# Research Analysis of Using tPA to Treat Cardiac Arrest

Tue, Feb 28, 2017 | By Amanda Polsinelli, MD , Elizabeth K. Powell, MD

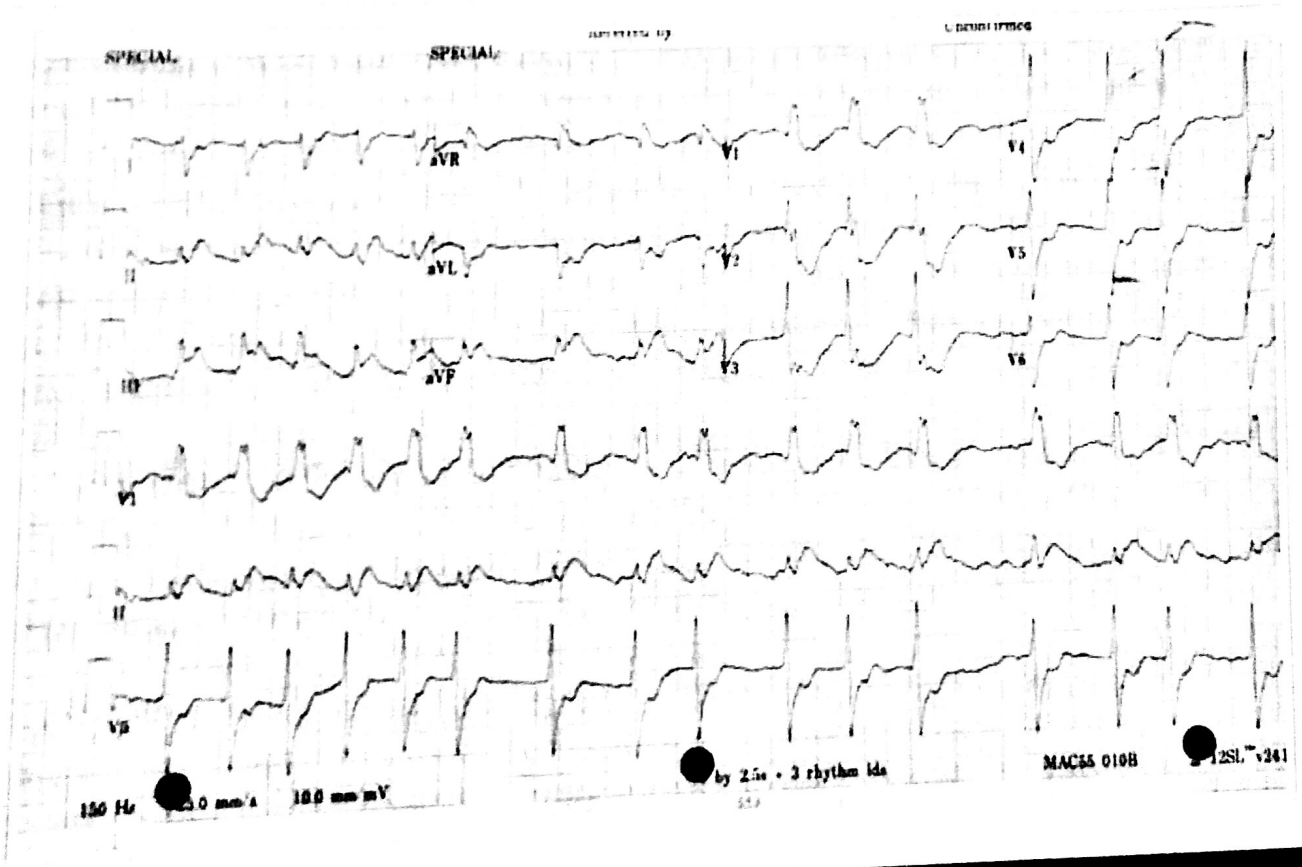


*Figure 1: ECG obtained 16 minutes after tPA showing STEMI*

James and his friend Brandon, a 41-year-old male with an initially unknown past medical history, are hanging out when Brandon goes into cardiac arrest just outside of his house. James calls 9-1-1 and begins CPR until EMS arrives.

James tells the arriving crew his friend could be hypoglycemic, so the lead paramedic administers an ampule of D50. A supraglottic airway is placed and compressions are continued, with end-tidal carbon dioxide ($EtCO_2$) through the supraglottic device noted to be in the 30s. The crew also sees Brandon is in v fib, so they shock him with 200 joules and administer 3 mg epinephrine. He's transported to the ED with continuous compressions and ventilation provided through the supraglottic device.

## Hospital Course

In the ED, pads are placed and his rhythm is again noted to be v fib. He's defibrillated with 200 joules without return of spontaneous circulation (ROSC). He's intubated and given continuous respirations with verification of tube placement by auscultation and $EtCO_2$ monitor. His initial $EtCO_2$ is still noted to be in the 30s.

Continuing CPR, nine 200-joule defibrillation attempts are made, and Brandon receives multiple code doses of epinephrine and amiodarone (300 mg, then 150 mg loading doses). He also receives an ampule each of sodium bicarbonate and calcium gluconate, and a finger stick of 230 mg/dL. The interventional cardiology department is called to discuss potential mechanical support options to catheterization. It's decided to continue resuscitation efforts in the ED, so, 13 minutes into the code on the sixth defibrillation attempt, 50 mg of tissue plasminogen activator (tPA) are given for presumptive myocardial infarction (MI) given v fib as the underlying rhythm.

After receiving the tPA, the patient is noted to be in v tach without a pulse. On the 10th defibrillation attempt, dual pads are placed and 200 joules are delivered through each. On the next pulse check the patient has ROSC after a total of 29 minutes of CPR. Interventional cardiology is consulted to begin emergent cardiac catheterization.

Post-ROSC, the patient is persistently hypotensive so he's started on an epinephrine infusion as well as amiodarone due to his v fib/v tach arrest. An arterial line and central line are placed in the left femoral artery and vein to preserve the right vessels for potential cardiac catheterization. An ECG confirms an ST elevation myocardial infarction with ST elevations in the inferior leads (II, III, aVF), reciprocal depressions in aVL, and ST depressions most pronounced in precordial leads V2–V4, suggesting right coronary artery (RCA) involvement. (See Figure 1, above.)

The patient goes into v fib again 15 minutes later, just prior to transfer to the cardiac catheterization lab. He's given an initial 200-joule defibrillation attempt, epinephrine

and lidocaine without ROSC. He's again defibrillated with dual pad placement at 200 joules each with ROSC on the next pulse check for a total of 10 minutes of CPR. Repeat ECG shows an idioventricular rhythm, which indicates possible early reperfusion. (See Figure 2, below.) A norepinephrine (levophed) infusion is added for additional vasopressor support and the patient is taken emergently to the cardiac catheterization lab.

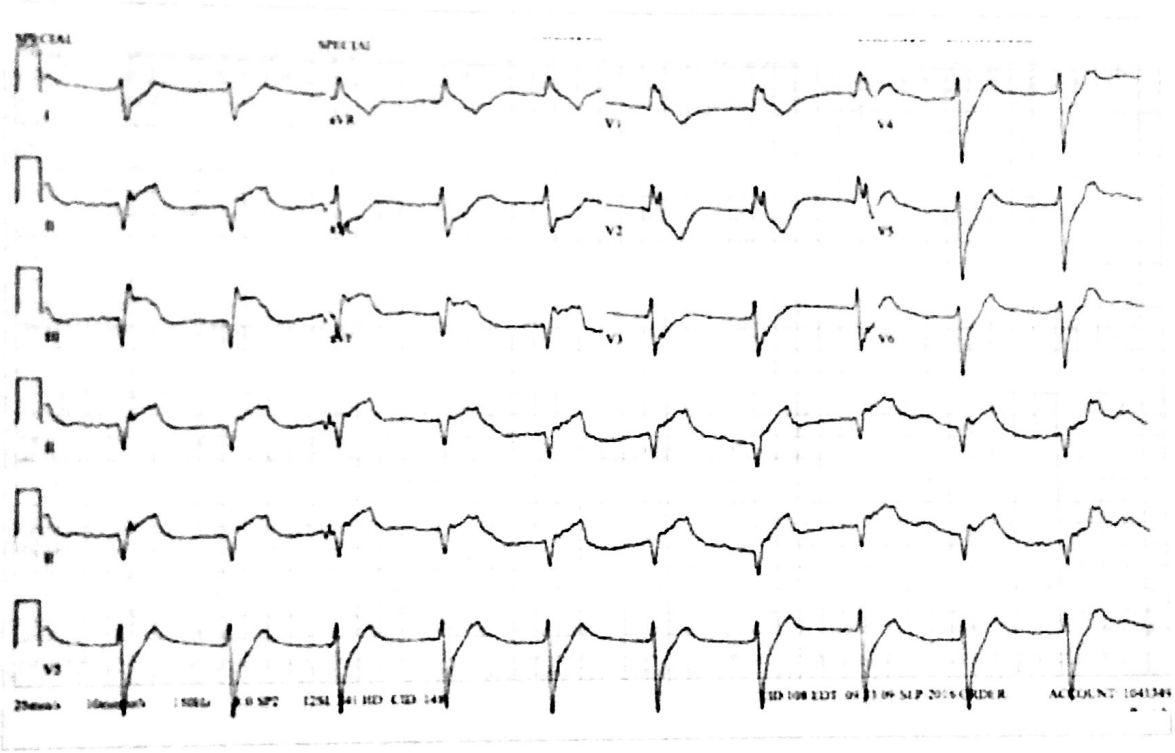

Figure 2: ECG obtained 27 minutes after tPA showing idioventricular rhythm

The coronary artery lesion is found to be a 100% proximal right coronary artery occlusion with a large clot burden. (See Figure 3, below.) A total of three stents are placed across the lesion. (See Figure 4, below.) The patient has multiple runs of ventricular tachycardia while in the procedure and requires lidocaine, but no vasopressor medications are required after stenting.

Figure 3: Right coronary artery (RCA) prior to angioplasty and stenting

Brandon is placed on the hypothermia protocol, cooled to 97 degrees F (36 degrees C) and transferred to the cardiovascular ICU to finish recovering.

## Discussion

Refractory v fib is a complex disease process to treat. Often, a cardiac cause should be suspected. The evidence for the use of tPA or other thrombolytics in CPR for patients with suspected acute MI is mixed and some do recommend thrombolytics in selected patients whose arrest is likely due to a thrombotic event.[1,2]

Over 300,000 people annually have an out-of-hospital EMS assessed cardiac arrest in the United States, with about 60% of all cardiac arrests treated by EMS.[3,4] Among those treated by EMS, 21.5% have a ventricular tachycardia or fibrillation that's treatable by defibrillation.[5] The American Heart Association's (AHA) Heart Disease and Stroke Statistics report from an unpublished Resuscitations Outcome Consortium (ROC) registry data that survival to hospital discharge in EMS-treated cardiac arrest in 2011 was 10.3% and survival to hospital discharge for bystander witnessed v fib was 31.4%.[3] Similarly, in the Cardiac Arrest Registry to Enhance Survival (CARES), survival to hospital discharge for EMS treated out-of-hospital arrest was 9.8%.[6]

Figure 4: RCA after angioplasty and stenting

The exact proportion of sudden cardiac death due to coronary heart disease is widely debated and difficult to ascertain. However, it's estimated that 80% of sudden cardiac death is attributable to coronary heart disease. Additionally, it's estimated that half of deaths from coronary heart disease are due to sudden cardiac death.[7]

Thrombolytics are known to improve mortality in acute MI both in the short term and at long-term follow up.[8,9] Given the proven benefit in patients with acute MI, it's reasonable to hypothesize that thrombolytics may have a benefit in sudden cardiac arrest thought to be attributable to acute MI. Additionally, thrombolysis has a theoretic benefit to cerebral micro-perfusion improvement, possibly improving neurologic outcomes after cardiac arrest.[10]

Use of tPA in cardiac arrest that's been refractory to conventional advanced cardiovascular life support (ACLS) has been investigated with mixed results. There had been some concern that tPA in patients undergoing CPR could lead to bleeding complications from the trauma associated with the mechanics of CPR, but this hasn't been demonstrated.[11,12] Retrospective studies of patients receiving tPA in cardiac arrest suspected to be due to MI showed promise with increased survival rates and favorable neurologic outcomes.[13–15] A meta-analysis of eight papers of retrospective and a non-randomized prospective trial showed a significant trend toward ROSC though

increased severe bleeding risk with 100 mg dose of tPA and heparin during cardiac arrest.[16]

The large randomized, double-blind, placebo-controlled prospective multicenter Thrombolysis in Cardiac Arrest (TROICA) trial published in 2008 looked at the 30-day survival rate for those either receiving tenecteplase or placebo in out-of-hospital witnessed cardiac arrest.[17] For inclusion, CPR had to be initiated within 10 minutes of arrest and continued for up to 10 minutes prior to randomization. In this trial, patients with pulseless electrical activity (PEA) arrest were immediately randomized upon IV placement and patients with initial shockable v fib/v tach rhythm were randomized after an initial three consecutive defibrillation attempts. Notably, heparin use was discouraged in this trial. Ultimately, the trial was stopped for futility. There was no significant difference in the primary endpoint or any of the secondary endpoints of hospital admission, ROSC, 24-hour survival, survival to discharge or neurologic outcomes.

The TROICA trial failed to show benefit. However, there are several factors that may have contributed to this and need further review. First, there were rapid response times of 18 minutes from call to tenecteplase administration for those enrolled in the trial with the overall survival to hospital discharge of the cohort well above the average (15.8% vs. 10.3%). These results in both groups may lead to a ceiling effect of current treatment, making it difficult to show survival benefit of the intervention. Additionally, many of the retrospective trials showed benefit with the use of heparin and aspirin in addition to thrombolytics, and the TROICA trial discouraged the use of heparin and aspirin. Platelet activation is one of the underlying mechanisms behind acute coronary syndromes, and thrombolytics themselves can be platelet activators, so the use of heparin and aspirin may actually improve patient outcomes.

Finally, the trial enrolled several patients in asystole prior to changing the protocol midway through the trial due to exceedingly low survival rates in this group. It also enrolled PEA arrest patients, which have a much higher likelihood of underlying pathology other than MIs.[18]

## Summary

The patient had a case of refractory v fib secondary to stent occlusion that was treated with tPA with successful ROSC, even though current guidelines recommend against the routine use of thrombolytics in CPR. Retrospective trials of thrombolytic use in out-of-

hospital arrest do suggest a potential benefit; however, the only large randomized study of thrombolysis in out-of-hospital arrest,TROICA, failed to show improved survival. Broad patient selection in TROICA and the failure to use antiplatelet therapy may have limited the efficacy of thrombolytics in this trial. Some do continue to advocate its use in select patients with a high likelihood of underlying thromboembolic disease leading to the arrest. In fact, there were no results in the TROICA trial to recommend against thrombolysis in patients with pathology that could theoretically benefit from its use. jems

**Amanda Polsinelli**, MD, earned her MD degree at the University of Wisconsin School of Medicine and Public Health. She's currently a third-year resident in emergency medicine and a flight physician with UC Health Air Care at the University of Cincinnati.

**Elizabeth K. Powell**, MD, is an emergency physician and assistant professor of emergency medicine at the University of Cincinnati. She's the medical director of UC Health Mobile Care, the associate medical director of UC Health Air Care, and an active flight physician.