Paramedic CAT (Critically Appraised Topic)

Title: Dual sequential external cardiac defibrillation for refractory VF/pVT in OHCA

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Clinical Scenario: An ALS paramedic crew is attending a cardiac arrest call for a witnessed sudden cardiac arrest of a 65yr old male. On initial assessment: the patient is found to be in a ventricular arrhythmia without a pulse. The paramedic crew follow ACLS management during resuscitation & provide external cardiac defibrillation. The patient rhythm does not respond and does not convert following defibrillation. The crew continue to manage the patient and deliver an additional two cardiac defibrillation treatments – the rhythm does not respond. The paramedic crew consider if applying a secondary set of cardiac defibrillation pads to the patient posteriorly & anteriorly as well as the standard placed pads will enhance the effectiveness of the treatment & terminate the refractory arrhythmia and produce a return of spontaneous circulation. Furthermore, will this treatment provide improved likelihood of positive neurological recovery following OHCA?

PICO (Population – Intervention – Comparison – Outcome) Question:
Population – Adult patients who experience cardiac arrest out-of-hospital.
Intervention – Dual sequential external defibrillation (DSED)
Comparison – Standard external pad placement/standard cardiac arrest management
Outcome – Impact or improvement of survival/ROSC/positive neurological outcome

Search Strategy: ((("Emergency Medical Services"[mh] OR "Emergency Medical Technicians"[mh] OR paramedic*[tiab] OR "emergency medical technician*"[tiab] OR prehospital[tiab] OR pre-hospital[tiab] OR "out of hospital"[tiab] OR first responder*[tiab] OR emergency responder*[tiab] OR ambulance[tiab])) AND ((cardiac arrest OR heart death OR "vital signs absent" OR ventricular tachycardia OR ventricular fibrillation))) AND ((("dual sequential" OR "double sequential") AND defibrillation))

Search Outcome: Results 40; run on 23 09 06

Relevant Papers:

AUTHOR, DATE	POPULATION: SAMPLE CHARACTERISTICS	DESIGN (LOE)	OUTCOMES	RESULTS	STRENGTHS/ WEAKNESSES
(Cheskes, 2022)	All patients who were at least 18 years of age and had an out-of-hospital cardiac arrest and refractory ventricular fibrillation	This was a cluster-randomized controlled trial with crossover.	Survival to hospital discharge.	<u>Survival to Hospital Discharge</u> A total of 38 patients (30.4%) in the DSED group survived to hospital discharge, as compared with 18 patients (13.3%) in the standard group (relative risk, 2.21;	<u>Strengths</u> This was a cluster-randomized trial design with crossover, which is a high level of evidence. There was near-complete outcome ascertainment by medics.

	of presumed cardiac causes were eligible for the trial. Refractory ventricular fibrillation was defined as an initial presenting rhythm of ventricular fibrillation or pulseless ventricular tachycardia that was still present after three consecutive rhythm analyses and standard defibrillations separated by 2-minute intervals of cardiopulmonary resuscitation (CPR). Patients with a traumatic cardiac arrest, patients with do-not-resuscitate medical directives, and patients with cardiac arrest due to drowning, hypothermia, hanging, or suspected drug overdose were excluded. 405 patients were randomized (450 patients were eligible, 45 excluded)	This is level 2 evidence. A random controlled study with the inability to meet sample size.	Termination of ventricular fibrillation Return of spontaneous circulation Good neurologic outcome at hospital discharge	95% confidence interval [CI], 1.33 to 3.67); In the generalized linear model, the overall test for differences in survival to hospital discharge according to the randomized treatment assignment was significant (P = 0.009 for the comparison among the three groups). <u>Termination of Ventricular Fibrillation</u> Occurred in 105 patients (84.0%) in the DSED group, as compared with 92 patients (67.6%) in the standard group (relative risk, 1.25; 95% CI, 1.09 to 1.44) <u>Return of Spontaneous Circulation</u> Occurred in 58 patients (46.4%) in the DSED group, as compared with 36 (26.5%) in the standard group (relative risk, 1.72; 95% CI, 1.22 to 2.42). <u>Good Neurological Outcome</u> Occurred in 34 patients (27.4%) who received DSED and in 15 patients (11.2%) who received standard defibrillation (relative risk, 2.21; 95% CI, 1.26 to 3.88	Continuous performance of high-quality CPR was performed by medics. The study identified the inclusion of outcomes that are important to patients, including survival to hospital discharge and good neurologic outcome at hospital discharge. The study was considered a blind study. Although treating paramedics had to be aware of the assigned defibrillation strategy, those assessing survival and neurologic outcomes were not aware of the treatment assignments. <u>Weakness/Limitations</u> The Covid-19 pandemic provided substantial challenges to the paramedics in enrolling patients while donning full personal protective equipment and in some instances performing aerosol-generating medical procedures The trial did not achieve the planned sample size, since it was stopped early by the data and safety monitoring board as a result of Covid-19–related operational challenges. It is possible that the treatment effect was overestimated, given the small number of events for the primary outcome. The trial protocol did not specify a fixed follow-up time, and outcomes were assessed until hospital discharge. The length-of-stay distributions across the trial centers is not known. Most of the patients enrolled in this study were in an urban environment where a second defibrillator was often available. That may mean that these findings are not appropriately generalizable to a more rural or remote setting. Possible confounding factors may exist that could have influenced patient outcomes. This is due to the prehospital nature of these emergencies that sometimes result in incomplete medical histories. Possible not replicable in all systems due to the high degree of medical oversight and paramedic feedback

AUTHOR, DATE	POPULATION: SAMPLE CHARACTERISTICS	DESIGN (LOE)	OUTCOMES	RESULTS	STRENGTHS/ WEAKNESSES
(Deakin, 2020)	Our population of interest was adult patients with a shockable (VF/ pVT) cardiac arrest rhythm in any setting. Review included 9 papers, which had a total of 1581 adult patients, 326 (20.6%) of whom had DSD applied.	This study was a systematic review. It is level 3 evidence, as it is a systematic review which contains case-series studies.	Survival to hospital admission Termination of VF/pVT Return of spontaneous circulation Survival and/or good neurological outcome at hospital discharge, 30 days, or greater than 30 days	<u>Survival to hospital admission</u> We found very-low-certainty evidence (downgraded for risk of bias and inconsistency) from five observational studies. Survival to hospital admission with DSD ranged from 22.2% (10/45) to 48.0% (12/45) and with standard defibrillation from 19.4% (34/175) to 50.4% (52/103) A case series reported by Merlin et al. found 57.1% (4/7) patients survived to hospital admission after the use DSD. <u>Termination of VF/pVT</u> We found low certainty of evidence (downgraded for risk of bias and imprecision) from one pilot RCT24 and very-low-certainty evidence from four observational studies. In the randomized study, Cheskes et al. reported VF termination with DSD of 76.4% (42/55) and 66.7% (24/36) with standard defibrillation. In a non-randomized study, Cheskes et al. reported a VF termination rate of 76.5% (39/51) with DSD vs. 78.1% (157/201) with standard defibrillation. The other three studies examining VF termination were all case series and reported rates of VF termination with DSD between 70% (7/10) and 75% (9/12). <u>Return of spontaneous circulation</u> We found low certainty of evidence (downgraded for risk of bias and imprecision) from one pilot RCT24 and very-low-certainty evidence (downgraded for risk of bias and inconsistency) from six observational studies. In the single pilot RCT, Cheskes et al. reported a ROSC rate of 40% (22/55) with DSD compared to 25% (9/36) with standard defibrillation. They also found that ROSC at emergency department arrival was 32.7% (18/55) with DSD compared to 19.4% (7/36) with standard defibrillation. (Fig. 5) In the non-randomized studies, Beck et al. found the rate of ROSC 39.4% (28/71) with DSD vs. 60.3% (144/239) with standard	<u>Strengths</u> A systematic and comprehensive literature search was conducted with a predefined search strategy. It included the use of multiple databases, as well as primary sources from unpublished research. It was then followed up later and with a hand search to ensure that studies had not been issued, and that no new studies were available. Data extraction and validation was done by multiple researchers independently and disagreements were resolved by consensuses or with a third researcher if required. The studies that were used in the review included trials Risk of bias of individual studies was assessed using the Robins-I tool for observational studies and the Cochrane Risk of Bias 2 (ROB-2) tool for clinical trials. The overall certainty of evidence is reported in accordance with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Guidelines The scope of the systematic review was clear and included predefined criteria for including and excluding patient populations, interventions and comparisons. A meta-analysis was not conducted, thus inappropriate analysis did not occur. The meta-analysis was not done due to heterogeneity between studies.

				defibrillation. There was a significant decrease in odds of ROSC (adjusted OR 0.46, 95% CI 0.25, 0.87) with the use of DSD. Cheskes et al. found 17.6% ROSC with DSD compared to 21.4% with standard defibrillation. Emmerson et al. observed 37.8% (17/45) ROSC with DSD compared to 34.9% (61/175) with standard defibrillation and Mapp et al. observed ROSC in 20% (5/25) with DSD compared to 40.8% (42/103) with standard defibrillation. Ross et al. found 28.0% (14/50) ROSC rate with DSD compared to 37.6% (86/229) with standard defibrillation. Cortez et al. reported a case series of seven patients and found 57.1% (4/7) patients had a ROSC with DSD. <u>Survival and/or good neurological outcome at hospital discharge, 30 days, or greater than 30 days</u> We identified very-low-certainty evidence (down-graded for risk of bias and imprecision) from five observational studies with a total of 947 patients. Ross et al. found 8.0% (4/50) survival with DSD and 14.4% (33/229) with standard defibrillation (unadjusted RR 0.56, 95% CI 0.21, 1.50). Mapp et al. found survival of 16.0% (4/25) with DSD compared to 23.3% (24/103) with standard defibrillation (unadjusted RR 0.69, 95% CI 0.26, 1.80) and Emmerson et al. found survival of 6.7% (3/45) with DSD and 6.3% (11/175) with standard defibrillation (unadjusted RR 1.06, 95% CI 0.31, 3.64). Beck et al. found survival of 14.1% (10/71) with DSD compared to 20.5% (49/239) with standard defibrillation (unadjusted RR 0.69, 95% CI 0.37, 1.29). No association was found between DSD and survival after adjusting for potential confounders (adjusted OR 0.63 95% CI 0.27, 1.45). Cabanas et al. found survival of 30.0% (3/10) in a case series of DSD cases.	<u>Weakness/Limitations</u> Most of the included studies had a critical risk of bias due to a lack of adjustment for potential confounders. Further, three of the included nine studies were case series, which represent a significant source of selection bias. The timing of DSD across the included observational studies varied, with most studies using DSD late in a resuscitation attempt after failure of standard resuscitation interventions. DSD was used from the third defibrillation attempt to up to 10 or more attempts. Therefore, there is a strong possibility of resuscitation time bias making it difficult to draw conclusions from the included studies on the effect of DSD. There is also no reporting of ACLS interventions in most studies, which has an unknown (potentially confounding) impact on defibrillation success and termination of VF. There is no uniform definition of what constitutes refractory VF in the included studies. There was also inconsistency around pad placement, energy dose delivered, and a lack of uniformity in the technique of DSD application.

Comments: It appears that there are limited numbers of high quality studies, with high level evidence. There seems to be interest in this question in the medical community, as can be seen in how more studies and research has been done in the recent future.

Consider: Currently DSD faces many challenges due to limited resources in emergency medicine. Pad placement inconsistency, time passed before initiation of DSD during cardiac arrest and availability of a second crew and monitor to perform the treatment. There is currently no uniform definition of refractory VF causing variations in approaches and possibly results found. Due to the limited number of high quality studies that have not yet had the opportunity to be replicable because of how new they are, hesitancy in drastically changing protocols may be prudent.

Clinical Bottom Line: Survival to hospital discharge appeared to be higher with DSED and VC defibrillation than with standard defibrillation among patients with refractory VF during OHCA. Specifically the two outcomes that are most important to patients, good neurological outcome and survival to hospital discharge appear to be increased with DSD.

References:

Cheskes, S., Verbeek, P. R., Drennan, I. R., McLeod, S. L., Turner, L., Pinto, R., ... & Scales, D. C. (2022). Defibrillation strategies for refractory ventricular fibrillation. *New England Journal of Medicine*, *387*(21), 1947-1956.

Deakin, C. D., Morley, P., Soar, J., & Drennan, I. R. (2020). Double (dual) sequential defibrillation for refractory ventricular fibrillation cardiac arrest: A systematic review. *Resuscitation*, *155*, 24-31.