Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial


SUMMARY:

- Ventricular fibrillation (VF) is the best initial rhythm for out-of-hospital cardiac arrest (OHCA), but the outcomes of shock-refractory VF are as poor as those of any of the other rhythm states (approximately 90% mortality).

- Pathophysiology has long suggested that patients with shock-refractory VF have a high probability of severe atherosclerotic heart disease, as compared with other pathologies that are more difficult to reverse (eg, pulmonary embolism or sepsis), and this has driven a desire to bring these patients into the catheterization laboratory (cath lab) to open up coronary arteries.

- However, that strategy has not worked: patients with initial-rhythm VF or ventricular tachycardia (VT) who have return of spontaneous circulation generally do not benefit from emergent transfer to the cath lab. Yet those patients had to have return of spontaneous circulation before transfer to the cath lab. Could extracorporeal membrane oxygenation (ECMO) be used as a bridge to get patients through the initial cardiac catheterization and stabilize them through the initial phase in the ICU?

- About a year ago, we covered an uncontrolled observational study on this topic that purported to show a survival benefit with this ECMO-based approach, but this trial reports the first randomized controlled data. The study is from Minnesota Medical Center and was conducted between August 2019 and June 2020.

- Patients with OHCA due to refractory VF were randomized to (1) usual care, ie, advanced cardiac life support in the ED or (2) immediate transfer to the cath lab while undergoing chest compressions with a LUCAS device, where they were immediately connected to peripheral venoarterial ECMO and underwent coronary angiogram stenting of the applicable vessels.

- Of note, according to the article, the inclusion criteria were fairly broad, comprising anyone 18-75 years old with OHCA, VF that did not recover after 3 shocks, and an estimated transport time <30 minutes. The authors excluded patients with trauma, drowning, cancer, and active GI bleeding, and patients in skilled nursing facilities. An exception from informed consent was obtained, and allocation was concealed until arrival at the ED.

- Patients in the intervention arm were brought to the angiography suite and underwent blood gas measurements. If the partial pressure of oxygen was <50, the end-tidal carbon dioxide was <10, the oxygen saturation was <85% or the lactate was >18; the patient was declared dead; otherwise, the patient was connected to ECMO, and underwent coronary catheterization and other aggressive procedures. The primary outcome was hospital survival, and the multiple secondary endpoints included functional outcomes at discharge, and 3 and 6 months.

- The authors screened only 36 patients and enrolled 30 patients, 15 in each group. All patients were treated at Minnesota Medical Center, a location with a large well-established ECMO unit. The mean age was 59, and the patients were 83% men; 1 patient withdrew consent in the treatment arm.

- Ultimately, 6/14 ECMO patients survived (43%) vs 1/15 patients (6.7%) in the standard-care group (a statistically significant result).

- At 6 months, 3/15 patients in the ECMO group had a Modified Rankin Scale score ≤2, vs 0/15 patients in the standard-care group.
In a fascinating turn, the NIH Data Safety Monitoring Board insisted that the authors stop the study at this 30-patient level because the probability of ECMO superiority was estimated to be 98%. This stoppage seems very early, especially given that the authors initially estimated that the difference between groups would be approximately 25% (37% vs 12%), and they would need 150 patients.

Other noteworthy points include that all patients in this trial had cardiac arrest in a public location and received bystander-assisted CPR, although these were not inclusion criteria. Patients not meeting these criteria might possibly have an initial VF/VT only rarely, if ever.

There are 3 main issues with this study and strategy: (1) What is the scientific truth: can we really believe that there is a significant mortality benefit on the basis of this small number (6 survivors vs 1)? What if 1 more person had survived in the control group, as should have been expected, because survival in this group is usually estimated at 10-12%? Do the authors or the NIH really expect physicians to adopt this protocol on the basis of 15 cases? (2) What is the actual cost of developing and maturing an ECMO program? Could this program really be established in most communities, given the need for extremely specialized training and facilities, and that the entire procedure must be completed in approximately 30 minutes, so the patient must be near a center that does ECMO. (3) What will the real-world effects be? How many people would actually benefit from this procedure if the findings are demonstrated to be true, and therefore the procedure is worth performing? Of note, the strategy is currently considered for only out-of-hospital refractory VF/VT, which is a rare situation.

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EDITOR’S COMMENTARY: These are the first randomized-trial data on an ECMO-driven resuscitative strategy for OHCA due to refractory VF. The results are favorable for this aggressive intervention strategy and are likely to prompt some medical centers to further develop such programs. However, because of the small sample size, early termination, and concerns about the generalizability of such a complicated and specialized intervention, the potential impact of widespread dissemination of this strategy remains mostly unknown.

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