Journal of Echocardiography (2019) 17:17–24
https://doi.org/10.1007/s12574-018-0408-2

REVIEW ARTICLE

# Utility of strain imaging in conjunction with heart failure stage classification for heart failure patient management

**Hidekazu Tanaka**[1]

Received: 29 October 2018 / Accepted: 7 November 2018 / Published online: 15 November 2018


## Abstract

The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) classification, based on structural changes and symptoms, classifies stages of heart failure (HF) development as Stages A–D. This HF classification emphasizes the development and progression of the disease and can be used to describe individuals and populations. Since HF is considered a progressive disorder that can be represented as a clinical continuum, individuals at a particular HF stage require specific management with the long-term goal of avoiding HF development and progression. Although early detection of subclinical left ventricular (LV) dysfunction is essential for delaying progression to HF, the assessment of such dysfunction can be challenging. While echocardiography plays a pivotal role in the quantification and early detection of LV structural findings, two-dimensional speckle-tracking echocardiographic parameters, especially global longitudinal strain (GLS), have recently been reported to be sensitive markers of early subtle abnormalities of LV myocardial performance. They are thus helpful for prediction of outcomes for various cardiac diseases, and superior to conventional echocardiographic indices such as LV ejection fraction, mitral inflow *E* and mitral *e′* annular velocities ratio. Strain imaging, especially GLS-guided management for patients at a particular stage of HF, may therefore have the potential to prevent progression to later HF stages and may offer new insights into the management of HF patients. This article reviews the utility of strain imaging, especially GLS in conjunction with HF stage classification, and future perspectives for HF patient management.

**Keywords** Heart failure stage classification · Speckle-tracking strain · Global longitudinal strain · Echocardiography

## Introduction

The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) classification, based on structural changes and symptoms, classifies stages of heart failure (HF) development into Stages A–D [1–3]. This HF classification emphasizes the development and progression of the disease and can be used to describe both individuals and populations. Although survival of HF patients has improved, a population cohort study reported that 5-year survival rates for Stages A, B, C, and D HF were 97%, 96%, 75%, and 20%, respectively [4]. Since HF is considered a progressive disorder that can be represented as a clinical continuum, individuals at a particular HF stage require specific management with the long-term goal of avoiding HF development. Although early detection of subclinical left ventricular (LV) dysfunction is essential for delaying progression to HF, the assessment of such dysfunction can be challenging. While echocardiography plays a pivotal role in the quantification and early detection of LV structural findings, it has been reported that speckle-tracking echocardiographic parameters are useful for the detection of early LV structural abnormalities. In particular, global longitudinal strain (GLS) assessed by two-dimensional speckle-tracking echocardiography has recently been reported to be a sensitive marker for early subtle abnormalities of LV myocardial performance, helpful for the prediction of outcomes for various cardiac diseases, and superior to conventional echocardiographic indices such as LV ejection fraction (LVEF), mitral inflow *E*, and mitral *e′* annular velocities ratio (*E*/*e′*) [5–9]. Moreover, recent studies suggest that GLS might be helpful for prediction of cardiovascular outcomes even for a general population [5, 10, 11]. Several manufacturers have devised various speckle-tracking echocardiographic

✉ Hidekazu Tanaka
tanakah@med.kobe-u.ac.jp

[1] Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, 7-5-2, Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan

approaches, although their basic approach is similar. Strain information is not dependent on the Doppler angle of incidence, thus making the analysis of longitudinal strain possible. According to the guidelines of the American Society of Echocardiography, GLS is determined as the averaged peak longitudinal strain of 18 LV segments from the three standard apical views (Fig. 1) [12].

This article reviews the utility of strain imaging, especially GLS in conjunction with HF stage classification, and future perspectives for the management of HF patients (Table 1).

## Utility of strain imaging for Stage A HF

Stage A HF patients have been described as being at high risk for HF even though they show no structural heart disease or symptoms of HF. High risk factors for HF include hypertension, diabetes mellitus (DM), obesity, metabolic syndrome, atherosclerotic disease, a history of using cardiotoxins, and a family history of cardiomyopathy [1–3]. The aim of strain imaging for Stage A HF is to predict subclinical LV dysfunction; it can be an early marker of LV dysfunction, thus possibly indicating cardiovascular morbidity and mortality. The next section will deal in more detail with the utility of GLS for Stage A HF patients with specific comorbidities, especially hypertension, DM, obesity, and a history of using cardiotoxins.

## Utility of strain imaging for hypertension

Hypertension is the most common risk factor for HF, with a proven population attributable risk of 39% for men and 59% for women [13]. Despite being diagnosed with hypertension, over 30% of Stage A HF patients had blood pressure above the target blood pressure during the survey period [14]. Previous studies have reported a prevalence of low GLS values, ranging from 15 to 42%, for patients with hypertension, depending on the severity and control of hypertension [15–17]. Soufi Taleb Bendiab et al.

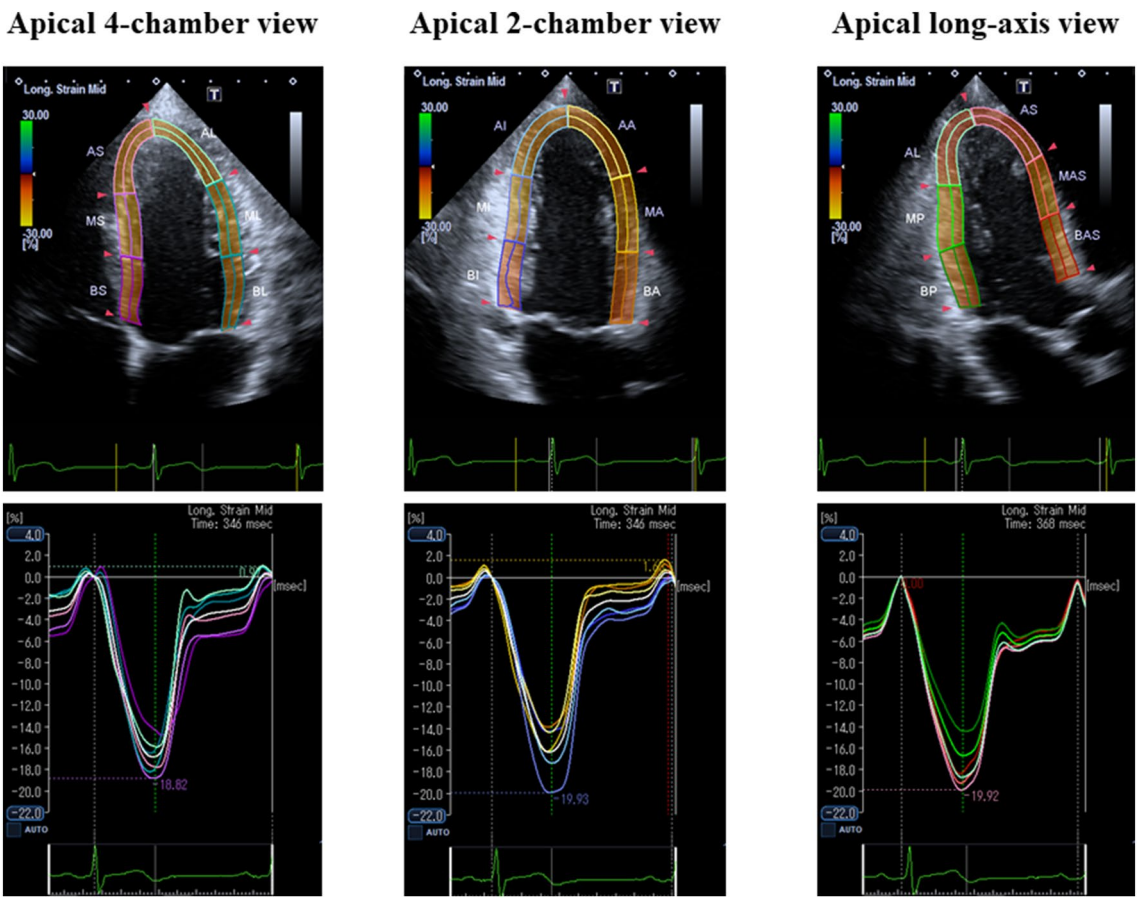


**Fig. 1** Example of the assessment of left ventricular (LV) longitudinal systolic myocardial function, known as global longitudinal strain (GLS), by means of two-dimensional speckle-tracking imaging, showing color-coded speckle-tracking images and corresponding longitudinal time–strain curves. GLS is determined as the average peak longitudinal strain of 18 segments from the three standard apical views and is expressed as an absolute value

found that 46% of their patients showed low GLS values (< 17%), and that low GLS was associated with long-lasting hypertension and uncontrolled blood pressure for 200 outpatients with hypertension with preserved LVEF but without overt HF. Moreover, Chen et al. reported that uncontrolled blood pressure (≥ 140/90 mmHg) was associated with low GLS regardless of LV hypertrophy for 276 patients with treated hypertension [17].

## Utility of strain imaging for DM

DM is another well-known risk factor for HF and as important a comorbid disease of Stage A HF as hypertension. Lack of DM control is an important predictor of new onset HF, with every 1% increase in HbA1c correlating with an 8–19% increase in HF incidence [18, 19]. The presence of LV longitudinal myocardial dysfunction has been identified in DM patients with preserved LVEF and without overt coronary artery disease or HF [20–28]. Nakai et al. reported that GLS in DM patients was significantly lower than that in age-matched normal subjects in spite of similar LVEF, and that 43% of DM patients showed LV longitudinal myocardial dysfunction defined as GLS < 17.2% [20], while Ernande et al. found that 23% of DM patients with preserved LVEF had LV longitudinal myocardial dysfunction defined as GLS < 18% [23]. In addition, Holland et al. reported that type 2 DM patients with preserved LVEF and GLS < 18.9% had significantly worse outcome than those with a higher percentage during a 10-year follow-up and concluded that GLS was independently associated with the primary end point [29]. DM is also a major cause of HF with preserved LVEF (HFpEF) as well as hypertension, with HFpEF usually presenting as LV diastolic dysfunction. Some investigators have maintained that LV longitudinal myocardial dysfunction, rather than LV diastolic dysfunction, should be considered as the first marker of a preclinical form of DM-related cardiac dysfunction in DM patients with preserved LVEF without overt HF [24, 30]. Ernande et al. demonstrated that LV longitudinal myocardial dysfunction detected as GLS < 18% was present even in DM patients with preserved LVEF and normal LV diastolic function [24]. Furthermore, Mochizuki et al. showed that GLS was a strong determinative factor for $e'$ and $E/e'$ independently of age [31]. For normal subjects, however, only age was associated with all LV diastolic parameters. It has thus been suggested that progression of uncontrolled DM leads to LV myocardial dysfunction as well as LV diastolic dysfunction, GLS is associated with LV diastolic function, and reduced GLS can occur together with LV diastolic dysfunction in DM patients with preserved LVEF, leading to HFpEF.

## Utility of strain imaging for obesity

Healthy lifestyle habits, including maintenance of normal body weight at body mass index (BMI) < 25 kg/m$^2$, are associated with lower lifetime risk of HF [32]. Compared to those with normal BMI, obese subjects were found to have twice the risk of developing HF, with a graded relationship between BMI and HF incidence, including for those in the overweight category [33]. Ho et al. observed that higher BMI was associated with low GLS in 6,231 participants [34]. They further showed that higher circulating leptin concentrations were also associated with low GLS, suggesting potential involvement of circulating adipokines in obesity-related LV damage. Suto et al. reported that GLS of overweight patients was significantly lower than that of non-overweight patients, and multiple regression analysis revealed that BMI as well as LV mass index were independent determinant parameters for GLS for 145 asymptomatic type 2 DM patients with preserved LVEF without coronary artery disease [35]. Finally, Leung et al. found that weight loss was associated with an increase in GLS in obese patients. They showed that in eight obese patients with type 2 DM with BMI of 44 ± 9 kg/m$^2$ who underwent sleeve gastrectomy, GLS improved from 13.2 ± 3.7% to 19.7 ± 2.2% after surgery [36].

## Utility of strain imaging for patients with history of using cardiotoxins

Cancer therapeutics-related cardiac dysfunction (CTRCD) has become a leading cause of morbidity and mortality for cancer survivors [37, 38], with the mortality rate for patients with CTRCD reportedly being as high as 60% by 2 years after treatment [39]. Patients without HF symptoms or LV structural abnormalities, but with a history of using cardiotoxins such as doxorubicin (Type I CTRCD) and trastuzumab (Type II CTRCD), are included in Stage A HF because of the irreversible LV myocardial changes due to anticancer drugs, such as myocyte loss, interstitial fibrosis leading to diminished LV contractility, reduced LV wall thickness, and progressive LV dilation. Recently, there has been a growing interest in the early detection of CTRCD by means of GLS, because it is a more sensitive and robust parameter for detecting subclinical LV dysfunction than other conventional LV functional parameters such as LVEF [40–43]. A systematic review of 1,504 patients during or after cancer chemotherapy showed that early changes in GLS appear to be the best gauge for predicting cardiotoxicity [42]. Specifically, a drop in LVEF or occurrence of HF, reflected in a 10–15% early reduction in GLS during chemotherapy, appears to be the most useful parameter for the prediction of cardiotoxicity. In addition, Hatazawa et al. recently reported that during a long-term follow-up, baseline GLS was identified as the

only independent predictor of Type I CTRCD for patients with malignant lymphoma, and that baseline GLS ≤ 19% was associated with the development of Type I CTRCD and hospitalization for HF [44].

## Utility of strain imaging for Stage B HF

Stage B HF refers to structural heart disease without signs or symptoms of HF. Most often, it is due to loss of functioning myocytes because of myocardial infarction, valvular disease, or LV hypertrophy secondary to hypertension. Transition from Stage B to C HF portends a fivefold increase in mortality risk for both men and women [4], but early intervention may delay or prevent the onset of overt HF in Stage B HF patients. Thus, the utility of strain imaging for Stage B HF patients is that it can identify patients more at risk of progressing to Stage C HF. Wang et al. showed that GLS was an additional echocardiographic parameter to help identify Stage B patients who are more at risk of progressing to symptomatic HF [45]. In our considered opinion, the the most promising application of GLS in this case for would be for Stage B HF asymptomatic patients with severe valvular diseases such as mitral regurgitation (MR), aortic stenosis (AS), and aortic regurgitation (AR) but with preserved LVEF.

### Utility of GLS for MR

Magne et al. used Cox multivariable analysis to show that GLS was independently associated with outcome for 135 asymptomatic patients with MR and preserved LVEF, and that the outcome for patients with GLS < 20% was unfavorable compared to that for patients with GLS ≥ 20% [46]. Mentias et al. examined 737 asymptomatic patients with more than moderate MR and preserved LVEF to evaluate the utility of GLS for predicting outcome and found that GLS < 21.7% was associated with poor outcome. In addition, Witkowski et al. showed that GLS < 19.9% was an independent predictor of long-term LV dysfunction (LVEF < 50%) after mitral valve repair in 233 patients with moderate–severe organic MR and preserved LVEF [47].

### Utility of GLS for AS

Yingchoncharoen et al. showed that GLS < 15% was associated with a significant excess of patient mortality. In addition, they found that for 79 asymptomatic patients with severe AS and preserved LVEF, GLS enhanced the prognostic accuracy of prediction of the outcome based on transaortic peak pressure gradient, aortic valve calcification, and valvulo-arterial impedance [48]. Moreover, Sato et al. demonstrated the utility of GLS as a predictor of outcome for patients with paradoxical low-flow, low-gradient severe AS, and that patients with GLS < 17% had significantly worse outcome [49].

### Utility of GLS for AR

Smedsrud et al. showed that GLS for patients with severe AR and preserved LVEF was significantly lower than that for healthy controls, but increased significantly postoperatively, although to a level still lower than in healthy controls [50]. In addition, Alashi et al. showed that for 1063 asymptomatic patients with severe AR and preserved LVEF, GLS ≥ 19.5% was associated with better longer-term mortality, enhanced prognostic accuracy and improved reclassification [51]. Furthermore, they showed that patients with GLS ≥ 19% showed excellent 5-year survival rates, whereas the risk of death continued to increase for those with GLS < 19%.

## Utility of strain imaging for Stage C–D HF

Stage C HF refers to structural heart disease with prior or current symptoms of HF, and Stage D HF to advanced stages of progression of the HF syndrome characterized by structural abnormalities of the heart and severe resting symptoms despite optimal medical, surgical, and device therapy. A proportion of Stage C HF patients will develop advanced symptoms, usually

**Table 1** Role of strain imaging in accordance with HF stage classification

| HF classification | Stage A HF | Stage B HF | Stage C HF | Stage D HF |
|---|---|---|---|---|
| HF definition | At high risk for HF, but without structural heart disease or symptoms of HF | Structural heart disease, but without signs or symptoms of HF | Structural heart disease with prior or current symptoms of HF | Refractory HF |
| Role of strain imaging | Prediction of subclinical LV dysfunction and can be an early marker of LV dysfunction | Identification of patients more at risk of progressing to Stage C HF | Identification of disease severity and prognosis | |

*HF* heart failure

**Table 2** Role of GLS for Stage A HF

| Authors (refs.) | Journal | Population | Main findings |
|---|---|---|---|
| Soufi Taleb Bendiab et al. [15] | Eur J Prev Cardiol 2017;24:1463–1472 | Hypertension ($n=200$) | GLS < 17% associated with long-lasting hypertension and uncontrolled blood pressure |
| Imbalzano et al. [16] | Echocardiography 2011;28:649–657 | Hypertension ($n=51$) | GLS reduced even in patients without LVH |
| Chen et al. [17] | Echocardiography 2016;33:1488–1494 | Hypertension ($n=276$) | Uncontrolled blood pressure (≥ 140/90 mmHg) associated with low GLS regardless of LVH |
| Nakai et al. [20] | Eur J Echocardiogr 2009;10:926–932 | DM ($n=60$) | GLS < 17.2% for 43% of patients |
| Ng et al. [21] | Am J Cardiol 2009;104:1398–1401 | DM ($n=47$) | DM independent predictor for GLS |
| Zoroufian et al. [22] | Echocardiography 2014;31:456–463 | DM ($n=37$) | Decrease in GLS irrespective of the presence or absence of LV diastolic dysfunction |
| Ernande et al. [23] | J Am Soc Echocardiogr 2014;27:479–488 | DM ($n=154$) | GLS < 18% associated with LV remodeling during 3-year follow-up |
| Ernande et al. [24] | J Am Soc Echocardiogr 2011;24:1268–1275 | DM ($n=114$) | GLS < 18% for 28% of patients even with normal LV diastolic function |
| Ernande et al. [25] | J Am Soc Echocardiogr 2010;23:1266–1272 | DM ($n=114$) | DM and gender associated with GLS < 18% |
| Mochizuki et al. [26] | Cardiovasc Diabetol 2015;14:37 | DM ($n=144$) | Diabetic nephropathy the highest risk factor for GLS < 18% |
| Mochizuki et al. [27] | Cardiovasc Diabetol 2015;14:47 | DM ($n=112$) | GLS of patients with diabetic neuropathy was significantly lower than of those without |
| Mochizuki et al. [28] | Circ J 2016;80:1957–1964 | DM ($n=198$) | Stepwise decrease in GLS in proportion to the degree of diabetic nephropathy, which correlated with both left atrial strain and albuminuria |
| Holland et al. [29] | Heart 2015;101:1061–1066 | DM ($n=230$) | GLS < 18.9% associated with worse outcome over 10 years follow-up; GLS independently associated with outcome |
| Mochizuki et al. [31] | Int J Cardiovasc Imaging 2017;33:1905–1914 | DM ($n=177$) | GLS a strong determinative factor for $e'$ and $E/e'$ in DM patients independently of age; only age associated with all LV diastolic parameters in normal subjects |
| Ho et al. [34] | Circ Heart Fail 2017;10:e003536 | Overweight/obesity ($n=6321$) | Higher BMI associated with lower GLS |
| Suto et al. [35] | Cardiovasc Diabetol 2017;16:145 | Overweight/obesity ($n=145$) | BMI as well as LV mass index independent determinant parameters for GLS |
| Leung et al. [36] | Obes Surg 2016;26:321–326 | Overweight/obesity ($n=8$) | Weight loss associated with increase in GLS |
| Negishi et al. [40] | Eur Heart J Cardiovasc Imaging 2014;15:324–331 | History of using cardiotoxins ($n=159$) | β-Blocker effective during 6-month follow-up for patients with ≥ 11% decrease in GLS by 7 months after chemotherapy |
| Negishi et al. [41] | J Am Soc Echocardiogr 2013;26:493–498 | History of using cardiotoxins ($n=81$) | Reduction in GLS of 11% by 6 months after chemotherapy strongly associated with subsequent decrease in LVEF during 12-month follow-up |

**Table 2** (continued)

| Authors (refs.) | Journal | Population | Main findings |
|---|---|---|---|
| Thavendiranathan et al. [42] | J Am Coll Cardiol 2014;63:2751–2768 | History of using cardiotoxins ($n=1504$) | 10–15% early reduction in GLS during chemotherapy most useful parameter for prediction of cardiotoxicity |
| Hatazawa et al. [44] | Circ J 2018;82:2566–2574 | History of using cardiotoxins ($n=73$) | Baseline GLS independent predictor of Type I CTRCD for patients with malignant lymphoma, and baseline GLS $\leq$ 19% associated with unfavorable outcome during long-term follow-up |

*HF* heart failure, *GLS* global longitudinal strain, *LVH* left ventricular hypertrophy, *DM* diabetes mellitus, *LV* left ventricular, *E/e′* mitral inflow *E* and mitral *e′* annular velocities ratio, *BMI* body mass index, *LVEF* left ventricular ejection fraction, *CTRCD* cancer therapeutics-related cardiac dysfunction

defined as NYHA functional class III–IV, which is refractory to optimal guideline-recommended therapy and therefore leads to Stage D HF. Kalogeropoulos et al. showed that 12.2% of 964 outpatients with Stage C HF with HFrEF receiving care in an academic center progressed to Stage D HF after 3 years Stage C HF [52]. They also reported that 25.1% of patients with Stage C HF had either progressed to Stage D HF or died. Thus, identification of disease severity or prognosis for Stage C–D HF patients is a clinically important task because treatments are inherently limited, morbidity is typically progressive, and survival is often short. Cameli et al. found that LV myocardial fibrosis and its grade as assessed using Masson's staining in 47 Stage D HF patients who had undergone cardiac transplantation strongly correlated with GLS, modestly with global circumferential strain and LV torsion, and weakly with mitral S′ wave and mitral annular plane systolic excursion but not with LVEF [53]. They also showed that GLS was most accurate for detecting LV fibrosis. Chimura et al. detected significant associations of GLS and late gadolinium enhancement on cardiac magnetic resonance imaging with long-term outcome for 179 consecutive symptomatic patients with dilated cardiomyopathy [54]. They also found that patients with GLS $\geq$ 8.3% showed a more favorable outcome than those with lower GLS. Reant et al. showed that reduced GLS was an independent factor associated with poor cardiac outcomes, and HF outcomes in particular, for 472 symptomatic patients with hypertrophic cardiomyopathy [55]. Moreover, it has been reported that GLS and LV dispersion, assessed as the standard deviation of time-to-peak longitudinal speckle tracking from 18 LV segments, are useful for predicting fatal ventricular arrhythmias in patients with dilated cardiomyopathy [56] and hypertrophic cardiomyopathy [57], although this study included a few Stage B HF patients.

## Future perspectives for the role of strain imaging in conjunction with HF stage classification

Prospects for strain imaging for the early detection of subclinical LV dysfunction seem to be promising for delaying progression to HF in patients with a particular stage HF. Interest is growing in the evaluation of subclinical LV dysfunction in Stage A HF patients by means of strain imaging and GLS in particular as the best means of preventing eventual progression to overt HF such as Stages C and D, while screening for comorbid diseases warrants closer attention (Table 2). This review article indicates that LV longitudinal myocardial dysfunction assessed in terms of low GLS can first appear in Stage A HF, which suggests the importance of the assessment of GLS for detecting subclinical LV dysfunction. These silent abnormalities may lead over time to symptomatic LV dysfunction, but such progression may be positively affected by early treatment. Thus, GLS-guided management of patients with hypertension, DM, obesity, and a history of using cardiotoxins may result in not only improvement in specific comorbid diseases, but also in prevention of future development of LV structural heart disease and symptomatic HF.

## Conclusion

Strain imaging, especially GLS-guided management for HF patients at a specific stage, may be able to help prevent progression to later HF stages and can offer new insights into the management of HF patients.

### Compliance with ethical standards

**Conflict of interest** Hidekazu Tanaka declares that he has no conflict of interest.

## References


1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation. 2013;128:1810–52.
2. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017;136:e137–61.
3. Writing Committee, Yancy CW, Jessup M, et al. 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2016;134:e282–93.
4. Ammar KA, Jacobsen SJ, Mahoney DW, et al. Prevalence and prognostic significance of heart failure stages: application of the American College of Cardiology/American Heart Association heart failure staging criteria in the community. Circulation. 2007;115:1563–70.
5. Biering-Sorensen T, Biering-Sorensen SR, Olsen FJ, et al. Global longitudinal strain by echocardiography predicts long-term risk of cardiovascular morbidity and mortality in a low-risk general population: the Copenhagen City Heart Study. Circ Cardiovasc Imaging. 2017;10:e005521.
6. Gorcsan J 3rd, Tanaka H 3rd. Echocardiographic assessment of myocardial strain. J Am Coll Cardiol. 2011;58:1401–13.
7. Stanton T, Leano R, Marwick TH. Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring. Circ Cardiovasc Imaging. 2009;2:356–64.
8. Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. Heart. 2014;100:1673–80.
9. Mignot A, Donal E, Zaroui A, et al. Global longitudinal strain as a major predictor of cardiac events in patients with depressed left ventricular function: a multicenter study. J Am Soc Echocardiogr. 2010;23:1019–24.
10. Russo C, Jin Z, Elkind MS, et al. Prevalence and prognostic value of subclinical left ventricular systolic dysfunction by global longitudinal strain in a community-based cohort. Eur J Heart Fail. 2014;16:1301–9.
11. Cheng S, McCabe EL, Larson MG, et al. Distinct aspects of left ventricular mechanical function are differentially associated with cardiovascular outcomes and all-cause mortality in the community. J Am Heart Assoc. 2015;4:e002071.
12. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the american society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr. 2015;28(1–39):e14.
13. Levy D, Larson MG, Vasan RS, et al. The progression from hypertension to congestive heart failure. JAMA. 1996;275:1557–62.
14. National Cholesterol Education Program Expert Panel on Detection E. Treatment of High Blood Cholesterol in A Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. Circulation. 2002;106:3143–421.
15. Soufi Taleb Bendiab N, Meziane-Tani A, Ouabdesselam S, et al. Factors associated with global longitudinal strain decline in hypertensive patients with normal left ventricular ejection fraction. Eur J Prev Cardiol. 2017;24:1463–72.
16. Imbalzano E, Zito C, Carerj S, et al. Left ventricular function in hypertension: new insight by speckle tracking echocardiography. Echocardiography. 2011;28:649–57.
17. Chen XJ, Sun XL, Zhang Q, et al. Uncontrolled blood pressure as an independent risk factor of early impaired left ventricular systolic function in treated hypertension. Echocardiography. 2016;33:1488–94.
18. Vaur L, Gueret P, Lievre M, et al. Development of congestive heart failure in type 2 diabetic patients with microalbuminuria or proteinuria: observations from the DIABHYCAR (type 2 DIABetes, Hypertension, CArdiovascular Events and Ramipril) study. Diabetes Care. 2003;26:855–60.
19. Iribarren C, Karter AJ, Go AS, et al. Glycemic control and heart failure among adult patients with diabetes. Circulation. 2001;103:2668–73.
20. Nakai H, Takeuchi M, Nishikage T, et al. Subclinical left ventricular dysfunction in asymptomatic diabetic patients assessed by two-dimensional speckle tracking echocardiography: correlation with diabetic duration. Eur J Echocardiogr. 2009;10:926–32.
21. Ng AC, Delgado V, Bertini M, et al. Findings from left ventricular strain and strain rate imaging in asymptomatic patients with type 2 diabetes mellitus. Am J Cardiol. 2009;104:1398–401.
22. Zoroufian A, Razmi T, Taghavi-Shavazi M, et al. Evaluation of subclinical left ventricular dysfunction in diabetic patients: longitudinal strain velocities and left ventricular dyssynchrony by two-dimensional speckle tracking echocardiography study. Echocardiography. 2014;31:456–63.
23. Ernande L, Bergerot C, Girerd N, et al. Longitudinal myocardial strain alteration is associated with left ventricular remodeling in asymptomatic patients with type 2 diabetes mellitus. J Am Soc Echocardiogr. 2014;27:479–88.
24. Ernande L, Bergerot C, Rietzschel ER, et al. Diastolic dysfunction in patients with type 2 diabetes mellitus: is it really the first marker of diabetic cardiomyopathy? J Am Soc Echocardiogr. 2011;24(1268–75):e1.
25. Mochizuki Y, Tanaka H, Matsumoto K, et al. Clinical features of subclinical left ventricular systolic dysfunction in patients with diabetes mellitus. Cardiovasc Diabetol. 2015;14:37.
26. Mochizuki Y, Tanaka H, Matsumoto K, et al. Association of peripheral nerve conduction in diabetic neuropathy with subclinical left ventricular systolic dysfunction. Cardiovasc Diabetol. 2015;14:47.
27. Mochizuki Y, Tanaka H, Tatsumi K, et al. Easy-to-use comprehensive speckle-tracking approach for cardiac resynchronization therapy. Circ J. 2014;78:2250–8.
28. Mochizuki Y, Tanaka H, Matsumoto K, et al. Impaired mechanics of left ventriculo-atrial coupling in patients with diabetic nephropathy. Circ J. 2016;80:1957–64.
29. Holland DJ, Marwick TH, Haluska BA, et al. Subclinical LV dysfunction and 10-year outcomes in type 2 diabetes mellitus. Heart. 2015;101:1061–6.
30. Cognet T, Vervueren PL, Dercle L, et al. New concept of myocardial longitudinal strain reserve assessed by a dipyridamole infusion using 2D-strain echocardiography: the impact of diabetes and age, and the prognostic value. Cardiovasc Diabetol. 2013;12:84.
31. Mochizuki Y, Tanaka H, Matsumoto K, et al. Impact of left ventricular longitudinal functional mechanics on the progression of diastolic function in diabetes mellitus. Int J Cardiovasc Imaging. 2017;33:1905–14.

32. Djousse L, Driver JA, Gaziano JM. Relation between modifiable lifestyle factors and lifetime risk of heart failure. JAMA. 2009;302:394–400.
33. Kenchaiah S, Evans JC, Levy D, et al. Obesity and the risk of heart failure. N Engl J Med. 2002;347:305–13.
34. Ho JE, McCabe EL, Wang TJ, et al. Cardiometabolic traits and systolic mechanics in the community. Circ Heart Fail. 2017;10:e003536.
35. Suto M, Tanaka H, Mochizuki Y, et al. Impact of overweight on left ventricular function in type 2 diabetes mellitus. Cardiovasc Diabetol. 2017;16:145.
36. Leung M, Xie M, Durmush E, et al. Weight loss with sleeve gastrectomy in obese type 2 diabetes mellitus: impact on cardiac function. Obes Surg. 2016;26:321–6.
37. Hooning MJ, Botma A, Aleman BM, et al. Long-term risk of cardiovascular disease in 10-year survivors of breast cancer. J Natl Cancer Inst. 2007;99:365–75.
38. Doyle JJ, Neugut AI, Jacobson JS, et al. Chemotherapy and cardiotoxicity in older breast cancer patients: a population-based study. J Clin Oncol. 2005;23:8597–605.
39. Felker GM, Thompson RE, Hare JM, et al. Underlying causes and long-term survival in patients with initially unexplained cardiomyopathy. N Engl J Med. 2000;342:1077–84.
40. Negishi K, Negishi T, Haluska BA, et al. Use of speckle strain to assess left ventricular responses to cardiotoxic chemotherapy and cardioprotection. Eur Heart J Cardiovasc Imaging. 2014;15:324–31.
41. Negishi K, Negishi T, Hare JL, et al. Independent and incremental value of deformation indices for prediction of trastuzumab-induced cardiotoxicity. J Am Soc Echocardiogr. 2013;26:493–8.
42. Thavendiranathan P, Poulin F, Lim KD, et al. Use of myocardial strain imaging by echocardiography for the early detection of cardiotoxicity in patients during and after cancer chemotherapy: a systematic review. J Am Coll Cardiol. 2014;63:2751–68.
43. Plana JC, Galderisi M, Barac A, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2014;27:911–39.
44. Hatazawa K, Tanaka H, Nonaka A, et al. Baseline global longitudinal strain as a predictor of left ventricular dysfunction and hospitalization for heart failure of patients with malignant lymphoma after anthracycline therapy. Circ J. 2018;82:2566–74.
45. Wang Y, Yang H, Huynh Q, et al. Diagnosis of nonischemic stage B heart failure in type 2 diabetes mellitus: optimal parameters for prediction of heart failure. JACC Cardiovasc Imaging. 2018;16:2601.
46. Magne J, Mahjoub H, Pierard LA, et al. Prognostic importance of brain natriuretic peptide and left ventricular longitudinal function in asymptomatic degenerative mitral regurgitation. Heart. 2012;98:584–91.
47. 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.
48. Yingchoncharoen T, Gibby C, Rodriguez LL, et al. Association of myocardial deformation with outcome in asymptomatic aortic stenosis with normal ejection fraction. Circ Cardiovasc Imaging. 2012;5:719–25.
49. Sato K, Seo Y, Ishizu T, et al. Prognostic value of global longitudinal strain in paradoxical low-flow, low-gradient severe aortic stenosis with preserved ejection fraction. Circ J. 2014;78:2750–9.
50. 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;24:1253–9.
51. Alashi A, Mentias A, Abdallah A, et al. Incremental prognostic utility of left ventricular global longitudinal strain in asymptomatic patients with significant chronic aortic regurgitation and preserved left ventricular ejection fraction. JACC Cardiovasc Imaging. 2018;11:673–82.
52. Kalogeropoulos AP, Samman-Tahhan A, Hedley JS, et al. Progression to stage D heart failure among outpatients with stage C heart failure and reduced ejection fraction. JACC Heart Fail. 2017;5:528–37.
53. Cameli M, Mondillo S, Righini FM, et al. Left ventricular deformation and myocardial fibrosis in patients with advanced heart failure requiring transplantation. J Card Fail. 2016;22:901–7.
54. Chimura M, Onishi T, Tsukishiro Y, et al. Longitudinal strain combined with delayed-enhancement magnetic resonance improves risk stratification in patients with dilated cardiomyopathy. Heart. 2017;103:679–86.
55. Reant P, Mirabel M, Lloyd G, et al. Global longitudinal strain is associated with heart failure outcomes in hypertrophic cardiomyopathy. Heart. 2016;102:741–7.
56. Haugaa KH, Goebel B, Dahlslett T, et al. Risk assessment of ventricular arrhythmias in patients with nonischemic dilated cardiomyopathy by strain echocardiography. J Am Soc Echocardiogr. 2012;25:667–73.
57. Debonnaire P, Thijssen J, Leong DP, et al. Global longitudinal strain and left atrial volume index improve prediction of appropriate implantable cardioverter defibrillator therapy in hypertrophic cardiomyopathy patients. Int J Cardiovasc Imaging. 2014;30:549–58.