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Editorial Comment

Ultrasound Tissue Characterization of the Diabetic Heart: Laboratory Curiosity or Clinical Tool?*

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Diabetes mellitus is a leading health problem in the United States, ranking among the 10 most common health-related causes of death (1). Its cardiovascular sequelae include vascular abnormalities ranging from large vessel atherosclerosis to widespread microangiopathic arteriolar changes. In addition, there is evidence (2–7) that abnormalities of ventricular function can occur in diabetes mellitus independent of coronary atherosclerosis or other causes of congestive heart failure. Hyaline changes of the arterioles and interstitial myocardial fibrosis appear to be features of a distinct, nonischemic cardiomyopathic process in diabetes (8–10).

The present study. One of the major problems in making the diagnosis of diabetic cardiomyopathy, particularly early in the course of the process, is the lack of specific diagnostic criteria. Sophisticated methods of conventional cardiac imaging, including echocardiography and radioisotope blood pool scanning, permit evaluation of ventricular systolic function at rest and with exercise (11–13); diastolic function is also of interest because filling abnormalities due to interstitial myocardial fibrosis (14) might occur separate from the development of frank abnormalities of contractile function (1). In this issue of the Journal, Pérez and coworkers (15) report that a technique of ultrasound myocardial tissue characterization may be an additional and very sensitive tool for identifying the diabetic patient with subclinical cardiomyopathy.

What is ultrasound tissue characterization? Ultrasound is attenuated and reflected differently by abnormal compared with normal soft tissue, including myocardium. Beginning in the 1970s, and largely through the pioneering work of scientists in the laboratory at Washington University from which the article by Pérez et al. originated, several quantitative indexes of soft tissue acoustic characteristics have been developed for detecting experimental and, more recently, clinical abnormalities of cardiac tissue structure (16). The chief acoustic variable found useful in this group's clinical studies has been the measurement of backscatter: an estimate of the amount of ultrasound energy reflected from myocardium back to the interrogating transducer. Similar to most phenomena involving the heart, ultrasound backscatter varies throughout the cardiac cycle, with peak levels of ultrasound reflected at end-diastole and a nadir of backscatter occurring near end-systole (17). This cyclic variation of backscatter, as well as other echo amplitude data, has been found to be present in normal myocardium by several investigative groups and techniques (17–21). Blunting of cyclic backscatter variation has been identified in pathologic states including ischemia (22), acute and chronic infarction (22,23), dilated cardiomyopathy (17) and other conditions (24).

What is the physiologic basis of the cyclic variation of backscatter? Because the contractile function of sarcomeres so closely parallels ventricular systole, it must be an important contributor to the cyclic variation. However, contractile function does not totally explain the phenomenon of cyclic variation, because it has been convincingly shown that after release of a coronary occlusion in an animal model of ischemia, cyclic variation of backscatter returns substantially before regional left ventricular wall contraction returns (25). Thus, factors other than sarcomere shortening must contribute to the phenomenon of cyclic variation of backscatter.

Cyclic myocardial backscatter variation in diabetes. In their study reported in this issue of the Journal, Pérez and coworkers (15) carefully studied a group of diabetic patients, including those with severe noncardiac complications such as retinopathy, neuropathy and nephropathy. Cyclic backscatter variation was less in the diabetic patients as a group than in a separate set of normal control subjects. Of potentially greater interest, it was most blunted when diabetes was associated with neuropathy or other severe noncardiac complications. These abnormalities in cyclic variation of backscatter occurred in patients who had generally normal standard echocardiographic measurements of chamber size, wall thickness and systolic function and only subtle abnormalities of diastolic function. Thus, Pérez et al. (15) correctly conclude that ultrasound backscatter evaluation appeared to indicate myocardial abnormalities at a very early stage, presumably in relation to collagen deposition or vessel wall abnormalities.

Clinical implications. The findings of this study (15) are intriguing and have two potentially important implications. For the clinician treating diabetic patients who have other noncardiac complications but apparently normal cardiac function, the measurement of cyclic variation of backscatter

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may provide evidence of early cardiomyopathic changes. Knowledge of early cardiomyopathy may lead to altered management strategies, possibly including institution of medical therapy for concomitant ischemia or for associated diastolic filling abnormalities (to improve relaxation) in selected patients. A second implication is that some of the techniques described, particularly the measurement of ultrasound backscatter throughout the cardiac cycle, are beginning to achieve sufficient maturity to be applied as independent diagnostic tools in the study of important physiologic problems.

Limitations. Two shortcomings of the present study (15) should dictate some caution in interpreting these data. First, no independent histologic or other direct evidence of myocardial abnormalities was available for the study subjects. Thus, although some subtle abnormalities in Doppler echocardiographic assessment of diastolic function were present, we have no definite proof that the patients with abnormal cyclic variation of backscatter did, in fact, have abnormalities of collagen deposition, collagen cross-linkage (26) or other tissue level changes (27). This problem was unavoidable because, as the investigators indicate, myocardial biopsy would not have been justified in these patients. Second, more readily available measures of myocardial function might have detected abnormalities in these patients without the use of the still investigational tool of ultrasound tissue characterization. For example, would radioisotope blood pool scans have revealed diastolic abnormalities of peak filling rate or time to peak filling? Would assessment of contractility using load-independent measures (11) have shown abnormalities in contractile reserve? Because the differences in cyclic variation between diabetic and control subjects and among the various subsets of patients with diabetes in the study by Pérez et al. (15) were subtle, these findings cannot be generalized to justify widespread clinical use of this technique for routine management of diabetic patients. However, with confirmatory studies by other investigators utilizing larger numbers of patients and, when possible, with independent confirmation of the presence of myocardial abnormalities, ultrasound tissue characterization may become a clinical tool useful in the management of patients with diabetic cardiovascular disease.

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