



Defibrillation Strategies for Refractory Ventricular Fibrillation

Key Article

Cheskes S, et al. *Defibrillation Strategies for Refractory Ventricular Fibrillation. N Engl J Med. 2022. Published online November 6, 2022.*

Background - Peter

- Out-of-hospital Cardiac Arrest accounts for > 350,000 deaths in North America each year
- 100,000 of these are attributed to VF or pulseless VT
- Approximately 50% of these patients have refractory VF despite multiple attempts, and medical treatments (amiodarone, lidocaine) have not been found to improve survival or neurologic outcomes.
- Double sequential external defibrillation (DSED) and vector-change (VC) defibrillation are two strategies that have been studied in the electrophysiology lab and suggested as an alternative to continued anterior-lateral defibrillation attempts.
- Traditionally, alternative defibrillation attempts have been performed and reported as case reports and from lower quality levels of evidence. Since earlier application of DSED may increase the rate of ROSC, timing of this alternative treatment is an important clinical question.

Objective - Peter

- To compare DSED and VC Defibrillation to standard defibrillation in patients with refractory VF during OHCA.

Methods - Rob

- 3-group, cluster-randomized controlled trial with crossover in 6 paramedic services in Canada.
 - Approximately 4000 paramedics from March 2018 – May 2022 in a mix of urban and rural communities.
 - Prehospital care for OHCA is standard ACLS by all paramedics
 - Brief enrollment, pause for 5 months in 2020 due to COVID (evaluation for ACLS safety)
 - Trial was stopped early in May 2022 by the DSMB (data and safety monitoring board) because of paramedic staffing shortages which made response times longer and affecting timely application of assigned type of defibrillation.
- Patients
 - Included
 - Adults aged 18 years of age or greater
 - Out-of-hospital cardiac arrest
 - Refractory VF defined as an initial VF rhythm or pulseless VT that was present after 3 intervals of defibrillation with 2-minutes of CPR.
 - Excluded
 - Non-cardiac causes
 - Traumatic arrest

- DNR directives
 - And hypoxic causes (hypothermia, hanging, drug overdose)
- Randomization
 - Random treatment sequences were computer-generated by the data coordinating center and assigned to paramedic services
 - Paramedic service clusters crossed over every 6 months to a different treatment group
- Interventions
 - Standard ACLS was provided to all patients
 - The first 3 defibrillations had pads placed in the standard anterior-lateral position
 - If still in VF or pulseless VT, patients then received either:
 - Standard Anterior-Lateral Defibrillation
 - Vector change defibrillation: Anterior-posterior pads
 - Double-sequential defibrillation: Anterior-Lateral + Anterior-Posterior pads with 2 separate defibrillators
- **Primary Outcome:** Survival to hospital discharge
- Secondary Outcomes
 - Termination of VF
 - Return of spontaneous circulation
 - Good neurologic outcome: Defined as a modified Rankin score of ≤ 2 at discharge
- A-prior Power analysis – Worth noting, because this is important
 - Estimated a 30-day survival of $12.4\% \geq 3$ shocks and estimated an 8% increase in survival to hospital discharge in the DSED/VC defibrillation groups over standard therapy.
 - *Based on estimates, the authors required 310 patients per group (930 patients total) for adequate power.*

Results - Mike

- In total, **405 patients were enrolled** before the DSMB suggested the trial be stopped.
 - Standard group: 136 patients (33.6%)
 - VC group: 144 patients (35.6%)
 - DSED group: 125 patients (30.9%)
- **12.3% of patients did not receive the assigned defibrillation treatment**
 - Most protocol violations were standard defibrillation for refractory VF in both groups
- Demographics
 - Age: 64 years old
 - 84% male
 - 68% bystander witnessed arrest
 - 58% received bystander CPR
 - Time to first defibrillation similar in all 3 groups (approx 10 min)
- Primary Outcome
 - (Brief Explanation for the listeners): Results listed as *adjusted relative risk* ratios: which mean if > 1 and the confidence interval does not include 1, the events are significantly more likely in the treatment groups (VC & DSED) than the control group.
 - Survival to hospital discharge
 - Standard defib: 13.3%
 - VC Defib: 21.7%; RR: 1.71 (1.01 – 2.88)
 - DSED group: 30.4%; RR: 2.21 (1.33 – 3.67)
- Secondary Outcomes

- Termination of VF
 - Standard defib: 67.6%
 - VC Defib: 79.9%; RR: 1.18 (1.03 – 1.36)
 - DSED group: 84.0%; RR: 1.25 (1.09– 1.44)
- ROSC
 - Standard defib: 26.5%
 - VC Defib: 35.4%; RR: 1.39 (0.97 – 1.99)
 - DSED group: 46.4%; RR: 1.72 (1.22-2.42)
- Good neurologic outcome
 - Std: 11.2%
 - VC defib: 16.2%
 - DSED: 27.4%

Limitations

- Stopped early – only enrolled 44% of target participants
- Incidence of outcomes are low, which usually leads to an overestimation of the treatment effect
- >10% of patients did not receive assigned treatment arm (patients kept in each group as an intention to treat)
- Vector change group had a fragility index of 1 for the primary outcome – meaning that the change in outcome of 1 patient would make the result no longer significant
- By using survival to hospital discharge as an outcome, it would be helpful to know more about the post-resuscitation care these patients received (TTM, PCI, and other confounders)

Take Home Points

- There is a signal here of benefit to using DSED and possibly VC defibrillation for refractory VF arrest.
- Still unclear if ready to be implemented as “usual care”