Editorial Commentary

Recurrent Takotsubo Cardiomyopathy:

An Opportunity to Clarify Causation and Prognosis

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akotsubo cardiomyopathy (TC), a persistently nebulous entity, continues to baffle its students.

This rare condition (<2% of acute coronary syndromes in women, 0.2% in men) is probably not often recognized clinically, because many forms are too mild and nonspecific. Deaths from TC are probably more prevalent than is usually assumed; some deaths occur outside a hospital environment at the onset of the acute (ischemic) phase and may be attributed to sudden death from ventricular fibrillation. Autopsies

are no reliable diagnostic criteria for TC in autopsies.⁴
Recurrent TC (2%–10% of clinical cases⁵) is particularly interesting. One would expect frequent relapse, especially if the causative factors are not treated. An important challenge is to understand the mechanism of self-healing and "spontaneous vaccina-

are rarely performed in such cases, and the results are usually negative because there

The variable behavior of TC (Table I) can be illustrated by some typical cases.

Takotsubo and Pheochromocytoma. When TC occurs in association with pheochromocytoma, patients have typically had high blood catecholamine levels for years, and they have had several hypertensive spells; however, they usually have only one episode of TC. Furthermore, TC occurs in association with only a few such tumors.⁷

Takotsubo and Psychological Stress. In patients adversely affected by anxiety, family deaths, or mental depression or upset, TC typically heals rapidly and does not recur, even if the patients' circumstantial distress continues.

Takotsubo and Chemotherapy. When TC occurs during chemotherapy, the chemotherapy is usually continued; however, the TC does not usually recur.

In all these instances, the behavior of TC defies normal explanation. However, a possible intervening factor that might be overlooked is transient endothelial dysfunc-

TABLE I. Pathway of Takotsubo Cardiomyopathy

tion" that an isolated episode of TC usually implies.6

	Phase	Characteristics
From: Department of Cardiology, Texas Heart Institute, Houston, Texas 77030	0	Preceding predisposing conditions are frequent but variable and are neither easy nor essential to identify in individual cases. The usual sign is endothelial dysfunction, as evidenced by positive acetylcholine test results.
Address for reprints: Paolo Angelini, MD, Texas Heart Institute, 6624 Fannin St., Suite 2780, Houston, TX 77030	1	Initial event. Critical functional myocardial ischemia (subtotal diffuse coronary obliteration or spasm) lasts 15 to 60 min. Intracoronary nitroglycerin administration within the first 15 min can abort the episode.
	2	Myocardial stunning (persistent myocardial hypokinesia, akinesia, or dyskinesia, upon disappearance of coronary obliteration) occurs in addition to territory-related left ventricular failure.
E-mail: pangelini@ leachmancardiology.com	3	The myocardium recovers (duration, 1–10 d); a longer recovery time may be due to an unrecognized recurrence of the acute phase.
	4	Histologic recovery of the myocardial structure takes place (duration, 1–3 mo).
© 2018 by the Texas Heart® Institute, Houston	5	A residual tendency to relapse is rare ("automatic vaccination," mechanism unknown) and can be described by means of acetylcholine test results. Calcium antagonists, nitrates, and L-arginine can help patients who test positive.

tion, thought to result from local metabolic changes, neurohumoral imbalance, or both.

Acetylcholine (Ach) testing can reveal transient endothelial dysfunction one to 15 days after an episode of TC. This simple, relatively safe procedure can stimulate clinical TC, verifiable by means of echocardiographic monitoring. Positive Ach test results are accompanied by transient, critical diffuse coronary narrowing of the TC-related territories. ^{5.6} The administration of intracoronary nitroglycerin usually abolishes the patient's chest pain, electrocardiographic changes, and apical ballooning within seconds.

In cases of recurrent TC, like those described in this issue of the *Texas Heart Institute Journal* by Korabathina and colleagues,⁸ Ach test results would probably provide crucial information about the nature and prognosis of events, before and after antispastic medication is given.

Patients whose TC recurs should certainly undergo Ach testing. Because the test is not available in every hospital, centers proficient in studying spastic coronary conditions can be of great help.

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