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To Beat or Not to Beat

Is Timing the Only Question? Survival after Delayed Defibrillation

SUDDEN cardiac death continues to be the leading cause of mortality in the developed world, claiming 400,000 lives annually in the United States alone.[1] The vast majority of these deaths are attributed to ventricular tachycardia/fibrillation (VT/VF). Currently, electrical defibrillation remains the only effective treatment for this otherwise fatal rhythm. Large-scale clinical trials have demonstrated that for out-of-hospital and intensive care unit cardiac arrests, the sooner defibrillation occurs, the greater the chance of patient survival.[2,3] It is in this context that the idioms "time is brain" or "time is myocardium" seem quite apt. The perioperative period constitutes an ideal setting to deliver quick defibrillation given the available monitoring and trained personnel. Nevertheless, perioperative patients constitute a complex and heterogeneous patient population quite different from the myocardial infarction patient found down in the field, and thus, the effectiveness of early defibrillation in this setting remains unproven. In this issue of ANESTHESIOLOGY, Mhyre *et al.*[4] report that delayed defibrillation occurs in approximately one in seven patients with identifiable VT/VF in the perioperative settings. Predictably, delayed defibrillation in the "off-site perioperative areas" is associated with reduced patient survival when compared with early defibrillation (31% *vs.* 62%). Surprisingly, no such association is seen for defibrillation in the operating room. To put such findings into context, one must first understand the pathophysiology of VT/VF and the unique attributes of cardiac arrests in the operating room environment.

VT/VF is created as a result of multiple reentrant waves of electrical excitation that meander erratically through the ventricular muscle.[5] Continued breakup of these electrical waves caused by dispersion of refractoriness in the myocardium leads to the disordered state of conduction that is VF. Factors that perpetuate wavebreak include preexisting myocardial tissue heterogeneity (fibrosis, ischemia/infarcts, myofiber orientation) and intrinsic electrophysiology properties of the ion channels and exchangers that influence wave stability. In diseased state or under abnormal electrophysiological conditions, VT/VF can become self-sustaining. Thus, with unstable hemodynamics, defibrillation becomes essential to stabilize the electrical waves and restore normal conduction quickly.

The latest work by Mhyre *et al.* sheds new light on the clinical effectiveness of perioperative defibrillation both inside and outside of the operating room. Their effort to analyze complex patient data in the National Registry of Cardiopulmonary Resuscitation should be commended. The results unfortunately demonstrate that even in highly monitored perioperative areas, delays in defibrillation are not uncommon, although substantially less frequent than delays observed in "nonperioperative" in-hospital patients (14% *vs.* 30%).[2,4] Lack of an association between time to defibrillation in the operating room and patient survival is interesting and may be explained by differences between arrests inside and outside of the operating room. For one thing, the cardioprotective and neuroprotective effects of anesthetics may confer improved survival when defibrillation is delayed. Furthermore, intraoperative monitoring may improve detection of evolving problems, allowing for actions that may mitigate the consequences of pulseless VT/VF. Such is generally not the case with arrests that occur in other areas of the hospital, likely explaining the much worse survival outcomes.[2,4]

The lack of demonstrable association between early defibrillation in the operating room and survival may also represent insurmountable study design hurdles. First, the rarity of documented intraoperative VT/VF arrests may have translated to insufficient statistical power. Second, it is conceivable that fast and successful intraoperative defibrillation interventions failed to trigger a "code blue" event and thus were not recorded in the medical record, creating a selection bias. Furthermore, the type of shock (biphasic *vs.* monophasic) and the exact energy of the therapeutic shock were not standardized, nor was the mechanism for measuring precise time to defibrillation. These study design limitations caused by varying clinical practices among participating centers can impact results and are addressed concisely in the manuscript. However, there exist methodological hurdles that do require further attention. For instance, although Mhyre *et al.* ana-

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lyzed their data according to the cardiac arrest site, no analysis based on the likely underlying cause of arrest was performed. In fact, the immediate cause of cardiac arrest of 80% of recorded patients was labeled "arrhythmia," highlighting the lack of clarity of precipitating events. Not surprisingly, in a retrospective data collection of code blue events, with the chaos that often ensues, the information gathered is frequently imperfect, as is the adherence to the recommended resuscitation protocols and attempts to seek the true etiology of cardiac arrest. In the intraoperative setting, VT/VF is often a final common pathway of a whole chain of unfortunate events, and limiting the focus of interventions to this final terminal event is akin to chasing the horse after it has left the stable. In that regard, it is important to note that clinical strategies aimed primarily at improving defibrillation times have failed to improve survival outcomes significantly.[6,7]

With these thoughts in mind, we propose that combating perioperative cardiac arrest requires a two-pronged strategy: (1) prevention of the arrest when possible, and (2) prompt diagnosis of the underlying cause with immediate treatment to reverse the catastrophe. Perioperative myocardial ischemia, especially when combined with respiratory depression and hypoxemia, creates fertile ground for a VF cardiac arrest to take root. VT/VF may not always be the presenting event, although it may appear so to a practitioner who fails to recognize the warning signs. Such warning signs are easily missed if the American Society of Anesthesiologists standard physiologic monitors are not utilized. Failure to implement this accepted monitoring in "off-site settings" is unfortunately a commonplace occurrence, as can be seen by the low (75%) rate of cardiac monitoring performed in the diagnostic suite in this study. This lies in stark contrast to the nearly universal monitoring performed in the other venues examined (operating room, catheterization laboratory, postanesthesia care unit). Practitioners often reduce monitoring and let their guard down when the perceived risk is low, such as at the end of a procedure.

Even when patients are fully monitored and our vigilance is at its peak, perioperative catastrophes may still occur, thus necessitating a unique differential diagnosis for cardiac arrest. Such a list should include massive blood loss, pulmonary embolus, hypoxemia, tension pneumothorax, pericardial tamponade, anaphylaxis, electrolyte/pH imbalance, and drug toxicity. Many of these complications can terminate in VT/VF and cardiac arrest; all are treatable, but each requires a unique intervention. Thus, to resuscitate a patient effectively, one must not only defibrillate quickly, but also treat and reverse the underlying cause. Diagnosis requires a high index of suspicion, often guided by timely imaging examinations. For instance, an intraoperative transesophageal echocardiography in a chest trauma patient can distinguish among pericardial tamponade, hemothorax, and systemic air embolus, each of which requires a vastly different definitive intervention to prevent further deterioration.

Because we cannot prevent all cases of cardiac arrest, we must develop a system that can maximize therapy while limiting treatment delay. When "time is patient survival," we must strive to eliminate the human factor, which inevitably leads to therapeutic delays, caused by both logistical hurdles and diagnostic errors. Just as the implantable cardioverter-defibrillator has revolutionized the treatment of sudden cardiac death for patients in the community, perhaps it is time to reevaluate the role of the automatic external defibrillator in large-scale clinical trials for improving outcomes for in-hospital cardiac arrests.[8] The possibility exists for all high-risk perioperative patients to be attached to an automatic external defibrillator that could administer a therapeutic shock before we humans could even muster the code blue distress signal. Only then could we truly know how important early defibrillation is to this population.

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References

1. Zheng ZJ, Croft JB, Giles WH, Mensah GA: Sudden cardiac death in the United States, 1989 to 1998. Circulation 2001; 104:2158–63
2. Chan PS, Krumholz HM, Nichol G, Nallamothu BK, American Heart Association National Registry of Cardiopulmonary Resuscitation Investigators. Delayed time to defibrillation after in-hospital cardiac arrest. N Engl J Med 2008; 358:9–17
3. American Heart Association. 2005 American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care, part 5: Electrical therapies: Automated external defibrillators, defibrillation, cardioversion, and pacing. Circulation 2005; 112:IV-35–IV-46
4. Mhyre JM, Ramachandran SK, Kheterpal S, Morris M, Chan PS, for the American Heart Association National Registry for Cardiopulmonary Resuscitation Investigators: Delayed time to defibrillation after intraoperative and periprocedural cardiac arrest. ANESTHESIOLOGY 2010; 113:782–93
5. Weiss JN, Qu Z, Chen PS, Lin SF, Karagueuzian HS, Hayashi H, Garfinkel A, Karma A: The dynamics of cardiac fibrillation. Circulation 2005; 112:1232–40
6. Edelson DP, Litzinger B, Arora V, Walsh D, Kim S, Lauderdale DS, Vanden Hoek TL, Becker LB, Abella BS: Improving in-hospital cardiac arrest process and outcomes with performance debriefing. Arch Intern Med 2008; 168:1063–69
7. Chan PS, Khalid A, Longmore LS, Berg RA, Kosiborod M, Spertus JA: Hospital-wide code rates and mortality before and after implementation of a rapid response team. JAMA 2008; 300:2506–13
8. Martínez-Rubio A, Kanaan N, Borggrefe M, Block M, Mäkijärvi M, Fedele F, Pappone C, Haverkamp W, Merino JL, Esquivias GB, Cinca J, European Powerheart Investigators. Advances for treating in-hospital cardiac arrest: Safety and effectiveness of a new automatic external cardioverter-defibrillator. J Am Coll Cardiol 2003; 41:627–32