Speckle Tracking Echocardiography & Valvular Heart Disease

Mohammad Abd Elwahab Fikry, Mohammad Abd Allah Eltahlawi, Alaa Elsayed Salama

Department of Cardiology, Faculty of Medicine, Zagazig University, Egypt

Corresponding author: Mohammad Abd Elwahab Fikry

E-mail: mafmody.mf@gmail.com, mafikry@medicine.zu.edu.eg

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Abstract

Recent advances in quantitative ultrasound technology have made speckle-tracking echocardiography an effective method for measuring myocardial function by analyzing the motion of speckles seen on standard 2-dimensional sonograms. It offers objective, non-Doppler quantification of left ventricular systolic and diastolic dynamics as well as myocardial deformation. After a sufficient amount of image acquisition, strain and the strain rate can be quickly determined offline by tracking the displacement of the speckles throughout the cardiac cycle. Speckle-tracking echocardiography has been shown to be feasible, accurate, and useful in a variety of clinical settings. The foundation of speckle-tracking echocardiography is the analysis of the spatial dislocation, or "tracking," of speckles, which are spots produced by the interaction of the ultrasound beam and myocardial fibres on standard 2-dimensional sonograms. Speckle-tracking echocardiography enables semi-automated elaboration of myocardial deformation in three spatial directions: longitudinal, radial, and circumferential by monitoring the displacement of speckles throughout the cardiac cycle. Additionally, left ventricle (LV) rotation's frequency, direction, and velocity can be assessed using speckle-tracking echocardiography

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Introduction:

Recent advances in quantitative ultrasound technology have made speckle-tracking echocardiography an effective method for measuring myocardial function by analyzing the motion of speckles seen on standard 2-dimensional sonograms. It offers objective, non-Doppler quantification of left ventricular systolic and diastolic dynamics as well as myocardial deformation. (1)

After a sufficient amount of image acquisition, strain and the strain rate can be quickly determined offline by tracking the displacement of the speckles throughout the cardiac cycle. Speckle-tracking echocardiography has been shown to be feasible, accurate, and useful in a variety of clinical settings. (2)

The foundation of speckle-tracking echocardiography is the analysis of the spatial dislocation, or "tracking," of speckles, which are spots produced by the interaction of the ultrasound beam and myocardial fibres on standard 2-dimensional sonograms. Speckle-tracking echocardiography enables semi-automated elaboration of myocardial deformation in three spatial directions: longitudinal, radial, and circumferential by monitoring the displacement of speckles throughout the cardiac cycle. Additionally, left ventricle (LV) rotation's frequency, direction, and velocity can be assessed using speckle-tracking echocardiography. (3)

Although this novel approach was initially developed for the sole purpose of analysing LV function, recent research has shown that it can also be applied to other cardiac chambers, such as the left atrium (LA). (4)

The name "speckle tracking" implies that the main foundation of this method is the analysis of speckles that occur during the cardiac cycle. Due to the unique arrangement of the speckles, single speckles merge into functional units (kernels) that can be uniquely identified. Each kernel, then, represents a kind of ultrasound fingerprint that can be tracked by software throughout the entire cardiac cycle. The system can calculate the displacement, the rate of displacement (velocity), the deformation (strain), and the rate of deformation (strain rate) of the chosen myocardial segments as well as the rotation of the left ventricle (LV) without the use of the Doppler signal. (1) [

Terminology and Definitions :

- **Strain :**

The term "strain" refers to a measurement that assesses the degree of segmental deformation in relation to the segment's original dimensions. A percentage is used to represent it. According to custom, a lengthening or thickening deformation is assigned a positive value, whereas a shortening or thinning deformation is assigned a negative value, depending on the direction. (5)

- **Strain Rate:**

The rate of myocardial deformation is represented by the strain rate. Units are expressed in terms of number/second, so the strain rate value will double if the same strain value is attained in half the time. According to experimental research, strain is more sensitive to changes in LV load than strain rate. However, the majority of clinical studies continue to use strain measurement because the strain rate signal is noisier and less dependable. (6)

- **Longitudinal Strain:**

Global peak systolic longitudinal strain (GLS), which measures LV function with high reliability and accuracy, is the ratio of the maximum change in myocardial longitudinal length in systole to the initial length. The term "longitudinal strain" refers to deformation of the myocardium that occurs from the base to the apex. The distance between individual kernels decreases as a result of the contraction of ventricular myocardial fibres during systole, which is depicted by negative trend curves. The LV function is better the more negative the value of GLS. **(7)**

Both regional strain values (relative to each of the 17 LV segments) and global strain values (global longitudinal strain) can be obtained through longitudinal strain analyses in 4-chamber, 2-chamber, and 3-chamber views. The average of the strain measurements across all 16 or 17 myocardial segments is known as the global strain. Roughly -18% is the average regional peak systolic strain in the longitudinal direction. **(8)**

Recently, global longitudinal strain has been proven to be a quantitative indicator of overall LV function. A same measurement can be used to determine the peak atrial longitudinal strain and the RV longitudinal strain in the speckle-tracking echocardiographic analysis of longitudinal myocardial deformation of the LA and right ventricle (RV), respectively. **(9)**

- **Radial Strain:**

The motion of the LV thickening and thinning during the cardiac cycle is represented by radial strain, which is myocardial deformation that is directed radially, or toward the centre of the LV cavity. As a result, given the progressive radial propulsion of individual kernels during systole, radial strain values are represented by positive curves. Speckle-tracking echocardiographic analysis of the basal and apical LV short-axis views yields radial strain values. **(10)**

- **Circumferential Strain:**

On a short-axis view, circumferential strain is a representation of the shortening of LV myocardial fibres around the circumference of the circle. Therefore, for circumferential speckle-to-speckle distance reduction during systole, circumferential strain measurements are represented by negative curves. As for longitudinal strain, a global circumferential strain value can be obtained. **(10)**

- **Twisting and Torsion :**

Speckle-tracking echocardiography has recently emerged as a new and promising tool for LV twisting analysis, replacing the previously required use of MRI for LV twisting evaluation. A crucial aspect of cardiac biomechanics is the left ventricular twisting, which is a part of the typical LV systolic contraction and results from the reciprocal rotation of the LV apex and base during systole. **(11)**

Analysis of the reciprocal rotation of the LV apex and base during systole enables the quantification of LV twisting by speckle-tracking echocardiography, which is intrinsic to its physiologic characteristics. The net difference in mean rotation between the apical and basal levels is then used to calculate left ventricular twisting. Left ventricular torsion is defined as LV twisting normalised with the base-to-apex distance. (12)

- **Untwisting**

The function of untwisting in diastolic LV filling mechanics has also received more attention recently. Because it appears to be less load-dependent than other diastolic parameters, untwisting velocity is relevant for studying diastole and, in particular, isovolumic relaxation. Untwisting velocity is also thought to be a critical initial manifestation of active relaxation. (13)

Image Acquisition :

Using conventional 2-dimensional grey scale echocardiography while holding breath while maintaining a stable electrocardiogram trace, you can obtain and record images for speckle-tracking echocardiographic analysis, which is currently done offline. The analysed myocardial structure must not be foreshortened in any view, and this will allow for a more accurate delineation of the endocardial border. Care must be taken to obtain true apical and short-axis images using established anatomic landmarks in each view. (3)

The range of 60 to 110 frames per second is considered to be the ideal frame rate for the acquisition of 2-dimensional images. These settings are advised to improve the viability of the frame-to-frame tracking technique and combine high temporal resolution with reasonably good spatial definition. (14)

For longitudinal strain and peak atrial longitudinal strain analyses, acquisitions from the apical 4, 3, and 2 chambers are required. With a standard parasternal probe position for the basal plane and a more distal anterior or anterolateral position for the apical plane, short-axis recordings can be obtained that are helpful for radial strain, circumferential strain, and rotation analysis. For the purpose of standardising acquisitions, the apical plane is defined as being distal to the papillary muscles, while the basal plane is defined as the plane containing the tips of the mitral leaflets. (15)

An offline semi-automated analysis of strain based on speckles is possible due to the processing of recordings using specific acoustic tracking software. A region of interest is created by manually tracing the endocardial surface in apical and/or short axis views of the myocardial segment being studied. The system then automatically generates the tracing of the epicardial surface. After the region of interest has been optimised, the software generates strain curves for each chosen myocardial segment. With the help of these curves, the operator can calculate local and global peak values by averaging values observed across all segments. If all three of the apical views are used for the longitudinal strain analysis, the software automatically creates a topographic representation of all 17 segments that were examined (bull's eye). **(3)**

Clinical applications:

The primary function of STE is to provide a quantitative, objective assessment of LV systolic function that is capable of accurately identifying minute changes in myocardial function. GLS seems to be the parameter that best fits this need among all the other myocardial deformation parameters. Compared to any other deformation parameters, it has higher reproducibility and is significantly more sensitive to the early myocardial damage. **(1)**

In contrast to the mid-myocardial and subepicardial fibres, which are responsible for the majority of the circumferential and radial strain and rotation, subendocardial fibres are primarily responsible for the longitudinal strain. Longitudinal strain is typically the first to become compromised because the subendocardial layers are typically the first to be affected by the majority of cardiac pathologies. In order to make up for the loss of the longitudinal function, the radial and circumferential strain is preserved, or in the early stages, may even be accentuated. **(5)**

The radial and circumferential strain also gradually deteriorate as the disease extends and becomes more transmural. As a result, radial and circumferential strain impairment is a relatively late phenomenon and frequently indicates more severe myocardial damage. However, circumferential strain and rotation may become compromised before longitudinal strain in some pathological conditions that affect the heart from the outside, such as constrictive pericarditis. **(16)**

A brief overview of the potential clinical uses of STE is given in the section below:

A -Detection of subclinical myocardial dysfunction:

As was previously mentioned, when enough myocardial damage has already been done, a decline in LVEF indicates that myocardial dysfunction is developing at a relatively late stage. One of the most promising indications for STE appears to be the early, subclinical detection of myocardial dysfunction, which may have significant diagnostic and therapeutic implications. **(17)**

For instance, patients receiving cancer chemotherapy may need to stop their treatment plan if their GLS is impaired despite their LVEF being preserved. also, The timing of the surgical intervention in patients with severe aortic stenosis or mitral regurgitation may also be aided by the presence of early myocardial damage in these patients. **(18)**

GLS dysfunction is also useful in identifying the involvement of the heart in a number of diseases and conditions, including diabetes, obesity, obstructive sleep apnea, amyloidosis, Fabry's disease, etc. It may also be useful in distinguishing hypertrophic cardiomyopathy from hypertensive heart disease or athletes' heart. **(19)**

B –Diabetes:

It has been demonstrated that speckle-tracking echocardiography has the potential to identify subclinical LV systolic dysfunction in asymptomatic diabetic patients with preserved LVEF, which is unmasked by the change in longitudinal strain. According to this perspective, speckle-tracking echocardiography could offer useful information about the occurrence of subclinical myocardial dysfunction in the context of diabetes before diabetic cardiomyopathy became overtly apparent. **(20)**

C - Monitoring response to treatment:

When evaluating the effectiveness of treatments aimed at enhancing LV contractile function, such as myocardial revascularization, stem cell therapy, medications, etc., GLS can be used as an objective, quantitative parameter. **(5)**

D - Role in acute coronary event:

GLS has been demonstrated to be a predictor of the final infarct size, patency of the infarct related artery, outcome after revascularization, and the extent of long-term LV remodelling in patients who present with acute coronary events. **(21)**

E - As a measure of myocardial ischemia and viability:

- The longitudinal strain increases the precision of the evaluation of myocardial ischemia and viability when combined with dobutamine echocardiography. However, due to issues with image quality, the longitudinal strain's predictive accuracy for this purpose is best for the anterior circulation (i.e., the territory of the left anterior descending artery) and less so for the posterior circulation. **(22)**

- It has been demonstrated that the resting longitudinal strain itself can predict myocardial viability. Additionally, a decrease in circumferential strain reflects a greater transmural extent of the infarct, which indicates a lack of myocardial viability. **(23)**

F - Role in cardiac resynchronization therapy:

- It has been demonstrated that radial strain measured by STE is a reliable predictor of the responsiveness to cardiac resynchronization therapy and a robust marker of intraventricular mechanical dyssynchrony.
- In order to place the LV lead, time to peak radial strain can also be used to determine the location of the most recent activation. **(24)**

G - Assessment of LV diastolic function:

Measures of LV diastolic function have included peak untwist velocity, early diastolic strain rate and time to peak untwist velocity with variable results. (25)

H -Assessment of RV function:

Like the LV, the RV free wall can also be used to measure longitudinal strain, which has been shown to be a reliable indicator of RV systolic function in a number of clinical conditions like pulmonary hypertension, RV cardiomyopathies, congenital heart diseases, etc. (26)

I -LA function:

Since STE is an angle-independent technique, LA strain can also be measured and used for the same diagnostic applications as LA volume. (27)

Other uses:

Early restriction of circumferential strain, as was previously discussed, may aid in distinguishing between constrictive pericarditis and restrictive cardiomyopathy. (28)

Limitations :

All measurements derived from speckle-tracking demand a higher level of image acquisition skill, and the accurate delineation of the endocardial border depends on the availability of sufficient echocardiographic views. Furthermore, strain measurements cannot even be performed on patients with non-sinus rhythms due to the close relationship between single-cardiac-cycle myocardial deformation analysis and speckle-tracking echocardiography. Another drawback of the technique is that results are highly dependent on the equipment used for the analyses. (15)

Speckle Tracking Echocardiography & Vavular Heart Disease

- **Assessing Cardiac Function in Valve Disease**

Ejection fraction versus strain

In order to intervene in asymptomatic patients with severe valvular dysfunction before irreversible LV damage occurs, LVEF is incorporated into the current guideline-recommended treatment strategies for valve diseases. Therefore, surgery is advised for asymptomatic patients with severe mitral regurgitation and early indications of LV systolic dysfunction (LVEF 60% and/or LV end-systolic diameter 45 mm). Patients with severe aortic regurgitation or aortic stenosis are advised to seek treatment when their LVEF is less than 50%. (29)

Systolic dysfunction in valvular heart disease, however, is difficult to assess. LVEF does not take into account the intricate nature of myocardial mechanics; it only represents a relative volume change from end-diastole to end-systole. When reflecting systolic function under altered loading (pressure and volume) conditions, which are inherently present in patients with valve diseases, this volume-based parameter has an important limitation. Since regurgitant valvular lesions frequently have LVEF in the "supernormal" range, it is a poor indicator of systolic myocardial function. (30)

LVEF overestimates cardiac function in mitral regurgitation because it accounts for both the volume of the aortic forward stroke and the volume of regurgitant fluid pumped into the low-pressure left atrium. As a result, LVEF can persist in the normal range for a long time and may conceal early, subtle contractility reductions. (31)

Stenotic lesions exhibit concentric remodelling with increased wall thickness and decreased cavity diameter; as a result, EF can be maintained despite lessened myofiber shortening. Because of this, LVEF can only identify LV systolic dysfunction at a relatively late stage of the disease when a pertinent myocardial contractile dysfunction has already appeared. (32)

However, myocardial deformation imaging may be superior at accurately detecting subtle dysfunction. (33) The part of LV mechanics that is most susceptible is longitudinal LV strain. Impaired longitudinal deformation is frequently compensated in the early stages of the disease by increased circumferential function, keeping the LVEF within normal limits. (32) It has been established that the contribution of circumferential strain to LV is greater than twice that of longitudinal strain. Therefore, one of the most promising applications of strain imaging is the early detection of cardiac dysfunction in valve disease. (34)

- **Recent Clinical Applications**

Recent research suggested that strain echocardiography could be helpful in determining the timing of interventions and enhancing the assessment of myocardial function in valve diseases. However, the majority of studies concentrated on mitral and aortic valve disease, and there is little information on right-sided valve diseases. (35)

- **Aortic stenosis**

In patients with aortic stenosis, GLS progressively impaired with increasing disease severity (from −18.2±2.1% in mild stenosis to −13.3±3.7% in severe stenosis). (36) Independent of stenosis severity, EF, or other established predictors, longitudinal strain has been demonstrated to be a potent predictor of all-cause mortality. (37)

Additionally, in all therapeutic strategies for either surgical or transcatheter aortic valve replacement, high-gradient or low-flow, low-gradient, preoperative GLS was linked to long-term postoperative cardiac mortality and morbidity in patients with symptomatic severe aortic stenosis. (38)

A GLS worse than -18.2% has been demonstrated to be associated with disease progression, as evidenced by the onset of symptoms and the requirement for valve intervention, in patients with asymptomatic severe aortic stenosis and normal EF. **(34)** Similar studies have demonstrated that excellent 5-year event-free survival is associated with a GLS better than -17%. **(39)** In a recent meta-analysis involving 1067 patients, a GLS worse than -14.7% was associated with a >2.5-fold higher risk of death and predicted mortality with 60% sensitivity and 70% specificity. **(40)**

According to recent studies, STE may help to identify asymptomatic patients with severe aortic stenosis who would benefit from earlier intervention than suggested by the most recent ESC/EACTS guidelines. **(29)** It's interesting to note that the Heart Valve Clinic International Database (HAVEC) team suggested incorporating GLS into therapeutic decision-making. **(41)** Patients with asymptomatic severe aortic stenosis and GLS worse than -16.0% may therefore be given interventional consideration if they also have other high-risk factors, such as high calcium scores on cardiac computer tomography and myocardial fibrosis detected by MRI. Dahl et al. recently proposed a similar algorithm. **(42)**

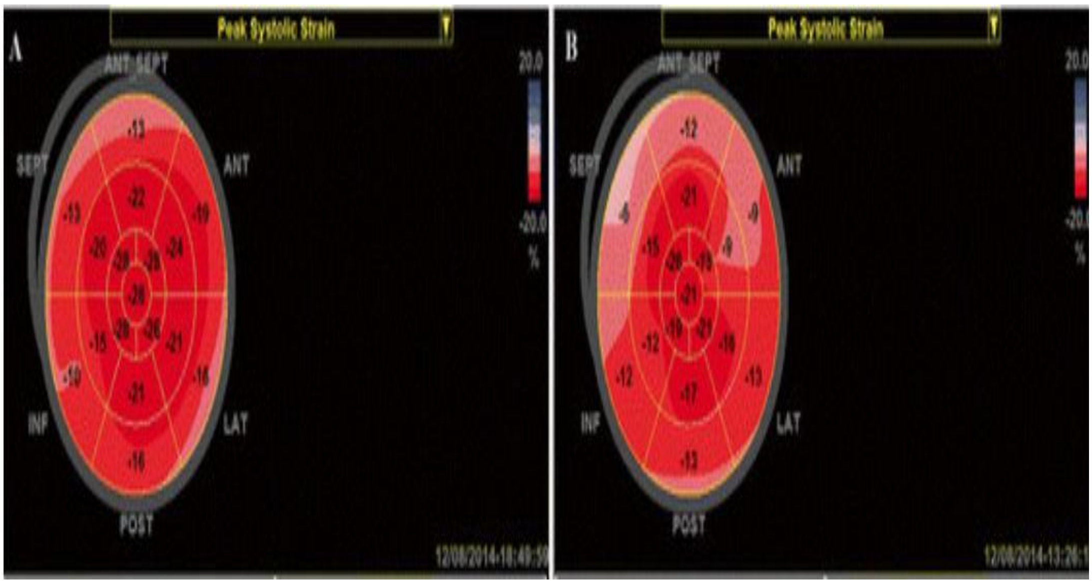

Figure (1): Measurement of left ventricular global longitudinal strain (GLS) in two asymptomatic patients with severe AS, a similar degree of concentric LVH, and LVEF greater than 60%. The first patient has reduced longitudinal deformation in the basal LV segments, but with a GLS value within the normal range (-20%). The second patient had impaired GLS (-15%) and significantly lower longitudinal deformation values in the basal segments. **(43)**

- <u>**Aortic regurgitation**</u>

Patients with moderate-to-severe and severe aortic regurgitation who are symptomatic have more impaired GLS than those who are completely asymptomatic (−14.9±3.0% vs. −16.8±2.5%). **(44)** As GLS worsens beyond -19% in asymptomatic patients, the risk of death rises steadily. In the same study, in asymptomatic patients with moderately severe or severe aortic regurgitation and preserved EF, GLS significantly improved the reclassification of mortality risk and was independently associated with the need for aortic valve surgery. **(45)**

Reduced long-term survival following surgical procedure was associated with preoperative GLS worse than -19% in patients having aortic valve surgery. **(46)**

- **Mitral regurgitation**

Preoperative GLS is an independent predictor of cardiovascular events and death in patients with severe primary mitral regurgitation undergoing interventions, and it appears to have incremental predictive value over traditional clinical and echocardiographic risk factors. **(47)**

One of the largest studies found that mitral valve surgery was beneficial for outcomes (all-cause mortality), especially in patients with GLS worse than -21% in those with asymptomatic severe mitral regurgitation.**(48)** Additionally, in patients undergoing mitral valve surgery, pre-operative GLS worse than -18.1% predicted post-procedural LV dysfunction. **(49)**

It is noteworthy that the GLS reported in these studies was higher than the cutoff value of normal, indicating that strain values that would otherwise be considered normal are already linked to a worse outcome in patients with primary mitral regurgitation. **(35)**

There aren't many comprehensive studies examining the clinical value of strain in secondary mitral regurgitation. Recent research found that GLS worse than -7.0% was linked to an increased risk for all-cause mortality, but LVEF was not. This research involved 650 patients with moderate to severe secondary mitral regurgitation. The specific high-risk patient population that was studied may help to explain why GLS found in this study was lower than that of patients with primary regurgitation. The majority of the study participants were people with advanced heart failure, with a mean EF of 29±10%, and ischemic cardiomyopathy adversely impacted half of them. **(50)**

- **Mitral stenosis and right-sided valve diseases**

Studies examining the clinical use of strain echocardiography in mitral stenosis or right-sided valve diseases are few and small. Patients with severe mitral stenosis have lower LV deformation, which is related to the severity of the disease. Within 72 hours of the balloon mitral valvuloplasty, an improvement in strain values was noted. **(51)**

Patients with significant tricuspid regurgitation showed the potential prognostic value of right ventricular (RV) longitudinal strain. Poorer than -23% RV free wall longitudinal strain was linked to a worse outcome and had prognostic significance beyond the usual RV systolic function echocardiographic parameters. **(52)**

Preinterventional RV longitudinal strain in patients with pulmonary valve disease undergoing percutaneous pulmonary valve implantation can predict improvement in exercise function after intervention. **(53)**

Future Perspectives There is no question about the future significance of strain imaging in valvular heart diseases due to mounting evidence. Longitudinal strain has been successfully demonstrated to have independent and additive prognostic value to conventional echocardiographic and clinical parameters. Before it is widely used in clinical practice, there are a few unresolved issues that need to be discussed. (35)

First, incorporating strain measurement into clinical guidelines and decision-making algorithms may be hindered by the variability of proposed GLS cutoffs in predicting clinical outcome. Cutoff values differ significantly between various valvular heart diseases, which may be due to the unique pathology and disease-related changes in chamber geometry and loading. As a result, disease-specific cutoffs must be identified. As a general rule, a strain value that is worse than average is linked to a worse outcome. A portion of the variability may also be attributed to technical factors, such as strain definitions and intervendor variability. Additionally, the definitions of clinical endpoints and follow-up times vary across studies. (35)

In addition, recent research has demonstrated the value of strain echocardiography for risk stratification of asymptomatic patients with severe valve disease, raising the possibility that GLS could be a crucial supplementary parameter for patient management decisions aimed at earlier interventions. These findings, however, come from past or present observational cohort studies. So, in order to assess the effectiveness of GLS and early interventions in asymptomatic patients with valve diseases, large randomised trials are required. Finally, a load-independent marker of systolic function is still required because strain measurements are load dependent. (35)

Conclusion

Strain echocardiography has proven to be a valuable complementary echocardiographic technique for valvular heart disease that can identify patients at risk of developing symptoms or having a poor prognosis and may help with therapeutic decision-making. To interpret myocardial deformation correctly and make the right decisions for patients with valve disease, you must have a thorough understanding of the intricate relationship between loading conditions, chamber geometry, and contractility. (35)

References:

1. **Perk G, Tunick PA, Kronzon I.** Non-Doppler two-dimensional strain imaging by echocardiography–from technical considerations to clinical applications. Journal of the American Society of Echocardiography. 2007 Mar 1;20(3):234-43.
2. **Blessberger H, Binder T.** Non-invasive imaging: two dimensional speckle tracking echocardiography: basic principles. 2007.Heart 96, 716e722.
3. **Teske AJ, De Boeck BW, Melman PG, Sieswerda GT, Doevendans PA, Cramer MJ.** Echocardiographic quantification of myocardial function using tissue deformation imaging, a guide to image acquisition and analysis using tissue Doppler and speckle tracking. Cardiovascular ultrasound. 2007 Dec;5(1):1-9.

4. **Sirbu C, Herbots L, D'hooge J, Claus P, Marciniak A, Langeland T, Bijnens B, Rademakers FE, Sutherland GR**. Feasibility of strain and strain rate imaging for the assessment of regional left atrial deformation: a study in normal subjects. European Journal of Echocardiography. 2006 Jun 1;7(3):199-208.
5. **Dandel M, Lehmkuhl H, Knosalla C, Suramelashvili N, Hetzer R**. Strain and strain rate imaging by echocardiography-basic concepts and clinical applicability. Current cardiology reviews. 2009 May 1;5(2):133-48.
6. **Marwick TH.** Measurement of strain and strain rate by echocardiography: ready for prime time?. Journal of the American College of cardiology. 2006 Apr 4;47(7):1313-27.
7. **Heimdal A, Støylen A, Torp H, Skjærpe T**. Real-time strain rate imaging of the left ventricle by ultrasound. Journal of the American Society of Echocardiography. 1998 Nov 1;11(11):1013-9.
8. **Brown J, Jenkins C, Marwick TH.** Use of myocardial strain to assess global left ventricular function: a comparison with cardiac magnetic resonance and 3-dimensional echocardiography. American heart journal. 2009 Jan 1;157(1):102-e1.
9. **Horton KD, Meece RW, Hill JC.** Assessment of the right ventricle by echocardiography: a primer for cardiac sonographers. Journal of the American society of echocardiography. 2009 Jul 1;22(7):776-92.
10. **Saito K, Okura H, Watanabe N, Hayashida A, Obase K, Imai K, Maehama T, Kawamoto T, Neishi Y, Yoshida K**. Comprehensive evaluation of left ventricular strain using speckle tracking echocardiography in normal adults: comparison of three-dimensional and two-dimensional approaches. Journal of the American Society of Echocardiography. 2009 Sep 1;22(9):1025-30.
11. **Notomi Y, Shiota T, Popović ZB, Weaver JA, Oryszak SJ, Greenberg NL, White RD, Thomas JD, Setser RM, White RD, Lysyansky P**. Measurement of ventricular torsion by two-dimensional ultrasound speckle tracking imaging. Journal of the American College of Cardiology. 2005 Jun 21;45(12):2034-41.
12. **Takeuchi M, Otsuji Y, Lang RM**. Evaluation of left ventricular function using left ventricular twist and torsion parameters. Current cardiology reports. 2009 May;11(3):225-30.
13. **Notomi Y, Popovic ZB, Yamada H, Wallick DW, Martin MG, Oryszak SJ, Shiota T, Greenberg NL, Thomas JD**. Ventricular untwisting: a temporal link between left ventricular relaxation and suction. American Journal of Physiology-Heart and Circulatory Physiology. 2008 Jan;294(1):H505-13.
14. **Serri K, Reant P, Lafitte M, Berhouet M, Le Bouffos V, Roudaut R, Lafitte S**. Global and regional myocardial function quantification by two-dimensional strain: application in hypertrophic cardiomyopathy. Journal of the American College of Cardiology. 2006 Mar 21;47(6):1175-81.

15. **Mondillo S, Galderisi M, Mele D, Cameli M, Lomoriello VS, Zacà V, Ballo P, D'Andrea A, Muraru D, Losi M, Agricola E**. Speckle-tracking echocardiography: a new technique for assessing myocardial function. Journal of Ultrasound in Medicine. 2011 Jan;30(1):71-83.
16. **Dal-Bianco JP, Sengupta PP, Mookadam F, Chandrasekaran K, Tajik AJ, Khandheria BK**. Role of echocardiography in the diagnosis of constrictive pericarditis. Journal of the American Society of Echocardiography. 2009 Jan 1;22(1):24-33.
17. **Edvardsen T, Helle-Valle T, Smiseth OA.** Systolic dysfunction in heart failure with normal ejection fraction: speckle-tracking echocardiography. Progress in cardiovascular diseases. 2006 Nov 1;49(3):207-14.
18. **Jurcut R, Wildiers H, Ganame J, D'hooge J, Paridaens R, Voigt JU**. Detection and monitoring of cardiotoxicity—what does modern cardiology offer?. Supportive Care in Cancer. 2008 May;16(5):437-45.
19. **Richand V, Lafitte S, Reant P, Serri K, Lafitte M, Brette S, Kerouani A, Chalabi H, Dos Santos P, Douard H, Roudaut R**. An ultrasound speckle tracking (two-dimensional strain) analysis of myocardial deformation in professional soccer players compared with healthy subjects and hypertrophic cardiomyopathy. The American journal of cardiology. 2007 Jul 1;100(1):128-32.
20. **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. European Journal of Echocardiography. 2009 Dec 1;10(8):926-32.
21. **Ersbøll MK**. Left ventricular global longitudinal strain in acute myocardial infarction--with special reference to neurohormonal activation, in-hospital heart failure and prognosis. Danish Medical Journal. 2013 Aug 1;60(8):B4697-.
22. **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. European heart journal. 2007 Jul 1;28(14):1765-72.
23. **Ng AC, Sitges M, Pham PN, Tran DT, Delgado V, Bertini M, Nucifora G, Vidaic J, Allman C, Holman ER, Bax JJ.** Incremental value of 2-dimensional speckle tracking strain imaging to wall motion analysis for detection of coronary artery disease in patients undergoing dobutamine stress echocardiography. American heart journal. 2009 Nov 1;158(5):836-44.
24. **Suffoletto MS, Dohi K, Cannesson M, Saba S, Gorcsan III** J. Novel speckle-tracking radial strain from routine black-and-white echocardiographic images to quantify dyssynchrony and predict response to cardiac resynchronization therapy. Circulation. 2006 Feb 21;113(7):960-8.
25. **Wang J, Khoury DS, Yue Y, Torre-Amione G, Nagueh SF**. Left ventricular untwisting rate by speckle tracking echocardiography. Circulation. 2007 Nov 27;116(22):2580-6.

26. **Chow PC, Liang XC, Cheung EW, Lam WW, Cheung YF.** New two-dimensional global longitudinal strain and strain rate imaging for assessment of systemic right ventricular function. Heart. 2008 Jul 1;94(7):855-9.
27. **Cameli M, Lisi M, Mondillo S, Padeletti M, Ballo P, Tsioulpas C, Bernazzali S, Maccherini M.** Left atrial longitudinal strain by speckle tracking echocardiography correlates well with left ventricular filling pressures in patients with heart failure. Cardiovascular ultrasound. 2010 Dec;8(1):1-9.
28. **Geyer H, Caracciolo G, Abe H, Wilansky S, Carerj S, Gentile F, Nesser HJ, Khandheria B, Narula J, Sengupta PP.** Assessment of myocardial mechanics using speckle tracking echocardiography: fundamentals and clinical applications. Journal of the American Society of Echocardiography. 2010 Apr 1;23(4):351-69.
29. **Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Munoz DR, Rosenhek R.** 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Kardiologia Polska (Polish Heart Journal). 2018;76(1):1-62.
30. **Marciniak A, Sutherland GR, Marciniak M, Claus P, Bijnens B, Jahangiri M.** Myocardial deformation abnormalities in patients with aortic regurgitation: a strain rate imaging study. European journal of echocardiography. 2009 Jan 1;10(1):112-9.
31. **Marciniak A, Claus P, Sutherland GR, Marciniak M, Karu T, Baltabaeva A, Merli E, Bijnens B, Jahangiri M**. Changes in systolic left ventricular function in isolated mitral regurgitation. A strain rate imaging study. European heart journal. 2007 Nov 1;28(21):2627-36.
32. **Stokke TM, Hasselberg NE, Smedsrud MK, Sarvari SI, Haugaa KH, Smiseth OA, Edvardsen T, Remme EW**. Geometry as a confounder when assessing ventricular systolic function: comparison between ejection fraction and strain. Journal of the American College of Cardiology. 2017 Aug 22;70(8):942-54.
33. **Smedsrud MK, Pettersen E, Gjesdal O, Svennevig JL, Andersen K, Ihlen H, Edvardsen T.** Detection of left ventricular dysfunction by global longitudinal systolic strain in patients with chronic aortic regurgitation. Journal of the American Society of Echocardiography. 2011 Nov 1;24(11):1253-9.
34. **Vollema EM, Sugimoto T, Shen M, Tastet L, Ng AC, Abou R, Marsan NA, Mertens B, Dulgheru R, Lancellotti P, Clavel MA.** Association of left ventricular global longitudinal strain with asymptomatic severe aortic stenosis: natural course and prognostic value. JAMA cardiology. 2018 Sep 1;3(9):839-47.
35. **Cvijic M, Voigt JU**. Application of strain echocardiography in valvular heart diseases. Anatolian Journal of Cardiology. 2020 May;23(5):244.
36. **Ng AC, Prihadi EA, Antoni ML, Bertini M, Ewe SH, Ajmone Marsan N, Leung DY, Delgado V, Bax JJ**. Left ventricular global longitudinal strain is predictive of all-cause mortality independent of aortic stenosis severity and ejection fraction. European Heart Journal-Cardiovascular Imaging. 2018 Aug 1;19(8):859-67.

37. **Kusunose K, Goodman A, Parikh R, Barr T, Agarwal S, Popovic ZB, Grimm RA, Griffin BP, Desai MY.** Incremental prognostic value of left ventricular global longitudinal strain in patients with aortic stenosis and preserved ejection fraction. Circulation: Cardiovascular Imaging. 2014 Nov;7(6):938-45.
38. **D'Andrea A, Carbone A, Agricola E, Riegler L, Sperlongano S, Tocci G, Scarafile R, Formisano T, Capogrosso C, Bigazzi MC, Bossone E.** Predictive value of left ventricular myocardial deformation for left ventricular remodeling in patients with classical low-flow, low-gradient aortic stenosis undergoing transcatheter aortic valve replacement. Journal of the American Society of Echocardiography. 2019 Jun 1;32(6):730-6.
39. **Huded CP, Masri A, Kusunose K, Goodman AL, Grimm RA, Gillinov AM, Johnston DR, Rodriguez LL, Popovic ZB, Svensson LG, Griffin BP.** Outcomes in asymptomatic severe aortic stenosis with preserved ejection fraction undergoing rest and treadmill stress echocardiography. Journal of the American Heart Association. 2018 Apr 12;7(8):e007880.
40. **Magne J, Cosyns B, Popescu BA, Carstensen HG, Dahl J, Desai MY, Kearney L, Lancellotti P, Marwick TH, Sato K, Takeuchi M.** Distribution and prognostic significance of left ventricular global longitudinal strain in asymptomatic significant aortic stenosis: an individual participant data meta-analysis. JACC: Cardiovascular Imaging. 2019 Jan;12(1):84-92.
41. **Dulgheru R, Pibarot P, Sengupta PP, Piérard LA, Rosenhek R, Magne J, Donal E, Bernard A, Fattouch K, Cosyns B, Vannan M.** Multimodality imaging strategies for the assessment of aortic stenosis: viewpoint of the Heart Valve Clinic International Database (HAVEC) Group. Circulation: Cardiovascular Imaging. 2016 Feb;9(2):e004352.
42. **Dahl JS, Magne J, Pellikka PA, Donal E, Marwick TH.** Assessment of subclinical left ventricular dysfunction in aortic stenosis. JACC: Cardiovascular Imaging. 2019 Jan;12(1):163-71.
43. **Călin A, Roşca M, Beladan CC, Enache R, Mateescu AD, Ginghină C, Popescu BA.** The left ventricle in aortic stenosis–imaging assessment and clinical implications. Cardiovascular ultrasound. 2015 Dec;13(1):1-3.
44. **Ewe SH, Haeck ML, Ng AC, Witkowski TG, Auger D, Leong DP, Abate E, Ajmone Marsan N, Holman ER, Schalij MJ, Bax JJ.** Detection of subtle left ventricular systolic dysfunction in patients with significant aortic regurgitation and preserved left ventricular ejection fraction: speckle tracking echocardiographic analysis. European Heart Journal-Cardiovascular Imaging. 2015 Sep 1;16(9):992-9.
45. **Alashi A, Mentias A, Abdallah A, Feng K, Gillinov AM, Rodriguez LL, Johnston DR, Svensson LG, Popovic ZB, Griffin BP, Desai MY.** Incremental prognostic utility of left ventricular global longitudinal strain in asymptomatic patients with significant chronic aortic regurgitation and preserved left ventricular ejection fraction. JACC: Cardiovascular Imaging. 2018 May;11(5):673-82.

46. **Alashi A, Khullar T, Mentias A, Gillinov AM, Roselli EE, Svensson LG, Popovic ZB, Griffin BP, Desai MY**. Long-term outcomes after aortic valve surgery in patients with asymptomatic chronic aortic regurgitation and preserved LVEF: impact of baseline and follow-up global longitudinal strain. Cardiovascular Imaging. 2020 Jan 1;13(1_Part_1):12-21.
47. **Hiemstra YL, Tomsic A, van Wijngaarden SE, Palmen M, Klautz RJ, Bax JJ, Delgado V, Ajmone Marsan N**. Prognostic value of global longitudinal strain and etiology after surgery for primary mitral regurgitation. Cardiovascular Imaging. 2020 Feb 1;13(2_Part_2):577-85.
48. **Mentias A, Naji P, Gillinov AM, Rodriguez LL, Reed G, Mihaljevic T, Suri RM, Sabik JF, Svensson LG, Grimm RA, Griffin BP**. Strain echocardiography and functional capacity in asymptomatic primary mitral regurgitation with preserved ejection fraction. Journal of the American College of Cardiology. 2016 Nov 1;68(18):1974-86.
49. **Kim HM, Cho GY, Hwang IC, Choi HM, Park JB, Yoon YE, Kim HK**. Myocardial strain in prediction of outcomes after surgery for severe mitral regurgitation. JACC: Cardiovascular Imaging. 2018 Sep;11(9):1235-44.
50. **Namazi F, van der Bijl P, Hirasawa K, Kamperidis V, van Wijngaarden SE, Mertens B, Leon MB, Hahn RT, Stone GW, Narula J, Ajmone Marsan N.** Prognostic value of left ventricular global longitudinal strain in patients with secondary mitral regurgitation. Journal of the American College of Cardiology. 2020 Feb 25;75(7):750-8.
51. **Roushdy AM, Raafat SS, Shams KA, El-Sayed MH.** Immediate and short-term effect of balloon mitral valvuloplasty on global and regional biventricular function: a two-dimensional strain echocardiographic study. European Heart Journal-Cardiovascular Imaging. 2016 Mar 1;17(3):316-25.
52. **Prihadi EA, van der Bijl P, Dietz M, Abou R, Vollema EM, Marsan NA, Delgado V, Bax JJ**. Prognostic implications of right ventricular free wall longitudinal strain in patients with significant functional tricuspid regurgitation. Circulation: Cardiovascular Imaging. 2019 Mar;12(3):e008666.
53. **Chowdhury SM, Hijazi ZM, Fahey JT, Rhodes JF, Kar S, Makkar R, Mullen M, Cao QL, Shirali GS.** Speckle-tracking echocardiographic measures of right ventricular function correlate with improvement in exercise function after percutaneous pulmonary valve implantation. Journal of the American Society of Echocardiography. 2015 Sep 1;28(9):1036-44