be of no benefit to our patients."[4] This statement is really quite contrary to studies that have shown that the time to administration of epinephrine during in-hospital cardiac arrest in nonshockable rhythms affects survival with favorable neurological outcomes. Caution should be taken in postoperative cardiac surgery patients.[5]

The PARAMEDIC2 trial provides little evidence of the value epinephrine during in-hospital cardiac arrest, particularly after cardiac surgery. The authors make a good argument that epinephrine should not be bolused indiscriminately in postoperative cardiac surgery patients who experience cardiac arrest. Indeed there may exist a number of quick reversible causes that should be the focus of the medical team while CPR is initiated, and preparations for emergency chest reopening are undertaken.

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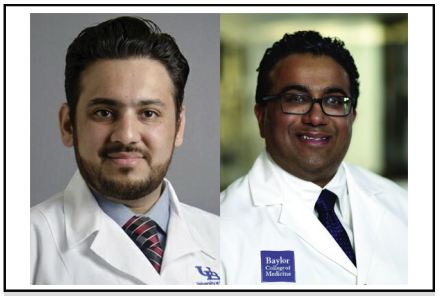
# Commentary: To epi or not to epi—that is the question

Nabeel H. Gul, MD, and Subhasis Chatterjee, MD



Nabeel H. Gul, MD, and Subhasis Chatterjee, MD, FACS, FACC, FCCP

**CENTRAL MESSAGE**

Standard resuscitation measures after postcardiotomy cardiac arrest require thoughtful consideration. Epinephrine should be used cautiously but not abandoned.

When evidence is not clear, perception can obscure reality. Epinephrine has been widely used in resuscitation after cardiac arrest; however, its role in improving long-term survival with a favorable neurologic outcome is questionable. In a review of the multicenter 2018 Prehospital Assessment of the Role of Adrenaline: Measuring the Effectiveness of Drug Administration in Cardiac Arrest (PARAMEDIC-2) trial,[1] Dunning and Trevis[2] ask in this issue of *Journal* whether the trial results can be extrapolated to postcardiotomy arrest.

The critical distinction is that the PARAMEDIC-2 trial focused exclusively on out-of-hospital cardiac arrest (OHCA); postcardiotomy arrest, in contrast, is an in-hospital cardiac arrest (IHCA). The all-comer survival rate after IHCA is approximately 25%, compared with 10% to 12% for OHCA, because IHCA is characterized by rapid initiation of basic life support and resuscitation medications in contrast to the 20 minutes seen in the PARAMEDIC-2 trial.[3] This is even more pronounced when results are compared across hospitals, with IHCA survival rates ranging from 8% to 31%.[4] Differences in cardiopulmonary resuscitation (CPR) quality or postarrest management, such as targeted temperature management,

From the Division of General and Cardiothoracic Surgery, Michael E. DeBakey Department of Surgery, Baylor College Medicine; and Department of Cardiovascular Surgery, Texas Heart Institute, Houston, Tex.

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Address for reprints: Subhasis Chatterjee, MD, Baylor College of Medicine, One Baylor Plaza, MS: BCM 390, Houston, TX 77030-3411 (E-mail: subhasis.chatterjee@bcm.edu).

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may explain the disparity in results. In an intensive care unit setting after cardiac surgery, CPR is performed by an experienced team by using an arterial line or end-tidal $CO_2$ monitoring to confirm the adequacy of CPR. The PARAMEDIC-2 trial, however, could not provide insight into variations in CPR quality or postarrest management.

In the PARAMEDIC-2 trial, the mean time interval between the emergency call and epinephrine administration was 20 minutes, which is significantly longer than that expected in a cardiac intensive care unit (average 3-4 minutes).[5] Each minute of delay in epinephrine administration after 10 minutes of OHCA increases the risk of unfavorable outcomes.[6] In a subgroup analysis of the PARAMEDIC-2 trial, the odds of return of spontaneous circulation in those receiving epinephrine immediately after cardiac arrest compared with placebo was more than twice as likely.[7] Therefore, the comparison of administering epinephrine within 20 minutes for the PARAMEDIC-2 trial versus 5 minutes for resternotomy is not a meaningful real-world comparison. In patients with postcardiotomy arrest, a dose of epinephrine would be administered in less than 5 minutes, under the direction of a senior clinician after pacing or defibrillation attempts and determining tamponade as unlikely, if appropriate.

Because of poor survival outcomes after using the 1-mg bolus dose of epinephrine in OHCA, others attempted low-dose (0.5 mg)[8] and high-dose (0.1-0.2 mg/kg)[9] epinephrine without improved results. An analysis of 21,000 patients examined whether the dosing period of epinephrine may be optimized for IHCA.[10] The results of this analysis suggested that perhaps the optimal frequency of epinephrine administration is less than that indicated in current resuscitation practices. Two randomized controlled trials showed improved survival rates with good neurologic outcomes after the combined use of vasopressin, epinephrine, and steroids during cardiac arrest, and the use of post-resuscitation stress-dose steroids.[11,12] Although one may question the optimum timing, dosage, combination, and frequency of administering epinephrine, current evidence is not convincing enough to completely reject the role of epinephrine in IHCA. The current guidelines of the Society of Thoracic Surgeons on resuscitation after cardiac surgery, as written by Dunning, state the following: "However, once a cardiac arrest has occurred, we recommend that epinephrine should only be administered by clinicians with experience in its use in cardiac surgery, and it should not be included in the routine arrest protocol."[13] It seems reasonable to infer that a postcardiotomy cardiac arrest run by a medicine-based code team may cause more harm than good, such as in a postaortic valve replacement patient who has a blood pressure of 250 mm Hg after the 1-mg epinephrine dose, resulting in mediastinal bleeding. An expert clinician who is familiar with the patient can better judge the optimum dosage, frequency, and delivery of the resuscitation medication.

The outcomes of the PARAMEDIC-2 trial confirm the epinephrine OHCA experience observed in other randomized and observational studies. However, in patients with IHCA after postcardiotomy arrest, epinephrine is a part of the expert clinician's armamentarium. When it comes to deciding whether to epi or not to epi, it is still reasonable to epi in select situations.

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