Comments on

To the Editor:
A recent article in Circulation Research by Momomura et al \(^1\) characterizes the metabolic alterations that are associated with changes in diastolic distensibility during pacing tachycardia in the setting of critical coronary stenoses. The authors demonstrate that ischemia produced in this model results in a right and upward shift of the left ventricular pressure vs. diastolic length relation, and therefore mimics the clinical findings that occur during angina pectoris. In contrast to these findings, a brief occlusion of the left anterior descending (LAD) coronary artery does not generate this shift in the pressure length relation, but instead produces abnormalities during systole manifested by holosystolic bulging. The metabolic findings revealed that the decline in high energy phosphate stores, myocardial pH, and subendocardial blood flow was greater in response to coronary artery occlusion than during pacing (demand)-type ischemia. The authors subsequently discuss four possible mechanisms that may be responsible for the absence of diastolic dysfunction during coronary occlusion. Briefly, these included: 1) the possible protective effects of myocardial acidosis in reducing diastolic tension; 2) the reciprocal effect of systolic dyskinesis allowing greater diastolic relaxation; 3) a decrease in myocardial stiffness associated with the reduction in vascular turgor that accompanied the diminished coronary flow; and 4) the potential salutary effect of excessive systolic stretch in rupturing contracture bonds and hence preserving ventricular compliance.

Aside from these possible explanations, the disparity in myocardial function may also be explained by an inconsistency in the model. During the pacing tachycardia portion of the protocol, critical stenoses were created in both the LAD and the left circumflex coronary artery (LCX) by placement of metal clips. Aside from the changes produced in the region supplied by the LAD, there was also a mild, though insignificant, reduction in systolic function in the region supplied by the LCX. However, the diastolic pressure/length relation in the region supplied by the LCX was not reported, and would provide useful information. It seems reasonable to postulate that changes in diastolic compliance that accompanied pacing tachycardia occurred not only in the apex, but also in the lateral wall. Hence, the shift in the left ventricular pressure/length relation during pacing tachycardia conceivably reflected a global phenomenon since a major portion of the ventricle was rendered ischemic, as evidenced by the 40% reduction in blood flow in both the LAD and LCX regions.

Following the pacing tachycardia portion of the study, the clips about the LAD and the LCX were removed. Consequently, during occlusion of the LAD, myocardial ischemia was produced in only the region supplied by the LAD. The region supplied by the LCX was not ischemic, and moreover, it is well known that the regions supplied by unobstructed vessels compensate for regional dysfunction in distant segments by improving contractility.\(^2\)\(^-\)\(^3\)

Therefore the absence of a change in diastolic distensibility during the LAD occlusion in this model may have reflected the ability of the lateral wall to compensate adequately for the ischemic apical segment. Creation of a critical stenosis in the LCX in the setting of pacing tachycardia precluded any such compensation in this phase of the study. That left ventricular end-diastolic pressure increased nearly twice as much (7 mm Hg) during atrial pacing compared with occlusion of the LAD (4 mm Hg) supports the contention that the former maneuver resulted in more global dysfunction than the latter. Perhaps a more consistent model to compare the changes in diastolic and systolic function is one where critical stenosis of the LCX is maintained throughout the entire study including the period of LAD occlusion. Under these circumstances one may see change in diastolic distensibility during a brief occlusion of the LAD. To justify compare differences in regional diastolic function in the LAD distribution, however, the LCX should ideally be unobstructed, both during pacing (demand) ischemia, and during occlusion of the LAD.

The study by Momomura et al \(^1\) is important and represents a metabolic analysis of a diastolic phenomenon noted in previous studies.\(^4\)\(^-\)\(^6\) However, further elucidation of the mechanisms involved in producing demand-type ischemia and ischemia associated with coronary occlusion requires standardization of the experimental protocol so that the changes produced are indeed regional and not a reflection of a global phenomenon.

Kenneth G. Warner
Michael D. Butler
Shukri F. Khuri
West Roxbury VAMC,
Brigham and Women’s Hospital,
and Harvard Medical School
1400 VFW Parkway
West Roxbury, MA 02132

References


Reply to the Preceding Letter

To the Editor:

We are grateful to Drs. Warner, Butler, and Khuri for their interest in our recent article.1 As they point out, there are multiple potential explanations for the differences in diastolic distensibility associated with demand ischemia (coronary stenoses plus pacing tachycardia) and primary ischemia (coronary occlusion). We have chosen to study dogs with multiple coronary stenoses since this model most closely mimics the clinical situation in patients with angina pectoris who exhibit an upward shift in the left ventricular diastolic pressure-volume relation. The upward shift apparently relates to the mass of ischemic myocardium.2 Of interest, we have noted previously3 that in dogs with coronary stenoses of the circumflex and left anterior descending coronary arteries, the animals showing the least systolic (contractile) dysfunction in response to pacing tachycardia showed the most pronounced upward shifts in diastolic pressure-segment length relations. As systolic function deteriorated (with more severe stenoses or pacing at higher heart rates) diastolic dysfunction tended to disappear. For this reason, we believe that the mechanisms underlying systolic and diastolic dysfunction associated with ischemia differ, and that the difference may lie in metabolic changes characteristic of the two different types of ischemia.

With regard to some of the specific questions raised by Warner et al., data regarding pressure-segment length relations in the circumflex distribution were not presented in this manuscript but are reported in our previous studies using this model; the pressure-segment length relation showed upward shifting for the circumflex distribution as well as the left anterior descending distribution. With regard to the possibility that the lateral wall might have adequately compensated for the ischemic apical segment, this is certainly possible concerning systolic (contractile) function but is unlikely concerning diastolic function. In order for this to happen, the segment would have had to exhibit increased distensibility. Since the nonischemic segment presumably had increased coronary blood flow, the vascular erectile effect would make it likely that distensibility decreased, if anything.

The explanations for abnormal diastolic function in association with transient demand ischemia still elude us, and the thoughtful points raised by Dr. Warner et al. are very much appreciated.

William Grossman
Department of Medicine
Harvard Medical School
and Beth Israel Hospital
330 Brookline Avenue
Boston, MA 02215

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Comments on "The relationship of high energy phosphates, tissue pH and regional blood flow to diastolic distensibility in the ischemic dog myocardium".
K G Warner, M D Butler and S F Khuri

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