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Editorial

Defibrillation trials: POSED a challenge

Compared to other early links in the Chain of Survival, the evidence surrounding defibrillation has lagged considerably. Defibrillation treatment recommendations by the International Liaison Committee on Resuscitation (ILCOR) are mostly based on very low to low certainty of evidence.[1–4] Despite being identified as a priority area for research in 2015,[5,6] questions still remain about the optimal shock strategy, including the optimal first and subsequent dose(s).[7] In fact, a 2022 systematic review found no studies examining optimal first-shock energy and only one study comparing fixed versus escalating energy strategies.[8] Thus, there was great excitement within the resuscitation community when the Prehospital Optimal Shock Energy for Defibrillation (POSED) trial protocol was registered and published for an out-of-hospital cardiac arrest trial of three defibrillation strategies (120–150–200 J, 150–200–200 J or 200–200–200 J).[9]

POSED is a three-arm cluster randomised controlled feasibility study.[9] Feasibility studies are a type of preliminary study that includes testing the design and whether the proposed research can be successfully carried out.[10] These studies consider broader concepts than a pilot study testing a trial protocol, including the barriers and enablers to implementation field[11] and often include qualitative components.[10] The feasibility elements of the POSED trial included protocol adherence, with the primary outcome being the proportion of eligible patients who received the study intervention, and interviews with study paramedics to identify barriers and facilitators to patient recruitment. POSED investigators aimed to recruit patients for two years or until 90 patients were reached. Unfortunately, for POSED, and many other prehospital resuscitation trials,[12,13] the 2020 pandemic impacted on the ability to recruit patients within the study and funding timeframe, and the study was stopped early.

In this issue of Resuscitation Plus, Pocock et al. [26] presents the results of the 38 patients enrolled in the POSED study and identifies important issues for future studies. The major issues identified were the movement of study defibrillators to non-study ambulances and the time and resources required to download the defibrillator data. Defibrillators continue to lag behind technologically, particularly in terms of geolocation and the ease of access to data.[14–16] Technological enhancements could improve the ability to conduct research, clinical data collection, patient monitoring, and the coordination of care. At least two other resuscitation trials have also adopted the use of mobile phone and computer applications to aid in the recruitment, randomisation and follow-up of patients in both the prehospital and in-hospital environments.[17,18] These applications are also capable of facilitating the notification of enrolments to the trial team in real-time,[18] potentially minimising delays in data collection and patient consent.

Cluster RCTs require high levels of protocol compliance, which can only be achieved through the engagement and education of frontline staff. Paramedic and healthcare provider involvement in clinical trials can often be challenging, particularly when the intervention seeks to withhold or reduce a standard of care,[19] as may be the case with defibrillation dosing. Although POSED investigators achieved a good adherence rate to the protocol (86%), achieving high rates of compliance in larger trials involving thousands of front-life staff may be more challenging. Ensuring all defibrillators in circulation are randomised to a treatment arm (pre-programmed) will help minimise missed opportunities for recruitment. It may also be necessary to restrict the ability of paramedics to manually override shock energy, particularly in situations where providers are not aware of the defibrillator's treatment assignment. Unfortunately, POSED investigators were unable to complete the qualitative component of their feasibility trial. Future trials should include this component to explore provider perceptions of the intervention and identify barriers to recruitment, which could also help address residual cultural, educational or logistical issues.[20,21].

One of the challenges with the generalisability of defibrillation trials relates to the myriad of defibrillation technologies available on the modern market. The POSED trial utilised Zoll X-series defibrillators with impedance-compensation technology which is said to adjust shock energy to optimise the delivery of current.[22] The technology employed by Zoll differs to other device manufacturers, which employ varying shock durations, waveforms, impedance compensation strategies, and initial shock doses.[23] It is unclear what dose energies (or currents) were delivered as part of the 3-arm POSED trial, making the generalisability to other systems challenging. Both animal and human studies have shown that impedance compensation technology can upward adjust dose energies by as much as 30%,[24] which could ultimately deliver 200 joules in cases where the preset strategy is 150 joules. Importantly, extrapolation of energy doses from one device to another may be misleading,[25] which would further limit the translatability of trial findings to other systems.

Nevertheless, the variability in defibrillation technology underscores the importance of contemporary defibrillation trials in resuscitation. POSED has demonstrated that a cluster RCT of escalating versus fixed defibrillation energy for out-of-hospital cardiac arrest patients is feasible in the UK and may pave the way for an appropriately powered RCT to measure impact on patient outcomes. The

POSED author's sample size calculation suggests 15,000 patients are required to detect a 20% improvement in survival to hospital discharge.[ADD reference] The viability of such a trial is bolstered by the absence of adverse events, patient and consumer support, and the practicality of integrating cloud-based technology and computer programming into modern defibrillators. The imperative for a trial of this nature is long overdue.

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Declaration of competing interest

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