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Transient Left Ventricular Apical Ballooning and Outflow Tract Obstruction

In the interesting syndrome of transient left ventricular apical ballooning (TLVAB) without coronary artery stenosis mimicking acute myocardial infarction, originally described by Tsuchihashi et al. (1), clinical manifestations in most patients were preceded by severe physical or emotional stress, suggesting a catecholamine-mediated mechanism. In a recent issue of the *Journal,* Abe et al. (2) described the clinical characteristics of a new series of 17 patients with TLVAB and disscuss and investigate different possible pathogenic mechanisms for this syndrome. The investigators could not identify any specific cause, suggesting neurogenic myocardial stunning induced by emotional or physical stress as the most probable etiology. Surprisingly, the previously suggested (1) possible role of a transient dynamic left ventricular outflow tract (LVOT) obstruction in the pathogenesis of this syndrome was not investigated by these researchers, who did not even mention the possible existence of such gradients in their patients. However, we believe there is much evidence indicating that this relation actually exist. In fact, a transient dynamic LVOT gradient was detected at initial evaluation in a substantial proportion of the patients described by Tsuchihashi et al. (1), and in other cases of this syndrome described elsewhere (3,4). In these patients, the clinical and hemodynamic situation improved as the gradient disappeared. Moreover, in some of the patients presenting with cardiogenic shock, this situation persisted until the dynamic obstruction was diagnosed and specifically treated (3).

Thus, at least in some patients, a possible mechanism for TLVAB could be a dynamic LVOT obstruction preceding the ischemic event. Once present, the dynamic obstruction elevates left ventricular filling pressures, increasing myocardial oxygen demand at the mid-to-apical cavity. If this situation persists, apical hypoperfusion and ischemia may result, with eventual apical infarction. In fact, it is well known that, even in normal hearts, exposure to an exogenous catecholamine, such as dobutamine infusion, can precipitate dynamic LVOT obstruction (5). Some patients, primarily women, may have geometric predisposition (sigmoid interventricular septum, small LVOT, reduced left ventricular volume) to dynamic LVOT obstruction, which may manifest only in the setting of intense adrenergic stimulation or hypovolemia (3,5). In these susceptible patients, increased adrenergic tone might produce primary LVOT obstruction leading to secondary ischemia and focal wall-motion abnormalities. Thus, the intense physical or emotional stress that precedes apical ischemia in most patients with TLVAB could be the trigger for the acute development of LVOT obstruction capable of producing severe apical ischemia.

Identification of acute dynamic LVOT obstruction as the possible initial mechanism in some of these patients may have important clinical and therapeutic implications, as the use of traditional measures to treat patients with chest pain and evidence of myocardial ischemia, including nitrates and afterload reduction, would actually increase the LVOT gradient, causing further clinical deterioration, while abolishing the gradient (with beta-blockers, intravenous fluids, or alpha-adrenergic receptor stimulation) might be beneficial and even life-saving (3). Moreover, treatment for secondary prevention would depend also on the suspected underlying mechanism. Eventually, in those patients in whom an acute dynamic LVOT obstruction mechanism is suspected, the possibility of performing tests of provocation, such as dobutamine stress echocardiography, should be considered.

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REPLY

We appreciate the comments and acknowledge the concerns of Dr. Penas-Lado and colleagues regarding the etiology of transient left ventricular apical ballooning described in our report (1). It may be quite reasonably argued that transient dynamic left ventricular outflow tract obstruction contributes to the pathogenesis of this syndrome (2). Tsuchihashi et al. (3) speculated on the inclusion of stress cardiomyopathy caused by vigorous stress (catecholamine exposure), dynamic midventricular obstruction due to basal hypercontraction, and/or secondary myocardial ischemia (increased wall tension) as an important etiological cause of this syndrome. However, they reported that only 18% of patients (12/72 patients) had left ventricular outflow tract obstruction and an intraventricular pressure gradient >30 mm Hg during the acute phase.

We did not discuss findings of left ventricular outflow tract obstruction in our report (1) for the following reasons. No patient showed left ventricular outflow tract obstruction with an intraventricular pressure gradient >30 mm Hg among 9 patients who underwent pressure recording during catheter withdrawal from the left ventricle and/or an accelerated flow in the left ventricular outflow tract in any of the 17 patients who underwent Doppler echocardiography during the acute phase. Moreover, little evidence was seen of geometric predisposition (sigmoid intraventricular septum, small left ventricular outflow tract, abnormal orientation of a slack mitral apparatus, reduced left ventricular volume) in our patients. However, pathological findings of the specimen obtained from left ventricular endomyocardial biopsy during the acute phase differed from those of myocardial ischemia (1,3,4). Moreover, Tawarahara et al. (5) recently reported a variant type of reversible severe left ventricular wall-motion abnormality of the basal segment with hypercontraction at the apex. It was considered that left ventricular outflow obstruction did not contribute to the etiology of this type of transient left ventricular abnormality. Thus, these findings suggested that left ventricular outflow obstruction was not a primary cause of this syndrome.

Kono et al. (6) reported that the mechanism of neurogenic stunned myocardium in patients with subarachnoid hemorrhage was mediated by the direct toxic effect of norepinephrine. Mann et al. (7) demonstrated the mechanism of catecholamine-mediated cardiac toxicity was that adrenergic stimulation leads to cyclic AMP-mediated calcium overload of cultures of adult cardiac muscle cells exposed to norepinephrine. Doshi et al. (8) reported that individual necrotic muscle fibers surrounded by macrophages and inflammatory cells and small foci of inflammatory cells between the muscle fibers with or without the presence of necrotic muscle fibers were observed histologically in patients with subarachnoid hemorrhage. These reports suggest that the direct toxicity of catecholamines could lead to myocyte damage.

Because none of our patients demonstrated neither significant left ventricular outflow tract obstruction nor intraventricular pressure gradient nor the evidence of geometric predisposition in our study, left ventricular outflow obstruction was not considered a primary cause. Therefore, we considered that this syndrome might be caused by the direct toxicity of catecholamines.

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Are Levels of C-Reactive Protein and Troponin T the Best Predictors of Mortality After Acute Coronary Syndrome?

We read with great interest the article by James et al. (1) in a recent issue of the *Journal*.

We were puzzled by the finding that C-reactive protein (CRP) was related to 30-day mortality, but not to the occurrence of myocardial infarction (MI). Indeed, as shown by Table 3, not only was CRP unrelated to MI, but patients with a CRP value ≥1.84 mg/l had a paradoxically lower probability of MI than did patients with values <1.84 mg/l (odds ratio 0.76, 95% confidence interval 0.59 to 0.98, $p = 0.03$). We believe that these findings can be explained by considering the potential relation (not addressed in the report) between high CRP values and impaired left ventricular (LV) function. Indeed, patients in the fourth CRP quartile had a higher rate of presentation with heart failure than did patients included in the other quartiles ($p < 0.001$). Moreover, as shown in Table 2 of the study, a strict relation existed between median troponin T values and CRP (0.04, 0.08, 0.1, and 0.3 μg/l being, respectively, the troponin T values in the four CRP quartiles, $p < 0.001$). It is likely that high CRP values would reflect large infarcts with impairment of LV function, an important predictor of early death, not necessarily related to the occurrence of a subsequent MI.

Unfortunately, the investigators (1) did not include in the multivariable analysis any index of LV function; therefore, the independent prognostic predictivity of CRP remains questionable.