular volumes before the late development of stone heart do not explain why defibrillation from brief VF typically results in a pulsatile rhythm with return of spontaneous circulation, whereas defibrillation from prolonged VF does not.

Use of Simpson’s method and the MRI technique applied in this work (ie, steady-state free precession) is well established and precise for measuring LV and RV volumes during normal sinus rhythm.22–26 The MRI technique provides ventricular measurements within 5% of the true gross anatomic measurements at autopsy.24,26 We have adapted this technique during VF. Extrapolating the accuracy and precision of this technique from normal sinus rhythm has face validity. Use of the technique is further supported by the clarity of the images and similarities in RV volume data from this experiment and the data of Steen et al obtained with different techniques. In addition, the interventricular septum width measurements with MRI were essentially the same during normal sinus rhythm compared with initial VF. LV volumes during initial VF were within the range of the end-systolic and end-diastolic volumes during normal sinus rhythm; however, the initial VF volumes were sometimes closer to the end-systolic volumes and sometimes closer to the end-diastolic volumes, apparently depending on when VF was induced in that animal. In contrast to LV volumes, RV volumes in VF were always higher than those in normal sinus rhythm, presumably because the RV was promptly distending even during the 10.5 to 12.5 seconds required to capture the initial VF MRI ventricular volume images.

As with all animal studies, caution is warranted with regard to direct extrapolation to humans. These animals were young, healthy, anesthetized, and free of atherosclerotic disease. The time course of these phenomena among humans in VF may be different. In addition, the swine weighed ∼27 kg, much smaller than a typical adult. Nevertheless, 25- to 35-kg swine are the animal model of choice for cardiac arrest and CPR studies because of their similarity to adults in terms of chest wall size and configuration and coronary artery anatomy.11,14,20,21,27–29

In conclusion, this study demonstrates that both RV and LV volumes increase substantially during the first minutes of untreated VF in swine with closed chest and closed pericardium. The implications of these findings for resuscitation from VF deserve further investigation.

References
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