European Review for Medical and Pharmacological Sciences 2022; 26: 3903-3910

2D speckle tracking: a diagnostic and prognostic tool of paramount importance

V.I. MORARIU[1,2,3], D.A. ARNAUTU[1,2,3], S.I. MORARIU[4], A.M. POPA[5], T. PARVANESCU[1,2,3], M. ANDOR[1,2,3], S. ABHINAV[4,6,7], V.L. DAVID[8], A. IONESCU[9], M.C. TOMESCU[1,2,3]

[1]Department of Semiology, [2]Multidisciplinary Heart Research Centre, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania
[3]Department of Cardiology, Timisoara Municipal Emergency Clinical Hospital, Timisoara, Romania
[4]Department of Occupational Health, "Vasile Goldis" Western University of Arad, Arad, Romania
[5]Timis Department of Public Health, Timisoara, Romania
[6]Department of Cardiology, University of Medicine and Pharmacy "Victor Babes", Timisoara, Romania
[7]Civil Medical Society Dr Rosca, Teremia Mare, Romania
[8]Department of Paediatric Surgery and Orthopaedics, [9]Department of Balneology, Medical Recovery and Rheumatology, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

Abstract. – OBJECTIVE: We aimed to conduct a review of the literature relevant to cardiac imaging techniques and summarize the use of different non-invasive imaging modalities in the assessment of ventricular size, function, and mechanics. The current review emphasizes the benefits of speckle tracking imaging (STI), highlighting its use in demonstrating myocardial strain. This robust technique is a recent addition to the existing imaging techniques that are used to assess the myocardium. In terms of effectively determining the left ventricle ejection fraction, it is a comparable technique to cardiac magnetic resonance. The use of STI method for image acquisition relies on semiautomatic identification of the border and deformation of the region of interest, and is also independent of the angle of insonation, thus it increases the inter-and intra-observer reproducibility in contrast to the conventional tissue doppler imaging.

MATERIALS AND METHODS: The databases of PubMed, Scopus, and Embase were thoroughly searched for the following keywords: 2- dimensional/ two-dimensional/ 2-D, speckle/strain tracking, systolic dysfunction, and heart failure. The studies selected described image acquisition techniques and the application of this imaging modality in various clinical settings. The selected journal articles were perused to provide the best possible analysis of STI.

RESULTS: Our comparative analysis demonstrated that the STI, when compared with the conventional echocardiography, is a more sensitive image acquiring technique for detecting subclinical myocardial dysfunction. Based on the analysis it can be stated that the STI can provide valuable information on both regional and global myocardial function, and it can also quantify cardiac synchronicity and rotation. Additionally, it serves as a better prognostic indicator.

CONCLUSIONS: The change in longitudinal strain can serve as an early marker of the left ventricular systolic dysfunction, and therefore, monitoring *via* STI has both diagnostic and prognostic value in heart failure, ischemic heart disease, valvulopathies, chemotherapy-induced cardiotoxicity, and cardiac resynchronization therapy. Despite the lack of standardization, the method is also effective in assessing the right ventricle and left atrial function and arterial rigidity.

Key Words:
Speckle tracking, Strain, Subclinical systolic dysfunction, Heart failure, Cardiology.

Introduction

Introduction in Strain Ultrasound Imaging – Basic Terminology and Principles

One of the parameters assessed during echocardiography is left ventricular ejection fraction (LVEF). Ample studies have demonstrated the usefulness of this parameter in assessing the systolic function of the left ventricle. Despite the universal use of this parameter, it lacks sensi-

Corresponding Author: Sharma Abhinav, MD; e-mail: sharma.abhinav@umft.ro

tivity in detecting early deterioration of systolic function and provides only a global assessment of the contractile function of the myocardium, thus not reflecting the subclinical changes in the complex geometry of the heart's cavities[1]. Moreover, the evaluation of the parameter is susceptible to inter-observer variation, making it less reliable despite advances in imaging techniques.

All these limitations seem to have been overcome in recent years, with the advances in strain ultrasound imaging- or speckle tracking-imaging (STI). This is a non-doppler imaging technique which is not reliant on the angle of insonation. Based on the alteration in length or strain of a particular myocardial segment, it analyses "speckle patterns" of the myocardium to determine any deformation[2,3].

Principals of Strain Ultrasound

Strain is defined as the percentage change in length of a certain segment of myocardium, when compared to its initial length (L0).

Strain (ε) = $\Delta L/L0$, where ΔL is the change in length (L-L0), representing either shortening (negative strain) or lengthening (positive strain).

Natural strain, or ε', is an instantaneous change in length, independent of time interval, and can be best applied to radial, circumferential or longitudinal deformation, and can be calculated using the following formula:

$$\text{Natural strain } (\varepsilon') = \ln\left(\frac{L}{L0}\right) \text{ (12).}$$

Shear strain represents the addition of angle of deformation to the equation, whereas strain rate can be defined as a temporal derivative, measured in units/s, as represented bellow:

$$\text{Strain rate } \varepsilon' = \left(\frac{d\varepsilon}{L0}\right) \text{ (12).}$$

The myocardium, as asserted by Torrent-Guasp[4] through their helical model, is primarily characterized by having 3 separate layers: an inner layer with longitudinal fibers (sub-endocardial layer), a middle layer with circumferential fibers, an outer layer with oblique fibers (sub-epicardial layer). Thus, the complex motion of the left ventricle during systole has 3 main components: an inward motion, a longitudinal one, and a twisting motion between base and apex (ventricular torsion).

As such, there are several types of myocardial strain, representing normal deformation (longitudinal, radial and circumferential), and shear deformation (base to apex twist, circumferential shear, as well as epicardial to endocardial longitudinal shear). Of all these components, the longitudinal strain, that is the result of the motion of subendocardial fibres, is the first to be affected when the myocardium is damaged in various pathological conditions (mentioned below), as opposed to the circumferential and radial strain that represent the change in subepicardial and midmyocardial fibres[1,5,6].

The longitudinal strain can be easily accessed through both TDI (Tissue Doppler Imaging), as well as STI. However, TDI is greatly dependent on insonation angle; tissue velocity is converted to strain rate, and then, to strain data, thus relying on user experience. Therefore, a broader clinical application of STI is necessary.

Each segment of the myocardium, when exposed to ultrasound, shows a particular pattern of acoustic reflection scatter, represented by patterns of specific grey scale values, or "speckles", which are monitored semi-automatically. Throughout the cardiac cycle, all in-plane velocity vectors determine the particular deformation of myocardium.

Several types of computational algorithms are used to automatically track the acoustic markers, such as monitoring the grey value conservation, block matching, following a specific speckle pattern, or kernel, and compare the similarities frame by frame to establish the deformation of a particular segment. High resolution images can be obtained by enhancing the radio frequency, however, higher frequencies require more regularization, such as, correcting vector velocity estimates. All velocity and movement characteristics of the speckles are independent of the transducer angle, and thus, corroborate with the semi-automated computational algorithms, providing better sensitivity and specificity[3,7].

Image Acquisition

For the left ventricle, the region of interest (ROI) is established at the end of the diastole by three lines, namely an endocardial border (outlined manually by the user), myocardial midline, and an epicardial border, the latter two being detected either automatically or by the user. In order to analyze the longitudinal strain of ROI of the left ventricle in 2D STI, apical 4 chamber, 3 chamber and 2 chamber images of the best quality must be acquired at an optimal frame rate of 60-110 fps, and a correct estimation of the endocardial border must be made, keeping the values of the width and depth to a minimal. For global circumferential and radial strain, the investigator must acquire parasternal short-axis images (apex, papillary muscle, base). Aortic, as well as mitral velocities (Doppler), are recorded for valve opening/closure timing. Cardiac cycles (usually 3) are recorded and analyzed offline for the software to semi-automatically assess the strain and strain rate; a 16 to 18 segment representation of the left ventricle is being used to illustrate deformation; the result is usually displayed as a polar map (analogous to the one used in SPECT), or curved anatomic monoplane mode (CAMM, for a particular ROI), as shown in Figure 1[8].

Both strain and strain rate are sensitive, robust and reproductible markers that can be used to evaluate both systolic and diastolic function of both ventricles, as well as the left atrium[9,10,].

Current Drawbacks of Strain Imaging

Though a robust indicator of both systolic and diastolic function, STI has certain drawbacks, such as, issues with acquisition of quality image, including frame rate (a high cardiac frequency is associated with a lower frame rate and hence low possibility of tracking) and out of plane movement of the kernel, a slight degree of variation in inter- and intra-observer reproducibility (albeit lesser than that of TDI), as well as incorrect tracking of epicardial border due to software algorithms[7].

Non-standardized definitions, and functional and image acquisition parameters are issues related to the assessment of the right ventricle and atria, however, efforts are being made to obtain higher inter-vendor similitude and dependability for perfecting right ventricle and atrial STE for clinical use[11].

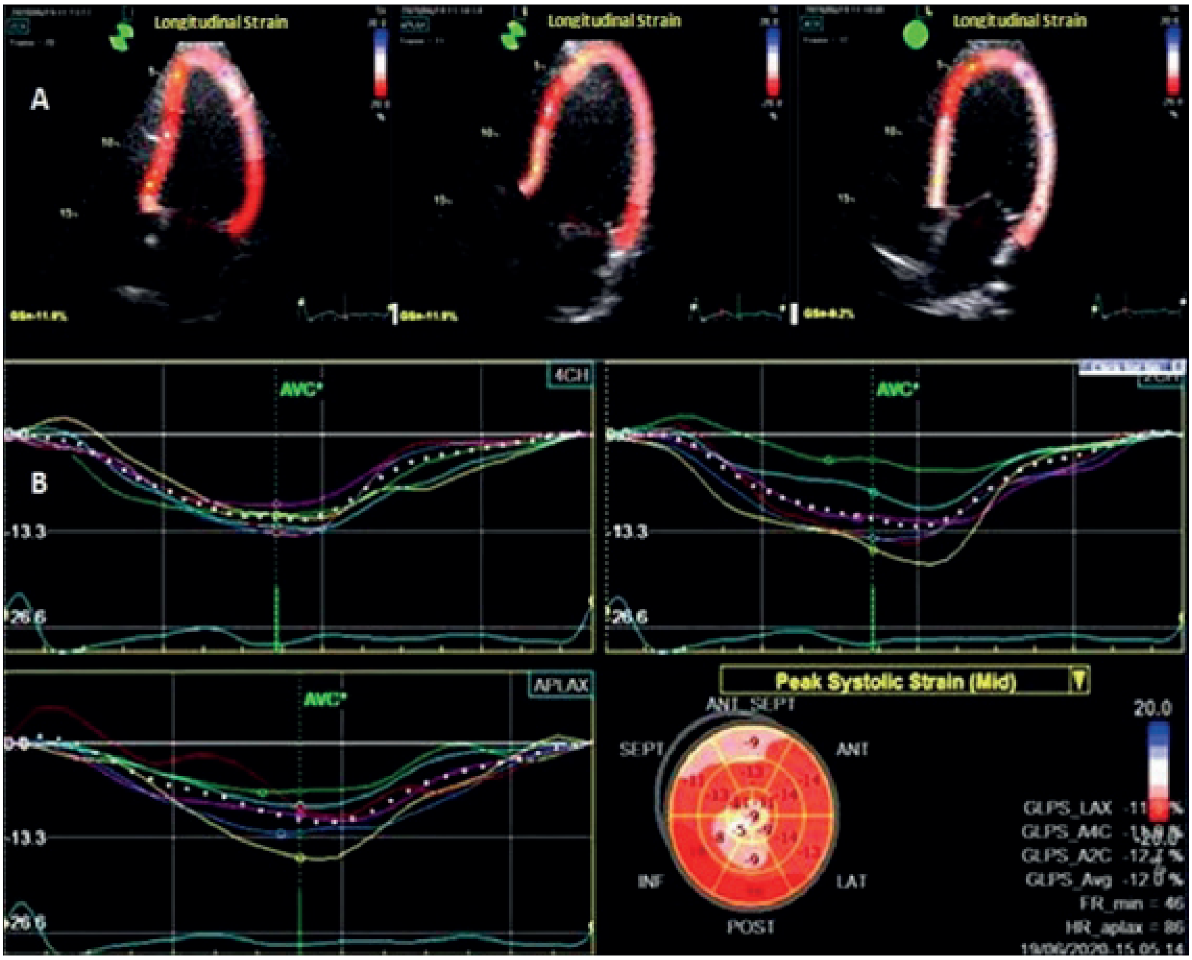

Figure 1. 2D STI of left ventricular longitudinal strain- apical two, three and four chamber views **(A)**, and polar map representation of strain values **(B)** (Bull's eye).

Application in Particular Clinical Settings

Advances in 2D strain imaging have led to higher accuracy of measurements[11] and standardization of global longitudinal strain (GLS), facilitating its clinical application in conditions analyzed in the following paragraphs.

Heart Failure

STI plays an important role in correctly assessing the systolic function of the left ventricle, GLS being more sensitive tool than the regular 2D left ventricle ejection fraction (LVEF) measurements, and MRI based LVEF[12,13].

Recent studies[9,15-18] have highlighted the role of GLS in not only detecting the subclinical LV systolic dysfunction, but also the heart failure with preserved ejection fraction (HFpEF) caused by hypertension and or ischemic cardiomyopathy, proving its potential as a diagnostic and prognostic tool. Altered GLS is an independent predictor of all-cause and HF related mortality in hospitalized HF patients[18]. Studies[20-23] have showed a powerful correlation between arrhythmic events (ventricular tachycardia) and patients with LV systolic dysfunction and altered basal GLS. Moreover, a decrease in segmental longitudinal strain (SLS) has also been identified in patients with diabetic myocardial dysfunction[24,25].

Strain and strain rate can also be utilized to assess right ventricle function, as well as left atrial deformation in patients with heart failure. The images are acquired in a similar way than LV STI, as can be seen in Figure 2[10,26].

Ischemic Heart Disease

Transmural infarction is usually associated with a decrease in both longitudinal and circumferential strain components, whereas subendocardial infarction is associated only with a decrease in longitudinal strain[27,28]. Subendocardial longitudinal fibers are the ones most sensitive to ischemia, and thus, they are affected in early stages of ischemic heart diseases. The proportional decrease in the systolic strain rate and the

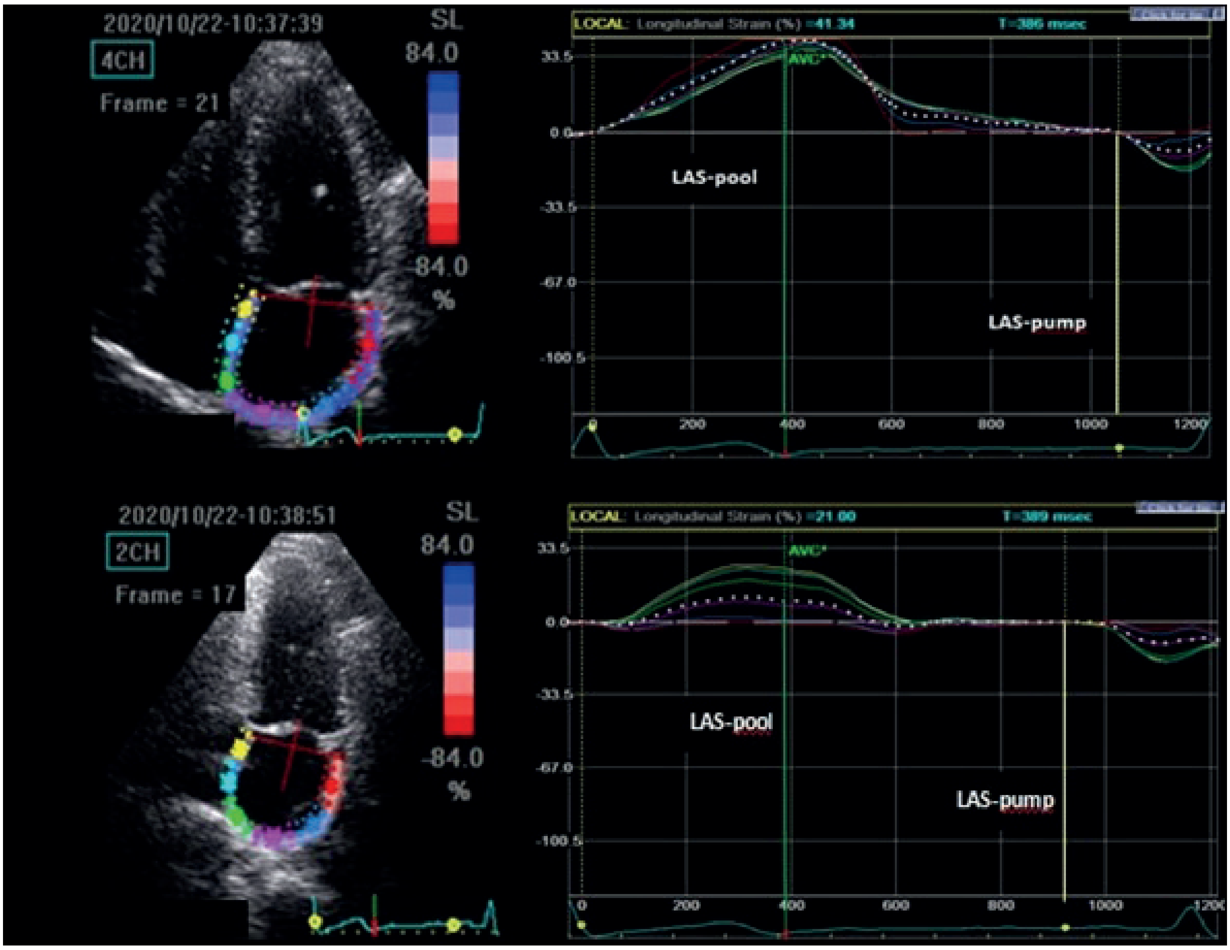

Figure 2. 2D STI of left atrium.

peak systolic strain, as measured by STI, reflects the severity of the ischemia in the ROI[29,30]. This attribute has a prognostic value, both before and after revascularization (decreased LS was associated with adverse remodeling-as shown in Figure 3)[27,31-34].

Also, one study[30] has indicated that the amount of post systolic deformation (PSD; contraction of the myocardium after aortic valve closure) also decreases proportionally to the degree of acute ischemia of a given ROI during dobutamine stress cardiac ultrasound.

Valvular Disease

Mitral regurgitation, and the subsequent volume overload can be better assessed using STI, alongside conventional ultrasound parameters, especially in asymptomatic patients and those needing mitral valve surgery. Dilatative deformation due to volume overload is associated with a comparatively larger stroke output (i.e., a normal LVEF) even with the declining contractile force, however, even the subtle decrease in the longitudinal strain and the strain rate is still detected by STI[29]. A recent review article indicated that a decreased GLS associated with a normal LVEF is a predictor of LV dysfunction after mitral valve surgery in patients with severe regurgitation.

Altered GLS has also been found to be an independent negative predictor for those suffering from severe atrial regurgitation, pressure overload leading to a higher parietal stress, and consequent decrease in GLS[35].

Chemotherapy Related Cardiotoxicity

Anthracycline induced cardiotoxicity is often related to mortality of patients post chemotherapy[35,36], thus necessitating periodic cardiologic monitoring. LVEF, obtained through 2D ultrasound, though widely used, is not sensitive enough and only detects variations greater than 10%. Studies have demonstrated that a decrease in GLS is indicative of chemotherapy induced early subclinical systolic dysfunction, proving that STI is a better prognostic tool when compared to the standard LVEF measurement[36,38,39].

Cardiac Resynchronization Therapy (CRT)

Asynchrony identified by STI can be used for the placement of LV leading for CRT. As asserted by several studies[40,41], radial strain asynchrony (can be demonstrated by images acquired through

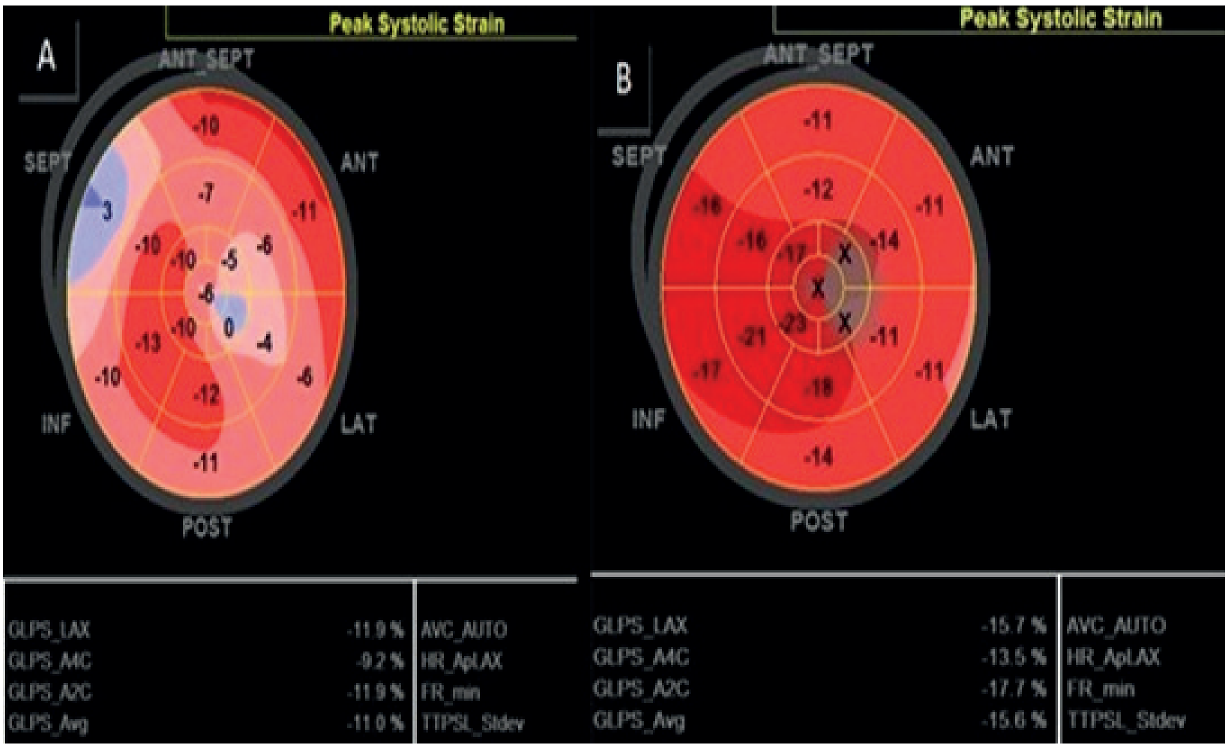

Figure 3. Polar Map of longitudinal strain of the left ventricle, 2D STI. **A,** Patient with ventricular remodelling post myocardial infarction. **B,** Patient without ventricular remodelling post myocardial infarction.

short axis view) positively correlates with patient survival post CRT.

Other Potential Applications of STI

Further studies[14,42] are required to assess the role that strain rate may play in the prognosis of other cardiovascular endpoints, such as stroke. Through the effective evaluation of carotid deformation parameters, circumferential strain and strain rate have proven their correlation with arterial rigidity and intima-media thickness, with their lower values indicating cerebrovascular disease.

Conclusions

Speckle tracking is a very useful tool, both in diagnosing subclinical systolic disfunction of the left ventricle and providing valuable information about the prognosis in a variety of clinical settings, something which was previously not possible using regular 2D cardiac ultrasound. STI rely on semiautomatic algorithms to aid image acquisition and is independent of the angle of insonation, and therefore, speckle tracking provides good inter and intra-observer reproducibility, conditions that were previously unmet by regular cardiac ultrasound imaging. Once the software standardization is achieved, STI is a diagnostic tool worth considering in cardiology, and deserves a greater level of implementation. However, further research regarding its use as a prognostic tool in other cardiovascular related pathologies, such as cerebrovascular disease, is required.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

These authors contributed equally as co-first authors: Vlad Ioan Morariu, Diana Aurora Arnautu, Stelian Ioan Morariu.

Funding

This research received no grant from any funding agency in the public, commercial or not-for-profit sectors.

References

1) 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. J Am Soc Echocardiogr 2010; 23: 351-369.
2) Dandel M, Lehmkuhl H, Knosalla C, Suramelashvili N, Hetzer R. Strain and strain rate imaging by echocardiography - basic concepts and clinical applicability. Curr Cardiol Rev 2009; 5: 133-148.
3) Biswas M, Sudhakar S, Nanda NC, Buckberg G, Pradhan M, Roomi AU, Gorissen W, Houle H. Two- and three-dimensional speckle tracking echocardiography: clinical applications and future directions. Echocardiography 2013; 30: 88-105.
4) Kocica MJ, Corno AF, Carreras-Costa F, Ballester-Rodes M, Moghbel MC, Cueva CN, Lackovic V, Kanjuh VI, Torrent-Guasp F. The helical ventricular myocardial band: global, three-dimensional, functional architecture of the ventricular myocardium. Eur J Cardiothorac Surg 2006; 29: 21-40.
5) Bansal M, Kasliwal RR. How do I do it? Speckle-tracking echocardiography. Indian Heart J 2013; 65: 117-123.
6) Bansal M, Sengupta PP. Longitudinal and circumferential strain in patients with regional LV dysfunction. Curr Cardiol Rep 2013; 15: 339.
7) Marwich TH, Yu CM, Sun JP. D'hooge J. Principles and Different Techniques for Speckle Tracking: Myocardial Imaging Tissue Dopler and Speckle Tracking. Wiley-Blackwell Hoboken 2007; 17-25.
8) Vitel A, Sporea I, Mare R, Banciu C, Bordejevic DA, Parvanescu T, Citu IM, Tomescu MC. Association Between Subclinical Left Ventricular Myocardial Systolic Dysfunction Detected by Strain and Strain-Rate Imaging and Liver Steatosis and Fibrosis Detected by Elastography and Controlled Attenuation Parameter in Patients with Metabolic Syndrome. Diabetes Metab Syndr Obes 2020; 13: 3749-3759.
9) Stoichescu-Hogea G, Buleu FN, Christodorescu R, Sosdean R, Tudor A, Ember A, Brie DM, Drăgan S. Contribution of Global and Regional Longitudinal Strain for Clinical Assessment of HFpEF in Coronary and Hypertensive Patients. Medicina (Kaunas) 2021; 57.
10) Parvanescu T, Vitel A, Sporea I, Mare R, Buz B, Bordejevic DA, Tomescu MC, Arnautu SF, Morariu VI, Citu IM. Significant Association Between Left Ventricular Diastolic Dysfunction, Left Atrial Performance and Liver Stiffness in Patients with Metabolic Syndrome and Non-Alcoholic Fatty Liver Disease. Diabetes Metab Syndr Obes 2021; 14: 1535-1545.
11) Badano LP, Kolias TJ, Muraru D, Abraham TP, Aurigemma G, Edvardsen T, D'Hooge J, Donal E, Fraser AG, Marwick T, Mertens L, Popescu BA, Sengupta PP, Lancellotti P, Thomas JD, Voigt JU. Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. Eur Heart J Cardiovasc Imaging 2018; 19: 591-600.

12) Bjork Ingul C, Stoylen A, Slordahl SA, Wiseth R, Burgess M, Marwick TH. Automated analysis of myocardial deformation at dobutamine stress echocardiography: an angiographic validation. J Am Coll Cardiol 2007; 49: 1651-1659.
13) 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. Am Heart J 2009; 157: 101-105.
14) Grund FF, Kristensen CB, Myhr KA, Vejlstrup N, Hassager C, Mogelvang R. Layer-Specific Strain Is Preload Dependent: Comparison between Speckle-Tracking Echocardiography and Cardiac Magnetic Resonance Feature-Tracking. J Am Soc Echocardiogr 2021; 34: 377-387.
15) Kundnani NR, Rosca CI, Sharma A, Tudor A, Rosca MS, Nisulescu DD, Branea HS, Mocanu V, Crisan DC, Buzas DR, Morariu S, Lighezan DF. Selecting the right anticoagulant for stroke prevention in atrial fibrillation. Eur Rev Med Pharmacol Sci 2021; 25: 4499-4505.
16) Rosca CI, Kundnani NR, Tudor A, Rosca MS, Nicoras VA, Otiman G, Ciurariu E, Ionescu A, Stelian M, Sharma A, Borza C, Lighezan DF. Benefits of prescribing low-dose digoxin in atrial fibrillation. Int J Immunopathol Pharmacol 2021; 35.
17) Pieske B, Tschöpe C, de Boer RA, Fraser AG, Anker SD, Donal E, Edelmann F, Fu M, Guazzi M, Lam CSP, Lancellotti P, Melenovsky V, Morris DA, Nagel E, Pieske-Kraigher E, Ponikowski P, Solomon SD, Vasan RS, Rutten FH, Voors AA, Ruschitzka F, Paulus WJ, Seferovic P, Filippatos G. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J 2019; 40: 3297-3317.
18) Marwick TH, Shah SJ, Thomas JD. Myocardial Strain in the Assessment of Patients With Heart Failure: A Review. JAMA Cardiol 2019; 4: 287-294.
19) Bertini M, Ng AC, Antoni ML, Nucifora G, Ewe SH, Auger D, Marsan NA, Schalij MJ, Bax JJ, Delgado V. Global longitudinal strain predicts long-term survival in patients with chronic ischemic cardiomyopathy. Circ Cardiovasc Imaging 2012; 5: 383-391.
20) Smiseth OA, Torp H, Opdahl A, Haugaa KH, Urheim S. Myocardial strain imaging: how useful is it in clinical decision making? Eur Heart J 2016; 37: 1196-1207.
21) Bertini M, Ng AC, Borleffs CJ, Delgado V, Wijnmaalen AP, Nucifora G, Ewe SH, Shanks M, Thijssen J, Zeppenfeld K, Biffi M, Leung DY, Schalij MJ, Bax JJ. Longitudinal mechanics of the periinfarct zone and ventricular tachycardia inducibility in patients with chronic ischemic cardiomyopathy. Am Heart J 2010; 160: 729-736.
22) Haugaa KH, Smedsrud MK, Steen T, Kongsgaard E, Loennechen JP, Skjaerpe T, Voigt JU, Willems R, Smith G, Smiseth OA, Amlie JP, Edvardsen T. Mechanical dispersion assessed by myocardial strain in patients after myocardial infarction for risk prediction of ventricular arrhythmia. JACC Cardiovasc Imaging 2010; 3: 247-256.
23) Gorcsan J, 3rd, Haugaa KH. Ventricular Arrhythmias and Reduced Echocardiographic Inferior Wall Strain: Is Regional Function an Important Risk Marker? Circ Cardiovasc Imaging 2017; 10.
24) Ernande L, Rietzschel ER, Bergerot C, De Buyzere ML, Schnell F, Groisne L, Ovize M, Croisille P, Moulin P, Gillebert TC, Derumeaux G. Impaired myocardial radial function in asymptomatic patients with type 2 diabetes mellitus: a speckle-tracking imaging study. J Am Soc Echocardiogr 2010; 23: 1266-1272.
25) Karagöz A, Bezgin T, Kutlutürk I, Külahçıoğlu S, Tanboğa IH, Güler A, Karabay CY, Oduncu V, Aksoy H, Kırma C. Subclinical left ventricular systolic dysfunction in diabetic patients and its association with retinopathy: A 2D speckle tracking echocardiography study. Herz 2015; 40: 240-246.
26) Morris DA, Belyavskiy E, Aravind-Kumar R, Kropf M, Frydas A, Braunauer K, Marquez E, Krisper M, Lindhorst R, Osmanoglou E, Boldt LH, Blaschke F, Haverkamp W, Tschöpe C, Edelmann F, Pieske B, Pieske-Kraigher E. Potential Usefulness and Clinical Relevance of Adding Left Atrial Strain to Left Atrial Volume Index in the Detection of Left Ventricular Diastolic Dysfunction. JACC Cardiovasc Imaging 2018; 11: 1405-1415.
27) Kansal MM, Panse PM, Abe H, Caracciolo G, Wilansky S, Tajik AJ, Khandheria BK, Sengupta PP. Relationship of contrast-enhanced magnetic resonance imaging-derived intramural scar distribution and speckle tracking echocardiography-derived left ventricular two-dimensional strains. Eur Heart J Cardiovasc Imaging 2012; 13: 152-158.
28) Antoni ML, Mollema SA, Delgado V, Atary JZ, Borleffs CJ, Boersma E, Holman ER, van der Wall EE, Schalij MJ, Bax JJ. Prognostic importance of strain and strain rate after acute myocardial infarction. Eur Heart J 2010; 31: 1640-1647.
29) Bijnens BH, Cikes M, Claus P, Sutherland GR. Velocity and deformation imaging for the assessment of myocardial dysfunction. Eur J Echocardiogr 2009; 10: 216-226.
30) Bijnens B, Claus P, Weidemann F, Strotmann J, Sutherland GR. Investigating cardiac function using motion and deformation analysis in the setting of coronary artery disease. Circulation. 2007; 116: 2453-2464.
31) Chan J, Hanekom L, Wong C, Leano R, Cho GY, Marwick TH. Differentiation of subendocardial and transmural infarction using two-dimensional strain rate imaging to assess short-axis and long-axis myocardial function. J Am Coll Cardiol 2006; 48: 2026-2033.
32) Hanekom L, Jenkins C, Jeffries L, Case C, Mundy J, Hawley C, Marwick TH. Incremental value

of strain rate analysis as an adjunct to wall-motion scoring for assessment of myocardial viability by dobutamine echocardiography: a follow-up study after revascularization. Circulation 2005; 112: 3892-3900.

33) Bordejevic DA, Pârvănescu T, Petrescu L, Mornoș C, Olariu I, Crișan S, Văcărescu C, Lazăr M, Morariu VI, Citu IM, Tomescu MC, Cozma D. Left Ventricular Remodeling Risk Predicted by Two-Dimensional Speckle Tracking Echocardiography in Acute Myocardial Infarction Patients with Midrange or Preserved Ejection Fraction in Western Romania. Ther Clin Risk Manag 2021; 17: 249-258.

34) Vacarescu C, Cozma D, Petrescu L, Dragan S, Mornos C, Crisan S, Feier H, Lazar MA, Cozlac RA, Luca CT. Exercise test is essential in LV-only fusion CRT pacing without right ventricle lead. Clin Interv Aging 2019; 14: 969-975.

35) Yingchoncharoen T, Gibby C, Rodriguez LL, Grimm RA, Marwick TH. Association of myocardial deformation with outcome in asymptomatic aortic stenosis with normal ejection fraction. Circ Cardiovasc Imaging 2012; 5: 719-725.

36) Cochera F, Dinca D, Bordejevic DA, Citu IM, Mavrea AM, Andor M, Trofenciuc M, Tomescu MC. Nebivolol effect on doxorubicin-induced cardiotoxicity in breast cancer. Cancer Manag Res 2018; 10: 2071-2081.

37) Doyle JJ, Neugut AI, Jacobson JS, Grann VR, Hershman DL. Chemotherapy and cardiotoxicity in older breast cancer patients: a population-based study. J Clin Oncol 2005; 23: 8597-8605.

38) Fallah-Rad N, Walker JR, Wassef A, Lytwyn M, Bohonis S, Fang T, Tian G, Kirkpatrick ID, Singal PK, Krahn M, Grenier D, Jassal DS. 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: 2263-2270.

39) Sawaya H, Sebag IA, Plana JC, Januzzi JL, Ky B, Tan TC, Cohen V, Banchs J, Carver JR, Wiegers SE, Martin RP, Picard MH, Gerszten RE, Halpern EF, Passeri J, Kuter I, Scherrer-Crosbie M. Assessment of echocardiography and biomarkers for the extended prediction of cardiotoxicity in patients treated with anthracyclines, taxanes, and trastuzumab. Circ Cardiovasc Imaging 2012; 5: 596-603.

40) Suffoletto MS, Dohi K, Cannesson M, Saba S, Gorcsan J, 3rd. Novel speckle-tracking radial strain from routine black-and-white echocardiographic images to quantify dyssynchrony and predict response to cardiac resynchronization therapy. Circulation 2006; 113: 960-968.

41) Tanaka H, Hirata K. Is speckle tracking actually helpful for cardiac resynchronization therapy? J Echocardiogr 2016; 14: 53-60.

42) Iino H, Okano T, Daimon M, Sasaki K, Chigira M, Nakao T, Mizuno Y, Yamazaki T, Kurano M, Yatomi Y, Sumi Y, Sasano T, Miyata T. Usefulness of Carotid Arterial Strain Values for Evaluating the Arteriosclerosis. J Atheroscler Thromb 2019; 26: 476-487.