The Emerging Role of Echocardiography in the Screening of Patients at Risk of Heart Failure

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A large number of patients without symptoms of heart failure (HF) have asymptomatic left ventricular (LV) dysfunction owing to the compensatory mechanisms acting through the autonomic nervous system and neurohormones. In the setting of screening for prevention, one must identify the subgroup of these patients at high risk for symptomatic HF to establish appropriate therapy. As a first step to identify the subgroup of patients at high risk, clinical screening scores and natriuretic peptide measurements are used. Second, the definite diagnosis of asymptomatic LV dysfunction must be confirmed with echocardiography, occasionally with the help of new technologic developments to establish prompt, appropriate treatment to prevent disease progression. Therefore, the screening role of echocardiography is the early identification of patients with structural cardiopathy who are at risk of developing symptomatic HF and detection of those without LV dysfunction (diabetic and hypertensive) whose condition is prone to advance rapidly to structural cardiopathy or to symptomatic HF. **(Am J Cardiol 2005; 96[suppl]:42L–51L)**

The incidence of chronic heart failure (HF) is progressively increasing because of the aging of the population and higher survival rates in patients with ischemic heart disease. This syndrome acts progressively, often beginning with asymptomatic left ventricular (LV) remodeling dysfunction (ALVD) and culminating in overt chronic HF with symptoms and signs of fluid overload and poor end-organ perfusion. Patients can have ALVD as a result of compensatory mechanisms involving the autonomic nervous system, neurohormones, and remodeling of cardiac structures and functions. At this stage it is essential to identify the subgroup of patients with ALVD whose condition can improve, despite these adaptations, in order to establish prompt, appropriate therapy.

The preclinical stages of chronic HF are featured in the current American College of Cardiology/American Heart Association practice guidelines for chronic HF.[1] These guidelines identify 4 stages of chronic HF, 2 of which (stages A and B) are asymptomatic: stage A is associated with a "high risk for [HF] but without structural heart disease," such as in patients with hypertension, diabetes mellitus (DM), or known atherosclerotic disease; and stage B is defined as in patients with "structural heart disease but without symptoms of chronic HF," including those with asymptomatic ischemic heart disease or reduced contractile function.

Echocardiography must be considered the second step in the screening process for chronic HF. The first step is identifying patients at high risk for developing symptomatic chronic HF; the second step is the diagnosis of ALVD (generally with echocardiography and its more precise new technologic developments) and treatment of ALVD to prevent progression to overt chronic HF. Therefore, in light of the new classification of chronic HF, echocardiography has a dual role: (1) early identification of patients with structural cardiopathy (chronic HF stage B) who are at risk of developing symptomatic chronic HF and (2) detection of patients without LV dysfunction (chronic HF stage A) who are prone to rapid development of structural cardiopathy or symptomatic chronic HF.

Therefore, screening with echocardiography has been performed in the entire population only for research purposes (prevalence studies[2–5]); however, in clinical practice, echocardiography must be performed only in a group selected by clinical, biohumoral, or electrocardiographic criteria.

Moreover, this type of screening has therapeutic significance: once patients are identified as having ALVD, one can reduce the rate of progression to symptomatic chronic HF with targeted therapy that has proved useful in large-scale clinical trials.[6,7]

Screening the General Population for Asymptomatic Left Ventricular Remodeling Dysfunction

Before being incorporated into a national health system program, the optimal strategy to screen the general popula-

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tion for ALVD must be cost-effective and must fulfill general criteria for usefulness.[8] Minimum requirements for such a screening strategy include (1) the ability to determine the presence of a disease or syndrome that is associated with a high prevalence as well as high morbidity/mortality; (2) utilization of a screening test sufficiently sensitive and specific; and (3) the ability to detect a disease early in its course, so effective treatment may be initiated to prevent disease progression or decrease morbidity and mortality. Although the high prevalence, morbidity, and mortality of ALVD have been established, as well as the efficacy and cost of therapy, no ideal screening test exists.

For use with the general population, an initially inexpensive treatment algorithm with sensitive indexes—that become progressively more specific—must be created. Different approaches have been proposed for initial screening before referral for echocardiography: (1) recording a single electrocardiogram; (2) evaluating brain natriuretic peptide (BNP) levels; or (3) examining the population with clinical risk factors, with or without determining BNP levels.

The initial screening for ALVD with a single electrocardiogram in the general population, although useful for its sensitivity for ischemia and arrhythmias, shows a low specificity for ALVD detection and, consequently, a low positive predictive value.[9]

A second screening strategy uses the simple direct measurement of natriuretic peptides, such as BNP, to detect ALVD. In fact, BNP levels are related to LV systolic dysfunction[10] (some studies are in disagreement[11]); they are independent predictors of mortality[12] and are rapidly and accurately assessed with bedside test kits.

However, the practical application of a single BNP measurement in screening the general population (primary care)[13] has been limited by difficulties in establishing a threshold for diagnosis and by suboptimal accuracy: sensitivity ranged from 26% to 92%, and specificity from 34% to 89%. An important explanation for the low accuracy of BNP levels in the screening for ALVD, found in some studies, may be that BNP levels depend on high LV filling pressures, regardless of whether systolic or diastolic ventricular dysfunction is the underlying cause. This may indicate a limited role for isolated BNP measurements in ALVD screening.[14]

Thus, a third screening strategy has been suggested, which selects patients with clinical characteristics associated with high risk for ALVD. The Framingham Heart Study reported that area under the curve (AUC) estimates for detecting LV systolic dysfunction by means of clinical characteristics were 0.72 in women and 0.75 in men.[3] Particularly, a model adding BNP levels to clinical characteristics did not result in a substantial improvement in AUC values. A recent composite scoring system (using several basal clinical parameters plus BNP levels) in a population of patients taking loop diuretics in a primary care setting identified patients with a worse prognosis without relying purely on a single threshold value for BNP.[15] However, use of this system is restricted to a specific subgroup of the general population, ie, patients taking loop diuretics; therefore, it is not established as a strategy broad enough to diagnose ALVD in the general population.

Moreover, another recent study in the primary care population tested a "clinical–BNP level" model to detect asymptomatic systolic or diastolic dysfunction.[4] Because of the prevalence of preclinical systolic or diastolic dysfunction and the predictive characteristics observed, Redfield and colleagues[4] concluded that using BNP levels to screen for ALVD would necessitate echocardiography in 10% to 40% of those screened, with most confirmatory echocardiograms being negative, and 10% to 60% of those affected would be missed.

Although BNP levels are useful in detecting moderate to severe preclinical systolic dysfunction, their limited use in detecting milder systolic and diastolic dysfunction as well as the high rate of confirmatory testing needed suggest that the search for a better screening tool should continue.

Prevalence of ALVD: The prevalence of ALVD in the community was reported in several studies, with estimates varying from 0.9% to 12.9% depending on the study design and setting, characteristics of the study sample, the definition of LV dysfunction, and the method for classifying participants as asymptomatic.

Population studies can be classified by design and setting in (1) community, longitudinal cohort studies, such as the Olmsted County Study,[16] Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) project,[17] the Rotterdam Study,[18] the Strong Heart Study,[19] and the Cardiovascular Health Study[20]; (2) random samples of population registries[21,22]; and (3) primary care practice studies.[23]

To justify the cost of screening for ALVD primarily with echocardiography, it is important to select subgroups at higher risk.[24] The prevalence of ALVD was found to be 2 to 8 times higher in men than in women and higher in elderly persons. When considering clinical characteristics, the prevalence was highest among those with known coronary artery disease (CAD) (range, 4.8% to 8.5%)[17,20,23] and high in patients who had hypertension or DM. Although racial differences were not well represented in all studies, the prevalence of ALVD was higher in the black population.[20]

A larger prevalence has been observed for diastolic ALVD.[16,25] In fact, the Framingham Study described prevalences of mild and moderate diastolic ALVD of 20.6% and 6.8%, respectively (systolic ALVD: ejection fraction [EF] <0.50 in 4.9% of patients and <0.40 in 1.1% of patients).[16]

Natural history of ALVD: The natural history of ALVD depends on the underlying disease, cardiac risk factors, and the degree of LV dysfunction. The role of echocardiography in identifying patients with ALVD who are at the highest risk of developing CHF is crucial because echocardiography can (1) often detect the etiology of LV dysfunction (ischemic or nonischemic), (2) determine the degree of LV systolic dysfunction (usually with EF

quantification) and diastolic dysfunction with its attendant increased end-diastolic pressure, and (3) detect associated cardiac diseases that can complicate the clinical course (mitral or aortic regurgitation, left atrial enlargement, and so forth).

Data on the rate of progression from ALVD to overt chronic HF in the community are based on relatively small numbers of chronic HF events because patients with ALVD are a small percentage of the basal population. Apart from this limitation, in the Cardiovascular Health Study,[5] there was an annual chronic HF incidence of 3% for patients with ALVD; such a good prognosis was found because the population was restricted to those without CAD. In multivariate modeling, echocardiographic indexes of systolic function (fractional shortening at the endocardium and at the midwall) and of diastolic function (peak Doppler E wave) independently predicted the incidence of chronic HF. Both high and low Doppler E/A–wave ratios were predictive of chronic HF incidence, confirming the poor prognosis indicated by both of the echocardiographic patterns of diastolic dysfunction (impaired relaxation, E/A ratio <1; and restrictive pattern, E/A ratio ≥ 1).[5]

With regard to prognosis, in community-based observational studies, ALVD was associated with increased cardiovascular mortality, all-cause mortality, and nonfatal cardiovascular events, such as myocardial infarction (MI) and stroke.[2,12,16,20]

In fact, large population studies observed that in a multivariate analysis adjusted for established risk factors for chronic HF and mortality (eg, age, sex, MI, systolic blood pressure, DM, ratio of total cholesterol to high-density lipoprotein cholesterol, valvular regurgitation or stenosis, smoking), ALVD was predictive of symptomatic chronic HF and mortality at long-term follow-up.[2,16] The presence of mild systolic ALVD (EF 0.40 to 0.50) and moderate to severe ALVD (EF <0.40) was associated with adjusted hazard ratios (HRs) for chronic HF of 3.3 and 7.8, respectively, compared with persons without ALVD.[2] Moreover, mild diastolic dysfunction (HR, 8.31) and moderate or severe diastolic dysfunction (HR, 10.17) were predictive of all-cause mortality (Figure 1). Thus, for screening purposes, LV dysfunction determined by Doppler techniques, whether systolic or diastolic, is associated with marked increases in risk of chronic HF and all-cause mortality.[2,16] Interestingly, similar results were also obtained with a simple echocardiographic measurement, such as LV end-systolic diameter.[3]

Conversely, it is possible to monitor the natural history and prognosis in a much larger group of patients with ALVD if patients in the placebo groups of randomized controlled trials are observed. However, in these patients, the annual mortality rate and the "progression to chronic HF" rate vary widely, depending on patient selection criteria, including the concomitance of renal insufficiency, atrial fibrillation, or DM. Thus these results should not be extrapolated to patients with ALVD in the general population because analyses in study groups are principally performed in patients recovering from myocardial infarction who are mildly symptomatic of chronic HF, who often have severe LV dysfunction (EF <0.40), and who are younger than patients with ALVD in the community.

Does treatment of ALVD improve outcome? The importance of screening patients with ALVD relies also on the opportunity to manage their condition with a different, effective therapeutic strategy.

For patients in chronic HF stage A, early recognition of clinical risk factors and their importance is necessary—when cardiac disease is worsening toward symptomatic chronic HF—in order to treat them more aggressively.

More direct evidence has been found in patients in chronic HF stage B. Pathophysiologic observations provide part of the data derived from large randomized trials as well as other data.

The first drug to generate a large evidence-based consensus regarding improved outcomes in patients with ALVD was an angiotensin-converting enzyme (ACE) inhibitor in the Studies of Left Ventricular Dysfunction (SOLVD) prevention trial.[6] Patients with ALVD (with 80% prevalence of postinfarction LV dysfunction) treated with enalapril had a 37% reduction in chronic HF incidence and a nonsignificant reduction in mortality. Therefore, the latest updated guidelines recommend "ACE inhibitors as first-line therapy in patients with a subnormal [EF], i.e., [0.40–0.45] with or without symptoms (recommendation I evidence A)," with or without previous MI, titrated up to the dosages shown to be effective in the large, controlled trials in HF (recommendation I evidence A).[7] However, in the community, most patients with ALVD who can be identified by screening would not have been eligible for participation in SOLVD. Thus, it remains unclear whether they would have benefited similarly from treatment.

Although there are few data on the use of β-blockers in patients with ALVD, recent trials demonstrated a beneficial effect of β-blockers in all patients with LV dysfunction.[26] In addition, the guidelines recommend β-blockers for all patients with LV dysfunction[7]: "(β-blockers) . . . should be added to the therapy in patients with ALVD, especially if following an acute [MI]." As previously noted, in contrast to clinical trials, persons with ALVD in community studies often do not report a history of MI and thus may not obtain the largest benefit from these drugs.

Minor studies are based on pathophysiology, whereas demonstration of efficacy may be the basis of randomized trials. With regard to digoxin, in the Digitalis Investigation Group trial, the small proportion of patients with diastolic dysfunction who received digoxin demonstrated benefits equal to or even more marked than those seen in other study participants: active treatment was associated with a lower incidence of the combined end point of death and hospitalizations for HF, perhaps due to its effect on heart rate and rhythm control.[27]

Angiotensin II receptor antagonists may also be benefi-

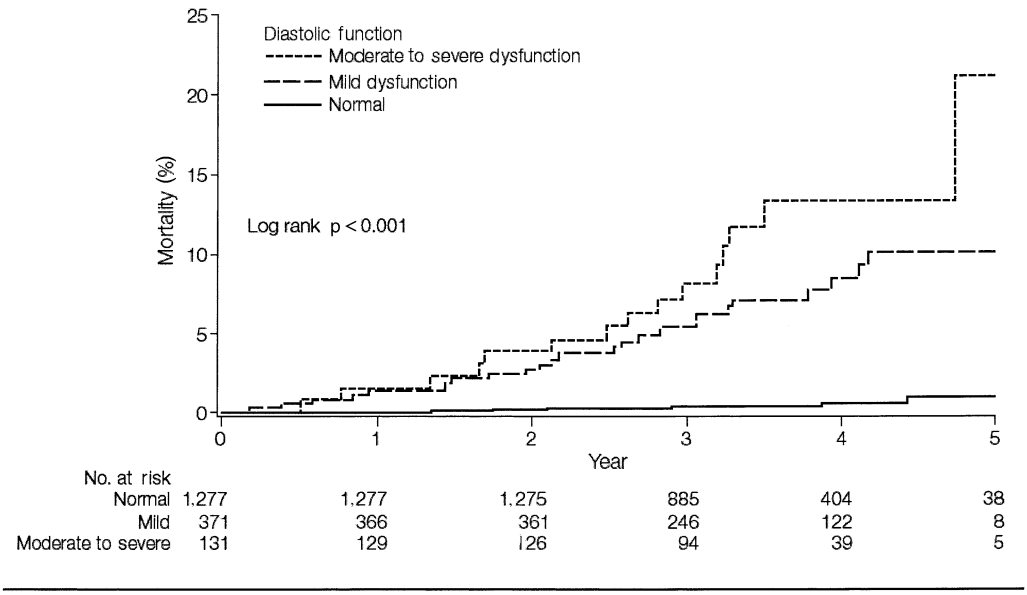

Figure 1. Kaplan-Meier mortality curves for participants with normal diastolic function versus subjects with mild or moderate to severe diastolic dysfunction. (Reprinted with permission from *JAMA*.[16])

cial in patients with ALVD because they help to deter fibrosis and improve intracellular calcium handling; the beneficial effect may be achieved through improvement in diastolic dysfunction. In patients with diastolic HF with preserved EF, the Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity-Preserved Trial (CHARM-Preserved) showed that candesartan reduced the number of hospital admissions for HF.[28]

Early Detection of Asymptomatic Left Ventricular Remodeling Dysfunction with New Echocardiographic Techniques

Diabetic cardiomyopathy: DM increases the risk for development of HF, even in the absence of coexisting heart pathologies such as CAD and hypertension.

This endocrine-generalized disease damages the heart at different levels, provoking epicardial coronary stenosis, autonomic dysfunction, diabetic cardiomyopathy, and coronary microvascular disease. Therefore, in patients with DM, echocardiography is important in the screening of asymptomatic chronic HF because it detects abnormalities early, when clinically apparent diabetic cardiomyopathy with consequent symptomatic chronic HF may take several years to develop.[29]

Ultrasonography, as well as other imaging techniques, can be used to study the different effects of DM on global (LV systolic, LV diastolic, and right ventricular) function[30] as well as on structural[31] and functional coronary microvasculature associated with coronary endothelial dysfunction[32] and coronary flow reserve impairment.[33]

Early echocardiographic signs of systolic LV dysfunction: Traditional echocardiographic measurements of systolic function in a large population study revealed that non–insulin-dependent DM (NIDDM) was an independent predictor of adverse cardiac effects. In fact, after adjusting the analysis for covariates (sex, age, body mass index, and blood pressure), women and men with NIDDM had greater LV mass and wall thickness and lower LV fractional shortening, midwall shortening, and stress-corrected midwall shortening than did their nondiabetic counterparts.[30] Pulse pressure/stroke volume, a measure of arterial stiffness, was higher in participants with DM than in healthy subjects. These are signs of the adverse cardiovascular effects of DM, independent of other cardiac risk factors, that may contribute to cardiovascular events in patients with diabetes.[5,30]

Moreover, systolic LV function studied at long-term follow-up (4 years) decreased in patients with DM compared with controls. All study subjects at baseline were free of cardiovascular disease and had comparable LVEFs. Worsening of LV function was greater in patients with insulin-dependent DM (IDDM) or NIDDM than in nondiabetic subjects and was associated with an abnormal LVEF response to exercise.[34]

Echocardiographic data on diastolic dysfunction: Several echocardiographic studies identified early diastolic abnormalities with preserved LVEF, such as reduced early diastolic filling, prolongation of isovolumetric relaxation, and increased atrial filling, indicating the classic features of diastolic dysfunction. Reduction in LV distensibility is characterized by an increased pre-ejection period and shorter LV ejection time, resulting in an increased pre-ejection period/LV ejection-time ratio. Such abnormalities have been demonstrated in patients who had DM and normal blood pressure without overt microvascular or macrovascular complications.[5,30]

These diastolic abnormalities are also seen often in patients with well-controlled type 2 DM who are free of clinically detectable heart disease: diastolic dysfunction was observed in approximately 60% of patients, of whom 28% had a pseudonormal pattern of ventricular filling and 32% had impaired relaxation.[35] Such a high prevalence suggests that screening for diastolic dysfunction should include the Valsalva maneuver and pulmonary venous recordings to unmask a pseudonormal pattern of ventricular filling.

Some echocardiographic indexes of diastolic dysfunction (E acceleration peak, E deceleration peak, and E peak filling rate) have also been found to be inversely related to myocardial phosphocreatine and adenosine triphosphate metabolism. Thus, altered myocardial energy metabolism may contribute to LV diastolic functional changes in patients with well-controlled and uncomplicated type 2 DM, indicating that the mechanisms underlying this diabetic cardiomyopathy may involve altered myocardial metabolism.[36]

However, diastolic evaluation with conventional Doppler techniques is limited by the dependence of transmitral flow on filling pressure as well as on LV relaxation and compliance. Conversely, tissue Doppler–derived parameters are less load-dependent and more sensitive to changes that are not recognized by conventional mitral Doppler inflow indexes.

Novel echocardiographic techniques to study systolic dysfunction:

TISSUE DOPPLER IMAGING (TDI) AND TISSUE CHARACTERIZATION: The sensitivity of conventional echocardiography in screening patients with DM for chronic HF depends on the population studied and on confounding pathologies such as hypertension or ischemic heart disease. Several studies showed that many of the frequently used echocardiographic indexes of LV systolic (such as LV fractional shortening and LVEF) and diastolic (such as E-wave velocity, isovolumic relaxation time, and E/A-wave ratio) performance can be within normal range or preload dependent and unable to discriminate myocardial dysfunction in the diabetic population.[37,38]

To differentiate the effects of hypertension from those of DM, conventional echo-Doppler and color Doppler M-mode parameters are limited, giving similar degrees of alterations in patients with DM with or without hypertension. A single conventional diastolic parameter—the deceleration time of early diastolic mitral flow—was found to be sensitive in detecting diabetic diastolic dysfunction because it was significantly longer in patients with hypertension associated with DM than in those with DM but without hypertension.[37,38]

Conversely, the new TDI parameters proved to be better than conventional echocardiography and better than plasma BNP measurements in identifying myocardial function impairment in patients with DM. In patients with DM who have either hypertension or normal blood pressure, peak systolic velocity was reduced compared with that in healthy subjects, as were diastolic indexes such as peak early diastolic velocity (E_m), isovolumic relaxation time (IRT), and to a lesser degree, peak early/peak late diastolic velocity ratio E_m/A_m).[37,38]

Also, the strain and strain rate calculated at baseline are reduced in patients with DM compared with control subjects; this reduction is greater in patients with DM who have LV hypertrophy.[37] Interestingly, the strain and strain rate in patients with DM are normalized during the dobutamine stress test,[39] raising the hypothesis of a "reverse ischemic cascade,"[29] as evidenced by a smooth contractile alteration at rest that is masked by the physiologic increase in contraction during dobutamine stimulation.

Moreover, different echocardiographic techniques can be useful in the staging of diabetic cardiomyopathy. Microvascular damage (see paragraph on coronary flow reserve below) can correspond to myocardial tissue fibrosis, which is visible as increased echo density at tissue characterization,[37,40] when TDI contractile indexes also begin to decrease. Even earlier, a reduction in contractility can be observed in the blunting of backscatter cyclic variations either in the entire myocardial wall or limited to the subendocardial layer only (Figure 2).[41,42] At a more advanced stage, a reduced inotropic reserve can be observed during exercise. Last, wall motion abnormalities at rest and a global reduction in EF can occur along with clinical signs of diabetic chronic HF.

Microvascular dysfunction studied with echocardiography: In the echocardiographic screening of chronic HF in patients with DM, it is important to recognize microvascular structural and functional disease. Besides structural wall thickening, lumen narrowing of the intramural coronary microvasculature, and capillary microaneurysms,[31] maximal coronary vasodilation capacity (known as coronary flow reserve)[40] is limited in patients with DM who have microvascular dysfunction and angiographically normal coronary arteries.[33]

A prognostic implication of microvascular dysfunction was confirmed in patients with type 2 DM who had angiographically normal coronary arteries. The reduced vasodilation capacity observed during cold pressor testing was associated with exercise-induced thallium myocardial perfusion abnormalities, and these patients had a higher number of ischemic events at 6-year follow-up than did healthy control subjects.[32]

A reduction in coronary flow reserve is more prominent in patients with than without diabetic retinopathy, especially in those with advanced diabetic retinopathy. Thus, the presence of diabetic retinopathy should be a hallmark of marked restriction of coronary flow reserve in patients with DM.[43]

Also, contrast echocardiography can detect diabetic microvascular dysfunction early. It was demonstrated that patients with IDDM had a reduction in microbubbles in the microcirculation, and administration of C-peptide was able to improve myocardial perfusion on contrast echocardiography.[44]

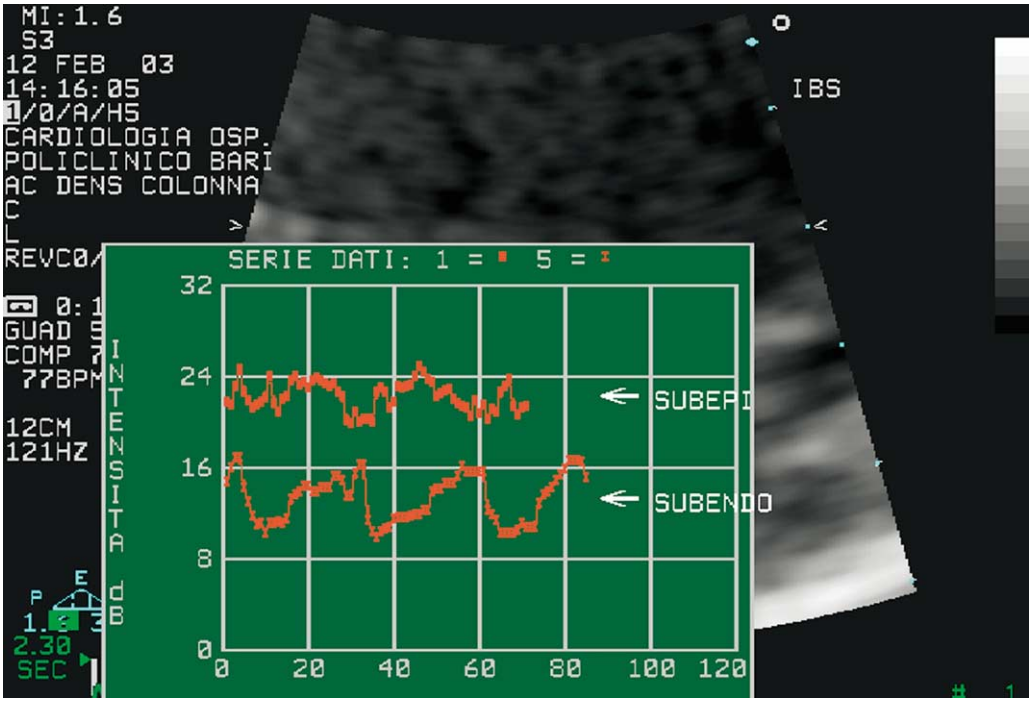

Figure 2. Integrated backscatter (IBS) cyclic variations in the different transmural layers of a normal myocardial segment. The region of interest has been separately placed in the subendocardium and then in the subepicardium of the posterior wall of the left ventricle. Graphs show that IBS cyclic variations are greater in the subendocardium (SUBENDO) than in the subepicardium (SUBEPI). MI = myocardial infarction (MI).

Right ventricular failure: In clinical practice, right ventricular dysfunction is relevant in a variety of disease states, affecting both the disease course and prognosis; therefore, one may assume that right ventricular performance is also an important issue in patients with DM. Recently, the possible involvement of the right ventricle in the pathologic process evoked by diabetes was described. Impairment in right ventricular diastolic function was evidenced mainly by TDI-derived indexes (decreased E_m and E_m/A_m ratio in both the basal and midsegments, and prolonged IRT in the midsegment of the right ventricular free wall) and by only 1 conventional Doppler parameter, right ventricular IRT.[45] Thus, TDI appears to prevail over other echocardiographic approaches in evaluating right ventricular myocardial abnormalities in patients with diabetes, and it seems to be more sensitive and more independent of various confounders such as preload or respiratory variations.

In screening for chronic HF, the discovery of subclinical right ventricular diastolic abnormalities may be essential both for prognostic purposes and for therapeutic planning to prevent symptomatic right ventricular dysfunction.

Early Detection of Asymptomatic Left Ventricular Dysfunction in Hypertensive Cardiomyopathy with New Echocardiographic Techniques

Similar to diabetes, systemic hypertension can affect LV shape as well as muscle architecture, thus determining the status of ALVD or symptomatic chronic HF. It is therefore important to find a screening technique capable of early identification of patients with systemic hypertension and LV hypertrophy who are at high risk of progression to LV dysfunction and chronic HF. In the >30-year follow-up of the Framingham Study, the screening potential of surface electrocardiography for chronic HF has been tested. The electrocardiographic pattern of LV hypertrophy indicated serious cardiovascular disease of all varieties, but the risk ratio was not great, especially in women. The electrocardiographic pattern of LV hypertrophy was more strongly associated with the occurrence of chronic HF than was radiographic enlargement; however, echocardiographic evidence of LV hypertrophy was even more strongly associated with the occurrence of chronic HF than was the electrocardiographic pattern.[46]

Early echocardiographic signs of LV dysfunction: The importance of early screening with echocardiography also depends on the strong link between systemic hypertension and the development of chronic HF.[47] The evaluation of systolic function (with the degree of LV hypertrophy and especially LV contractility) in patients with hypertension who are still asymptomatic improves the stratification of cardiovascular risk. However, despite normal EF, overall LV performance can be depressed.[48]

A very specific echocardiographic index of LV function is the midwall shortening fraction; when it decreases it can predict an adverse prognosis in adults with systemic hyper-

tension. Moreover, midwall shortening, although dependent on increased LV mass, adds a prognostic indicator for the development of subsequent cardiac events.[49]

This early parameter of systolic LV dysfunction is also related to the conventional pattern of LV diastolic dysfunction. Patients with chronic HF and normal LV function have a high prevalence of arterial hypertension, and the presence of chronic HF is often attributed to isolated diastolic LV dysfunction.[50] In accordance with this concept, Doppler echocardiographic studies in patients with hypertension have revealed a high prevalence of diastolic filling abnormalities.

In this process, cardiac work during systole is balanced by "internal" work during diastole to restore the energy spent during systole. Therefore, in diastolic dysfunction, the impairment occurring during diastole should be reflected during systole. This interconnection makes it difficult to separate diastolic and systolic abnormalities from mechanical or energetic standpoints.

Moreover, in evaluating diastolic function, the determination of the change in volume during diastole can quantify the relaxation slope. In fact, automated border detection may also be regarded as complementary to Doppler echocardiography. The waveform of LV area obtained by the automated border detection technique identifies phases of the cardiac cycle and correlates with Doppler values of LV diastolic function. Therefore, automated border detection can have potential uses in the assessment of LV diastolic function.[51]

Novel echocardiographic techniques to study dysfunction in LV hypertrophy: Further advances have recently demonstrated that systolic TDI velocity indexes are lower in patients who are hypertensive without apparent global systolic dysfunction than such indexes in control subjects.[52,53] In fact, EF and fractional shortening may have limitations as measures of LV contractile properties. The global assessment of LV performance by means of EF does not take regional contractile function into consideration, and fractional shortening primarily reflects radial LV contraction caused by predominant circular myocardial fibers. The outer and inner subendocardial longitudinal myocardial fiber contractions may not be clearly reflected by these LV systolic measurements.[41] To overcome this problem, in the recent past TDI (quantifying myocardial mechanical activity) showed a decreased LV peak systolic velocity in patients with hypertension and hypertrophy.[52]

However, TDI does not efficiently discriminate between actively contracting and "tethered" myocardium. Conversely, strain and strain rate imaging are new echocardiographic modalities based on TDI, and they may be used to assess LV regional systolic shortening independent of the effects of tethering and translation. The segmental myocardial strain rate analysis showed positive strain rate in some myocardial segments with hypertrophy in patients with hypertension, indicating segments with abnormal regional systolic function with either myocardial stretching or no motion. Furthermore, peak systolic strain rate was significantly lower in all LV segments in patients with hypertension and diastolic dysfunction than in those with normal diastolic function. This finding may be explained by the presence of regional subendocardial myocardial ischemia[41,42] as well as increased perivascular and interstitial fibrosis,[54] which has previously been demonstrated in hypertension.[37,38]

These studies provide new insight into myocardial function in hypertension that may improve pathophysiologic understanding and identification of patients at high risk who may benefit from regression of LV hypertrophy with a more aggressive antihypertensive treatment program; this improvement can occur even when EF and fractional shortening are normal, and therefore are earlier markers of myocardial dysfunction than are conventional measures. However, a possible limitation is the angle dependence—correct analysis is done only in myocardial walls perpendicular to the ultrasound beam—and the high interobserver variability of the measurements of strain rate and strain.

Another novel echocardiographic technique used to study dysfunction in LV hypertrophy is tissue characterization with integrated backscatter cyclic variations. This technique can detect ultrastructural alterations in the hypertensive heart, confirmed by morphologic features such as the increase in collagen volume fraction in the hypertrophied left ventricle. Interstitial fibrosis, perivascular fibrosis, and replacement fibrosis of necrotic myocytes as well as plexiform fibrosis are the specific findings of histologic analysis.

Tissue characterization with integrated backscatter cyclic variations can also be used to forecast increases in LV mass in patients with essential hypertension and to predict changes in function before such changes in fractional shortening occur.[54] Patients with hypertension have low backscatter cyclic variations, and these are substantially independent of LV mass: these variations are present when LV mass is within normal limits as well as in the presence of mild to moderate degrees of LV hypertrophy. The reduction in cyclic variation index observed in patients who were hypertensive with normal fractional shortening can be considered an early independent index of abnormal intrinsic contractility.[54] Moreover, LV mass regression (consequent to pharmacologic therapy) induces a normalization of backscatter parameters.[54]

With regard to the use of integrated backscatter cyclic variations to determine differences in myocardial pathology,[41] hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension can be differentiated on the basis of quantitative analysis of the transmural gradient in integrated backscatter, which is present only in hypertrophic cardiomyopathy.[55]

Therefore, this technique may be ancillary in the screening of patients at risk of developing complications of hypertensive cardiopathy. The major limitation of this technique is its low predictive value and the angle dependence of the backscatter technique.

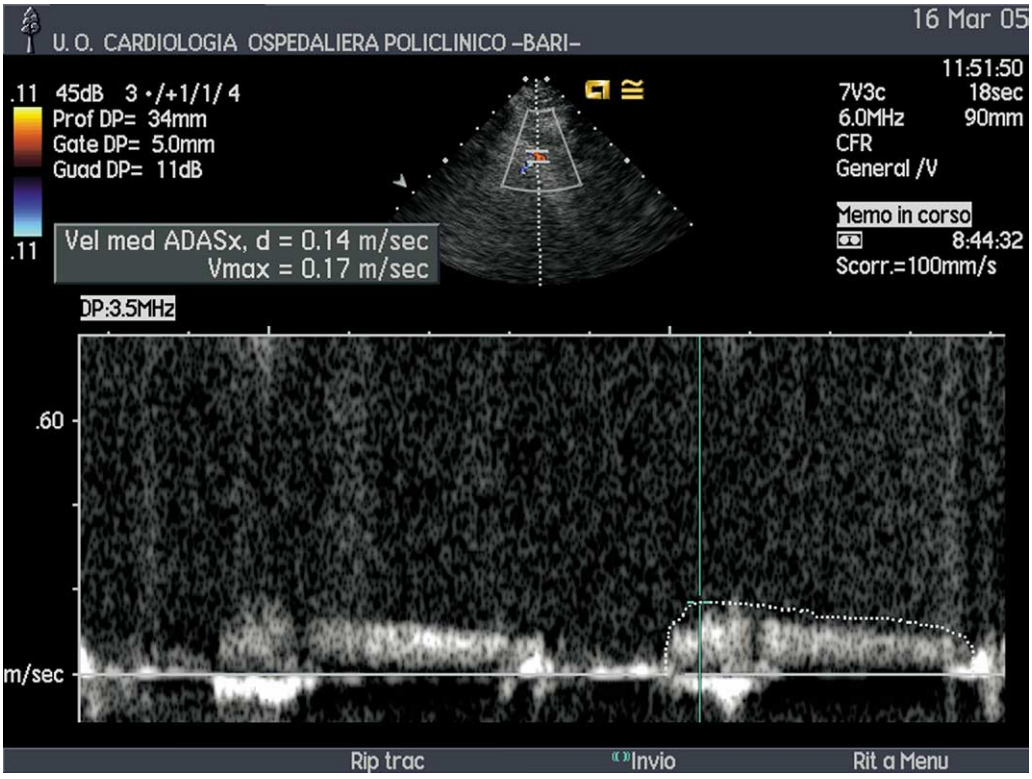

Figure 3. Coronary flow velocity in the left anterior descending coronary artery measured with posterior wall Doppler echocardiography.). It is possible to measure the mean and maximum velocity of the different components of coronary flow (the diastolic contour is outlined).

Altered vasodilation capacity studied with echocardiography in LV hypertrophy: Another key point is that microvascular function has an important prognostic role in patients with systemic hypertension with or without LV hypertrophy. In fact, an essential part of the cardiovascular risk of hypertensive cardiopathy has been attributed to impairment in coronary artery structure and vasodilative capacity, which underlies the increased prevalence of myocardial ischemia, arrhythmias, and sudden cardiac death.[56] The altered capacity of coronary flow velocity in response to vasodilation has been demonstrated in patients who have hypertension with or without LV hypertrophy; this can also be seen with positron emission tomography. The reduction in coronary flow reserve may be due to the increased basal blood demand (derived from the increased LV mass) or to a reduction in maximal flow primarily due to altered microvascular function. In fact, the increase in LV mass can be compensatory (appropriate for the increased cardiac workload stimulus) or overcompensatory (excessive for the stimulus). In this second case the excessive increase in LV mass has a bad prognostic meaning. Similarly, a more severe impairment in coronary flow reserve has been demonstrated in patients who are hypertensive with inappropriately high LV mass—which is associated with worse myocardial systolic performance—and LV diastolic filling pattern.[57] Part of the reduction in coronary reserve may be due to diastolic dysfunction in hypertension.[58] Consequently, these functional abnormalities may reflect an increased susceptibility to myocardial ischemia and HF,[47] which can be identified on screening with novel echocardiographic techniques (Figure 3).

Conclusion

The importance of echocardiography in screening for chronic HF is the early identification of patients with structural cardiopathy—patients at risk of developing symptomatic HF—and the early detection of patients who have diabetes or hypertension without LV dysfunction, who are prone to the rapid development of structural cardiopathy or symptomatic HF. A screening strategy must consider use of a clinical screening score and measurement of natriuretic peptides the first step in identifying a subgroup of patients at high risk. The second step would be to confirm the diagnosis of ALVD with new echocardiographic technologies to allow the earliest and most complete treatment to delay or prevent disease progression.

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