Published in final edited form as:

Resuscitation. 2008 September ; 78(3): 355–358. doi:10.1016/j.resuscitation.2008.04.002.

Post-Resuscitation Hemodynamics and Relationship to the Duration of Ventricular Fibrillation

James J. Menegazzi, PhD, Ramiro Ramos, MD, Henry E. Wang, MD, MPH, and Clifton W. Callaway, MD, PhD

Department of Emergency Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

Abstract

Objective—We have observed consistent hemodynamic patterns after restoration of spontaneous circulation (ROSC) after ventricular fibrillation (VF) cardiac arrest. We sought to characterize the time-course of these patterns, and to determine whether these differed based on duration of the VF insult.

Methods—We performed a retrospective review of data from a randomized animal experiment that was conducted in an AAALAC-approved animal laboratory. We used mixed-breed domestic swine of either sex. Animals were anesthetized and instrumented for continuous recording of ECG and blood pressures. VF was induced electrically and allowed to progress for various times ranging from brief (22s) to moderate (less than 3 minutes) to prolonged (3 to 10 minutes). All animals were initially shocked (150J) up to three times. If ROSC was not achieved on the 3 initial shocks, a standardized treatment protocol was followed. We defined cardiovascular collapse as a SBP < 90 mmHg sustained for one minute. For statistical purposes, we classified animals as having VF of <3 minutes, or >3minutes duration. Data were analyzed with Fisher's exact test and survival analysis.

Results—A hyperdynamic phase, consisting of very high blood pressures and tachycardia, was seen in all animals immediately after ROSC. This lasts from 1 to 4 minutes. Post-resuscitation cardiovascular collapse occurred in 2/7 (29%) animals in the <3 minute group and 13/14 in the >3 minute group (93%) $p=0.006$. Onset of cardiovascular collapse was highly related to duration of VF (log-rank $p=0.004$).

Conclusions—There are two distinct phases of hemodynamic change after resuscitation of VF. The first phase is a brief hyperdynamic phase. The second phase is either stabilization or cardiovascular collapse. When VF is brief, blood pressures often return to normal without exogenous support. When VF was prolonged animals were rescued with exogenous pressor. Healthcare providers should be prepared to provide pressor support for patients having ROSC after prolonged VF.

Corresponding Author: James J. Menegazzi, PhD, Department of Emergency Medicine, 230 McKee Place, Suite 500, Pittsburgh, PA 15213, Phone: 412.647.7992, Fax: 412.647.4670, Email: menegazz+@pitt.edu.

Presented: National Association of EMS Physicians Annual Meeting, Tucson, Arizona, January 2004.

Conflict of interest statement

Drs. Menegazzi and Callaway receive royalty payments from a licensing agreement between the University of Pittsburgh and Medtronic Physio-Control. This technology is not related to this study. None of the other authors have any conflict of interests to declare in regards to this study.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Keywords

Heart arrest; ventricular fibrillation; cardiopulmonary resuscitation; hemodynamic phenomena; electric countershock; electrocardiography

Introduction

Sudden cardiac death remains the most significant public health problem in the United States.¹ Approximately 325,000 such deaths occur annually, with only 6% of these patients surviving to hospital discharge.^{2,3} Many patients who suffer an out-of-hospital cardiac arrest (OOHCA) have their pulses restored in the field but do not survive to be admitted to the hospital. For example, of 1,474 OOHCA patients treated by the City of Pittsburgh EMS, 32% had pulses restored in the field while only 25% still had pulses at arrival to the emergency department (a 22% loss of pulses after initial resuscitation).⁴

This loss of circulation may be explained in part by post-resuscitation instability that often occurs after the prolonged global ischemia that occurs during cardiorespiratory arrest. This instability is the result, in part, of left ventricular dysfunction and loss of vascular tone.^{5–7} In our laboratory, we have observed post-resuscitation hemodynamic patterns that seem to be dependent on the duration of the antecedent ventricular fibrillation (VF). Better understanding of these patterns might help healthcare providers anticipate the need for exogenous pressor support, thereby preventing the loss of pulses during the transport of OOHCA patients.

We sought to determine whether the nature and time-course of these post-ROSC hemodynamic patterns were temporally associated with the duration of VF. We also sought to describe the phenomenon of post-resuscitation cardiovascular collapse. We hypothesized that post-resuscitation cardiovascular collapse would be associated with the duration of VF, i.e. that brief periods of VF would have delayed or no post-resuscitation cardiovascular collapse, while prolonged VF would have rapid onset of post-resuscitation cardiovascular collapse.

Materials and Methods

This investigation was approved by the University of Pittsburgh Institutional Animal Care and Use Committee (IACUC). We retrospectively analyzed the data from 24 mixed-breed domestic swine of either sex that were a subset of another experiment.⁸ These animals were selected because they both represented variety in the duration of VF and were treated with immediate defibrillation attempts as the first therapy (i.e. these animals did not receive any drug treatment before the first 1–3 rescue shocks).

The animals ranged in mass from 19.5 to 25.7 kgs. The preparation of these animals has been previously described in detail.⁸ In brief, animals were sedated with ketamine and xylazine, anesthetized with alpha-chloralose, orotracheally intubated, and paralyzed with pancuronium. Micro-manometer-tipped catheters (Mikro-Tip Catheter Transducers SPR-471A and SPC-370-S, Millar Instruments, Houston, Texas) were advanced into the aorta and right atrium. Pressures were recorded continuously throughout the experiments using a computerized data acquisition system and software package (Chart, v.5.3, ADInstruments, Castle Hill, Australia). Arterial blood gases were drawn periodically to establish the physiologic stability of the preparation, and any time the ventilator was adjusted (i-STAT Portable Clinical Analyzer, Heska Corporation, Waukesha, WI).

At the end of the preparation, VF was induced with a 3s, 60 Hz, 100 mA transthoracic shock. VF was then untreated until the animals' ECG displayed a predetermined level of organization

(scaling exponent value). Animals were then treated with up to 3 fixed-dose countershocks (150J, biphasic waveform), depending on the post-shock ECG rhythm. If these shocks failed, mechanical CPR was begun (Thumper, Model 1007, Michigan Instruments, Grand Rapids, MI) and standardized care was given.⁸

We defined ROSC as an organized post-shock ECG rhythm combined with a systolic blood pressure of at least 90 mmHg sustained for one minute continuously. We defined the hyperdynamic phase, *a priori*, as post-ROSC systolic blood pressure of 150 mmHg or greater. We defined post-resuscitation cardiovascular collapse as a post-ROSC systolic blood pressure below 90 mmHg sustained continuously for at least 60 seconds. This was also the point at which exogenous pressor support with norepinephrine was begun. For the purposes of time-to-event analyses, we dichotomized the classification of VF duration into <3 minutes VF and >3 minutes VF.

We compared the proportions of animals attaining ROSC and the proportion of animals experiencing post-resuscitation cardiovascular collapse in each group and compared these with Fisher's exact test. We compared time to post-resuscitation cardiovascular collapse using survival analysis.⁹

Results

The distribution of VF duration for the two groups is shown in Figure 1. Twenty-one of twenty-four animals achieved ROSC; 7/7 (100%) in the <3 minute VF group and 14/17 (71%) in the >3 minute VF group. Time to event (stabilization or cardiovascular collapse) data were not available for 3 animals and these were excluded from further analyses.

There were two distinct phases of post-ROSC hemodynamics. First, there is an immediate hyperdynamic phase characterized by very high aortic blood pressures combined with tachycardia. This was observed in all animals that had ROSC, regardless of duration of VF, and lasts for 1–4 minutes. This was followed by either a stabilization period or cardiovascular collapse. Fifteen of twenty-one animals experienced post-resuscitation cardiovascular collapse; 2/7 (29%) in the <3 minute VF group and 13/14 (93%) in the >3 minute VF group ($p=0.006$). Five of seven animals who had VF <3 minutes needed no exogenous pressor support (stabilization), while 13/14 who had VF >3 minutes did. Representative aortic pressure tracings from the two groups are displayed in Figure 2.

Survival analysis showed that time to collapse was highly related to duration of VF (log-rank $p=0.004$). The overall median time to cardiovascular collapse was 11.1 minutes (95% CI: 8.6–13.3 minutes). The median time to post-resuscitation cardiovascular collapse in the <3 minute VF group was 22.2 minutes, and the median time to same in the >3 minute VF group was 9.1 minutes ($p=0.004$). Results of the survival analysis are shown in Figure 3.

Discussion

We have observed consistent post-ROSC hemodynamic patterns and have shown these to be associated with the duration of VF. There are two distinct phases. The first is a hyperdynamic phase, and this was seen in all animals. The second phase takes one of two courses, either hemodynamic stabilization or cardiovascular collapse. The former is associated with brief periods of VF and the latter with prolonged VF. This might occur clinically when the cardiac arrest is witnessed by a caregiver, is in an intensive care unit, or where the patient may be in close proximity to an automated external defibrillator.^{10, 11} In such cases, defibrillation may occur in a few minutes. However, in most cases of OOHCA and many cases of in-hospital cardiac arrest (in non-intensive care beds) VF is prolonged before defibrillation can occur. Thus, profound hypotension may be eminent once pulses are restored and should be considered

by healthcare providers. By anticipating this precipitous drop in pressure, pressor support could be readied and delivered at the first sign of deteriorating blood pressure.

There may be several factors contributing to the fact that prolonged VF more frequently results in cardiovascular collapse. First, prolonged VF usually requires more defibrillation attempts to achieve ROSC. This could result in electrical injury that could affect myocardial efficiency after ROSC.^{12, 13} Second, the myocardium is more likely to be stunned after prolonged VF.¹⁴ So reperfusion injury and impaired pump function will be more pronounced when VF has been prolonged compared to a brief ischemic insult.¹⁵ Third, during VF high-energy phosphates become depleted.^{16,17} So when pulses are restored after prolonged VF what little high-energy phosphates remain will be rapidly diminished. This will be exacerbated if myocardial perfusion during early ROSC is impaired.¹⁸ Fourth, the physical and mechanical derangements of myocytes will be more pronounced when VF is prolonged.^{19,20}

There are several important limitations to this study. First, these were healthy swine without any apparent cardiovascular disease. As such, their response may differ from animals with atherosclerotic heart disease. Second, VF was induced electrically and was not preceded by an ischemic insult. This method of inducing VF may have produced results that could differ from ischemia-induced VF, with the latter being worse. Third, we gave norepinephrine to support blood pressure by protocol when the aortic systolic pressure dropped below 90 mmHg. Therefore, we cannot know whether some of the animals in our study who received norepinephrine would have stabilized and recovered spontaneously without exogenous pressor support. Another major limitation is that the animals were anesthetized, as required by our IACUC. While this could have affected hemodynamics in this model, we specifically selected α -chloralose as the anesthetic agent because of its benign cardiovascular effects. Still, we have no way of knowing what impact anesthesia may have had here. Finally, while we cannot extrapolate these findings to human sudden cardiac death we have demonstrated that this porcine model does produce ROSC rates that are very similar to human clinical experience.²¹

Conclusions

There are two distinct phases of hemodynamic patterning after resuscitation of VF. There is a brief hyperdynamic phase that lasts 1–4 minutes. This is followed by either stabilization or cardiovascular collapse. When VF is brief, blood pressures return to normal and stabilize without exogenous support. When VF is prolonged cardiovascular collapse occurs. Healthcare providers should be prepared for cardiovascular collapse in patients having ROSC after prolonged VF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Funding

Dr. Menegazzi is supported in part by National Heart, Lung, and Blood Institute grant RO1HL080483-01. Dr. Ramos was supported by a National Institutes of Health one year supplemental research grant. Partial support for this study came from an unrestricted research grant from Medtronic Physio-Control, Redmond, WA.

References

1. Becker, LB. The epidemiology of sudden death. In: Paradis, NA.; Halperin, H.; Nowak, R., editors. *Cardiac Arrest: The Science and Practice of Resuscitation Medicine*. Baltimore, MD: Williams & Wilkins; 1996.

2. American Heart Association, American Stroke Association. Heart disease and stroke statistics: 2007 Update. [Accessed March 28, 2007]. at <http://circ.ahajournals.org/cgi/content/short/CIRCULATIONAHA.106.179918>
3. Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989–1998. *Circulation* 2001;104:2158–2163. [PubMed: 11684624]
4. Unpublished data, City of Pittsburgh Bureau of EMS, 1998–2001.
5. Kusuoka H, Porterfield JK, Weisman HF, Weisfeldt ML, Marban E. Pathophysiology and pathogenesis of stunned myocardium. Depressed Ca^{2+} activation of contraction as a consequence of reperfusion-induced cellular calcium overload in ferret hearts. *Journal of Clinical Investigation* 1987 Mar;79(3): 950–61. [PubMed: 3818956]
6. Tabayashi K, McKeown PP, Miyamoto M, Luedke AE, Thomas R, Breazeale DG, Misbach GA, Allen MD, Ivey TD. Diastolic mechanical properties of the left ventricle after global ischemia. *Journal of Cardiovascular Surgery* 1991 Mar-Apr;32(2):250–8. [PubMed: 2019630]
7. Sunderdick U, Schmitz-Spanke S, Korbmacher B, Gams E, Schipke JD. Left ventricular dysfunction and disturbed O_2 -utilization in stunned myocardium: influence of ischemic preconditioning. *European Journal of Cardio-Thoracic Surgery* 2001 Oct;20(4):770–6. [PubMed: 11574223]
8. Menegazzi JJ, Callaway CW, Sherman LD, Hostler DP, Wang HE, Fertig KC, Logue ES. Ventricular fibrillation scaling exponent can guide timing of defibrillation and other therapies. *Circulation* 2004;109:926–931. [PubMed: 14757695]
9. Young KD, Menegazzi JJ, Lewis RJ. Statistical methodology: IX. survival analysis. *Academic Emergency Medicine* 1999 Mar;6(3):244–9. [PubMed: 10192678]
10. Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. *New England Journal of Medicine* 2000;343:1206–1209. [PubMed: 11071670]
11. Caffrey SL, Willoughby PJ, Pepe PE, Becker LB. Public use of automated external defibrillators. *New England Journal of Medicine* 2002 Oct 17;347(16):1242–7. [PubMed: 12393821]
12. Karch SB. Resuscitation-induced myocardial necrosis. Catecholamines and defibrillation. *Am J Forensic Med Pathol* 1987;8(1):3–8. [PubMed: 3578203]
13. Dahl CF, Ewy GA, Warner ED, Thomas ED. Myocardial necrosis from direct current countershock. Effect of paddle electrode size and time interval between discharges. *Circulation* 1974;50(5):956–61. [PubMed: 4430099]
14. Bolli R. Mechanism of myocardial “stunning”. *Circulation* 1990 Sep;82(3):723–38. [PubMed: 2203553]
15. Kloner RA, Jennings RB. Consequences of brief ischemia: stunning, preconditioning, and their clinical implications: part 1. *Circulation* 2001 Dec 11;104(24):2981–9. [PubMed: 11739316]
16. Neumar RW, Brown CG, Robitaille PL, Altschuld RA. Myocardial high energy phosphate metabolism during ventricular fibrillation with total circulatory arrest. *Resuscitation* 1990;19:199–226. [PubMed: 2164245]
17. Neumar R, Brown C, Van Ligten P, Hoekstra J, Altschuld R, Baker P. Estimation of myocardial ischemic injury during ventricular fibrillation with total circulatory arrest using high-energy phosphates and lactate as metabolic markers. *Annals of Emergency Medicine* 1991;20:222–229. [PubMed: 1996814]
18. Heusch G, Schulz R. Perfusion-contraction match and mismatch. *Basic Research in Cardiology* 2001 Feb;96(1):1–10. [PubMed: 11215527]
19. Korvald C, Elvenes OP, Aghajani E, Myhre ES, Myrnes T. Postischemic mechanoenergetic inefficiency is related to contractile dysfunction and not altered metabolism. *American Journal of Physiology - Heart & Circulatory Physiology* 2001 Dec;281(6):H2645–53. [PubMed: 11709434]
20. Karch SB, Billingham ME. Myocardial contraction bands revisited. *Hum Pathol* 1986;17(1):9–13. [PubMed: 2417934]
21. Rittenberger JC, Menegazzi JJ, Callaway CW. Association of delay to first intervention with return of spontaneous circulation in a swine model of cardiac arrest. *Resuscitation* 2007;73(1):154–160. [PubMed: 17223246]

VF DURATION DISTRIBUTION

Figure 1.
Distribution of the duration of VF, in seconds, for animals categorized as having either <3 minutes VF or >3minutes VF.

COMPARISON OF VF DURATION

Figure 2.

Representative blood pressure tracings immediately after ROSC for an animal with <3 minutes of VF and one with >3 minutes of VF. Note stabilization without exogenous pressor in the <3 minute animal, and the cardiovascular collapse needing norepinephrine in the >3 minute animal.

Figure 3. Survival curves depicting onset of cardiovascular collapse after ROSC (log-rank $p=0.004$).