Editorials

Tako-Tsubo Cardiomyopathy and Cardiac Magnetic Resonance Imaging

Address for correspondence:
Carsten Schmalfuss, MD
Section of Cardiology
Malcom Randall VA Medical Center
1601 SW Archer Road
Gainesville, FL 32608
carsten.schmalfuss@va.gov

Carsten Schmalfuss, MD
Section of Cardiology, Malcom Randall VA Medical Center, and Division of Cardiovascular Medicine, University of Florida, Gainesville, Florida

See Article on Page 178

Tako-tsubo cardiomyopathy (TCMP), also known as apical ballooning syndrome, is an acute, reversible dysfunction of the apical and/or midventricular segments of the left ventricle (LV). Patients present with sudden onset of ischemia-like chest pain and varying degrees of congestive heart failure. They are predominantly postmenopausal females and often describe a recent, emotionally stressful event. Other acute findings are elevated cardiac biomarkers and ST-segment abnormalities, including ST elevations.

The initial presentation of TCMP is often indistinguishable from an acute coronary syndrome (ACS), and the patients commonly undergo urgent/emergent invasive coronary angiography as their first diagnostic test. Usually there are no significant stenoses or unstable plaques in the major branches of the coronaries; the ventriculography reveals characteristic apical and/or midventricular akinesis or dyskinesis with compensatory hyperkinesis of the basal segments of the LV. The treatment is supportive and includes the use of angiotensin-converting enzyme inhibitors, long-acting beta-blockers, and diuretics as needed, at least until the ventricular function normalizes. The course of TCMP is most often benign, with full resolution of the myocardial dysfunction within days or weeks.

The exact pathophysiology of TCMP is not known. It has been suggested that an aborted ST-elevation myocardial infarction (MI) with spontaneous lysis of thrombus may be responsible; however, this theory does not explain the wall-motion abnormalities extending beyond a single coronary artery distribution. Similarly, transient vasospasm of multiple coronaries has been postulated as a possible cause, but pharmacologically induced vasospasm could be shown only in some patients with TCMP. Another hypothesis is that of microcirculatory dysfunction causing transient ischemia. Several studies have been published showing ischemia in the same apical and midventricular myocardial segments that are dyskinetic. This microvascular dysfunction may be caused by transient catecholamine excess secondary to emotionally stressful events. Wittstein et al[1] found significantly higher levels of catecholamines and their metabolites in patients presenting with TCMP compared with patients with acute MI and similar degrees of heart failure. However, endomyocardial biopsy done in a subgroup of these patients showed histological signs of myocardial injury, with contraction band necrosis and mononuclear infiltrates often seen with catecholamine-mediated direct cardiomyocyte toxicity rather than with microvascular dysfunction.

Cardiac magnetic resonance imaging (CMRI) has the unique ability to noninvasively demonstrate myocardial tissue injury through the presence of edema and/or prolonged retention of gadolinium contrast (early and late gadolinium enhancement, or LGE) in myocardial extracellular matrix. The differential diagnosis of TCMP includes ACS and myocarditis, and it has been demonstrated in multiple studies that the location and distribution of edema and LGE can accurately differentiate acute MI from acute myocarditis. The absence of any LGE is a common criterion for the diagnosis of TCMP in most CMRI centers.

In this issue of *Clinical Cardiology*, Avegliano et al[2] provide evidence for a previously not described unique morphological pattern of LGE in patients with TCMP on early CMRI. A total of 8 patients with TCMP were enrolled. The diagnosis was based on transient apical or midventricular wall-motion abnormalities beyond the distribution of a single coronary artery, absence of significant coronary artery stenosis, presence of new ST-T segment changes, or elevation in cardiac troponin, and absence of pheochromocytoma and myocarditis. All subjects underwent CMRI within 72 hours of cardiac catheterization as well as repeat CMRI at 90 days after the initial admission. The CMRI protocol consisted of cine imaging for wall-motion assessment, as well as T2 (edema imaging) and LGE sequences 10 minutes after gadolinium contrast administration. Evaluation of CMR images was done qualitatively. The CMRI on admission showed typical wall-motion abnormalities and reduced LV function in all patients. All 8 patients had mild transmural LGE in all segments with abnormal contractility, compared with no LGE in segments with normal contractility. In the 5 patients with evaluable T2 (edema imaging) sequences, the segments with transmural myocardial edema matched the segments with abnormal contractility. The CMRI on follow-up revealed normal wall motion and absence of LGE in all patients. The authors conclude that early imaging with CMRI in patients with TCMP reveals a characteristic pattern of reversible, mild transmural LGE suggestive of diffuse myocardial and microcirculatory damage.

Prior studies have very rarely reported LGE in patients with TCMP.[3,4] A large observational study (Sharkey et al) found LGE in only 1 of 95 patients with TCMP undergoing CMRI.[5] However, the CMRIs in this study were done at

The author has no funding, financial relationships, or conflicts of interest to disclose.

Received: January 12, 2011
Accepted: January 19, 2011

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.20898

the discretion of the treating physician (only in 95 of 136 patients), and the time from admission to CMRI and time of LGE imaging after the administration of gadolinium contrast were not standardized. These factors may have led to selection of healthier or recovering patients with a lesser degree of myocardial inflammation and more time for contrast washout resulting in no detectable LGE.

It seems important to perform CMRI early after admission to detect LGE, as shown recently by Rolf et al.[6] The researchers performed LGE imaging in 15 patients with TCMP within 24 hours of admission. All patients also underwent LV endomyocardial biopsy acutely to determine the amount of extracellular matrix. In the acute phase, 5 patients (30%) had LGE and a significantly higher amount of extracellular matrix compared with patients without LGE. The LGE signal intensity was much lower in TCMP compared with LGE in myocarditis or acute MI. As in the current study, the LGE signal was no longer present on follow-up CMRI 2 weeks later, and repeat LV biopsies also showed normalization of the extracellular matrix. The authors concluded that presence of LGE does not rule out TCMP, but rather defines a subgroup with larger transient increase in extracellular matrix in response to the myocardial inflammation.

The present study[2] shows mild transient LGE not only in some, but in all patients. It is possible that there is not only the global gender predisposition for the development of TCMP, but also a strong regional predisposition for a larger increase in extracellular matrix in response to TCMP. Most of the earlier studies that did not show any or very little LGE were performed with patients from North America and Europe,[3–5] whereas the present study enrolled only subjects from South America. Together, this predisposition and the CMRI performed early after admission may explain the finding of mild transmural LGE in all patients.

With their study, Avegliano et al[2] have added to the increasing body of evidence that, due to its unique ability to noninvasively demonstrate and distinguish various types of myocardial tissue injury, CMRI is very useful to help make the initial diagnosis of and provide follow-up of patients with TCMP. Some old and new questions remain: What is the exact etiology of TCMP? What is the basis for the female predisposition for TCMP? Is there a genetic difference beyond gender to explain the differences in the myocardial response to TCMP as seen on CMRI? Future multicenter, long-term, longitudinal studies combining imaging technology, histology, and genetic evaluation may be able to provide answers to these questions.

References

1. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med.* 2005;352:539–548.
2. Avegliano G, Huguet M, Ronderos R, et al. Morphologic pattern of late gadolinium enhancement in Takotsubo syndrome detected by early cardiovascular magnetic resonance. *Clin Cardiol.* 2011;34:178–1802.
3. Haghi D, Fluechter S, Suselbeck T, et al. Cardiovascular magnetic resonance findings in typical versus atypical forms of the acute apical ballooning syndrome (Takotsubo cardiomyopathy). *Int J Cardiol.* 2007;120:205–211.
4. Eitel I, Behrendt F, Schindler K, et al. Differential diagnosis of suspected apical ballooning syndrome using contrast-enhanced magnetic resonance imaging. *Eur Heart J.* 2008;29:2651–2659.
5. Sharkey SW, Windenburg DC, Lesser JR, et al. Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy. *J Am Coll Cardiol.* 2010;55:333–341.
6. Rolf A, Nef HM, Möllmann H, et al. Immunohistological basis of the late gadolinium enhancement phenomenon in tako-tsubo cardiomyopathy. *Eur Heart J.* 2009:30:1635–1642.

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.20898