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Esmolol in persistent ventricular fibrillation/tachycardia with de-emphasised adrenaline – Introducing the REVIVE project

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Dear Professor Perkins,

Out-of-hospital cardiac arrest (OHCA) secondary to refractory or recurrent ventricular fibrillation or pulseless ventricular tachycardia (rVF/VT) presents a unique challenge for pre-hospital clinicians, and typically has worse outcomes than non-refractory VF/VT. In a recent registry study 56 % of patients presenting in a shockable rhythm fulfilled the most common definition of refractory VF (3 or more shocks)¹. Unfortunately, refractory and recurrent shockable rhythms have often been lumped together, mostly due to the unavailability of 'see through technology' and the pragmatic nature of clinical trials in this field². We have therefore chosen to coin the term 'persistent VF/VT' to encompass true refractory, but also recurrent VF/VT.

Excessive catecholamines that co-exist in persistent VF/VT exacerbate myocardial ischemia, induce tachyarrhythmias, and impair the heart's ability to respond to defibrillation. Esmolol is a short-acting beta-1 selective blocker that decreases myocardial oxygen demand, heart rate, and ventricular arrhythmias. By blocking beta-1 receptors, esmolol may improve the heart's responsiveness to defibrillation, stabilise electrical activity and reducing myocardial damage. In this letter, we briefly summarise the evidence for esmolol in persistent VF/VT and introduce a new trial group.

Table 1 Collates the current body of knowledge for the management of rVF/VT with esmolol alone, or in conjunction with other

therapies. Most of the studies are small, retrospective and observational. The area lacks a definitive RCT. Despite this, there is a signal that esmolol and/or adrenaline dose reduction increases the likelihood of achieving a return of spontaneous circulation (ROSC). We believe the signal is strong enough to pursue more rigorous research into this treatment modality.

We therefore introduce REVIVE – **RE**fractory **VF** **I**nter**V**ention with **E**smolol, a collaborative project between Hampshire & Isle of Wight Air Ambulance, Thames Valley Air Ambulance, Dorset & Somerset Air Ambulance, the Isle of Wight NHS Trust Ambulance Service and University Hospital Southampton NHS Foundation Trust. REVIVE is a mixed-methods project, including a national survey of pre-hospital emergency care services to establish the current landscape of treatment protocols and guidelines for this patient cohort (REVIVE-1), a retrospective observational review of a national database (REVIVE-2), and a pilot study (REVIVE-3). The pilot study will be a multi-centre feasibility randomised controlled trial, evaluating the combination of esmolol and de-emphasised adrenaline when compared to standard care for OHCA secondary to persistent VF/VT. Should the pilot study be successful, a larger randomised controlled trial can be pursued. We hope that our research collaborative will add to the evidence base for the management of this complex patient group.

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Table 1 –

No.	Date	Authors	Methods	N=	Results
1	2024	Watson et al. ³	Retrospective observational review of patient care records, single centre HEMS. De-emphasised adrenaline & esmolol administration.	124	'De-emphasised' adrenaline associated with sustained ROSC
2	2023	Stupca et al. ⁴	Retrospective cohort study of medical records, multicentre ambulance service. Esmolol, de-emphasis of adrenaline and vector change defibrillation vs standard care.	126	Intervention group less likely to obtain ROSC, similar incidence of neurologically intact survival between groups.
3	2022	Patrick et al. ⁵	Retrospective observational cohort study, single ambulance service. Esmolol vs standard care.	133	Esmolol may be associated with increased likelihood of ROSC.
4	2020	Miraglia et al. ⁶	Systematic review & meta-analysis	66	Likely greater rate of sustained ROSC, survival to ICU, survival to discharge and survival favourable neurological outcome with esmolol
5	2019	Gottlieb et al. ⁷	Systematic review & meta-analysis.	115	Greater rate of ROSC (temporary and sustained), survival to ICU, survival to discharge and survival favourable neurological outcome with esmolol
6	2016	Lee et al. ⁸	Retrospective observational review of patient care records, single centre ED. Esmolol vs standard care.	41	Greater rate of sustained ROSC, survival to ICU, survival to discharge and survival favourable neurological outcome with esmolol
7	2014	Driver et al. ⁹	Retrospective observational review of patient care records, single centre ED. Esmolol vs standard care.	25	Greater rate of ROSC (temporary and sustained), survival to ICU, survival to discharge and survival favourable neurological outcome with esmolol
8	2000	Nademanee et al. ¹⁰	Prospective observational study, single centre ED comparing multiple forms of sympathetic blockade (including esmolol) to standard ACLS.	49	Higher survival rate in patients with sympathetic blockade, when compared to standard ACLS.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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