Journal of Echocardiography
https://doi.org/10.1007/s12574-022-00576-7

ORIGINAL INVESTIGATION

Association between cardiovascular risk factors and left ventricular strain distribution in patients without previous cardiovascular disease

Tomonori Takahashi[1] · Kenya Kusunose[1] · Robert Zheng[1] · Natsumi Yamaguchi[2] · Yukina Hirata[2] · Susumu Nishio[2] · Yoshihito Saijo[1] · Takayuki Ise[1] · Koji Yamaguchi[1] · Shusuke Yagi[1] · Hirotsugu Yamada[3] · Takeshi Soeki[1] · Tetsuzo Wakatsuki[1] · Masataka Sata[1]

Received: 12 February 2022 / Revised: 31 March 2022 / Accepted: 26 April 2022

Abstract

Background Some cardiovascular (CV) risk factors, such as hypertension and diabetes mellitus, have been reported to reduce left ventricular (LV) longitudinal strain (LS) even in patients with preserved LV ejection fraction. We hypothesized that multiple CV risk factors might cause changes in myocardial strain. Our study aimed to assess the association between multiple CV risk factors and strain in patients without previous CV disease (CVD).

Methods We retrospectively evaluated 137 patients without CVD, who underwent echocardiography at our institution between May 2017 and February 2020. They were divided into four groups based on the number of risk factors (group 0: no risk factor, group 1: one risk factor, group 2: two risk factors, and groups 3: three or four risk factors). Risk factors were hypertension, dyslipidemia, diabetes mellitus, and chronic kidney disease. Absolute values of global LS (GLS) and relative apical LS ratio (RALSR) defined using the equation: average apical LS/(average basal LS + average mid LS) and was used as a marker of strain distribution.

Results Out of 137 patients, group 0 had 35 patients, group 1 had 35 patients, group 2 had 32 patients, and group 3 had 35 patients. GLS was 22.4 ± 2.0%, 21.7 ± 2.1%, 21.3 ± 1.8%, 20.7 ± 2.2%, and RALSR was 0.64 ± 0.06, 0.66 ± 0.06, 0.68 ± 0.08, 0.69 ± 0.07 in groups 0–3, respectively. The one-way ANOVA detected significant differences between groups in GLS ($p = 0.005$) and RALSR ($p = 0.037$), respectively. Group 3 had a significantly lower GLS and higher RALSR than group 0 ($p < 0.05$).

Conclusion In patients without previous CVD, LS decreased especially from the basal segment as the number of cardiovascular risks increased. The segmental LS may be markers of occult LV dysfunction in patients with CV risk factors.

Keywords Echocardiography · Strain · Risk factors · Systolic function

Introduction

Cardiovascular (CV) risk factors are highly prevalent in an aging society, and their management remains an essential factor of CV disease (CVD) [1, 2]. It is well known that CVD is generally a chronic process with atherosclerosis-driven pathophysiology [3]. Plaque formation has been demonstrated to occur more than 20 years prior to the onset of cardiovascular symptoms. Thus, subclinical alterations in cardiac structure and function might develop in patients with CV risk factors. On the other hand, the impact of multiple CV risk factors on subclinical dysfunction of the heart is not well understood.

Quantitative assessment of myocardial deformation is an emerging field of clinical cardiac imaging. Strain imaging is a reproducible and widely used technique for measuring left ventricular (LV) longitudinal deformation. In hypertensive and diabetic patients, global longitudinal strain (GLS) and regional strain were found to be reduced, even when LV ejection fraction was preserved [4–6]. A recent clinical study

✉ Kenya Kusunose
kusunosek@tokushima-u.ac.jp

[1] Department of Cardiovascular Medicine, Tokushima University Hospital, 2-50-1 Kuramoto, Tokushima, Japan

[2] Ultrasound Examination Center, Tokushima University Hospital, Tokushima, Japan

[3] Department of Community Medicine for Cardiology, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan

Published online: 13 May 2022

using speckle tracking imaging showed significant differences in regional strain through several cardiomyopathies, even in the absence of ischemia. The LV strain distribution patterns can be helpful in diagnosing contractile pericarditis, cardiac amyloidosis, hypertrophic cardiomyopathy, and hypertensive heart disease [7–11]. The distribution pattern might be used to identify potential LV dysfunction. We hypothesized that multiple CV risk factors could cause changes in GLS and local strain distribution patterns. This study aimed to evaluate the association between multiple CV risk factors and LS parameters in patients without a history of CVD.

Materials and methods

Study population

We designed a retrospective observational study to assess the association between multiple CV risk factors and GLS in patients without previous CVD. Patients were referred to our echocardiographic examination center between May 2017 and February 2020. Figure 1 shows the selection of eligible patients and enrollment process. The exclusion criteria were as follows: patients with cancer, cerebrovascular disease, collagen disease, and known cardiovascular diseases. We defined each cardiovascular disease was as follows: cardiac arrhythmia, coronary artery disease, more than mild valvular heart disease, and cardiomyopathy. Subjects were also excluded if they had poor echocardiographic images. One hundred thirty-seven patients fulfilled all criteria for the final analysis. This study was approved by the local ethics committee and Institutional Review Board.

Clinical characteristics

We evaluated the overlap of four risk factors: hypertension, dyslipidemia, diabetes, and chronic kidney disease. Hypertensive patients were defined as those with a systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or individuals receiving antihypertensive medications. Dyslipidemia patients were defined as those with a low-density lipoprotein cholesterol (LDL-C) level ≥ 140 mg/dL, a triglyceride level ≥ 150 mg/dL, a high-density lipoprotein cholesterol (HDL-C) level < 40 mg/dL, or individuals receiving lipid-lowering medications. Diabetic patients were defined as individuals receiving insulin or oral hypoglycemic agents, or those with a glycated hemoglobin (HbA1c) level ≥ 6.5%, fasting plasma glucose level ≥ 126 mg/dL, or non-fasting plasma glucose level ≥ 200 mg/dL. CKD patients were defined as those with proteinuria level ≥ 0.15 g/gCr or albuminuria level ≥ 30 mg/

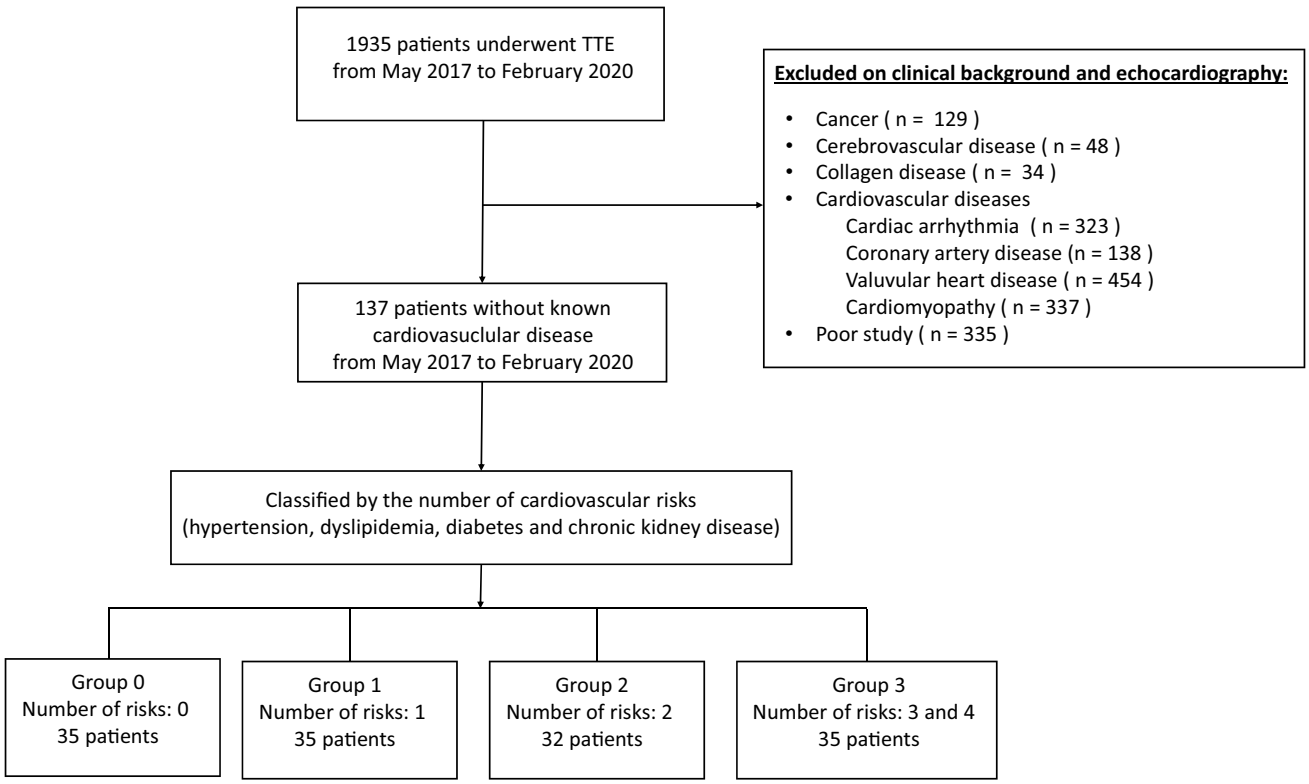

Fig. 1 Patient selection. *TTE* transthoracic echocardiography

gCr, and/or glomerular filtration rate (GFR) < 60 ml/min/1.73 m^2 for at least 3 months. Patients were divided into four groups based on the number of risk factors (group 0: no risk factor, group 1: one risk factor, group 2: two risk factors, and groups 3: three or four risk factors).

Echocardiographic assessment

Transthoracic echocardiography was performed by experienced sonographers/doctors using a commercially available ultrasound machine (EPIQ7G, Philips Healthcare, Amsterdam, the Netherlands) equipped with a 2.5 MHz phased-array transducer. Measurements and recordings were obtained according to the American Society of Echocardiography recommendations [12, 13]. LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), left atrial volume (LAV), and LVEF were calculated by the biplane method of disks using two-dimensional images and indexed to body surface area. The early diastolic (*e*') mitral annular tissue velocity was also measured in the apical four-chamber view. The sample volume was positioned at the lateral and septal mitral annulus, and average *e*' velocity was computed. The trans-tricuspid pressure gradient (TRPG) was calculated by the modified Bernoulli's equation using maximal continuous-wave Doppler velocity of the tricuspid regurgitant (TR) jet. Tricuspid annular plane systolic excursion (TAPSE) was measured as the distance of systolic movement of the junction between the tricuspid valve and the RV free wall using M-mode following current guidelines. The wall motion score index (WMSi) was calculated as the average of all segments visualized LV wall motion that was analyzed individually in multiple views. The following scoring system was used: (1) normal or hyperkinetic, (2) hypokinetic (reduced thickening), (3) akinetic (absent or negligible thickening), and (4) dyskinetic (systolic thinning or stretching).

Strain echocardiography

Peak systolic LS measurements were obtained from gray-scale images recorded in the apical four-chamber, two-chamber, and long-axis views. The frame rate was maintained at a level of > 50 frame/s. LV strain was analyzed offline using speckle tracking software (IntelliSpace Cardiovascular R1.2, Philips Healthcare, Amsterdam, The Netherlands). Good image quality was defined as having clear endocardial border detection throughout the cardiac cycle, and regions of interest at the apex and annulus were ensured. After manual definition of the LV endocardial border, the endocardium was automatically tracked throughout the cardiac cycle. The software algorithm automatically divided the LV apical view into six segments for speckle tracking throughout the cardiac cycle. Global LS (GLS) was obtained by averaging all segmental strain values from the apical four-chamber, two-chamber, and long-axis views. Strain values for the six basal, six mid, and five apical segments of the LV were averaged to obtain regional LS values (basal, mid, and apical, respectively) [13, 14]. Relative apical LS ratio (RALSR) was calculated by dividing the apical LS by the sum of the basal and mid LS values [9]. These offline analyses were independently performed by one expert observer who was not involved in the image acquisition and had no knowledge of examination dates and other echocardiographic or clinical data.

Statistical analysis

For continuous variables, the normality of distribution was assessed using the Shapiro–Wilk test. Variables with normal distributions were presented as mean values ± standard deviation, otherwise as medians and the lower and upper quantile ($Q1$–$Q3$). The categorical data were presented as the percentage and number of patients. Statistical significance of differences between the groups was assessed using the Student's *t* test for data with normal distribution. The Mann–Whitney *U* test was used for data that were not normally distributed. For categorical variables, the Fisher's exact test was used. When equality of variance was found between each group using the Levene's test, one-way general linear model analysis of variance, followed by Tukey–Kramer post hoc test analysis was used to assess the difference between parameters in patients with CVD risks versus without CVD risks. The Kruskal–Wallis followed by Conover post hoc test was used for data that were not equal of variance between groups. Statistical analysis was performed using standard statistical software packages (MedCalc Software 17; Mariakerke, Belgium). Statistical significance was defined by $p < 0.05$.

Results

Clinical characteristics of subjects

Out of 137 patients, group 0 (no risk factors) had 35 patients, group 1 (one risk factor) had 35 patients, group 2 (two risk factors) had 32 patients, and group 3 (three or four risk factors) had 35 patients. Baseline characteristics of the study group are presented in Table 1. The mean age of the study sample was 63 ± 15 years, and 48% were male. Age, body mass index, systolic blood pressure, serum urea nitrogen, creatinine, and hemoglobinA1c level, and prevalence of each CVD risk were significantly different between the groups. In terms of the patient's medication status, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, sodium-glucose transport protein 2 inhibitor, statins, oral hypoglycemic agent were different between the groups.

Table 1 Clinical characteristics

Variable	All ($n=137$)	Group 0 ($n=35$)	Group 1 ($n=35$)	Group 2 ($n=32$)	Group 3 ($n=35$)	p value for trend
Demographics						
Age, years	63 ± 15	53 ± 17	65 ± 14*	65 ± 12*	67 ± 12*	0.005
Male sex, *n* (%)	66 (48)	13 (37)	18 (51)	16 (50)	19 (54)	0.186
Clinical						
Systolic BP, mmHg	130 ± 22	122 ± 21	133 ± 24	128 ± 19	136 ± 24*	0.049
Diastolic BP, mmHg	74 ± 13	73 ± 11	74 ± 13	74 ± 11	76 ± 17	0.864
Heart rate, beats/min	69 ± 14	69 ± 12	69 ± 12	70 ± 13	68 ± 17	0.913
Hypertension, *n* (%)	89 (65)	0 (0)	25 (71)	30 (94)	34 (97)	< 0.001
Diabetes mellitus, *n* (%)	47 (34)	0 (0)	3 (9)	17 (53)	27 (77)	< 0.001
Dyslipidemia, *n* (%)	43 (31)	0 (0)	4 (11)	10 (31)	29 (83)	< 0.001
Chronic kidney disease, *n* (%)	30 (22)	0 (0)	3 (9)	7 (22)	20 (57)	< 0.001
Laboratory data						
BUN, mg/dL	14 (11–17)	12 (11–15)	13 (11–17)	16 (11–18)*	17 (13–23)*	< 0.001
Cre, mg/dL	0.77 (0.61–0.93)	0.67 (0.58–0.79)	0.70 (0.59–0.87)	0.78 (0.66–0.91)	0.95 (0.73–1.12)*	< 0.001
eGFR, mL/min/1.73	71 (58–83)	81 (68–87)	74 (63–79)	69 (59–79)*	54 (40–78)*	< 0.001
HbA1c, %	5.8 (5.6–6.4)	5.6 (5.3–5.7)	5.7 (5.6–6.0)*	6.1 (5.7–6.6)*	6.3 (5.8–7.2)*	< 0.001
BNP, pg/mL	23.5 (10.8–42.7)	27.0 (5.9–46.9)	20.1 (14.3–34.1)	17.3 (8.2–28.5)	33.8 (16.6–51)	0.139
Medication						
ACE-I/ARB	56 (41)	0 (0)	15 (43)	20 (63)	21 (60)	< 0.001
β-Blocker	8 (6)	0 (0)	2 (6)	3 (9)	3 (9)	0.100
SGLT-2i	6 (4)	0 (0)	0 (0)	1 (3)	5 (14)	0.003
CCB	65 (47)	0 (0)	20 (57)	25 (78)	20 (57)	< 0.001
Statin	30 (22)	0 (0)	5 (14)	7 (22)	18 (51)	< 0.001
OHA	30 (22)	0 (0)	1 (3)	10 (31)	19 (54)	< 0.001

BP blood pressure, *BUN* blood urea nitrogen, *Cre* creatinine, *eGFR* estimated glomerular filtration rate, *HbA1c* hemoglobin A1c, *BNP* brain natriuretic peptide, *ACE-I* angiotensin-converting enzyme inhibitor, *ARB* angiotensin II receptor blocker, *SGLT2i* sodium glucose cotransporter 2 inhibitor, *CCB* calcium channel blocker, *OHA* oral hypoglycemic agent

*$p < 0.05$, each group versus group 0

Conventional echocardiographic parameters

Baseline echocardiographic assessments of the study group are presented in Table 2. Left ventricular mass index (LVMi) was significantly different between the groups. There was no significant difference between the groups for the other conventional echocardiographic variables, including left atrial size, ejection fraction, and diastolic parameters. The wall motion score was one in all groups, because cases with regional wall motion abnormalities were excluded at the enrollment stage.

Strain measurements and evaluation of regional strain

The overall mean GLS of the study was 21.5 ± 2.1%, and the mean GLS in groups 0 to 3 was 22.4% ± 2.0%, 21.7% ± 2.1%, 21.3% ± 1.8%, 20.7% ± 2.2%, respectively. The one-way ANOVA detected significant differences between groups in GLS (F (3,133) = 4.438, $p = 0.005$).

Figure 2 demonstrates the typical patterns of regional strain seen in the different groups (group 0 and group 3) classified by the number of cardiovascular risks included in this study. The patient in group 3 shows a reduction in basal segmental LS compared to a patient from group 1. There were significant differences between groups in basal segment (F (3,133) = 9.212, $p < 0.001$) but no significant differences between groups in apical segment (F (3,133) = 1.314, $p < 0.272$). The average RALSR was 0.64 ± 0.06, 0.66 ± 0.06, 0.68 ± 0.08, 0.69 ± 0.07 in group 0–3, respectively. The one-way ANOVA also detected significant differences between groups in RALSR (F (3,133) = 2.908, $p = 0.037$). Group 3 had a significantly higher RALSR than group 0, after post hoc Tukey–Kramer test ($p < 0.05$). We also examined which of the four CV risk factors was most associated with RALSR. After adjustment of age, hypertension was the most associated with RALSR (standardized coefficients β 0.223, $p = 0.014$).

Figure 3 shows the ratio of the average value of LS for each of the 17 segments between group 0 and groups 1–3. In group

Table 2 Echocardiographic parameters

Variable	All ($n=137$)	Group 0 ($n=35$)	Group 1 ($n=35$)	Group 2 ($n=32$)	Group 3 ($n=35$)	p value for trend
LVMi, g/m^2	74.4 ± 13.3	67.5 ± 10.2	75.1 ± 13.4	79.0 ± 15.1*	76.4 ± 11.9*	0.002
RWT	0.36 ± 0.05	0.33 ± 0.05	0.35 ± 0.05	0.38 ± 0.05*	0.36 ± 0.04	0.001
LVEDVi, ml/m^3	51.1 ± 10.3	54.0 ± 11.1	51.4 ± 9.3	49.1 ± 9.2	49.6 ± 10.7	0.191
LVESVi, ml/m^3	32.9 ± 6.5	18.8 ± 5.1	18.7 ± 4.1	17.4 ± 4.2	17.8 ± 4.2	0.522
LAVi, ml/m^3	26.6 ± 6.7	24.4 ± 6.3	27.4 ± 7.6	26.4 ± 6.6	28.0 ± 5.8	0.130
LVEF, %	64 ± 4	65 ± 4	64 ± 3	65 ± 4	64 ± 3	0.223
E/e'	8.7 ± 3.2	7.8 ± 2.7	9.1 ± 3.8	8.1 ± 2.9	9.5 ± 3.2	0.112
TRPG, mmHg	20.8 ± 4.2	20.0 ± 3.7	20.4 ± 4.6	21.2 ± 3.6	21.7 ± 4.6	0.499
TAPSE, mm	21.4 ± 3.7	22.5 ± 3.3	21.5 ± 2.7	20.8 ± 5.4	21.0 ± 2.9	0.267
WMSi	1	1	1	1	1	–
GLS, %	21.5 ± 2.1	22.4 ± 2.0	21.7 ± 2.1	21.1 ± 1.8*	20.7 ± 2.2*	0.005
RALSR	0.67 ± 0.07	0.64 ± 0.06	0.66 ± 0.06	0.68 ± 0.08	0.69 ± 0.07*	0.037

LVMi left ventricular mass index, *LVEDVi* left ventricular end-diastolic volume index, *LVESVi* left ventricular end-systolic volume index, *LAVi* left atrial volume index, *LVEF* left ventricular ejection fraction, *TRPG* trans-tricuspid pressure gradient, *TAPSE* tricuspid annular plane systolic excursion, *WMSi* wall motion score index, *GLS* global longitudinal strain, *RALSR* relative apical longitudinal strain ratio

*$p<0.05$, each group versus group 0

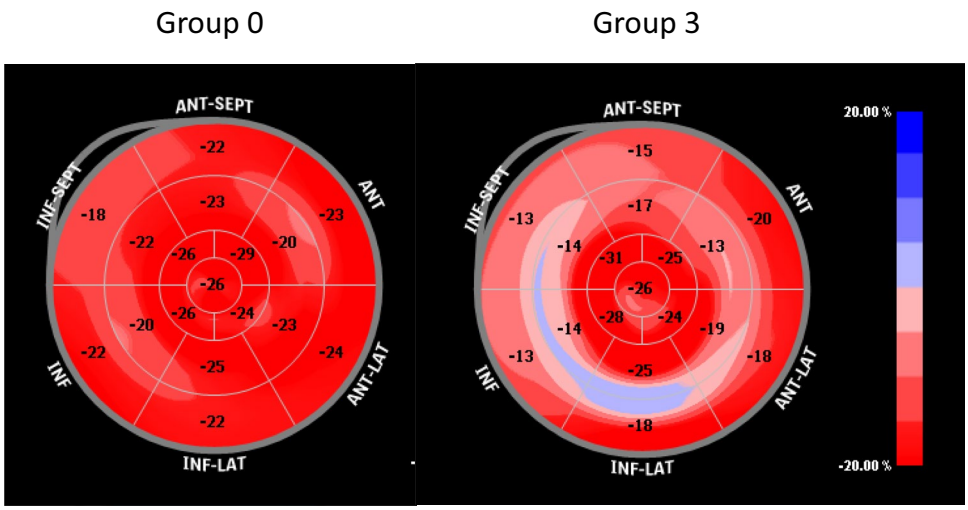

Fig. 2 Representative cases of Group 0 and Group 3 in bull's-eye maps *AFI* automated function imaging

3, seven segments (basal anterior, basal inferoseptal, basal inferior, basal inferolateral, mid inferoseptal, mid inferior, and mid anterolateral) were significantly smaller compared to that in group 0. In groups 1 and 2, two segments (group 1: basal inferoseptal and mid anterolateral, group 2: basal inferior and mid inferoseptal) were significantly smaller compared to group 0. These results showed a greater regional strain reduction from the basal segment of LV, in groups with more CV risk factors.

Discussion

Our study brings several new insights into the understanding of LV strain distribution in patients with CVD risk factors: (1) GLS decreased as the number of cardiovascular risks increased (2) the decrease of LS was more profound in the basal segments of patients with multiple CV risk factors. In clinical practice, this information might be

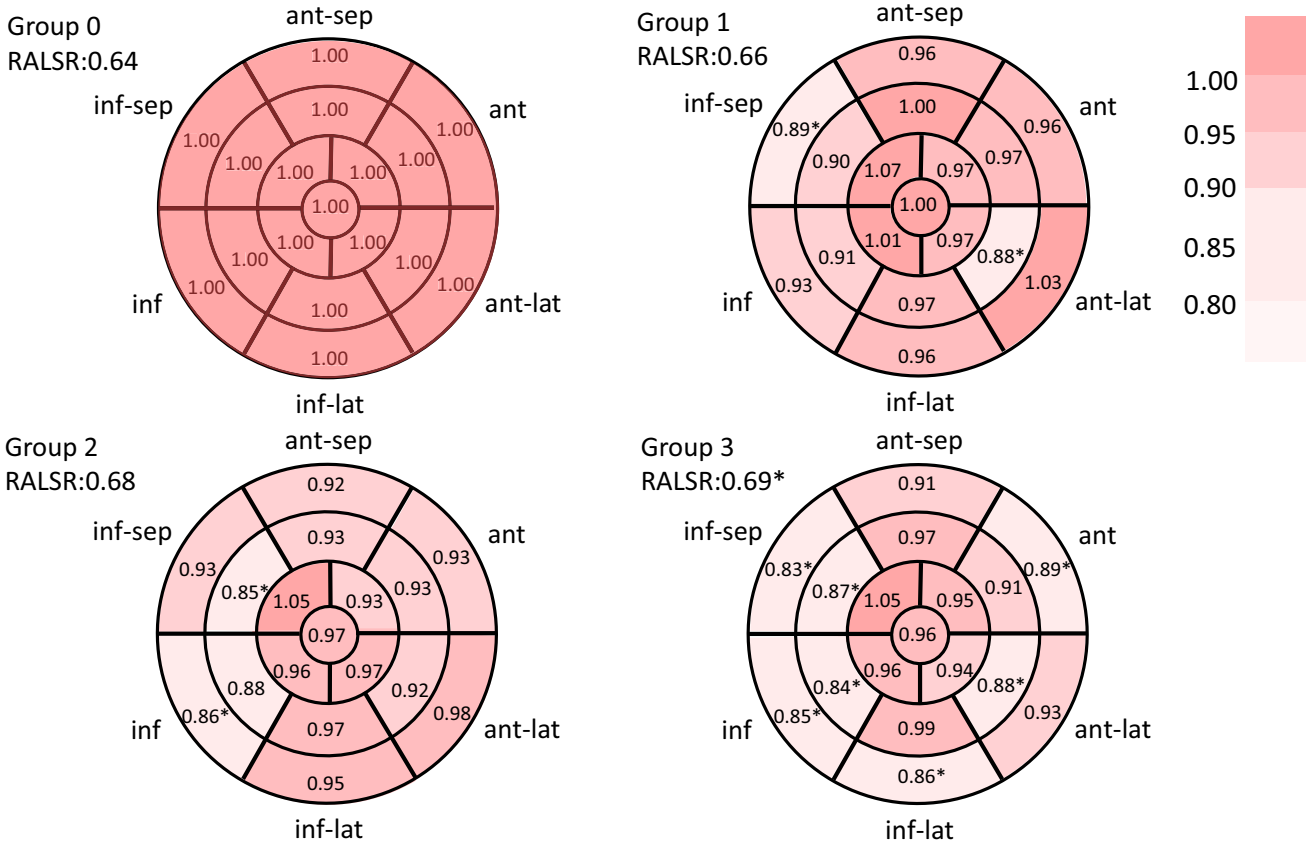

Fig. 3 Strain distribution each bull's-eye map shows the ratio of the local LS mean values for each group compared to group 0. Longitudinal strain; *RALSR*, relative apical LS ratio. *$p < 0.05$, each group versus group 0

useful for the early detection of subclinical LV dysfunction in patients with multiple CV risk factors.

Global longitudinal strain and cardiovascular risk factors

Although LVEF or LV volume were not significantly different in each group, GLS decreased with increased CVD risk. It is known that GLS changes despite preserved LV ejection fraction in conditions that precipitate cardiovascular diseases, such as hypertension, diabetes mellitus, and renal dysfunction. It is reasonable to assume that combining these multiple risk factors could lead to significant changes in GLS. The etiology of this effect on the myocardium is thought to be multifactorial, including microvascular damage, altered myocardial metabolism, structural changes in the myocardium, and increased fibrosis. Microvascular abnormalities commonly found in renal dysfunction or diabetes may be associated with increased resistance in smaller micro vessels. Even in increased medication use for CV risk factors, the GLS was lower in the group with more overlapping CV risks. Thus, the presence of the CV risk factors itself may contribute to the decrease in GLS.

Strain distribution and cardiovascular risk factors

The heterogeneity of LV systolic dysfunction related with CV risk factors has been debated. In asymptomatic diabetes patients with normal LVEF, several reports focused on regional LV longitudinal dysfunction [4, 5]. Reduction of LS in the basal segment was reported in patients with hypertension and LV hypertrophy [6]. In major kidney diseases and Fabry disease, impaired basal strain suggested early myocardial changes even when LV wall thickness was normal [15]. Moreover, this phenomenon was also observed in the COVID-19 infection [16]. Reduced basal LV strain was commonly found in patients with COVID-19. The regional LS reduction may be an early marker of LV dysfunction in several diseases [7–11].

The mechanism of regional LV impairment in these cases has not been precise. But it is assumed to be due to Laplace's law [17]. The cross-sectional radius of curvature in the basal segment is more significant than that of the other segments, and the myocardium and endocardium in the basal segment might be more susceptible to damage by wall stress than the other segments. In addition, some investigators have reported that the increase in myofiber and sheet

shear remodeling in the basal segment was also significantly more significant than in the apical segment as a result of earlier remodeling in response to volume loading [18, 19]. In healthy individuals, these adverse effects are subtle and do not significantly impact cardiac function. These previous findings, along with those of our current study, raise the possibility that this basal injury pattern may reflect the sensitivity of specific myocardial regions to inflammatory or systemic stressors. Further studies are needed to elucidate the pathophysiology of basal LV dysfunction in the context of multiple overlapping factors.

Clinical implications

To the best of our knowledge, this is the first report on strain distribution in patients with multiple CV risk factors. It is well known that mortality is higher when more CV risks are present [20, 21]. Early detection of cardiac dysfunction using the GLS and strain distribution may prove beneficial in the management of patients with multiple CV risk factors. GLS and RALSR may allow for risk stratification of cardiovascular events before echocardiographic abnormalities are detected. Although this study suggests an association between strain distribution and CV risk factors, the results should be verified in a larger cohort.

Limitations

This study was a single-center trial in a selected patient population. The sample size was small. Despite excluding known cardiovascular diseases, the potential impact of other unknown etiologies on myocardial mechanics may not have been avoided. Lack of outcome data is a significant limitation of this study. The strain pattern of decreased RALSR is also commonly observed in cardiac amyloidosis, and the group of patients with decreased RALSR in this study may include potential patients with early cardiac amyloidosis. Based on these limitations, we believe that this study should be considered a proof of concept and that a larger multicenter study is warranted.

Conclusions

In patients without known CVD, LS decreased especially in the basal segment as the number of cardiovascular risks increased. The LS and segmental strains may be markers of occult LV dysfunction in patients with CV risk factors.

Author contributions Design of the work: TT and KK. Conduct of the work and data acquisition: RZ, NY, YH, SN, YS, TI, KY, SY, HY, TS, and TW. Data analysis and interpretation: TT and KK. Drafting the work: TT, KK and RZ. Reviewing the work and providing input: all authors. Final approval: all authors.

Funding This work was supported by Takeda Science Foundation (to K. Kusunose). The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Declarations

Conflict of interest The author declares that they have no conflict of interest.

References

1. Matsuoka M, Inoue T, Shinjo T, et al. Cardiovascular risk profile and frailty in Japanese outpatients: the Nambu Cohort Study. Hypertens Res. 2020;43:817–23.
2. Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2021;143:e984–1010.
3. Lloyd-Jones DM, Braun LT, Ndumele CE, et al. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease: a special report from the American Heart Association and American College of Cardiology. Circulation. 2019;139:e1162–77.
4. Nakai H, Takeuchi M, Nishikage T, Lang RM, Otsuji Y. Subclinical left ventricular dysfunction in asymptomatic diabetic patients assessed by two-dimensional speckle tracking echocardiography: correlation with diabetic duration. Eur J Echocardiogr. 2009;10:926–32.
5. Zoroufian A, Razmi T, Taghavi-Shavazi M, Lotfi-Tokaldany M, Jalali A. 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.
6. Frimodt-Moeller K, Olsen F, Biering-Soerensen S, et al. 3149 Regional strain patterns according to hypertension and left ventricular hypertrophy in the general population. Eur Heart J. 2019;40(ehz745):0037.
7. Phelan D, Thavendiranathan P, Popovic Z, et al. Application of a parametric display of two-dimensional speckle-tracking longitudinal strain to improve the etiologic diagnosis of mild to moderate left ventricular hypertrophy. J Am Soc Echocardiogr. 2014;27:888–95.
8. Kusunose K, Dahiya A, Popovic ZB, et al. Biventricular mechanics in constrictive pericarditis comparison with restrictive cardiomyopathy and impact of pericardiectomy. Circ Cardiovasc Imaging. 2013;6:399–406.
9. Phelan D, Collier P, Thavendiranathan P, et al. Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis. Heart. 2012;98:1442–8.
10. Foell D, Jung B, Germann E, Staehle F, Bode C, Markl M. Hypertensive heart disease: MR tissue phase mapping reveals altered left ventricular rotation and regional myocardial long-axis velocities. Eur Radiol. 2013;23:339–47.
11. Chang SA, Kim HK, Kim DH, et al. Left ventricular twist mechanics in patients with apical hypertrophic cardiomyopathy: assessment with 2D speckle tracking echocardiography. Heart. 2010;96:49–55.

12. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr. 2010;23:685–713 ((**quiz 786-8**)).
13. 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.
14. Kusunose K, Zhang Y, Mazgalev TN, Thomas JD, Popovic ZB. Left ventricular strain distribution in healthy dogs and in dogs with tachycardia-induced dilated cardiomyopathy. Cardiovasc Ultrasound. 2013;11:43.
15. Zada M, Lo Q, Boyd AC, et al. Basal segmental longitudinal strain: a marker of subclinical myocardial involvement in Anderson-Fabry disease. J Am Soc Echocardiogr. 2021;34(405–413): e2.
16. Goerlich E, Gilotra NA, Minhas AS, Bavaro N, Hays AG, Cingolani OH. Prominent longitudinal strain reduction of basal left ventricular segments in patients with coronavirus disease-19. J Card Fail. 2021;27:100–4.
17. Basford JR. The law of Laplace and its relevance to contemporary medicine and rehabilitation. Arch Phys Med Rehabilit. 2002;83:1165–70.
18. Badke FR, Covell JW. Early changes in left ventricular regional dimensions and function during chronic volume overloading in the conscious dog. Circ Res. 1979;45:420–8.
19. Ashikaga H, Omens JH, Covell JW. Time-dependent remodeling of transmural architecture underlying abnormal ventricular geometry in chronic volume overload heart failure. Am J Physiol Heart Circ Physiol. 2004;287:H1994-2002.
20. Li D, Jia Y, Yu J, et al. Adherence to a healthy lifestyle and the risk of all-cause mortality and cardiovascular events in individuals with diabetes: the ARIC study. Front Nutr. 2021;8: 698608.
21. Barr EL, Zimmet PZ, Welborn TA, et al. Risk of cardiovascular and all-cause mortality in individuals with diabetes mellitus, impaired fasting glucose, and impaired glucose tolerance: the Australian Diabetes, Obesity, and Lifestyle Study (AusDiab). Circulation. 2007;116:151–7.