THE CCU CORNER

Takotsubo Cardiomyopathy, or When an ACS Is Not an ACS

BY GEORGE PHILIPPIDES, M.D., AND ERIC H. AWTRY, M.D.
EDITED BY DR. THOMAS RYAN

The Problem

Approximately 400,000 cases of acute ST-segment elevation myocardial infarction (STEMI) occur in the United States each year. However, occasionally patients who present with a clinical syndrome consistent with STEMI do not have significant coronary artery disease. Among this group of patients, a subset has been increasingly recognized that develop characteristic, transient, left ventricular dysfunction—so-called takotsubo cardiomyopathy.

The Patient

A 58-year-old woman presented after developing acute chest pain and dyspnea during "an exhilarating prayer service with wild singing and celebrating." Her initial ECG revealed anterior ST elevation and her troponin was elevated at 3.04 ng/mL. Cardiac catheterization revealed insignificant coronary arter disease and mildly elevated filling pressures. Left ventriculography revealed her left ventricle (LV) to be hyperdynamic at the base and dyskinetic from midlevel to apex ("apical ballooning"), with an ejection fraction (EF) of 25%.

She was treated with diuretics, angiotensin-converting enzyme inhibitors, and β-blockers, and several days later an echocardiogram revealed improving wall motion abnormalities with an ejection fraction of 45%.

A repeat echocardiogram 6 weeks later demonstrated normalization of her LV function.

Clinical Presentation

Patients with takotsubo cardiomyopathy (also referred to as apical ballooning syndrome, acute stress-induced cardiomyopathy, catecholamine-mediated cardiomyopathy, and the broken heart syndrome) usually present with anginal-type chest pain that is often associated with dyspnea, and which characteristically develops in the setting of a preceding emotional or physical stressor. The syndrome occurs predominantly in postmenopausal women, and in several recent series, accounts for 1%-2% of patients presenting to the hospital with suspected acute coronary syndromes (ACS). The ECG usually reveals ST-segment elevation in the anterior leads, although isolated anterior T-wave inversions have also been described.

Myocardial biomarkers are normal or only mildly elevated, and cardiac catheterization reveals no significant coronary artery disease. However, the LV function is impaired with characteristic findings on echocardiography and ventriculography: apical and/or mid ventricular akinesis or dyskinesis, with hyperdynamic function of the basilar segments, resulting in a LV in systole that is similar in shape to a Japanese octopus trap, or tako-tsubo, hence the name. The apex of the right ventricle is occasionally involved and development of a dynamic LV outflow tract gradient has been described.

Overall prognosis is good, although cardiac complications have been described in the acute setting. While frank pulmonary edema and cardiogenic shock are uncommon in these patients, mild pulmonary congestion is frequently noted. Both atrial and ventricular arrhythmias have been noted, and left ventricular apical thrombi and subsequent thromboemboli have been described. Although the vast majority of these patients have normalization of ventricular function within several weeks, recurrence of the LV dysfunction has been seen in as many as 6% of patients.

Pathophysiology

The pathophysiology of the transient ventricular dysfunction has not yet been determined, although several theories exist. Multivessel coronary spasm has been proposed as a possible mechanism; however, the absence of vasospasm during coronary angiography in the majority of these patients and the nonanatomic distribution of LV dysfunction suggest vasospasm is unlikely the sole cause. Several lines of evidence suggest that endothelial dysfunction is present in patients with this syndrome, although it is unclear if the microvascular dysfunction is the cause of the disorder or a secondary response.

The precipitation of this syndrome by significant stressors suggests that catecholamine excess likely plays a role. In this regard, elevated levels of norepinephrine and other catecholamines have been demonstrated in these patients. The increased catecholamines may contribute either through oxidative stress-induced myocyte injury, or through the development of an acute severe LV outflow tract or midcavitary obstruction resulting in subendocardial ischemia and LV dysfunction.

Our Experience:

Over the past several years we have seen multiple patients with features consistent with this syndrome.

Obvious precipitating events were present in the vast majority of patients, and have included emotional stressors (surprise birthday parties or hearing of the death of a family member), physical stressors (trying to push a car out of the way of a snowplow), systemic illness (sepsis, acute blood loss, pheochromocytoma), and in at least one case, administration of exogenous catecholamines for the treatment of hypotension.

Prospective differentiation of these patients from those truly presenting with an STEMI is difficult, and it has been our approach to treat these patients as having ACS until the diagnosis is clarified at the time of angiography.

Short-term treatment of this syndrome is directed at specific complications—heart failure, arrhythmias, and shock are managed similar to that in other settings.

Given the potential role of catecholamines, it seems appropriate to treat these patients with β-blockade, at least in the short term.

Since relatively rapid improvement in LV function is expected, we routinely repeat an echocardiogram several days after admission, and again 1-3 months after discharge.

If LV dysfunction persists, treatment with ACE inhibitors should be initiated, and short-term anticoagulation should be considered if apical akinesis is present.

The appropriate duration of this pharmacologic therapy is currently unknown; however, we usually treat patients empirically for several months, and at least until normalization of LV function is documented.

DR. AWTRY is assistant professor of medicine and director of education at Boston Medical Center. DR. PHILIPPIDES is assistant professor of medicine and director of the Coronary Care Unit at BMC. To respond to this column or suggest topics for consideration, write to our editorial offices or e-mail us at cardnews@elsevier.com.

GIK Infusion Not Beneficial and Possibly Harmful in STEMI

BY MARY ANN MOON
Contributing Writer

Infusion of glucose, insulin, and potassium yielded no benefit for patients with ST-segment elevation myocardial infarction in two large clinical trials, and the treatment may even cause harm, suggests an analysis of data on almost 23,000 patients.

Twenty-four-hour glucose-insulin-potassium (GIK) infusion exerted no favorable effect on any important clinical end point, and it appeared to raise mortality in the early postinfarction period, researchers wrote in the JAMA.

Several small studies have supported the use of GIK infusion to treat STEMI, but the Clinical Trial of Reviparin and Metabolic Modulation in Acute Myocardial Infarction Treatment and Evaluation—Estudios Clinicos Latino America (CREATE-ECLA), which enrolled more than 20,000 subjects, showed only a neutral effect.

A second large-scale clinical study assessing the treatment—the Organization for the Assessment of Strategies for Ischemic Syndromes-6 (OASIS-6) trial—was halted early when the CREATE-ECLA results were announced. The data from the first 2,748 subjects in the OASIS-6 trial have just been analyzed and combined with the CREATE-ECLA findings.

Dr. Rafael Diaz of Estudios Cardiologica Latin America, Rosario, Argentina, and his associates have reported the 30-day outcomes for 22,943 subjects in both studies.

GIK infusion exerted no favorable effect on any important clinical end point, and it appeared to raise mortality in the early postinfarction period.

There were no differences between STEMI patients who received GIK infusions and control subjects who received standard care in 30-day rates of death (9.7% vs. 9.3%), heart failure (16.5% vs. 16.7%), or the combined end point of death or heart failure (20.3% vs. 20.4%) in the combined analysis. Similarly, in subgroup analyses comparing patients who were treated immediately (within 2 hours) after symptom onset, those treated soon (within 4 hours), and those treated later (after 4 hours), GIK infusion did not reduce mortality in any group.

"We observed a higher rate of death and the composite of death or heart failure at 3 days in patients allocated to GIK therapy, compared with controls. Between 4 and 30 days, there were lower rates of death and the composite of death or heart failure in the GIK infusion group than in the control group, and the overall effect of GIK therapy on 30-day outcomes was neutral.

"It is possible that despite its early harmful effects, GIK therapy may have delayed benefits that neutralize its early hazard, but a more likely explanation for the observed 'late benefit' is post-trandomization (survivor) bias," the investigators said (JAMA 2007;298:2399-405).

It appears that rather than simply ensuring normalized glucose levels, potassium levels, and fluid balance after STEMI, GIK infusion may actually induce hyperglycemia, hyperkalemia, and net fluid gain, they said.

The OASIS-6 trial was funded by Sanofi Aventis, Organon, and GlaxoSmithKline. ■