Current Cardiology Reviews, 2017, *13*, 32-40

REVIEW ARTICLE

Incremental Value of Two Dimensional Speckle Tracking Echocardiography in the Functional Assessment and Characterization of Subclinical Left Ventricular Dysfunction

Prasad Gunasekaran, Sidakpal Panaich, Alexandros Briasoulis, Shaun Cardozo and Luis Afonso*

Division of Cardiology, Detroit Medical Center, Wayne State University, Detroit, MI, United States

ARTICLE HISTORY

Received: May 24, 2016
Revised: June 26, 2016
Accepted: June 29, 2016

DOI: 10.2174/1573403X12666160712095938

Abstract: Subclinical left ventricular (LV) dysfunction refers to subtle abnormalities in LV function which typically precede a reduction in the left ventricular ejection fraction (LVEF). The assessment of myocardial function using LVEF, a radial metric of systolic function, is subject to load dependence, intra-observer and inter-observer variability. Reductions in LVEF typically manifest late in the disease process thus compromising the ability to intervene before irreversible impairment of systolic performance sets in. 2-Dimensional speckle tracking echocardiography (2D-STE), a novel strain imaging modality has shown promise as a sensitive indicator of myocardial contractility. It arms the clinician with a powerful and practical tool to rapidly quantify cardiac mechanics, circumventing several inherent limitations of conventional echocardiography. This article highlights the incremental utility of 2D-STE in the detection of subclinical LV dysfunction.

Keywords: Subclinical left ventricular dysfunction, 2-dimensional speckle tracking echocardiography, Global longitudinal strain.

INTRODUCTION

Strain refers to the change in the length of a segment of the myocardium relative to its original length and strain rate refers to the net change in strain per unit time. 2-Dimensional speckle tracking echocardiography (2D-STE), an angle-independent technique, employs automated algorithms to analyze temporal variations (frame to frame) in the mobility of acoustic speckle markers of 20-40 pixels size along different spatial orientations such as longitudinal, circumferential and radial planes to then quantitatively derive respective strain or deformational parameters. The endocardium contributes maximally to longitudinal strain (LS). Location of the endocardium farthest away from the epicardial coronary arteries and its exquisite sensitivity to ischemia makes it vulnerable to a variety of insults thereby making LS a highly sensitive indicator of LV dysfunction. In contrast, radial strain (RS), circumferential strain (CS) and torsional strains (TS) are affected later in the disease and are widely acknowledged to have lower inter- and intra-observer reproducibility [1].

*Address correspondence to this author at the Division of Cardiology, Wayne State University, Detroit Medical Center, 3990 John R, 8-Brush, Harper University Hospital, Detroit, Michigan-48201. United States; Tel: 313-745-2620; Fax: 313-745-8643; E-mail: lafonso@med.wayne.edu

One of the utilities of myocardial strain might be timely identification of subclinical left ventricular (LV) dysfunction, which could provide the clinician with a wider therapeutic window to potentially arrest or delay progression to clinically evident cardiovascular disease or impairment of myocardial performance. In this article, subclinical LV dysfunction refers to a compromise in LV function prior to reduction in LVEF $\leq$ 50%. The focus of this article is to highlight: 1. The clinical entities where subclinical LV dysfunction has been described by 2D-STE and 2. The potential incremental value of 2D-STE over conventional 2D-echocardiography in the management of these patients.

APPLICATIONS OF STRAIN

i) Valvular Heart Disease

A clear consensus on the timing of valve repair or replacement in asymptomatic patients with preserved LVEF is currently lacking [2]. In addition to the detection of subclinical LV dysfunction, strain parameters have shown promise for the prediction of post-surgical LV dysfunction. Myocardial strain could plausibly assist in the identification of high-risk patients who might benefit from early surgical intervention prior to a decline in the LVEF below guideline recommended threshold levels for surgical intervention (Table **1**). Adaptive remodeling in early aortic regurgitation (AR) preserves LVEF by a compensatory rise in RS and CS for the

1875-6557/17 $58.00+.00

Table 1. Studies evaluating strain in valvular heart disease with speckle tracking echocardiography.

Study	Sample size with description	Imaging modality (vendor name)	Objective	Outcomes
Aortic Regurgitation				
Mizariene *et al.* [41]	Chronic AR:NT-proBNP<400 (n=44) vs. >400 vs. controls (n=64)	2D-STE (EchoPac-GE)	Effect of LV strain on NT-proBNP	GLS>-16% predicts levels>400
Olsen *et al.* [5]	Chronic AR: Surgical (n=29) vs. conservative (n=35)	2D-STE (EchoPAC-GE)	Strain indices in AR progression	Progression correlates with reduced systolic (-1.04 vs. -1.19s^{-1}), early diastolic (1.2 vs. 1.6s^{-1}) and myocardial SR (-16.3 vs. -19%)
Smedsrud *et al.* [6]	Chronic AR (n=47) vs. controls (n=31)	2D-STE (EchoPAC-GE)	GLS impairment and early LV dysfunction	Reduced GLS (-17.5 vs.-22.1%) identifies subclinical LV dysfunction; GLS and not LVEF correlates with post-operative LV function
Kaneko *et al.* [37]	Chronic AR (n=36) vs. controls (n=15)	2D-STE (Toshiba)	GRS decline-marker of myocardial dysfunction?	Endocardial GRS loss (28.9 vs. 37.1%) predicts myocardial dysfunction
Di Salvo *et al.* [4]	Stable (n=17) vs. progressive AR (n=9)	2D-STE (EchoPAC)	Strain parameters and AR progression	LV LS (cut-off >-19.5%) - only predictor for AR Progression
Aortic Stenosis				
Van Dalen *et al.* [11]	AS (n=60) vs. controls (n=30)	2D-STE (QLAB-Philips)	Twist indices and severity of AS, subendocardial ischemia	Elevated peak systolic LV twist (13.6 vs. 11.4) and endocardial twist-shortening ratio (0.6vs.0.4) correlates with ischemia and AS severity
Ng *et al.* [9]	Aortic sclerosis (n=118) vs. Mild (n=81) vs. moderate (n=109) vs. severe (n=112) AS	2D-STE (EchoPAC-GE)	Strain and severity of AS	Sequential deterioration in LS, CS, RS and SR correlates with progressive reduction in valve area
Levy *et al.* [42]	Severe symptomatic AS	2D-STE (EchoPAC-GE)	GLS on post-surgical atrial fibrillation rates	GLS>-15% predicts post-surgical atrial fibrillation
Delgado *et al.* [10]	Severe AS (n=73) vs. controls (n=40)	2D-STE (EchoPAC-GE)	Changes in LV strain pre and post-surgery	GLS (-14.6 vs. -20.3%) and SR-impaired despite pEF. LS, CS and RS improved following valve replacement
Mitral Stenosis				
Ozdemir *et al.* [12]	Mild-moderate MS (n=60) vs. controls (n=52)	2D-ECHO, STE (EchoPAC-GE)	LV dysfunction in MS with pEF	GLS (-17 vs.-19%) and GLS rate compromised in MS
Mitral Regurgitation				
Isla *et al.* [7]	Chronic severe MR (n=38)	2D, 3D-ECHO, Doppler ECHO and 2D-STE (Q-Lab)	Preoperative strain on post-operative LV dysfunction	Longitudinal SR at mid interventricular septal level <-0.8s^{-1} best predictors of LVEF reduction > 10%
Kim *et al.* [43]	Chronic severe MR (n=59) vs. controls (n=34)	2D-ECHO,angiography and 2D-STE (EchoPac-GE)	Strain assessment of latent LV dysfunction	Peak systolic radial SR of 2.0 s^{-1} best correlates with peak dP/dt; short axis function offers better prediction

(Table 1) Contd….

Study	Sample size with description	Imaging modality (vendor name)	Objective	Outcomes
Florescu *et al.* [8]	Severe primary MR (n=28) vs. controls (n=10)	2D-ECHO, TVI and STE (EchoPac-GE)	Pre-op strain and post-valve replacement LV function	Systolic TVI and the combination of systolic TVI and LS are main independent predictors of post-operative LVEF drop >10%
Pandis *et al.* [44]	Degenerative MR (n=40)	2D, 3D-ECHO, and 2D-STE (TomTec)	Predictors of recurrent MR post-surgery	Mid-lateral RS≤-27 and apical lateral RS ≤-25-significant predictors
Mascle *et al.* [45]	Severe degenerative MR: post op LVEF≥50% (n=73) + LVEF<50% (n=15)	2D-ECHO, 2D-STE and TDI (EchoPAC-GE)	Pre-operative GLS on post-operative LV dysfunction	GLS >-18% predicts post-operative LVEF drop to <50%

2D, 2 dimensional; 3D, 3 dimensional; AS, aortic stenosis; AR, aortic regurgitation; CS, circumferential strain; ECHO, echocardiography; GLS, global longitudinal strain; GRS, global radial strain; LS, longitudinal strain; LV, left ventricle; LVEF, left ventricular ejection fraction; MS, mitral stenosis; MR, mitral regurgitation; NT-proBNP, N terminal-pro brain natriuretic peptide; pEF, preserved ejection fraction; RS, radial strain; SR, strain rate; TDI, tissue Doppler imaging; TVI, tissue velocity imaging.

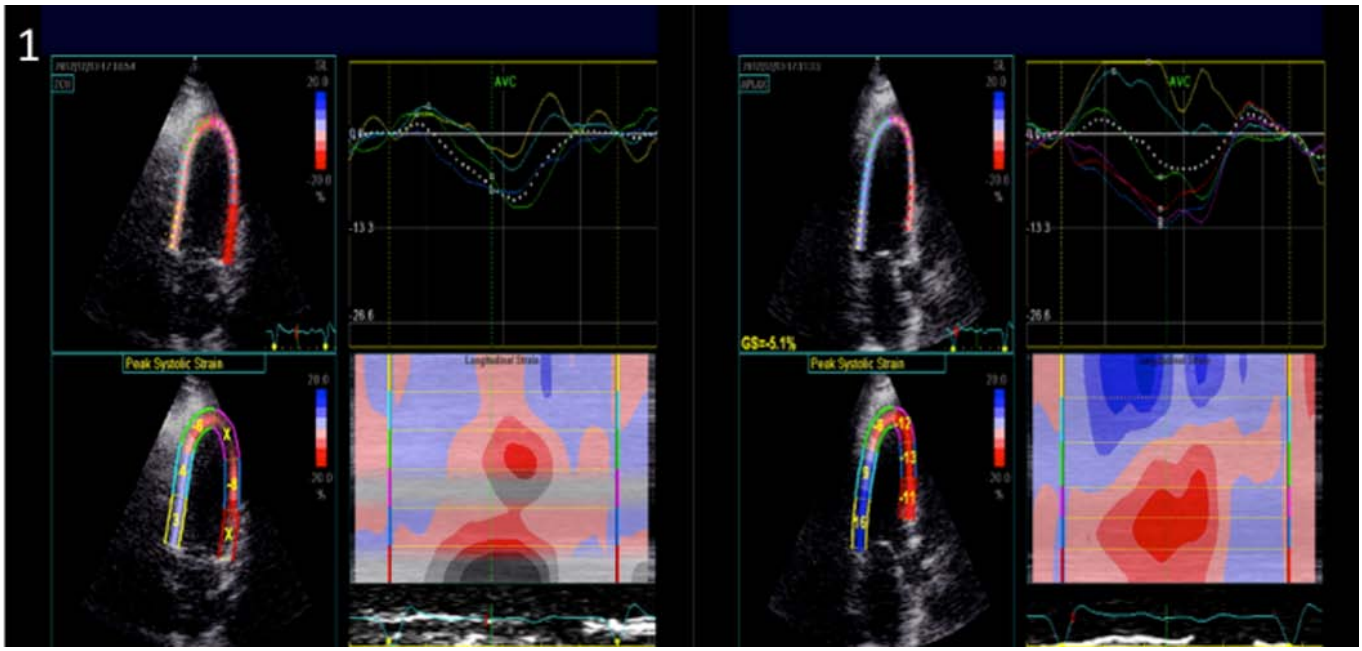

Fig. (1). Paradoxical longitudinal strain in inferior and inferolateral walls in a patient admitted with uremic pericarditis and found to have newly reduced systolic function without any wall motion abnormalities, suggestive of perimyocarditis. The systolic function recovered following treatment for pericarditis in an echocardiogram performed 2 weeks later.

early loss of LS with additional compensation provided by LV hypertrophy and increase in LV volume [3]. Reduction in LVEF to <50% in asymptomatic AR heralds an increase in the rate of progression to symptoms, a surgical indication, from 4.3% to 25% per year [2]. Amongst patients with preserved ejection fraction (pEF), LS attenuation >-19.5% is 77% sensitive and 94% specific for symptomatic progression of asymptomatic moderate-severe AR [4]. Pre-operative GLS attenuation, but not LVEF, has been associated with post-operative LV dysfunction [5, 6]. Likewise, in mitral regurgitation, pre-operative GLS impairment (GLS<-18 %) has been shown to identify subclinical LV dysfunction in patients with LVEF>60% and also predict post-operative LV dysfunction [7, 8].

In aortic stenosis (AS), the degree of strain deterioration correlates significantly with lower aortic valve (AV) area and severity of AS [9] while strain recovery has been noted post AV replacement [10], even prior to recovery of LVEF. Furthermore, altered twist mechanics in AS offers a non-invasive means of predicting subendocardial ischemia [11]**.** Similarly, identification of subclinical LV dysfunction by attenuated GLS and GLS rate in asymptomatic or minimally symptomatic mitral stenosis (MS) [12] might aid in optimal

Table 2. Studies highlighting utility of speckle tracking echocardiography in subclinical coronary artery disease.

Study	Sample size with description	Imaging modality with vendor name	Objective	Outcomes
Nucifora *et al.* [46]	Non-obstructive (n=60) vs. obstructive (n=63) vs. no CAD (n=59)	CT angiography and 2D-STE (EchoPAC-GE)	GLS prediction of obstructive CAD	GLS≥-17.4% predicts obstructive CAD better than diastolic dysfunction or Duke clinical scores
Hanekom *et al.* [47]	Significant CAD (150)	2D-STE, TVI, DSE and coronary angiography (EchoPAC-GE)	Strain from STE vs. TVI during DSE in predicting obstructive CAD	STE-equally efficacious to TVI in anterior but not in posterior circulation
Liang *et al.* [17]	Obstructive (n=39) vs. non-obstructive or no CAD (n=15)	2D-STE, coronary angiography (EchoPAC-GE)	Diastolic strain in obstructive CAD	Early diastolic SR impairment is superior to systolic strain: 77% sensitive, 93% specific
Tsai *et al.* [16]	CAD (n=75) vs. no CAD (n=77)	STE, coronary angiography (EchoPAC-GE)	LS in prediction of obstructive CAD	Sensitivity, specificity of GLS>-19%: 75%, 81%; peak segmental LS difference/peak systolic GLS ratio>1: 77%, 79%
Smedsrud *et al.* [15]	Significant (n=43) vs. non-significant CAD (n=43)	2D-STE, coronary angiography (EchoPac-GE)	Does duration of early systolic lengthening predict significant CAD?	Early systolic lengthening (cutoff 58 milliseconds) predicts significant CAD better than peak systolic LS attenuation

2D-STE, 2 dimensional-speckle tracking echocardiography; CAD, coronary artery disease; CT, computerized tomography; DSE, dobutamine stress echocardiography; GLS, global longitudinal strain; LS, longitudinal strain; pEF, preserved ejection fraction; SR, strain rate; TVI, tissue velocity imaging.

timing of mitral valve (MV) interventions prior to permanent myocardial remodeling [13, 14].

ii) Coronary Artery Disease

2D-STE is robust in terms of its prognostic utility and reproducibility in the assessment of subclinical CAD (Table **2**) [15]. Various strain parameters such as early myocardial systolic lengthening (15), ratio of peak systolic LS difference to peak systolic GLS [16] and a combination of early systolic and early diastolic SR [17] provide incremental value over GLS for obstructive CAD. Strain assessment during dobutamine stress echocardiography (DSE) could enhance the sensitivity of conventional 2D-echo by minimizing inter-observer variability in delineating endocardial borders and interpreting wall motion abnormalities as demonstrated by using software such as automated functional imaging (AFI). Strain rate imaging offers incremental value over DSE derived wall motion scores in the prediction of mortality [18]. Additionally, a remarkable coronary territorial correlation between AFI derived strain and angiography with a sensitivity >90% in the anterior and >79% in the posterior circulations has been demonstrated [16, 18].

iii) Hypertension and Diabetes Mellitus

Attenuation of 2D-STE derived GLS presents a vital differentiating parameter between hypertensive heart disease and an athlete's heart while providing excellent correlation with the magnitude of diastolic dysfunction in hypertensives [19]. Detection of LS impairment by 2D-STE precedes detection by tissue Doppler imaging (TDI) in hypertensives with preserved LVEF even prior to the development of left ventricular hypertrophy (LVH) [20] thus providing an early opportunity to arrest progression to LVH. Indeed, preserved CS and consequential wall thickening despite reduction in LS has been posited to explain preservation of LVEF in patients with systemic hypertension [21].

2D-STE derived GLS attenuation might be useful for risk stratification in asymptomatic diabetics via prediction of subclinical systolic LV dysfunction with the decrease in LS being proportional to diabetes duration [22]. Furthermore, impairment of GLS has been associated with higher coronary artery calcium scores in diabetics, a surrogate for subclinical coronary atherosclerosis [23].

iv) Heart Failure with Preserved Ejection Fraction (HFpEF)

Although diastolic dysfunction is believed to be the underlying pathophysiology in HFpEF, recent studies have indicated abnormalities of systolic function in these patients [24]. Indeed, traditional diastolic dysfunction parameters were absent in approximately one-third of the HFpEF trial cohorts [25, 26]. Systolic impairment of strain parameters (LS, CS) has been demonstrated in HFpEF patients, with LS attenuation being associated with higher NT-pro BNP levels [27]. 2D-STE derived increases in LS delay index and time to achieve peak longitudinal velocity unveil the dysfunctional systolic component of HFpEF indicating dyssynchronous and ineffective ventricular contraction [28] (Table **3**). Previous studies have hypothesized that reduction of dyssynchrony by cardiac resynchronization therapy could translate into energy efficient contractility and mitigate progression to systolic failure [28].

Table 3. Evaluation of heart failure with preserved ejection fraction with speckle tracking echocardiography.

Study	Sample size with description	Imaging modality with vendor name	Objective	Outcomes
Phan *et al.* [48]	HfPEF (n=47) vs. young (n=27) vs. old controls (n=26)	2D-ECHO, 2D-STE (EchoPAC-GE)	Comparing strain profiles: HfPEF vs. age related changes	Increased TS seen with ageing. CS increase (-24.7% vs. -20%) differentiates HfPEF from old controls
Phan *et al.* [28]	HfPEF (n=38) vs. controls (n=33)	2D-ECHO and 2D-STE (EchoPAC-GE)	Dyssynchrony assessment in HfPEF	Systolic and diastolic dyssynchrony observed. LS impairment (-17.6% vs. -19.9%) and higher LV dyssynchrony (LS delay index-14.4% vs.-10.7%) noted
Donal *et al.* [39]	HfPEF (n=21) vs. controls (n=15)	2D-ECHO, exercise stress testing and 2D-STE (EchoPAC-GE)	To characterize resting and exercise induced strain changes	GLS impaired at rest [Rest: (-16% vs. -20%) and aggravated by stress: (-17% vs. -23%); similar trend with global CS
Kraigher-Krainer *et al.* [27]	HfPEF (n=219) vs. controls (n=50) and Hypertensive Heart Disease (n=44)	Vendor independent STE Software	Strain parameters in HfPEF	Lower LS and CS in HfPEF (-14.6±3.3 vs.. 20.0±2.1 in controls); Lower LS values co-related with higher NT-ProBNP

2D, 2 dimensional; CS, circumferential strain; ECHO, echocardiography; GLS, global longitudinal strain; HfPEF, heart failure with preserved ejection fraction; LS, longitudinal strain; RS, radial strain; STE, speckle tracking echocardiography; TS: torsional strain; BNP: Brain Natiuretic Peptide.

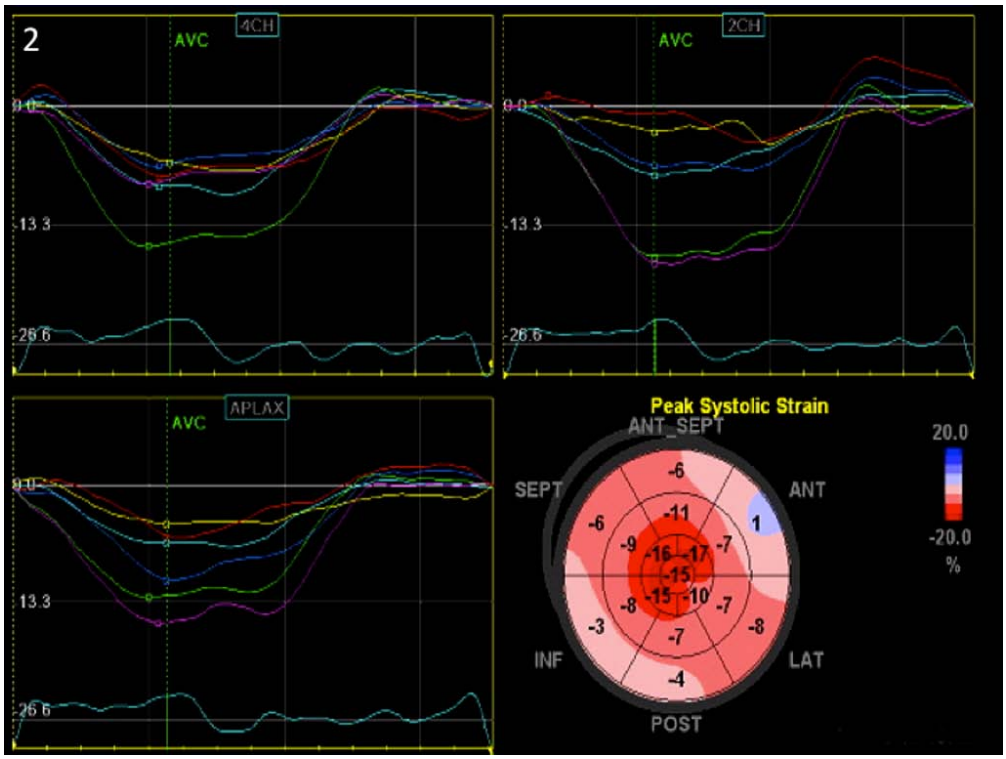

Fig. (2). Reduced basal and mid-segmental strain values with apical sparing suggestive of amyloidosis in the presence of normal systolic function.

v) Perimyocarditis

Incipient myocardial dysfunction has been demonstrated in acute perimyocarditis with compromise in GLS and twist angle preceding reduction of LVEF [29] (Fig. **1**). Impairment of CS and TS with intact LS in constrictive pericarditis as opposed to impaired LS and intact CS in restrictive cardiomyopathy effectively differentiates these conditions [30].

vi) Cancer Chemotherapy

Routine serial assessment of LV strain parameters could aid in earlier identification of chemotherapy-induced cardiotoxicity prior to conventional changes in LVEF (Table **4**). Attenuation of 2D-STE derived LV apical cap peak systolic strain [31], GLS, torsion, twisting and untwisting rates occur as early as 1 month after anthracycline (AT) therapy, preced-

Table 4. Strain imaging in the assessment of chemotherapy associated cardio toxicity.

Study	Sample size with description	Imaging modality with vendor name	Objective	Outcomes
Tsai *et al.* [40]	Hodgkin's lymphoma and radiotherapy (n=47) [AT (n=27), No AT (n=20)] vs. controls (n=20)	2D-ECHO and 2D-STE (EchoPAC-GE)	LV dysfunction with anthracycline (AT) and radiotherapy (RT)	Higher GLS impairment in RT+AT (-16.1%) than RT and no AT (-17.5%); CS-similar trend; pEF-all groups
Poterucha *et al.* [31]	AT (n=19) vs. controls (n=19)	2D-ECHO and 2D-STE (EchoPAC-GE)	Temporal changes in strain and LVEF	Longitudinal PSS reduction started at 4 months (8.7%) and worsened by 8 months (9.2%) with AT. LVEF decreased by 4.3% only at 8 months.
Motoki *et al.* [32]	AT therapy (n=25)	2D-ECHO, TDI and 2D-STE (EchoPAC-GE)	Torsional strain and subclinical LV dysfunction	Impairment in GLS, TS, twisting and untwisting rates occur as early as 1 month; LVEF, TDI indices-preserved
Ho *et al.* [49]	AT (n=19) vs. AT+TZ (n=51) vs. controls (n=50)	2D-ECHO, Doppler ECHO and 2D-STE (EchoPAC-GE)	Subclinical LV dysfunction in combination therapy (AT+TZ)	Reduced GLS in AT (-17.7) vs. AT+TZ (-19.2) vs. controls (-19.6). No additive cardiotoxicity with TZ
Fallah-Rad *et al.* [50]	No toxicity (n=10) vs. TZ toxicity (n=32)	TVI, CMR and 2D-STE (EchoPac-GE)	Detection of TZ cardiotoxicity with various techniques	2D-STE impairment in GLS (-19.9 ± 1.8% to. -16.4 ± 1.1%) and GRS (42.4 ± 10.5% to. 32.5 ± 15.2%) occur earliest (3 months). LVEF preserved until 6 months

2D-ECHO, 2 dimensional echocardiography; 2D-STE, 2 dimensional speckle tracking echocardiography; AT, anthracycline; CMR, cardiac magnetic resonance; CS, circumferential strain; GLS, global longitudinal strain; GRS, global radial strain; LV, left ventricle; LVEF, left ventricular ejection fraction; pEF, preserved ejection fraction; PSS, peak systolic strain; RS, radial strain; RT, radiotherapy; TS, torsional strain; TDI, tissue Doppler imaging; TZ, trastuzumab.

ing impairment in LVEF and Doppler parameters and also offers excellent correlation with cumulative AT dose [32]. AT therapy has been associated with a 16% prevalence of higher LV systolic dyssynchrony index reflective of energy inefficient contraction, positing a role for cardiac resynchronization therapy in these patients. Likewise, strain imaging has been shown to recognize pre-clinical changes in systolic function in prospectively followed breast cancer patients on adjuvant trastuzumab therapy [31].

MISCELLANEOUS CONDITIONS

Apical sparing, evidenced by relative apical LS>1 (mean apical LS/mean basal LS+ mean mid-LS) discriminates cardiac amyloidosis from AS or hypertrophic cardiomyopathy induced LVH with a sensitivity>90% and specificity>80% [32] (Fig. **2**). LS impairment is associated with elevated NT-proBNP in Behcet's disease (Table **5**). In Fabry's disease, systolic strain attenuation in the basal postero-lateral segments offers a sensitivity and specificity of 90% and 97% respectively, for the identification of MRI confirmed fibrotic arrhythmogenic foci [33]. Systemic Sclerosis is characterized by impairment of global and LV longitudinal peak systolic strain (PSS) with higher attenuation in the basal segments and sparing of the apical and medial segments [34]. Moreover, reduced GLS and global CS were independently predictive of ventricular arrhythmias in systemic sclerosis patients [35].

Strain derived radial LV wall motion discoordination was shown to be an independent predictor of decline in cardiac output in acute pulmonary embolism [54]. Subclinical LV dysfunction inherent to preeclampsia has been identified by a higher decline in global LS, RS and CS than in non-proteinuric hypertension [55]. Sickle cell crisis results in transient LV dysfunction with reversal of regional LS impairment on crisis resolution [38].

OBLIGATORY NEED FOR STANDARDIZATION IN SPECKLE TRACKING ECHOCARDIOGRAPHY

Marwick *et al*. have described discordant strain values from different vendors to result from three components: 1) Image procurement and storage resolution; 2) Processing of image data for strain quantification and 3) Hemodynamic status [35]. Image acquisition with vendor specific ultrasound machines, heterogeneity in frame rates used for compression (30 frames/sec for vendor neutral software), differences in the methodology of algorithms used to derive strain, types of strain used (natural or Lagrangian strain), anatomical regions studied to derive strain (endocardial, epicardial or both), phase of the cardiac cycle in which images are acquired and blood pressure variations during image procurement are all sources of discrepancies [35]. Head-to-head comparisons between different combinations of ultrasound machines and vendor specific versus vendor neutral post-processing software has depicted higher variations from post-processing and not image acquisition [36]. When vendor neutral software is used, standardization of methods to derive strain has been shown to minimize GLS variations even at frame rates as low as 30 frames/second [39, 40].

Table 5. Miscellaneous conditions underscoring the clinical applicability of speckle tracking echocardiography.

Study	Sample size with description	Imaging modality with vendor name	Objective	Outcomes
Yagmur *et al.*	Behcets disease (n=32) vs. controls (n=27)	2D-ECHO and 2D-STE (QLab-Philips)	Detection of subclinical LV dysfunction	Reduced LS (-17.8 ± 2.7%) in disease vs. controls (-20.5 ± 1.8%); NT-proBNP independent corelate of mean LS
Liu *et al.* [51]	Hemodialysis patients (n=102)	2D-ECHO, TDI and 2D-STE (EchoPac-GE)	Predictors of significant CAD despite pEF in hemodialysis patients	Reduction in LS ≥-15% in ≥6 myocardial segments predicts CAD
Dedobbeleer *et al.* [52]	Friedreich's ataxia (n=20) vs. controls (n=20)	2D-ECHO and 2D-STE (Qlab-Philips)	Stain profiling, detection of subclinical LV dysfunction	Reduced GLS (-15.3 vs. -17.5%), peak LV twist and untwisting rates
Caputo *et al.* [53]	At least 1 cardiovascular risk factor (n=70)	2D-ECHO, TDI and 2D-STE (EchoPAC-GE)	Abnormal LV strain in overweight (BMI) despite pEF	Peak LS of LV-reduced in overweight vs. normal BMI (-17.2% vs. -18.7%)
Takamura *et al.* [54]	Acute PE (n=25) vs. controls (n=25)	2D-ECHO and 2D-STE (EchoPAC-GE)	Impact of acute RV pressure overload on LV strain	Global LS (-16 vs. -20), CS (-17 vs. -24) and RS (44 vs. 59) reduced in acute PE, recover with the resolution of pressure overload
Shahul *et al.* [55]	Preeclampsia (n=11) vs. non-proteinuric hypertension (n=11) vs. normotensives (n=17)	2D-ECHO and 2D-STE (TomTec)	Is subclinical LV dysfunction inherent to preeclampsia?	Impaired GLS (-13.7 vs. -15.9 vs. -20.1), GRS (22.4 vs. 40.7 vs. 39.8) and GCS (-17.9 vs. -28.2 vs. -21.6) in preeclampsia. pEF in all groups
Inoue *et al.* [56]	RV apical pacing (n=51)+ RV septal pacing (n=52) vs. controls (n=50)	2D-ECHO and 2D-STE (EchoPAC-GE)	Subclinical LV dysfunction with RV apical pacing	Maximal impairment of GLS with RV apical pacing [-14.3 vs. -16.8 vs. -18.2]
Miszalski-Jamka *et al.* [57-59]	Wegener's granulomatosis (n=22) vs. controls (n=22)	2D-ECHO and 2D-STE (EchoPAC-GE)	Subclinical LV dysfunction identification	Global LS (-17.9 vs.-19.7), CS (-18.4 vs. -21.6) and RS (38.8 vs. 50.1) impairment noted, correlate with disease severity.

2D-ECHO, 2 dimensional echocardiography; 2D-STE, 2 dimensional speckle tracking echocardiography; BMI, body mass index; CAD, coronary artery disease; CS, circumferential strain; GCS, global circumferential strain, GRS, global radial strain; LS, longitudinal strain; LV, left ventricle; PE, pulmonary embolism; pEF, preserved ejection fraction; RS, radial strain; RV, right ventricle; TDI, tissue Doppler imaging.

A concerted effort to standardize strain software between a conglomerate of vendors supported by the American Society of Echocardiography and the European Society of Echocardiography is afoot. It is hoped that this endeavor will eventually culminate into standardization of postprocessing software to minimize variability between vendor offerings.

FUTURE DIRECTIONS

Barriers to use of strain imaging in routine practice include physician reluctance to adopt innovative technology with perceived complexity, lack of standardization and reimbursement limitations. Whether interventions following identification of subclinical LV dysfunction could translate into reduced cardiovascular morbidity and mortality needs further appraisal in prospective randomized controlled trials. Further technologic refinements targeting these limitations could transform 2D-STE into a robust modality for the routine detection of subclinical myocardial dysfunction, given its increasing ease of use and wide applicability.

LIST OF ABBREVIATIONS

2D-ECHO = 2-dimensional echocardiography

2D-STE = 2-dimensional speckle tracking echocardiography

AF = Atrial fibrillation

AFI = Automated functional imaging

AR = Aortic regurgitation

AS = Aortic stenosis

AT = Anthracycline

AV = Aortic valve

CAD = Coronary artery disease

CS = Circumferential strain

DSE = Dobutamine stress echocardiography

GLS = Global longitudinal stain

HFpEf = Heart failure with preserved ejection fraction

LS = Longitudinal strain

LV = Left ventricle

LVEF = Left ventricular ejection fraction

MS = Mitral stenosis

MV = Mitral valve

NT-proBNP = N terminal-pro brain natriuretic peptide

pEF = Preserved ejection fraction

PSS = Peak systolic strain

RS = Radial strain

RV = Right ventricle

SR = Strain rate

TS = Torsional strain

TDI = Tissue doppler imaging

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Leischik R, Dworrak B, Hensel K. Intraobserver and interobserver reproducibility for radial, circumferential and longitudinal strain echocardiography. Open Cardiovasc Med J 2014; 8: 102-9.

[2] Bonow RO, Carabello BA, Chatterjee K, *et al*. 2008 Focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation 2008; 118(15): e523-661.

[3] Iida N, Seo Y, Ishizu T, *et al*. Transmural compensation of myocardial deformation to preserve left ventricular ejection performance in chronic aortic regurgitation. J Am Soc Echocardiogr 2012; 25(6): 620-8.

[4] Di Salvo G, Rea A, Mormile A, *et al*. Usefulness of bidimensional strain imaging for predicting outcome in asymptomatic patients aged </= 16 years with isolated moderate to severe aortic regurgitation. Am J Cardiol 2012; 110(7): 1051-5.

[5] Olsen NT, Sogaard P, Larsson HB, *et al*. Speckle-tracking echocardiography for predicting outcome in chronic aortic regurgitation during conservative management and after surgery. JACC Cardiovasc Imaging 2011; 4(3): 223-30.

[6] Smedsrud MK, Pettersen E, Gjesdal O, *et al*. Detection of left ventricular dysfunction by global longitudinal systolic strain in patients with chronic aortic regurgitation. J Am Soc Echocardiogr 2011; 24(11): 1253-9.

[7] de Isla LP, de Agustin A, Rodrigo JL, *et al*. Chronic mitral regurgitation: a pilot study to assess preoperative left ventricular contractile function using speckle-tracking echocardiography. J Am Soc Echocardiogr 2009; 22(7): 831-8.

[8] Florescu M, Benea DC, Rimbas RC, *et al*. Myocardial systolic velocities and deformation assessed by speckle tracking for early detection of left ventricular dysfunction in asymptomatic patients with severe primary mitral regurgitation. Echocardiography 2012; 29(3): 326-33.

[9] Ng AC, Delgado V, Bertini M, *et al*. Alterations in multidirectional myocardial functions in patients with aortic stenosis and preserved ejection fraction: a two-dimensional speckle tracking analysis. Eur Heart J 2011; 32(12): 1542-50.

[10] Delgado V, Tops LF, van Bommel RJ, *et al*. Strain analysis in patients with severe aortic stenosis and preserved left ventricular ejection fraction undergoing surgical valve replacement. Eur Heart J 2009; 30(24): 3037-47.

[11] van Dalen BM, Tzikas A, Soliman OI, *et al*. Assessment of subendocardial contractile function in aortic stenosis: a study using speckle tracking echocardiography. Echocardiography 2013; 30(3): 293-300.

[12] Ozdemir AO, Kaya CT, Ozcan OU, *et al*. Prediction of subclinical left ventricular dysfunction with longitudinal two-dimensional strain and strain rate imaging in patients with mitral stenosis. Int J Cardiovasc Imaging 2010; 26(4): 397-404.

[13] Wang B, Xu ZY, Han L, *et al*. Impact of preoperative atrial fibrillation on mortality and cardiovascular outcomes of mechanical mitral valve replacement for rheumatic mitral valve disease. Eur J Cardiothorac Surg 2013; 43(3): 513-9.

[14] Ancona R, Comenale Pinto S, Caso P, *et al*. Two-dimensional atrial systolic strain imaging predicts atrial fibrillation at 4-year follow-up in asymptomatic rheumatic mitral stenosis. J Am Soc Echocardiogr 2013; 26(3): 270-7.

[15] Smedsrud MK, Sarvari S, Haugaa KH, *et al*. Duration of myocardial early systolic lengthening predicts the presence of significant coronary artery disease. J Am Coll Cardiol 2012; 60(12): 1086-93.

[16] Tsai WC, Liu YW, Huang YY, *et al*. Diagnostic value of segmental longitudinal strain by automated function imaging in coronary artery disease without left ventricular dysfunction. J Am Soc Echocardiogr 2010; 23(11): 1183-9.

[17] Liang HY, Cauduro S, Pellikka P, *et al*. Usefulness of two-dimensional speckle strain for evaluation of left ventricular diastolic deformation in patients with coronary artery disease. Am J Cardiol 2006; 98(12): 1581-6.

[18] Bjork Ingul C, Rozis E, Slordahl SA, Marwick TH. Incremental value of strain rate imaging to wall motion analysis for prediction of outcome in patients undergoing dobutamine stress echocardiography. Circulation 2007; 115(10): 1252-9.

[19] Galderisi M, Lomoriello VS, Santoro A, *et al*. Differences of myocardial systolic deformation and correlates of diastolic function in competitive rowers and young hypertensives: a speckle-tracking echocardiography study. J Am Soc Echocardiogr 2010; 23(11): 1190-8.

[20] Imbalzano E, Zito C, Carerj S, *et al*. Left ventricular function in hypertension: new insight by speckle tracking echocardiography. Echocardiography 2011; 28(6): 649-57.

[21] Sengupta SP, Caracciolo G, Thompson C, Abe H, Sengupta PP. Early impairment of left ventricular function in patients with systemic hypertension: New insights with 2-dimensional speckle tracking echocardiography. Indian Heart J 2013; 65(1): 48-52.

[22] Nakai H, Takeuchi M, Nishikage T, Lang RM, Otsuji Y. Subclinical left ventricular dysfunction in asymptomatic diabetic patients assessed by two-dimensional speckle tracking echocardiography: correlation with diabetic duration. Eur J Echocardiogr 2009; 10(8): 926-32.

[23] Scholte AJ, Nucifora G, Delgado V, *et al*. Subclinical left ventricular dysfunction and coronary atherosclerosis in asymptomatic patients with type 2 diabetes. Eur J Echocardiogr 2011; 12(2): 148-55.

[24] Borlaug BA, Lam CS, Roger VL, Rodeheffer RJ, Redfield MM. Contractility and ventricular systolic stiffening in hypertensive heart disease insights into the pathogenesis of heart failure with preserved ejection fraction. J Am Coll Cardiol 2009; 54(5): 410-8.

[25] Persson H, Lonn E, Edner M, *et al*. Diastolic dysfunction in heart failure with preserved systolic function: need for objective evidence:results from the CHARM Echocardiographic Substudy-CHARMES. J Am Coll Cardiol 2007; 49(6): 687-94.

[26] Zile MR, Gottdiener JS, Hetzel SJ, *et al*. Prevalence and significance of alterations in cardiac structure and function in patients with heart failure and a preserved ejection fraction. Circulation 2011; 124(23): 2491-501.

[27] Kraigher-Krainer E, Shah AM, Gupta DK, *et al*. Impaired Systolic Function by Strain Imaging in Heart Failure with Preserved Ejection Fraction. J Am Coll Cardiol 2014; 63(5): 447-56.

[28] Phan TT, Abozguia K, Shivu GN, *et al*. Myocardial contractile inefficiency and dyssynchrony in heart failure with preserved ejection fraction and narrow QRS complex. J Am Soc Echocardiogr 2010; 23(2): 201-6.

[29] Leitman M, Bachner-Hinenzon N, Adam D, *et al*. Speckle tracking imaging in acute inflammatory pericardial diseases. Echocardiography 2011; 28(5): 548-55.

[30] Sengupta PP, Krishnamoorthy VK, Abhayaratna WP, *et al*. Disparate patterns of left ventricular mechanics differentiate constrictive pericarditis from restrictive cardiomyopathy. JACC Cardiovasc Imaging 2008; 1(1): 29-38.

[31] Poterucha JT, Kutty S, Lindquist RK, Li L, Eidem BW. Changes in left ventricular longitudinal strain with anthracycline chemotherapy in adolescents precede subsequent decreased left ventricular ejection fraction. J Am Soc Echocardiogr 2012; 25(7): 733-40.

[32] Phelan D, Collier P, Thavendiranathan P*, et al.* Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis. Heart 2012; 98(19): 1442-8.

[33] Kramer J, Niemann M, Liu D, *et al*. Two-dimensional speckle tracking as a non-invasive tool for identification of myocardial fibrosis in Fabry disease. Eur Heart J 2013; 34(21): 1587-96.

[34] Spethmann S, Dreger H, Schattke S, *et al*. Two-dimensional speckle tracking of the left ventricle in patients with systemic sclerosis for an early detection of myocardial involvement. Eur Heart J Cardiovasc Imaging 2012; 13(10): 863-70.

[35] Yiu KH, Schouffoer AA, Marsan NA*, et al.* Left ventricular dysfunction assessed by speckle-tracking strain analysis in patients with systemic sclerosis: relationship to functional capacity and ventricular arrhythmias. Arthritis Rheumatism 2011; 63(12): 3969-78.

[36] Negishi K, Lucas S, Negishi T, Hamilton J, Marwick TH. What is the primary source of discordance in strain measurement between vendors: imaging or analysis? Ultrasound Med Biol 2013; 39(4): 714-20.

[37] Kaneko A, Tanaka H, Onishi T, *et al*. Subendocardial dysfunction in patients with chronic severe aortic regurgitation and preserved ejection fraction detected with speckle-tracking strain imaging and transmural myocardial strain profile. Eur Heart J Cardiovasc Imaging 2013; 14(4): 339-46.

[38] Sengupta SP, Jaju R, Nugurwar A, Caracciolo G, Sengupta PP. Left ventricular myocardial performance assessed by 2-dimensional speckle tracking echocardiography in patients with sickle cell crisis. Indian Heart J 2012; 64(6): 553-8.

[39] Nelson MR, Hurst RT, Raslan SF*, et al.* Echocardiographic measures of myocardial deformation by speckle-tracking technologies: the need for standardization? J Am Soc Echocardiogr 2012; 25(11): 1189-94.

[40] Risum N, Ali S, Olsen NT*, et al.* Variability of global left ventricular deformation analysis using vendor dependent and independent two-dimensional speckle-tracking software in adults. J Am Soc Echocardiogr 2012; 25(11): 1195-203..

[41] Mizariene V, Grybauskiene R, Vaskelyte J, *et al*. Strain value in the assessment of left ventricular function and prediction of heart failure markers in aortic regurgitation. Echocardiography 2011; 28(9): 983-92.

[42] Levy F, Debry N, Labescat AL, *et al*. Echocardiographic prediction of postoperative atrial fibrillation after aortic valve replacement for aortic stenosis: a two-dimensional speckle tracking left ventricular longitudinal strain multicentre pilot study. Arch Cardiovasc Dis 2012; 105(10): 499-506.

[43] Kim MS, Kim YJ, Kim HK, *et al*. Evaluation of left ventricular short- and long-axis function in severe mitral regurgitation using 2-dimensional strain echocardiography. Am Heart J 2009; 157(2): 345-51.

[44] Pandis D, Grapsa J, Athanasiou T, Punjabi P, Nihoyannopoulos P. Left ventricular remodeling and mitral valve surgery: prospective study with real-time 3-dimensional echocardiography and speckle tracking. J Thorac Cardiovasc Surg 2011; 142(3): 641-9.

[45] Mascle S, Schnell F, Thebault C, *et al*. Predictive value of global longitudinal strain in a surgical population of organic mitral regurgitation. J Am Soc Echocardiogr 2012; 25(7): 766-72.

[46] Nucifora G, Schuijf JD, Delgado V, *et al*. Incremental value of subclinical left ventricular systolic dysfunction for the identification of patients with obstructive coronary artery disease. Am Heart J 2010; 159(1): 148-57.

[47] Hanekom L, Cho GY, Leano R, Jeffriess L, Marwick TH. Comparison of two-dimensional speckle and tissue Doppler strain measurement during dobutamine stress echocardiography: an angiographic correlation. Eur Heart J 2007; 28(14): 1765-72.

[48] Phan TT, Shivu GN, Abozguia K, *et al*. Left ventricular torsion and strain patterns in heart failure with normal ejection fraction are similar to age-related changes. Eur J Echocardiogr 2009; 10(6): 793-800.

[49] Ho E, Brown A, Barrett P, *et al*. Subclinical anthracycline- and trastuzumab-induced cardiotoxicity in the long-term follow-up of asymptomatic breast cancer survivors: a speckle tracking echocardiographic study. Heart 2010; 96(9): 701-7.

[50] Fallah-Rad N, Walker JR, Wassef A, *et al*. The utility of cardiac biomarkers, tissue velocity and strain imaging, and cardiac magnetic resonance imaging in predicting early left ventricular dysfunction in patients with human epidermal growth factor receptor II-positive breast cancer treated with adjuvant trastuzumab therapy. J Am Coll Cardiol 2011; 57(22): 2263-70.

[51] Liu YW, Su CT, Wang SP, *et al*. Application of speckle-tracking echocardiography in detecting coronary artery disease in patients with maintenance hemodialysis. Blood Purif 2011; 32(1): 38-42.

[52] Dedobbeleer C, Rai M, Donal E, Pandolfo M, Unger P. Normal left ventricular ejection fraction and mass but subclinical myocardial dysfunction in patients with Friedreich's ataxia. Eur Heart J Cardiovasc Imaging 2012; 13(4): 346-52.

[53] Caputo M, Urselli R, Zaca V, *et al*. Detection of Early Left Ventricular and Atrial Dysfunction in Overweight Patients with Preserved Ejection Fraction: A Speckle Tracking Analysis. Echocardiography 2013; 30(5): 551-7.

[54] Takamura T, Dohi K, Onishi K, *et al*. Reversible left ventricular regional non-uniformity quantified by speckle-tracking displacement and strain imaging in patients with acute pulmonary embolism. J Am Soc Echocardiogr 2011; 24(7): 792-802.

[55] Shahul S, Rhee J, Hacker MR, *et al*. Subclinical left ventricular dysfunction in preeclamptic women with preserved left ventricular ejection fraction: a 2D speckle-tracking imaging study. Circ Cardiovasc Imaging 2012; 5(6): 734-9.

[56] Inoue K, Okayama H, Nishimura K, *et al*. Right ventricular septal pacing preserves global left ventricular longitudinal function in comparison with apical pacing: analysis of speckle tracking echocardiography. Circ J 2011; 75(7): 1609-15.

[57] Miszalski-Jamka T, Szczeklik W, Nycz K, *et al*. Two-dimensional speckle-tracking echocardiography reveals systolic abnormalities in granulomatosis with polyangiitis (Wegener's). Echocardiography 2012; 29(7): 803-9.

[58] Witkowski TG, Thomas JD, Debonnaire PJ, *et al*. Global longitudinal strain predicts left ventricular dysfunction after mitral valve repair. Eur Heart J Cardiovasc Imaging 2013; 14: 69-76.

[59] Ternacle J, Berry M, Alonso E, *et al*. Incremental value of global longitudinal strain for predicting early outcome after cardiac surgery. Eur Heart J Cardiovasc Imaging 2013; 14: 77-84.