Foundations of Emergency Medicine
Foundations III: Guided Small Group Experience

Session 23: Advanced ACLS
Unit: Critical Care

- **Agenda and Learning Objectives**
  - Case 1 – Recognition and treatment of refractory ventricular fibrillation (20 min)
    - Know the definition of refractory ventricular fibrillation
    - Understand the pathophysiology and etiologies of refractory ventricular fibrillation
    - Learn potential therapies for the treatment of refractory ventricular fibrillation
  - Case 2 – Recognition and treatment of severe shock, also known as "pseudo-PEA" (20 min)
    - Define PEA and review provoking etiologies of PEA
    - Learn to recognize the difference between PEA and a severe shock state (pseudo-PEA)
    - Explain the different treatment ramifications for a patient with severe shock compared with PEA
  - Review (10 min)
    - Review session teaching points

- **The goal of this Foundations case is to create discussion around cardiac arrest considerations beyond ACLS. Some of these concepts are controversial. As with many cardiac arrest treatment paradigms, the level of evidence is generally weak. Before your session, we encourage you to review some of the source literature on the use of esmolol for refractory ventricular fibrillation, double sequential defibrillation, and the concept of pseudo-PEA. This will prepare you best for an active discussion regarding the potential pros and cons of adopting some of these strategies in your practice.**

- **Case 1 - Recognition and treatment of refractory ventricular fibrillation (20 min)**

  A 62 year-old male with a past medical history of hypertension and diabetes has suffered a witnessed cardiac arrest. The family states that he was at home in normal health when he acutely started "breathing funny" and suddenly collapsed. The patient's son started CPR. EMS arrived 5 minutes later. EMS established an IV and performed three rounds of ACLS. The patient was found in ventricular fibrillation with each rhythm check. He has received three defibrillations, a total of 3 mg epinephrine, and a 300 mg bolus of amiodarone. A King airway is in place with adequate breath sounds on lung auscultation. The patient's blood glucose was 88. He is now arriving in your CPR bay.

- **Discussion Questions with Teaching Points**
  - **How do you define refractory ventricular fibrillation?**
    - Ventricular fibrillation is considered refractory if still present after the following:

- Three defibrillation attempts
- 3 mg of epinephrine
- 300 mg of amiodarone
- > 10 min of CPR without return of spontaneous circulation (ROSC)

- **What are common etiologies of refractory ventricular fibrillation?**
  - Ischemia
  - Electrolyte abnormalities (such as hypokalemia, hypomagnesemia, and hyperkalemia)
  - Prolonged QT due to both congenital and acquired causes.

- **Any other drugs you would consider giving?**
  - If your initial anti-arrhythmic does not work, then consider giving others as well. For example, you should consider also giving lidocaine and magnesium. If clinically suspected, then you may also empirically treat for hyperkalemia.

- **Current ACLS recommendations are controversial in regard to refractory ventricular fibrillation. Why may this be so?**
  - ACLS is designed to give a streamlined approach to cardiac arrest for all practitioners that may encounter it, however, this one size fits all approach could be counterproductive in some circumstances.
  - Current recommendations on epinephrine advise administering 1 mg IV every 3-5 minutes indefinitely.
    - Epinephrine is a potent arterial vasoconstrictor used to increase coronary blood flow. It also has potent chronotropic and ionotropic effects on the heart.
    - In a fibrillated heart, there is approximately a four-fold increase in myocardial oxygen consumption. Eventually the vasoconstrictive effects of epinephrine are likely counterproductive as it works to restrict coronary arterial circulation.
    - Some studies have shown that beta stimulation of the myocardium may lead to hyperphosphorylation of ryanodine receptors (calcium receptors). This in turn would lead to a high influx of calcium into myocardial cells and ultimately lead to heightened electrical instability.
    - It has been suggested that epinephrine may not be the best pressor to use during cardiac arrest, but more research is needed.
    - The Paramedic2 Trial, published in NEJM in 2018, showed that while use of epinephrine led to higher 30-day survival, there was no difference in neurologically intact survival.
    - Theories of time-sensitive phases of cardiac arrest, particularly when due to shockable rhythms, advocate that the maximal benefit of epinephrine may be in the first 10-15 minutes.

- **How may this information change your approach?**

- You may consider setting a ceiling on your aggregate epinephrine dosing.
- There are practitioners who believe that the administration of more than 3 mg of epinephrine is counterproductive, especially in a case of refractory ventricular fibrillation.
- There is some weak evidence that beta blockade could counteract the potentially deleterious effects of high dose epinephrine by preventing the beta agonist induced hyperphosphorylation of ryanodine receptors mentioned before. This could lead to less electrical instability and improve the odds of defibrillating out of ventricular fibrillation.

- **What beta blocker would you use? What is the evidence behind this?**
  - Esmolol can be given at an initial bolus dose of 500 mcg/kg followed by an infusion of 0-100 mcg/kg/min.
  - There are two small studies that have been published on this topic
    - Driver et. al in 2014 studied 24 patients, only 6 of them receiving esmolol. They reported that the esmolol group was more likely to survive to hospital discharge (50% vs. 16%) and was more likely to be neurologically intact at time of discharge (50% vs. 11%).
    - Lee et. al in 2016 studied 41 patients, 16 of whom received esmolol, and reported an improvement in sustained ROSC and survival to ICU admission (56% vs. 16%). They did not show a statistically significant effect on mortality.
  - Be encouraged to review these studies yourself. The evidence is weak, but suggests potential benefit.

- **What else can you consider in refractory ventricular fibrillation?**
  - Double sequential cardiac defibrillation (DSCD)

- **How do you perform DSCD?**
  - Use two defibrillators simultaneously. Have one set up with anterior/posterior pads, and the other with parasternal/axillary pads. Charge both for defibrillation and administer the shock from each machine simultaneously by pressing the shock buttons at the same time.

- **What's the evidence for this?**
  - The evidence is mostly sourced from case reports. There are three theories for why this may work:
    - DSCD delivers a shock through two separate vectors, so It may get a higher proportion of defibrillated cardiac myocytes compared with one defibrillator alone.
    - DSCD could work by the first defibrillation reducing the ventricular defibrillation threshold enough for the second defibrillation to be successful.
    - DSCD may work just because of the higher total energy delivered, though this is the most contested proposed explanation of the three.

- **Any surgical considerations in this case?**
  - Remember to consult your ECMO team, if available, early in the course of treatment of refractory ventricular fibrillation. Observational and retrospective studies have shown benefit in the right candidates. Think ECMO particularly in patients with:
    - Witnessed circulatory arrest
    - Bystander CPR
    - Age < 75 years old
    - No ROSC after 10 minutes of professionally administered CPR

After receiving your patient into the resuscitation bay, ACLS was continued. An amiodarone drip was initiated. You elected to not continue giving more epinephrine after the 3 mg delivered by EMS. You administered an esmolol bolus and performed DSCD, achieving ROSC and a normal sinus rhythm. The patient was admitted to the ICU.

❖ **Case 2 – PEA (20 min)**

After finishing your last case, you're pulled into another resuscitation bay because EMS has arrived with a patient receiving chest compressions. They report the patient is a 68-year-old female who has had a cold for the last four days. Her husband and she were getting ready to come to the ER because she did not feel well, after which she became suddenly unresponsive. He started CPR on scene and called 911. Overall, downtime has been 8 minutes and EMS has seen PEA on all rhythm checks. She has received epinephrine 1 mg three times. She is intubated. You confirm clinically that the ETT is in appropriate position. Her POC glucose is 116.

- **Can you define PEA and list its common precipitants?**
  - There is no one unifying definition of PEA, but from a 2013 article in Circulation, the authors defined it as "a syndrome characterized by the absence of a palpable pulse in an unconscious patient with organized electrical activity other than ventricular tachyarrhythmia on EKG."
  - The differential includes the 5 H's and T's, as follows:
    - Hypovolemia
    - Hypoxia
    - Hydrogen ions (Acidosis)
    - Hyperkalemia or hypokalemia
    - Hypothermia
    - Tamponade
    - Thrombosis from MI
    - Thrombosis from PE
    - Tension pneumothorax
    - Toxins
  - It is also important to consider hypoglycemia and trauma, both of which have been removed from the 5 H's and T's compared with prior years. Routine blood glucose

checks should cover for hypoglycemia. Trauma should be evident based off presentation.

- Decide for yourself a way to systematically run a code while covering for the differential. You may have the 5 H's and T's on hand with a card or smartphone. You may decide that once you check a glucose, get a history, and perform a POCUS, that all you have to consider further is toxins, acidosis, and/or hyperkalemia and you're all set.
- The most important thing is using a systematic method each time to cover the differential in a manner that cognitively unloads you as much as possible during a cardiac arrest.

- **What is pseudo-PEA and how is this diagnostically important?**
  - Pseudo-PEA is a state of severe shock where the patient appears to be in PEA arrest but actually has cardiac function on POCUS with a measurable pulse by POCUS or arterial line.

- **What are ways, besides manual palpation, you can check for a pulse during a cardiac arrest?**
  - Studies have shown manual pulse checks are neither highly specific or sensitive for determining the presence of a pulse.
  - There are two other ways to augment your pulse checks:
    - Using the linear probe at the femoral artery to check for pulsations
    - Early insertion of a femoral arterial line
  - An arterial line is preferable, if manpower allows it. Its insertion will obviate the need to stop compressions for pulse checks.

- **How do I establish pseudo-PEA from PEA and how do we treat it differently?**
  - You can establish that the patient is in a high shock state if you notice a blood pressure by US at the femoral artery or by A-line, in conjunction with an organized rhythm on telemetry.
  - If you see this, quickly ultrasound the heart to assess for contractility. If present, CPR should be discontinued and the patient should be managed as being in severe shock.

- **Can the ultrasound lead to harm?**
  - Continuous high-quality chest compressions with limited pauses are essential to CPR, yet two studies in 2017 showed that the addition of POCUS to standard CPR increased the average pause for rhythm and pulse checks from 11 seconds to 21 seconds.
  - One study by Edelson found an average pause of 15.3 seconds from the beginning of a pulse check to the subsequent defibrillation. It also showed every five-second decrease in that pause was associated with an almost doubling of shock success.
  - In summary, extended pauses for the sake of an ultrasound likely lead to patient harm.

- **How can we limit prolonged pauses?**

- Be ready in position with your US before the pulse check arrives. Have an imaging goal before the pulse check. For example, this next pulse check, I'm going to check a subxyphoid cardiac window for pericardial effusion. Get in and out, continue CPR, and be ready for your next POCUS goal at the following pulse check.
- Limit the pause in compressions to no more than 10 seconds. Ideally have another party in charge of cutting off the sonographer.

❖ **Case Concludes (10 min)**

After the first round of compressions, no one is able to palpate a pulse. You place the linear probe on the femoral artery and see active pulsations in conjunction with an organized rhythm on telemetry. US also shows organized cardiac activity. You stop compressions and start a norepinephrine drip titrated to a goal MAP of 65. Follow-up CXR shows multi-focal pneumonia. The patient is admitted to the ICU for septic shock.

❖ **Case Teaching Points Summary**

- Refractory Ventricular Tachycardia/Fibrillation
  - Think refractory ventricular tachycardia and fibrillation if it continues after 3 defibrillations, 3 mg epinephrine, and a loading dose of your anti-arrhythmic of choice
  - Use 2 defibrillators, one anterior/posterior and one parasternal/apex. Deliver both defibrillations simultaneously
  - Consider an esmolol bolus and drip
  - Be liberal with the use of additional anti-arrhythmics

- Pseudo-PEA/High Shock State
  - Employ a method to run your PEA differential in a manner that limits your cognitive load
  - Use an ultrasound or an arterial line to assess for the difference between true PEA and a high shock state with severe hypotension
  - If a severe shock state is identified, proceed with treatment for severe shock and discontinue CPR
  - Remember to limit pulse checks when performing an ultrasound

❖ **Facilitator Background Information**

Ventricular fibrillation or “electrical storm” can be challenging to manage. It is defined as ventricular fibrillation that is resistant to at least three defibrillation attempts, 3 mg of epinephrine, 300 mg of amiodarone, and does not exhibit ROSC after >10 min of CPR (Lee, Resuscitation).

If refractory ventricular fibrillation is identified, one should consider the use of esmolol. There is some weak evidence showing its potential benefit. The goal of using beta blockers is to counteract the sympathomimetic surge from exogenous catecholamines that accumulate with the continued use of epinephrine. This build-up of catecholamines in patients with very low cardiac output can cause myocardial ischemia and can lead to lowering the ventricular fibrillation threshold, making successful defibrillation more challenging. The use of esmolol to counteract these potentially negative effects was first studied in animal models but has now been studied in humans. In a 2016 study, esmolol was shown to improve the return of sustained ROSC and to increase survival to ICU admission (56% vs 16%) but did not have a statistically significant effect mortality. Another study in 2014, which only studied 24 patients, with 6 of them receiving esmolol, showed that patients who received esmolol were more likely to survive to hospital discharge (50% vs 16%) and more likely to be neurologically intact at time of discharge (50% vs 11%). To reiterate, these studies were both very small, so the quality of evidence is low.

One should remember to consider giving other anti-arrhythmic medications too. If you start with amiodarone, consider giving lidocaine and magnesium too.

Double sequential cardiac defibrillation (DSCD) can be attempted alongside esmolol. The evidence for DSCD mostly comes from case reports, yet the concept is simple. There are three theories as to why this works: 1) The application of two sets of defibrillation pads instead of one set may help completely depolarize the myocardium 2) the first shock reduces the ventricular defibrillation threshold which allows the second shock to be more effective and 3) a larger amount of energy is more effective than a smaller amount of energy (though this last point has been contested in the literature). This approach may be especially useful for patients with large body habitus that impedes the transmission of electricity to the heart.

Finally, we should start to think of PEA and severe shock or “pseudo-PEA” as two different disease process. The way to differentiate the two is by using methods to assess for the difference between someone with no blood pressure versus someone with a blood pressure, but at a low enough level such that a pulse is difficult or impossible to palpate. Manually checking a pulse during cardiac arrests is poorly sensitive and specific for ROSC. POCUS provides us with a much more reliable method by using the linear probe over the femoral artery and assessing for arterial pulsations. If the manpower is available, the insertion of an arterial line is even more ideal. If there is the suggestion of arterial pulsations by US, then POCUS can be used to confirm organized cardiac activity to finalize the diagnosis of a high-shock state. Treatment implications are significant. A patient in a high shock state likely benefits more from aggressive treatment of shock rather than continued ACLS care with high dose epinephrine and continued chest compressions.

- **References**
  - **Author:** Dr. Isabel Malone

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- **References:**

1. Clattenburg, Eben J, et al. "Point-of-Care Ultrasound Use in Patients with Cardiac Arrest Is Associated Prolonged Cardiopulmonary Resuscitation Pauses: A Prospective Cohort Study." *Resuscitation*, vol. 122, 2018, pp. 65–68., doi:10.1016/j.resuscitation.2017.11.056.
2. Driver, B. E., Debaty, G., Plummer, D. W., & Smith, S. W. (2014). Use of esmolol after failure of standard cardiopulmonary resuscitation to treat patients with refractory ventricular fibrillation. *Resuscitation, 85*(10), 1337-1341. doi:10.1016/j.resuscitation.2014.06.032
3. Edelson DP, Abella BS, Kramer-Johansen J, et al: "Effects of compression depth and pre-shock pauses predict defibrillation failure during cardiac arrest." Resuscitation. 2006;71(2):137–145.
4. Ewy, G. "The Time-Sensitive Role of Vasopressors During Resuscitation of Ventricular Fibrillation." *Journal of the American College of Cardiology*, vol. 64, 2014, pp. 2368-70.
5. Gardner, Kevin F., et al. "The Cardiac Arrest Sonographic Assessment (CASA) Exam – A Standardized Approach to the Use of Ultrasound in PEA." *The American Journal of Emergency Medicine*, vol. 36, no. 4, Apr. 2018, pp. 729–731.,doi:10.1016/j.ajem.2017.08.052.
6. Perkins, G, et al. "A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest." *NEJM.* Vol. 379, 2018, pp. 711-21.
7. Hemmy, Davida. "Ultrasound Use During Cardiopulmonary Resuscitation Is Associated with Delays in Chest Compressions." *The Journal of Emergency Medicine*, vol. 54, no. 1, 2018, p. 140., doi:10.1016/j.jemermed.2017.11.007.
8. Larabee, Todd M., et al. "A Novel Hands-Free Carotid Ultrasound Detects Low-Flow Cardiac Output in a Swine Model of Pulseless Electrical Activity Arrest." *The American Journal of Emergency Medicine*, vol. 29, no. 9, 2011, pp. 1141–1146., doi:10.1016/j.ajem.2010.05.013.
9. Leacock, B. W. (2014). Double Simultaneous Defibrillators for Refractory Ventricular Fibrillation. *The Journal of Emergency Medicine, 46*(4), 472-474. doi:10.1016/j.jemermed.2013.09.022
10. Lee, Y. H., Lee, K. J., Min, Y. H., Ahn, H. C., Sohn, Y. D., Lee, W. W., . . . Park, S. M. (2016). Refractory ventricular fibrillation treated with esmolol. *Resuscitation, 107*, 150-155. doi:10.1016/j.resuscitation.2016.07.243
11. Myerberg, Robert J, et al. "Pulseless Electrical Activity: Definition, Causes, Mechanisms, Management, and Research Priorities for the Next Decade: Report From a National Heart, Lung, and Blood Institute Worksho." *Circulation* , vol. 128, no. 23, 3 Dec. 2013, www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.113.004490.
12. Rezaie, Salim. "REBEL Cast Ep 54: What the Heck Is Pseudo-PEA?" *REBEL EM - Emergency Medicine Blog*, 27 June 2018, rebelem.com/rebel-cast-ep-54-what-the-heck-is-pseudo-pea/.
13. Rezaie, Salim. "September 2016 REBEL Cast: Refractory Ventricular Fibrillation." *REBEL EM - Emergency Medicine Blog*, 17 Aug. 2017, rebelem.com/september-2016-rebel-cast-refractory-ventricular-fibrillation/.
14. Tibballs, J., and P. Russell. "Reliability of Pulse Palpation by Healthcare Personnel to Diagnose Paediatric Cardiac Arrest." *Resuscitation*, vol. 77, Jan. 2009, doi:10.1016/j.resuscitation.2008.03.098.

15. Tibballs, James, and Cyveen Weeranatna. "The Influence of Time on the Accuracy of Healthcare Personnel to Diagnose Paediatric Cardiac Arrest by Pulse Palpation." *Resuscitation*, vol. 81, no. 6, June 2010, pp. 671–675., doi:10.1016/j.resuscitation.2010.01.030.
16. Yates, James*. The Resus Room*, theresusroom.co.uk/double-sequential-defibrillation/.

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