The 2015 American Heart Association CPR/ACLS update categorizes amiodarone and lidocaine as IIb drugs that “may be considered” for ventricular fibrillation or pulseless ventricular tachycardia unresponsive to CPR, defibrillation, or vasopressors. Out-of-hospital use of these drugs has previously been shown to increase survival rate to hospital admission, but not necessarily to hospital discharge.

The effects of amiodarone and lidocaine on the rate of survival to hospital discharge are addressed in a recent randomized, double-blind, out-of-hospital trial comparing amiodarone, lidocaine, and placebo in the treatment of shock-refractory ventricular fibrillation or pulseless ventricular tachycardia (N Engl J Med. 2016;374[18]:1711-1722). This study was conducted by the Resuscitation Outcomes Consortium (ROC) in 3,026 patients at 10 US and Canadian sites. The ROC authors concluded that “overall, neither amiodarone nor lidocaine resulted in a significantly higher rate of survival or favorable neurologic outcome than the rate with placebo.” But the article raises concerns about its methodology, appropriateness of its primary and secondary outcomes to out-of-hospital (or prehospital) care, and the manner in which its findings were reported.

Because of the condition (unconscious) and circumstances (out of hospital) of the patients at the time medication or placebo must be administered, this NIH-supported trial was conducted under exception from informed consent in emergency research, with FDA and Health Canada oversight, and with approval by trial-site Institutional Review Boards. Notwithstanding the list of regulatory bodies that approved the exception, is the trial appropriate for drugs previously demonstrated to be efficacious in improving survival rates to hospital admission—long considered the goal of prehospital care—when subsequent care from admission to hospital discharge is not standardized or controlled across multiple sites in two countries?

Another concern is the way the results were reported. Will the authors’ conclusion that overall, neither amiodarone nor lidocaine resulted in a significantly higher rate of survival suggest to hurried readers that there is no benefit to any patient to hospital discharge from either antiarrhythmic agent? In the results section, the authors report “active drugs were associated with a survival rate that was significantly higher than the rate with placebo among patients with bystander-witnessed arrest but not among those with unwitnessed arrest.” Also noted in the accompanying editorial entitled “Out-of-Hospital Cardiac Arrest—Are Drugs Ever the Answer?” (N Engl J Med. 2016;374[18]:1781-1782), both drugs were associated with nonsignificant increases in survival rate, fewer subsequent shocks, and less administration of rhythm-control medications or need for CPR during hospitalization, compared with patients’ courses after placebo.

The ROC trial is not the first or only out-of-hospital trial to use survival to hospital discharge as its primary outcome measure. A 1990-1991 study using death or discharge home to determine survival from out-of-hospital cardiac arrests in New York City found that of the 2,329 patients who met entry criteria for that study, overall survival was only 1.4%—which the authors attributed partly to lengthy elapsed time intervals at every step in the chain of survival, lack of adequate bystander CPR, and possibly sociodemographic features common to victims of cardiac arrest in large cities (JAMA. 1994;271[9]:678-683). The poor results led to increases in first responders and AED availability but not the abandonment of properly performed CPR and ACLS. In the ROC trial, length of time from cardiac arrest to administration of medications clearly was shown to be a significant outcome determinant and was emphasized in the accompanying editorial. Here too shouldn’t we concentrate on optimizing the setting and timing of CPR and ACLS measures?

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