Speckle-Tracking Echocardiography

A New Technique for Assessing Myocardial Function

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Speckle-tracking echocardiography has recently emerged as a quantitative ultrasound technique for accurately evaluating myocardial function by analyzing the motion of speckles identified on routine 2-dimensional sonograms. It provides non-Doppler, angle-independent, and objective quantification of myocardial deformation and left ventricular systolic and diastolic dynamics. By tracking the displacement of the speckles during the cardiac cycle, strain and the strain rate can be rapidly measured offline after adequate image acquisition. Data regarding the feasibility, accuracy, and clinical applications of speckle-tracking echocardiography are rapidly accumulating. This review describes the fundamental concepts of speckle-tracking echocardiography, illustrates how to obtain strain measurements using this technique, and discusses their recognized and developing clinical applications.

Key Words—cardiac function; echocardiography; speckle tracking; strain; torsion

Speckle-tracking echocardiography is a new noninvasive ultrasound imaging technique that allows for an objective and quantitative evaluation of global and regional myocardial function independently from the angle of insonation and from cardiac translational movements.[1–4] Speckle-tracking echocardiography is based on an analysis of the spatial dislocation (referred to as tracking) of speckles (defined as spots generated by the interaction between the ultrasound beam and myocardial fibers) on routine 2-dimensional sonograms. Before the introduction of this sophisticated echocardiographic technique, only tagged magnetic resonance imaging (MRI) had enabled an accurate analysis of the several deformation components that characterize myocardial dynamics.[5] Although tagged MRI may be considered the reference standard in this area of study, its routine use is limited by its high costs, poor availability, relative complexity of acquisitions, and time-consuming image analysis.[6,7]

By tracking the displacement of speckles during the cardiac cycle, speckle-tracking echocardiography allows semiautomated elaboration of myocardial deformation in 3 spatial directions: longitudinal, radial, and circumferential. In addition, speckle-tracking echocardiography offers an evaluation of the occurrence, direction, and velocity of left ventricle (LV) rotation.[8] The semiautomated nature of speckle-tracking echocardiography guarantees good intraobserver and interobserver reproducibility.[9] Nonetheless, although this new technique was introduced for the exclusive analysis of LV function, several studies have recently extended its applicability to other cardiac chambers, such as the left atrium (LA).[10–15]

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Abbreviations

EF, ejection fraction; LA, left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; MRI, magnetic resonance imaging; RV, right ventricle

This review explains the fundamental concepts of speckle-tracking echocardiography, provides a practical guide to the acquisition and interpretation of data, and discusses the clinical applicability of these new echocardiographic parameters, which recently have become a subject of great interest for clinicians.

Main Technical Considerations

The term *speckle tracking* implies that this technique is principally based on the analysis of speckles during the cardiac cycle. Single speckles are merged in functional units (kernels) that are in turn univocally identifiable given the peculiar disposition of the speckles. As a result, each kernel constitutes a sort of ultrasound fingerprint that can be tracked by software during the entire cardiac cycle. Through analysis of the motion of each kernel that composes a routine 2-dimensional gray scale image, the system, without using the Doppler signal, can calculate displacement, the rate of displacement (velocity), deformation (strain), and the rate of deformation (strain rate) of the selected myocardial segments and LV rotation.[1]

According to the indications derived from the literature and to reduce random noise, each sample for a speckle-tracking echocardiographic analysis must be obtained by averaging at least 3 consecutive heart cycles, setting the frame rate of the routine 2-dimensional image acquisition between 60 and 110 frames per second.[8,16] Considering the close dependence of speckle-tracking echocardiography and single-cardiac-cycle strain analysis, it is not possible to even conduct a study in patients with nonsinus rhythms.

Speckle-tracking echocardiography–derived measurements have recently been validated against sonomicrometry and tagged MRI, showing high feasibility and reproducibility.[17] Substantial potential limitations of this new technique are its strict dependence on the frame rate and on high-quality 2-dimensional images, which are necessary for obtaining an optimal definition of the endocardial border.

Terminology and Definitions

A summary of the terminology used for this echocardiographic technique and described in the text is given in Table 1.

Strain

Strain represents a measure that evaluates the degree of deformation of the analyzed segment in relation to its initial dimensions. It is expressed as a percentage. The strain equation (ε) is as follows:

$$\varepsilon = L - L_0/L_0,$$

where L is the length of the object after deformation, and L_0 is the basal length of the object. By convention, depending on the direction, a lengthening or thickening deformation is given a positive value, whereas a shortening or thinning deformation is given a negative one.

Strain Rate

The strain rate (ε') represents the myocardial deformation rate. It is expressed as seconds^{-1}; in other words, if the same strain value is reached in half the time, the strain rate value will be doubled. Experimental studies have shown that the strain rate is less dependent on LV load variations than strain.[18] However, because the strain rate signal is noisier and less reproducible, most clinical studies still use strain measurements.

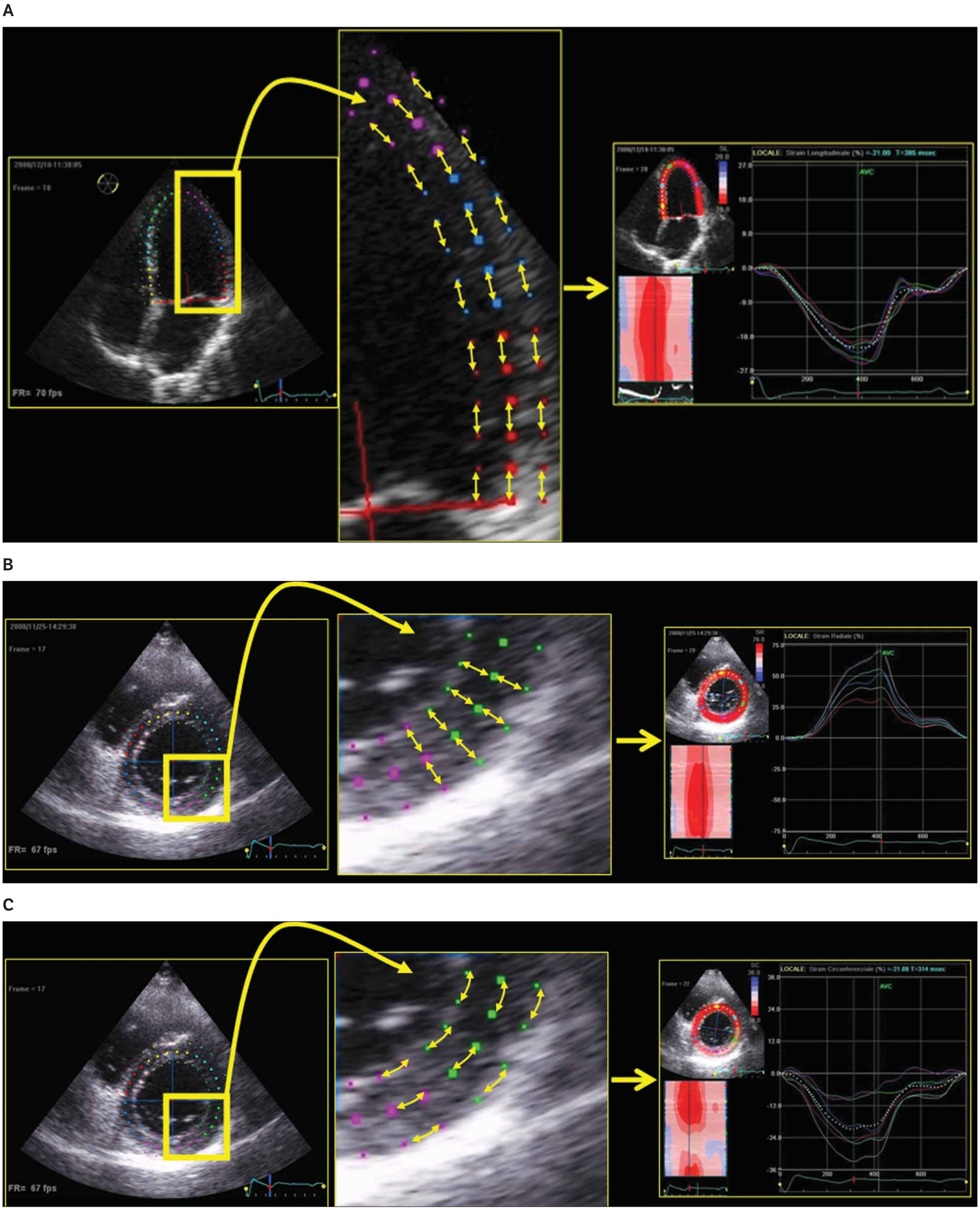
Longitudinal Strain

Longitudinal strain represents myocardial deformation directed from the base to the apex. During systole, ventricular myocardial fibers shorten with a translational movement from the base to the apex; the consequent reduction of the distance between single kernels is represented by negative trend curves (Figure 1A).[19] Through

Table 1. Speckle-Tracking Echocardiographic Terminology

Term	Definition
Strain	Myocardial deformation
Strain rate	Myocardial deformation rate velocity
Longitudinal strain	Base-to-apex–directed myocardial deformation
Radial strain	Myocardial deformation directed radially toward the center of the left ventricular cavity
Circumferential strain	Left ventricular myocardial shortening along the circular perimeter observed in a short-axis view
Twisting	Net difference between mean apical and basal rotation in the systolic phase
Torsion	Twisting normalized with the base-to apex distance
Untwisting	Net difference between mean apical and basal rotation in the diastolic phase
Untwisting rate	Untwisting velocity
Bull's-eye	Strain value topographic representation for all 17 segments
Post-systolic index	Percentage of the postsystolic strain value compared to the maximum strain peak

Figure 1. Speckle-tracking echocardiographic analysis of myocardial deformation showing measurements of longitudinal strain (**A**), radial strain (**B**), and circumferential strain (**C**). See "Terminology and Definitions" for details.



longitudinal strain analyses in 4-chamber, 2-chamber, and apical long-axis views, both regional (relative to each of the 17 LV segments) and global strain values (global longitudinal strain) can be obtained. Global longitudinal strain recently has been validated as a quantitative index for global LV function.[20] The same measurement can be applied to the speckle-tracking echocardiographic analysis of longitudinal myocardial deformation of the LA and right ventricle (RV), obtaining the peak atrial longitudinal strain[15] and the RV longitudinal strain,[21] respectively.

Radial Strain

Radial strain represents radially directed myocardial deformation, ie, toward the center of the LV cavity, and thus indicates the LV thickening and thinning motion during the cardiac cycle. Consequently, during systole, given the progressive radial propulsion of single kernels, radial strain values are represented by positive curves (Figure 1B). Radial strain values are obtained by speckle-tracking echocardiographic analysis of both basal and apical LV short-axis views.[22]

Circumferential Strain

Circumferential strain represents LV myocardial fiber shortening along the circular perimeter observed on a short-axis view (Figure 1C).[22] Consequently, during systole, for circumferential speckle-to-speckle distance reduction, circumferential strain measurements are represented by negative curves. As for longitudinal strain, it is possible to obtain a global circumferential strain value.

Twisting and Torsion

Until recently, the evaluation of LV twisting has been possible only through MRI,[6] but currently, speckle-tracking echocardiography has emerged as a new promising tool for LV twisting analysis.[23,24] Left ventricular twisting is a component of the normal LV systolic contraction that arises from the reciprocal rotation of the LV apex and base during systole and constitutes an important aspect of cardiac biomechanics.[25–27] Intrinsic to its physiologic characteristics, the quantification of LV twisting by speckle-tracking echocardiography is made possible by analyzing the reciprocal rotation of the LV apex and base during systole. Left ventricular twisting is then calculated as the net difference in mean rotation between the apical and basal levels (Figure 2). Left ventricular torsion is defined as LV twisting normalized with the base-to-apex distance.[28–30]

Untwisting

Growing attention has been also recently given to the role of untwisting in diastolic LV filling mechanics.[31,32] Untwisting velocity is thought to be a critical initial manifestation of active relaxation, which makes this measurement relevant for investigating diastole and, mainly, isovolumic relaxation because it seems to be less dependent on load compared to other diastolic parameters.[31]

How to Obtain Strain Parameters

Image Acquisition

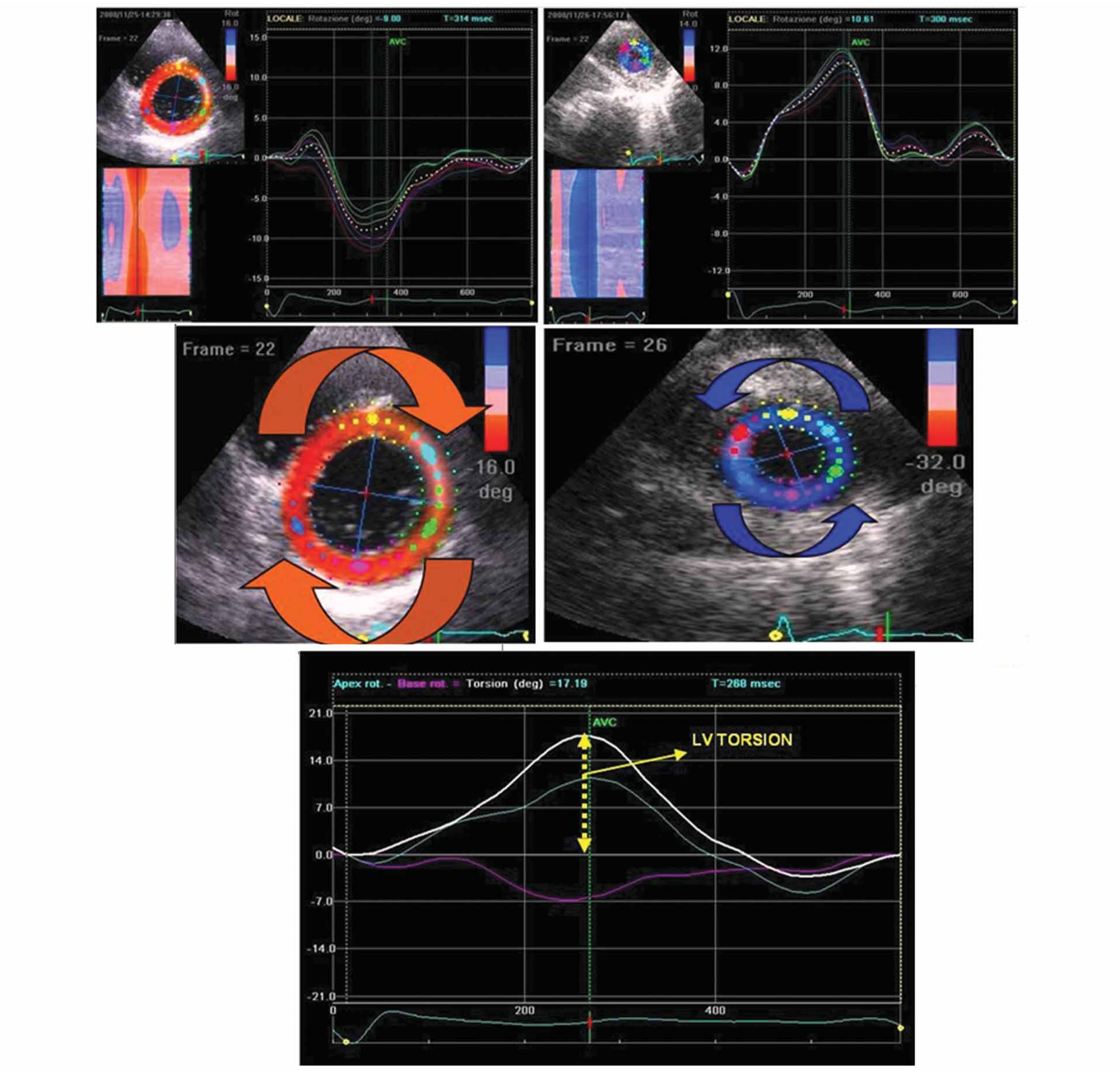
Images for speckle-tracking echocardiographic analysis, currently performed offline, are obtained and recorded by using conventional 2-dimensional gray scale echocardiography during breath holding with stable electrocardiographic tracing. Care must be taken to obtain true apical and short-axis images using standard anatomic landmarks in each view and to avoid foreshortening of the analyzed myocardial structure, thus allowing a more reliable delineation of the endocardial border. The optimal frame rate for the 2-dimensional image acquisition is set between 60 and 110 frames per second.[8,16] These settings are recommended to combine high temporal resolution with acceptable spatial definition and to enhance the feasibility of the frame-to-frame tracking technique. It is recommended to begin with speckle-tracking echocardiographic analysis of an apical long-axis chamber view to select the frame corresponding to the aortic valve closure, which is a useful reference for the subsequent analysis. Apical 4- and 2-chamber view acquisitions are necessary for longitudinal strain and peak atrial longitudinal strain analyses (see above). Short-axis recordings, useful for radial strain, circumferential strain, and rotation analysis, are obtained from a standard parasternal probe position for the basal plane and from a more distal anterior or anterolateral position for the apical plane. To standardize acquisitions, the basal plane is identified as the plane including the tips of the mitral leaflets, whereas the apical plane is identified distally to the papillary muscles as the plane just proximal to the level at which LV cavity end-systolic obliteration occurs.[9] Particular attention should be paid to making the LV cross section as circular as possible.

Offline Analysis

Recordings are processed using specific acoustic-tracking software usually available on dedicated workstations, allowing for an offline semiautomated analysis of speckle-based strain. The endocardial surface of the myocardial segment analyzed is manually traced in apical and/or short axis views by a point-and-click approach. An epicardial surface tracing is then automatically generated by the system, thus creating a region of interest. After manual adjustment of the region of interest width and shape, the software automatically divides the region of interest into 6 segments, and the resulting tracking quality for each segment is automatically scored as either acceptable or unacceptable, with the possibility of further manual correction. Segments for which no adequate image quality can be obtained are rejected by the software and excluded from the analysis. Last, once the region of interest is optimized, the software generates strain curves for each selected myocardial segment (Figure 1). From these curves, the operator can obtain regional and global (by averaging values observed in all segments) peak and time-to-peak values.

If the longitudinal strain analysis is performed in all 3 apical views, the software automatically generates a topographic representation of all 17 analyzed segments (bull's-eye; Figure 3A). With a simple input, the operator can also obtain the longitudinal strain time to peak and the postsystolic index (ie, the percentage of the postsystolic strain

Figure 2. Graphic depiction of left ventricular rotational dynamics showing rotation of the cardiac base (left) and apex (right). In the bottom panel, a diagram of left ventricular (LV) twisting measurement is represented as the net difference between mean apical and basal rotation; left ventricular torsion is calculated by normalizing left ventricular twisting with the base-to-apex distance. AVC indicates aortic valve closure.



value compared to the maximum strain peak of the evaluated segment) bull's-eye (Figure 3B), both shown to be useful in preliminary studies for the analysis and detection of potentially ischemic or dyssynchronous myocardial areas.[33]

Clinical Applications

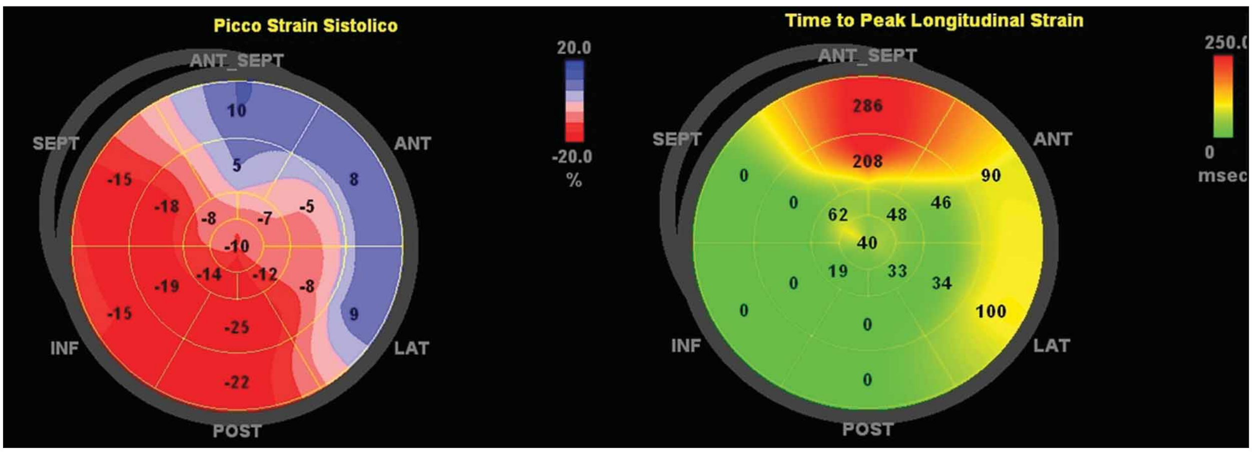
In general, speckle-tracking echocardiography may allow an unprecedented in-depth evaluation of myocardial systolic and diastolic dynamics across a broad range of physiologic and pathologic conditions beyond traditional echocardiographic techniques. For example, not only has a good correlation between longitudinal strain and the left ventricular ejection fraction (LVEF) been shown in several studies,[20,34] but in addition, longitudinal strain provides a quantitative myocardial deformation analysis of each LV segment, also allowing for early systolic dysfunction detection in patients with a preserved LVEF.[35]

Hypertension

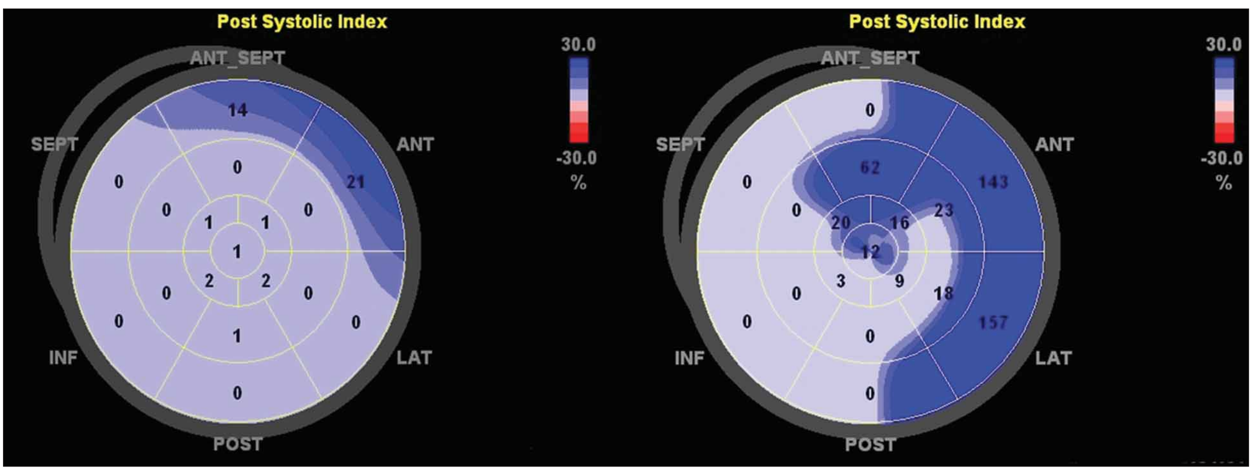
Arterial hypertension is an ideal model for assessing the changes in different varieties of deformation occurring hand in hand with the development of LV concentric

Figure 3. Topographic bull's-eye representations of different strain measures. **A**, Representation of longitudinal strain (left) and time-to-peak longitudinal strain (right) in a patient with severe stenosis of the left anterior descendent artery. Note the chromatic individuation of the ischemic area (left), also showing delayed contraction (red area with contraction delay of 286 milliseconds; right). **B**, Postsystolic speckle-tracking echocardiographic index measurement at baseline (left) and under physical stress (50 W; right) in a patient undergoing stress exercise echocardiography. Note the worsening of the LV contraction delay in the anterolateral territory. Subsequent coronary angiography showed left main and left anterior descendent artery disease. ANT indicates anterior; ANT_SEPT, anteroseptal; INF, inferior; LAT, lateral; and POST, posterior.

A



B



geometry (concentric remodeling and concentric LV hypertrophy). This is a crucial issue because experiences using standard echocardiography have shown that impairment of midwall fractional shortening of the circumferential fibers precedes the reduction of the LVEF.[36] Speckle-tracking echocardiography has furthered the understanding that the interaction of the different deformations is much more complex under these circumstances. In particular, it seems that longitudinal and radial strain are impaired when circumferential strain is still normal and LV torsion, also maintained in the normal range, acts as mechanistic compensation to preserve a normal ejection fraction (EF).[37] These data are further sustained by the demonstration that in hypertensive patients with a preserved LVEF, impaired longitudinal strain and increased LV torsion are associated with serum levels of the tissue inhibitor of matrix metalloproteinase 1, a marker of myocardial fibrosis, which represents the main determinant of LV diastolic dysfunction. These findings suggest therefore that the change in collagen turnover and the myocardial fibrotic process may cause early LV contractile dysfunction[38] when the LVEF is still normal, and LV functional abnormalities seem to mainly affect the diastolic properties of the myocardium.

Diabetes

In asymptomatic diabetic patients with a preserved LVEF, it has been shown that speckle-tracking echocardiography has the potential for detecting subclinical LV systolic dysfunction, which is unmasked by the alteration of longitudinal strain. In this view, speckle-tracking echocardiography might provide useful information about the development of subclinical myocardial dysfunction in the diabetic setting before the overt appearance of diabetic cardiomyopathy.[39,40] This evidence confirms previous experiences using either color tissue velocity imaging or Doppler-derived strain rate imaging.[41]

Coronary Artery Disease

Choi et al[42] reported that a lower longitudinal strain value in asymptomatic patients without wall motion abnormalities is a strong predictor of stable ischemic cardiopathy. Studies in patients with acute myocardial infarction found that longitudinal strain is related to peak levels of cardiac troponin T[33] and the LV infarct size.[43] Moreover, when measured immediately after reperfusion therapy, longitudinal strain is an excellent predictor of LV remodeling and adverse events, such as congestive heart failure and death.[44] In addition, it has been shown that longitudinal strain correlates with the global and regional extent (transmurality) of scar tissue as evaluated by contrast-enhanced MRI.[45,46] A radial peak strain cutoff value of 17.2% predicts LV functional recovery after revascularization with accuracy similar to that of a cutoff value of 43% hyperenhancement on MRI.[45] A cutoff value of –4.5% for regional longitudinal strain discriminates between segments with a viable myocardium and those with transmural scar tissue on contrast-enhanced MRI, with sensitivity of 81.2% and specificity of 81.6%.[47] Recently, Voigt et al[47] used speckle-tracking echocardiography to validate an analysis of post-systolic motion, identified as LV regional myocardial motion after aortic valve closure, and showed that the post-systolic index represents an important quantitative marker for analysis of the ischemic myocardium (Figure 3B). However, data from studies on large populations are still lacking.

Valvular Heart Disease

Speckle-tracking echocardiographic analysis in patients with valvular heart disease has been mainly performed for the evaluation of LV function with stress (exercise or pharmacologic) testing.[48] Lancellotti et al[49] have shown that in asymptomatic patients with degenerative mitral regurgitation undergoing valvular surgery, limited exercise-induced longitudinal LV contractile recruitment, as assessed by speckle-tracking echocardiography with global longitudinal strain, predicts postoperative LV dysfunction. In patients with aortic stenosis or aortic regurgitation immediately after aortic valve replacement, there is a substantial increase in radial and circumferential strain, suggestive of how these myocardial deformation parameters critically depend on LV load conditions.[50]

Heart Failure

It has been shown that in hypertensive patients with heart failure and in patients with heart failure and a normal EF, LV longitudinal strain progressively deteriorates from New York Heart Association class I to class IV, with additional LV radial and circumferential systolic impairment occurring in New York Heart Association functional classes III and IV.[51,52] As for LV rotation and torsion analysis, Park et al[53] reported that systolic twisting, torsion, and diastolic untwisting are significantly increased in patients with mild diastolic dysfunction (as shown in 2 representative cases in Figure 4). In patients with advanced diastolic dysfunction and increased filling pressures, these parameters are normalized or reduced.[53,54] However, it remains to be elucidated whether increased LV torsion is a compensatory mechanism for reduced myocardial relaxation or a consequence of reduced LV filling in the early stage of diastolic dysfunction. The first longitudinal study conducted in patients with heart failure and a reduced EF found global circumferential strain to be a powerful predictor of cardiac events.[55] Another study indicated that global longitudinal strain is a superior outcome predictor compared to the EF and wall motion score index.[56]

Mechanical Dyssynchrony

Cardiac resynchronization therapy is an effective treatment option for patients with New York Heart Association functional class III and IV heart failure who have an LVEF of 35% or less and QRS prolongation and who remain symptomatic despite optimal medical therapy. However, about 30% of patients fail to show a substantial benefit with cardiac resynchronization therapy, and several efforts have been made in recent years to identify nonresponders before implantation. A variety of echocardiographic parameters potentially suitable for predicting the response to cardiac resynchronization therapy have been tested.[57] In a recent multicenter trial, none of 12 conventional and tissue Doppler-based echocardiographic indices of dyssynchrony was shown to be a reliable predictor of the response to cardiac resynchronization therapy.[58] However, strain parameters recently have been shown to have good reproducibility and accuracy in discriminating healthy patients from cardiac resynchronization therapy volumetric responders.[59] In addition, a recent study showed that longitudinal 2-dimensional strain rate imaging is a promising potential echocardiographic parameter for predicting benefits from cardiac resynchronization therapy in patients with heart failure.[60] Also, radial strain dyssynchrony analysis has been used successfully to predict the LV functional response to cardiac resynchronization therapy.[61–63] Prospective randomized trials using speckle-tracking echocardiography for predicting the response to cardiac resynchronization therapy are still lacking.

Cardiomyopathies

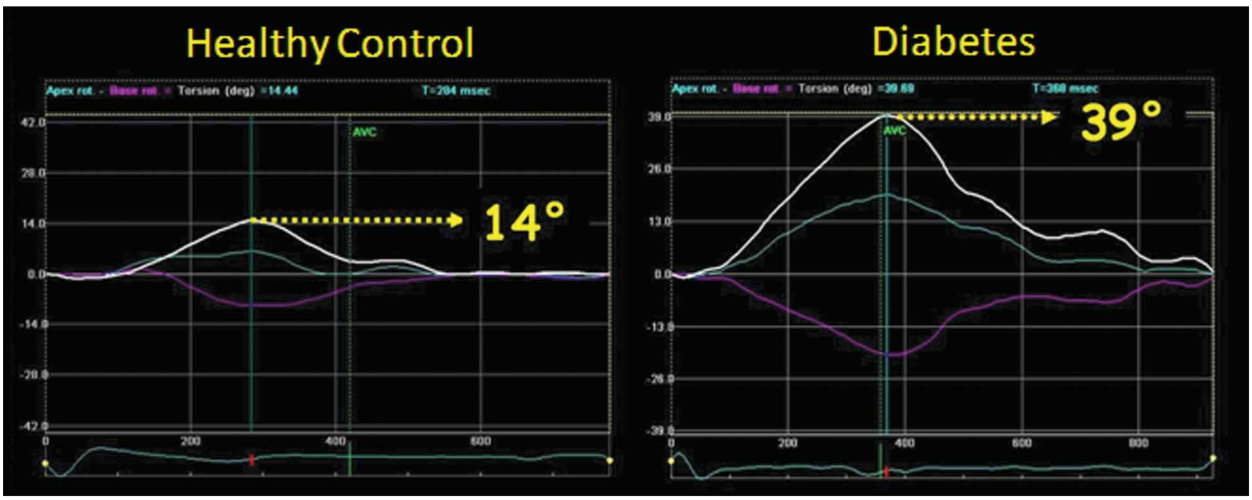
In patients with nonobstructive hypertrophic cardiomyopathy and a preserved EF, speckle-tracking echocardiography has shown the capability to identify early major abnormalities of all strain components of myocardial deformation (longitudinal, circumferential, and radial strain).[16] Another potential clinical application of speckle-tracking echocardiography is for differentiation of hypertrophic cardiomyopathy from athlete's LV hypertrophy[64–66] based on the lower longitudinal strain values in patients with hypertrophic cardiomyopathy who have a normal LVEF.[67] Other interesting findings have recently been shown for other cardiomyopathies.[68–71]

Emerging Areas of Application

Heart Transplantation

Cameli et al[72] recently reported impairment in LV twisting, LV torsion, and untwisting rates in heart transplant recipients compared to age-matched controls and to patients undergoing other types of cardiac surgery. These findings are suggestive of a potential role of heart denervation in the determinism of LV torsion depression (Figure 5).[72]

Figure 4. Comparative representation of left ventricular twisting measurements in a diabetic patient with a preserved left ventricular ejection fraction (right) and an age-matched healthy individual (left). The ventricular twisting function appears substantially increased in the diabetic patient.



Left Atrial Function

Preliminary data on speckle-tracking echocardiography of LA myocardial deformation as assessed by measurement of the peak atrial longitudinal strain[15,73] have suggested that both arterial hypertension and diabetes have a major impact on LA function, even in the absence of LA enlargement.[74] The coexistence of both conditions further impairs LA performance in an additive manner (Figure 6), and the magnitude of LA dysfunction is strictly related to LV filling pressures.[74–76]

Identification of Subclinical Dysfunction During Chemotherapy

With new anticancer therapies, many patients can have a long life expectancy. For this reason, treatment-related comorbidities become an issue for cancer survivors. Considering that cardiac toxicity remains an important side effect of anticancer therapies, early detection of cardiac injury is crucial because it may facilitate early therapeutic measures.[77] In contrast to only EF analysis, new speckle-tracking echocardiographic parameters have been shown to reliably detect preclinical abnormalities in both regional and global myocardial function at an early stage.[78,79]

Limitations

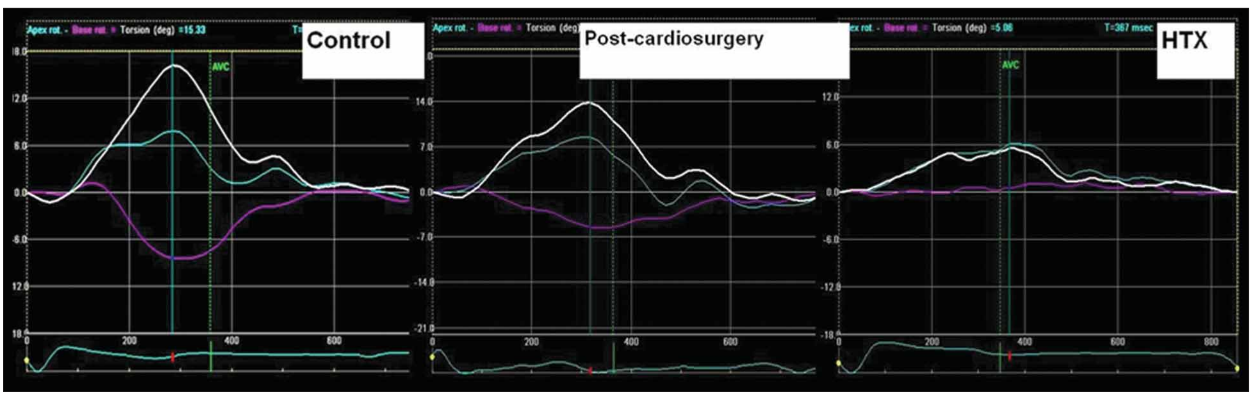
All speckle-tracking–derived measurements require more capability in image acquisition and, to obtain correct endocardial border delineation, are contingent on the presence of adequate echocardiographic views. Furthermore, considering the close dependence of speckle-tracking echocardiography and single-cardiac-cycle myocardial deformation analysis, it is not possible to even conduct strain measurements in patients with nonsinus rhythms. An additional limitation of the technique is that results depend critically on the machine with which the analyses are performed, and they are not interchangeable among different manufacturers.

Conclusions

Speckle-tracking echocardiography is a sophisticated new echocardiographic technique that, working with standard 2-dimensional images devoid of the limitations of Doppler techniques, provides a comprehensive analysis of global and regional myocardial deformation evaluated in all spatial directions. In addition, speckle-tracking echocardiography enables evaluation of LV rotational and torsional dynamics, aspects of LV function that were exclusively analyzed by MRI before the introduction of this technique.

Within the last 3 years, a growing body of evidence has accumulated, showing the good feasibility, reproducibility, and accuracy of speckle-tracking echocardiography in several clinical applications. However, prospective clinical trials for the validation of this technique in large populations are still lacking. A recently developed 3-dimensional speckle-tracking technique showed promising preliminary results in analyses of 3-dimensional images data sets.[22,80] This further technologic advance will presumably provide an even more comprehensive and detailed analysis of cardiac dynamics, bringing echocardiography closer to the most advanced imaging techniques while maintaining its particular availability at the patient's bedside.

Figure 5. Comparative representation of left ventricular twisting measurements in an age-matched healthy individual (left), a patient after nontransplant cardiac surgery (middle), and in a heart transplant (HTX) recipient (right). The ventricular twisting function appears strongly reduced after heart transplantation.



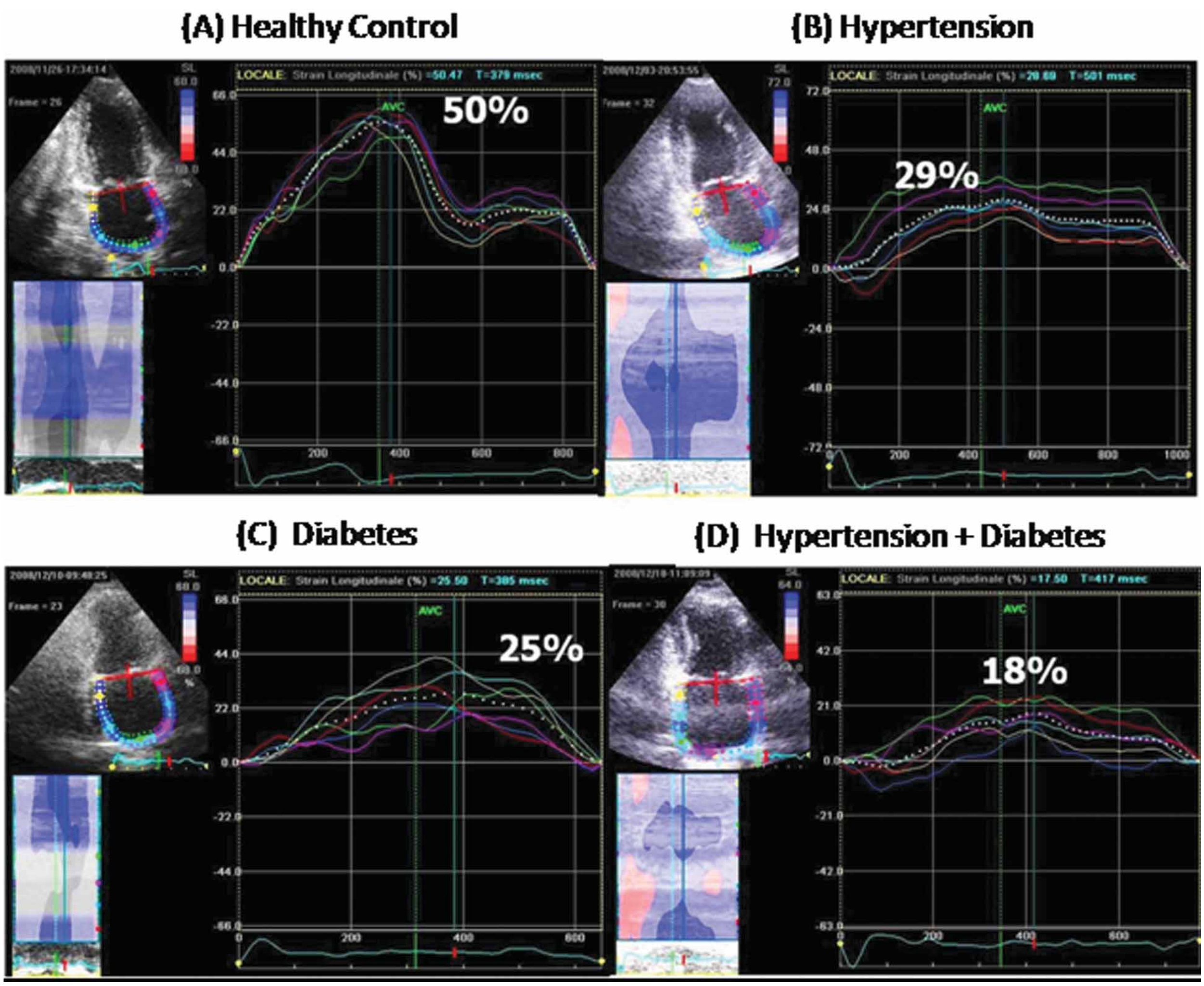


Figure 6. Left atrial function analysis by speckle-tracking echocardiography showing sample peak atrial longitudinal strain measurements in a healthy individual (**A**), a hypertensive patient (**B**), a diabetic patient (**C**), and a hypertensive and diabetic patient (**D**) with a preserved ejection fraction and no enlargement of the left atrium. Both hypertension and diabetes have a major impact on left atrial myocardial deformation. Coexistence of both conditions further impairs left atrial performance in an additive manner.

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