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ORIGINAL PAPER

Initial application of three-dimensional speckle-tracking echocardiography to detect subclinical left ventricular dysfunction and stratify cardiomyopathy associated with Duchenne muscular dystrophy in children

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Abstract
Three-dimensional (3D) speckle-tracking echocardiography (STE) is a new imaging modality used for quantitative analysis of left ventricular (LV) function. The aim of this study is to assess the value of 3D STE in early detection of subclinical myocardial involvement in children with Duchenne muscular dystrophy (DMD). Fifty-six children with DMD (mean age, 8.8 ± 1.9 years) and 31 age-matched control subjects were studied. Patients were subdivided into two groups by age: ≤ 8 or > 8 years. Standard echocardiography examinations were performed to measure LV size and ejection fraction (EF). 3D STE was performed to assess LV 3D global strain and LV end-diastolic volume (EDV), end-systolic volume (ESV), and EF. Standard and 3D echocardiography measures were compared between children with DMD and those in the control group as well as between different patient groups. The areas under the receiver-operating characteristic (ROC) curve were calculated to determine the capability of 3D global strain indices to discriminate between patients and control subjects. No significant difference was detected in either LVEF derived from M-mode or 3D echocardiography between the two groups, and they were both within the normal range. Compared with control subjects, children with DMD had significantly reduced LV 3D global longitudinal strain (GLS; − 16.6 ± 4.7 vs. − 19.5 ± 3.7, $p = 0.003$), global circumferential strain (GCS; − 13.7 ± 2.9 vs. − 15.8 ± 2.6, $p = 0.001$), global radial strain (GRS; 42.5 ± 9.7 vs. 50.3 ± 10.4, $p = 0.001$), and global area strain (GAS; − 25.3 ± 4.9 vs. − 30.7 ± 4.1, $p = 0.000$). The older DMD children (age > 8 years) had lower GLS (− 15.1 ± 4.43 vs. − 18.6 ± 4.35, $p < 0.05$), GCS (− 12.8 ± 3.48 vs. − 14.8 ± 2.83, $p < 0.001$), GAS (− 23.8 ± 4.7 vs. − 29.0 ± 5.4, $p < 0.001$), and GRS (40.7 ± 8.8 vs. 47.3 ± 11.5, $p < 0.05$) than younger patients (age ≤ 8 years). The AUC of GAS was 0.80, and the cutoff value of − 29.5 had a sensitivity of 85.7% and a specificity of 71.0% for differentiating DMD patients from control. 3D speckle-tracking echocardiography is useful for detecting subclinical myocardial dysfunction and stratifying cardiomyopathy in children with DMD.

Keywords Three-dimensional speckle-tracking echocardiography · Cardiomyopathy · Duchenne muscular dystrophy · Area strain · Children

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Introduction

Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder dystrophy occurring in approximately 1 of every 3500 live-born males [1]. It is caused by muscle dystrophin deficiency, which is due to translational reading-frame shift or nonsense mutations in the dystrophin gene. The glycoprotein structure of the muscle sarcolemma is less stable without dystrophin. Membrane instability initially leads to muscle inflammatory cascade contributing further to muscle damage, necrosis, and fibrosis [2]. Because dystrophin is expressed not only in skeletal muscle but also in heart, cardiac involvement is an integral part of DMD. All patients with DMD are at risk of developing dilated cardiomyopathy and frequently manifest congestive heart failure. Clinically apparent DMD cardiomyopathy starts in the first decade of life [3]. However, preclinical cardiac involvement is present at less than 6 years of age, with persistent tachycardia commonly noted [4]. DMD-associated cardiomyopathy is the leading cause of death in DMD patients because the use of corticosteroids and supportive respiratory care has improved noncardiac outcomes [5]. The prevalence of cardiomyopathy increases with age in DMD patients, but early manifestations of decrease in cardiac function often go unrecognized because of a lack of classic signs and symptoms [6]. Previous investigators have demonstrated that early detection of myocardial dysfunction in the subclinical phase may facilitate timely intervention [7]. Hence, identification of early cardiac involvement in DMD patients is important.

Echocardiography is the main imaging modality for the assessment of left ventricular (LV) function in children with DMD. However, functional abnormalities are rarely detected by traditional echocardiography during the first decade of life [8]. Although studies have shown some new technology of echocardiography [9, 10] and magnetic resonance imaging (MRI) [11] for the early detection of impaired cardiac function, these new methods have their limitations, such as angle dependence of tissue Doppler imaging, failure to track speckles moving out of the two-dimensional (2D) planes of 2D strain, great monetary cost, and the large amount of time needed to perform MRI. Recent investigators have reported that three-dimensional (3D) speckle-tracking echocardiography (STE) is effective for noninvasively quantifying LV deformation [12–14]. The aim of this study was to investigate the value of 3D STE in the early detection of subtle myocardial dysfunction in children with DMD.

Methods

Subjects

Sixty-two children with DMD who were admitted to Shenzhen Children's Hospital were initially recruited. Of the 62 patients, 56 (90.3%) with quality LV 3D echocardiography data were included in the final analysis. None of the patients had cardiac symptoms at the time of study or a history of taking drugs to improve cardiac function. The diagnosis of DMD was confirmed by analysis of DNA through muscle biopsy that showed a characteristic dystrophin mutation in all patients. The patients were divided into two groups according to age: ≤ 8 years ($n=25$) or >8 years ($n=31$). Thirty-one control subjects were studied. All the control subjects were free of cardiac disease and medical illnesses affecting cardiac function, and were screened by history and physical examination. The body weight and height of all subjects were measured, and the body surface area was calculated accordingly. The ethical committee of Shenzhen Children's Hospital approved the study, and all patients and their parents gave informed written consent.

Standard 2D echocardiography examinations

Transthoracic standard 2D echocardiography examination was performed in all subjects with a M5S-D probe using a Vivid E9 system (GE Healthcare, USA). Images of the left ventricles were obtained from an apical or parasternal view with patients lying in the left lateral decubitus position. Three consecutive cardiac cycles were stored in cine loop format for analysis. LV end-diastolic inner diameter, LV end-systolic inner diameter, and left atria diameter were measured according to the recommendation of the American Society of Echocardiography. LV ejection fraction (LVEF) was measured by Simpson biplane method using the apical four-chamber view and two-chamber view.

Three-dimensional STE assessment

Real-time 3D echocardiography imaging was performed with an active matrix 3D-volume phased array probe (4V-D, 1.5–4.0 MHz, GE Healthcare). Volumetric data acquisition was performed from an apical window using the full-volume mode, in which sequential acquisition of narrow subvolumes were scanned during four consecutive heart beats without moving the transducer. These subvolumes were subsequently stitched together to form an entire pyramidal data set. The minimum frame rate (volume/s) was no less than 30 for reliable recognition of speckles. The sector width was adjusted to ensure that the entire LV cavity was included within the full-volume data set. Data sets were stored digitally in raw data format.

Offline analysis of the data sets was performed by the 4D-LVQ method using EchoPAC PC software (GE Healthcare). Triplanes were displayed for tracing of the endocardium and epicardium on the basis of the 3D volume data set. The LV epicardium and endocardium were traced semiautomatically with refinement by further manual adjustments. After generation of the left ventricle 3D cast, the LV end-systolic and end-diastolic volumes and EF were derived automatically. After LV volumes and EF measurements, an automatic trace of the epicardial border was displayed to identify the region of interest required for LV mass and myocardial deformation measurements. The left ventricle was further automatically divided into 17 segments. On the basis of the time-strain curves for each of the LV segments, the software provided four global and segmental 3D strain components: longitudinal strain, circumferential strain, radial strain, and area strain, and a color-coding 17-segment bull's-eye. Segmental data were not analyzed. The 3D volume data set was analyzed by two expert sonographers who were blinded to clinical data.

Intra- and inter-observer reproducibility

Twenty randomly selected subjects (10 patients and 10 control subjects) were analyzed offline at different times for intra- and inter-observer variability. Blinding was ensured by measuring the 3D global strain parameters using selected data sets on different days by the same observer for intraobserver variability and by independent assessments by two observers for interobserver variability.

Statistical analysis

All data are expressed as mean ± SD. The LV size and volumes were normalized by body surface area. Differences in demographic and echocardiography parameters between patients and control subjects and different patient groups were compared using unpaired Student's *t* test. The area under the receiver-operating characteristic (ROC) curve was calculated to determine the capability of various echocardiography indices to discriminate between patients and control subjects. Interobserver and intraobserver variability of 3D echocardiography indices were examined using the intraclass correlation coefficient and Bland–Altman analysis. Two-tailed p values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS version 19.0 (SPSS, Inc., Chicago, IL).

Results

Subjects and 2D echocardiography parameters

Data from 56 children with DMD (aged 8.8 ± 1.9 years) and 31 control subjects (aged 8.4 ± 1.8 years) were collected for this study. Demographic data and 2D echocardiographic parameters of the DMD patients and control subjects were not significantly different (Table 1).

3D STE parameters

No significant difference was detected in 3D LVEF between the two groups, and they were both in the normal range. Compared with control subjects, children with DMD had significantly reduced LV 3D global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), and global area strain (GAS) (Fig. 1). Table 2 summarizes the 3D STE parameters of patients and control subjects. Representative illustrations of reduced LV 3D GLS, GCS, GRS, and GAS in a patient compared with a control subject are shown in Fig. 2. The older children with DMD (age > 8 years) had lower 3D global strains than younger patients (age ≤ 8 years), but there was no significant difference in LVEF (61.9 ± 3.6 vs. 62.3 ± 3.0, $p > 0.05$) between the two groups (Table 3).

Table 1 Comparisons of demographic data and 2D echocardiography parameters between DMD patients and control subjects

Parameter	Patients (n = 56)	Control subjects (n = 31)	p
Age (year)	8.8 ± 1.9	8.4 ± 1.8	0.27
Height (cm)	128.6 ± 10.1	132.1 ± 10.4	0.14
Weight (kg)	27.9 ± 6.6	28.9 ± 7.2	0.49
BSA (m^2)	0.99 ± 0.14	1.02 ± 0.15	0.28
LVEDD (mm)/m^2	38.2 ± 4.6	36.4 ± 4.4	0.09
LVESD (mm)/m^2	25.4 ± 3.7	24.6 ± 2.4	0.27
LAD (mm)/m^2	21.7 ± 3.7	22.4 ± 4.1	0.73
LVEF	62.1 ± 3.3	60.9 ± 4.5	0.18

BSA body surface area, *EDD* end-diastolic inner diameter, *ESD* end-systolic inner diameter, *LAD* left atria diameter, *LV* left ventricular, *LVEF* LV ejection fraction

ROC analysis

Table 4 summarizes the ROC analyses of 3D GLS, GCS, GRS, and GAS to detect patients and control subjects. The areas under the curve (AUCs) of GAS, GRS, GLS, and GCS were 0.80, 0.74, 0.71, and 0.70, respectively. Of all the parameters, GAS had the greatest area under the ROC curve (Fig. 3). The GAS cutoff of − 29.5 had a sensitivity of 85.7% and a specificity of 71.0% in differentiating patients from control subjects.

Intra- and inter-observer variability

The reproducibility of 3D strain measurements was determined in 20 randomly selected subjects, including 10 patients and 10 control subjects. Figure 4 shows the Bland–Altman analysis graphs of 3D global strain. The intraclass correlation coefficients of intra- and inter-observer variability for GLS were 0.853 (95% confidence interval [CI] 0.628–0.942, $p < 0.001$) and 0.815 (95% CI 0.532–0.927, $p < 0.001$), for GCS were 0.810 (95% CI 0.521–0.925, $p < 0.001$) and 0.809 (95% CI 0.517–0.924, $p < 0.001$), for GRS were 0.843 (95% CI 0.647–0.935, $p < 0.001$) and 0.807 (95% CI 0.575–0.919, $p < 0.001$), and for GAS were 0.896 (95% CI 0.737–0.959, $p < 0.001$) and 0.892 (95% CI 0.728–0.957, $p < 0.001$).

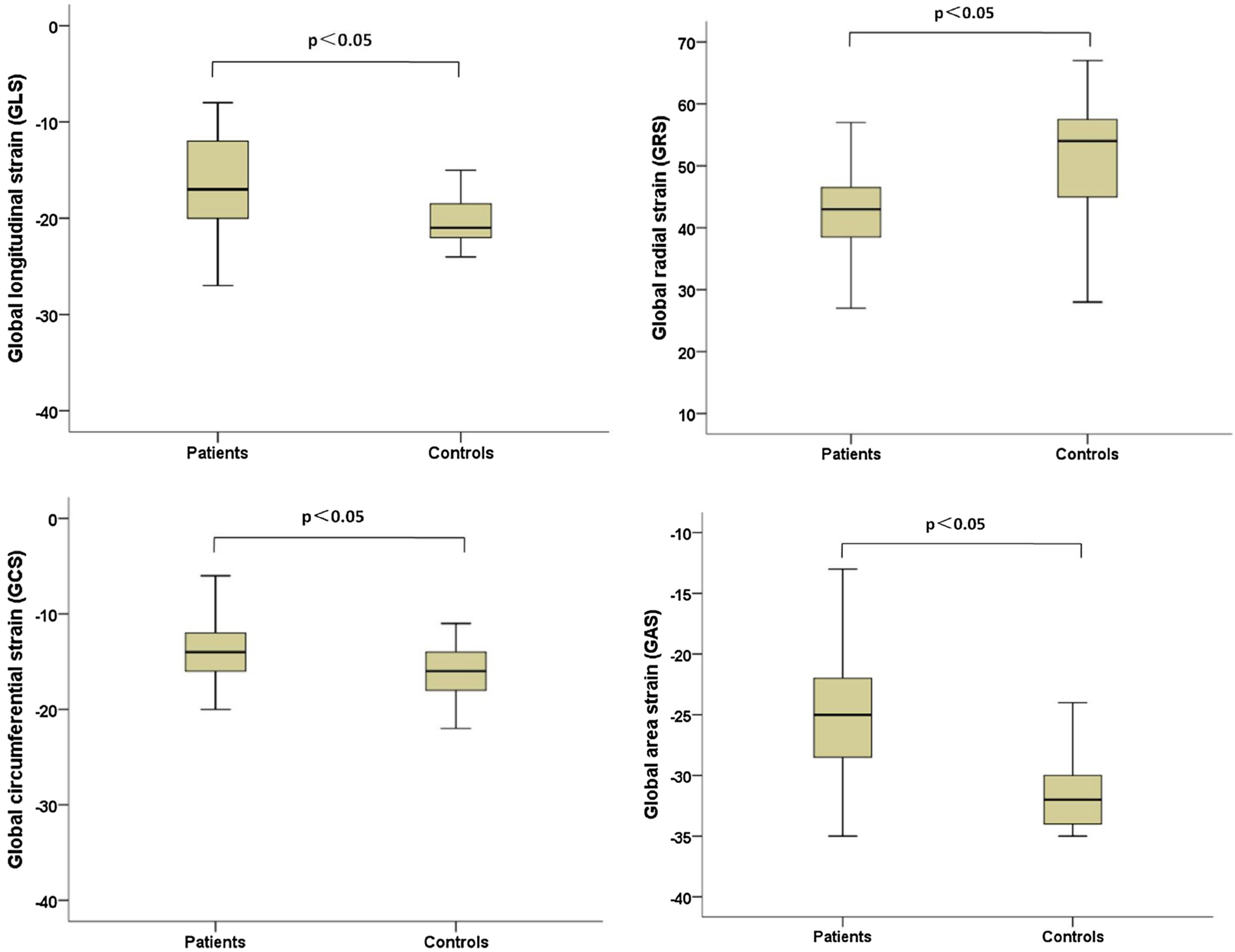

Fig. 1 Three-dimensional (3D) global longitudinal strain (GLS), 3D global radial strain (GRS), 3D global circumferential strain (GCS), and 3D global area strain (GAS) of the left ventricles in patients and control subjects

Table 2 3D speckle tracking echocardiography indices in patients and control subjects

Parameter	Patients (n = 56)	Control subjects (n = 31)	p
LV EDV (ml/m^2)	49.1 ± 6.3	49.1 ± 5.6	0.99
LV ESV (ml/m^2)	19.5 ± 3.5	20.0 ± 2.9	0.49
3D-LVEF (%)	60.1 ± 4.5	60.0 ± 4.2	0.90
GLS (%)	− 16.6 ± 4.7	− 19.5 ± 3.7	0.003*
GCS (%)	− 13.7 ± 2.9	− 15.8 ± 2.6	0.001*
GRS (%)	42.5 ± 9.7	50.3 ± 10.4	0.001*
GAS (%)	− 25.3 ± 4.9	− 30.7 ± 4.1	0.000*

3D-LVEF left ventricular ejection fraction derived from 3D speckle tracking echocardiography, *EDV* end-diastolic volume, *ESV* end-systolic volume, *GAS* global area strain, *GCS* global circumferential strain, *GLS* global longitudinal strain, *GRS* global radial strain, *LV* left ventricular

*Statistically significant

Discussion

In the present study, our findings showed impairment of global myocardial deformation in the left ventricle using 3D STE in children with DMD despite normal LVEF. Another important finding of this study was that older (≥ 8 years) patients with DMD had lower 3D strain values. The ROC analyses showed that 3D global strains had high sensitivity and specificity for differentiating patients from control subjects.

The decline of LV function in children with DMD is caused by corresponding pathological changes. Histologic changes in the hearts of DMD patients have been identified as fibrosis, degeneration, and fatty infiltration [2, 15]. Cardiac magnetic resonance has been used to confirm myocardial fibrosis in DMD patients [16]. As is well known, the pathogenesis of DMD is loss of membrane integrity leading to degeneration of myocytes; intermittent tears in the

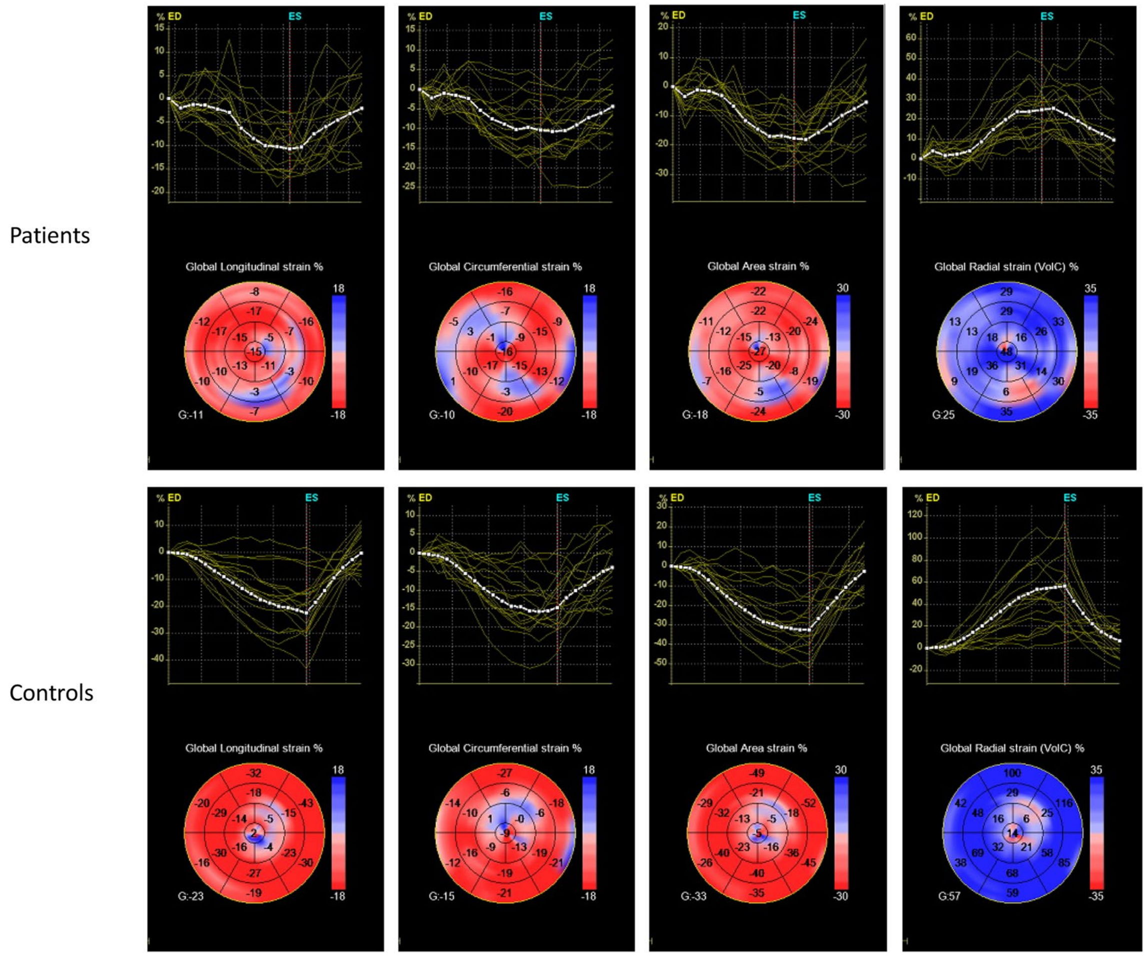

Fig. 2 Representative curves and bull's-eyes of left ventricular three-dimensional (3D) global strain GLS, GCS, GRS, and GAS in a patient and a control subject. Reduced strain (upper panel) was illustrated in the curves derived from the patient. *GAS* global area strain, *GCS* global circumferential strain, *GLS* global longitudinal strain, *GRS* global radial strain

Table 3 3D speckle tracking Echocardiography indices in older and younger DMD patients

Parameter	Older patients (n = 23)	Younger patients (n = 33)	p
3D-LVEF (%)	61.9 ± 3.6	62.3 ± 3.0	0.56
GLS (%)	− 15.1 ± 4.43	− 18.6 ± 4.35	0.004*
GCS (%)	− 12.8 ± 3.48	− 14.8 ± 2.83	0.025*
GAS (%)	− 23.8 ± 4.7	− 29.0 ± 5.4	0.000*
GRS (%)	40.7 ± 8.8	47.3 ± 11.5	0.009*

3D-LVEF left ventricular ejection fraction derived from 3D speckle tracking echocardiography, *EDV* end-diastolic volume, *ESV* end-systolic volume, *GAS* global area strain, *GCS* global circumferential strain, *GLS* global longitudinal strain, *GRS* global radial strain, *LV* left ventricular

*Statistically significant

cell membrane permit influx of calcium that then functions as a primary inducer of a destructive cascade, culminating in myocyte necrosis and replacement fibrosis [17–19]. In a word, these processes lead to progressive cardiac dysfunction. The cardiac involvement caused by DMD progresses ultimately toward cardiomyopathy and is responsible for death in approximately 40% of patients [2, 3, 20]. Unfortunately, most DMD patients remain asymptomatic for years, despite the progression of cardiac dysfunction. It is therefore important to screen patients using a noninvasive method to identify those at high-risk of developing heart failure.

Whereas echocardiography is the most common imaging modality used to assess LV size and function in patients with DMD, traditional echocardiography could not detect abnormalities until the development of overt cardiac complications. Many studies have demonstrated the early detection of myocardial changes in patients with DMD. Tissue Doppler might reveal cardiac dysfunction in patients with DMD when conventional echocardiography

Table 4 Receiver operative characteristic analyses of three-dimensional speckle tracking echocardiographic parameters

Parameter	Area under the curve	95% confidence interval	Cutoff value (%)	Sensitivity (%)	Specificity (%)	NND
GAS (%)	0.80	0.70–0.90	−29.5	85.7	71.0	2
GRS (%)	0.74	0.62–0.86	48.5	82.1	71.0	2
GLS (%)	0.71	0.59–0.82	−20.5	82.1	51.6	3
GCS (%)	0.70	0.59–0.81	−16.5	80.4	48.4	3

GAS global area strain, *GCS* global circumferential strain, *GLS* global longitudinal strain, *GRS* global radial strain, *NND* number needed to diagnose

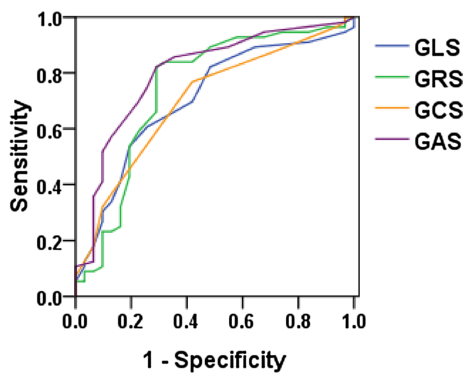

Fig. 3 The receiver-operating characteristic curve for the four three-dimensional (3D) speckle-tracking echocardiography parameters to discriminate between patients and control subjects. *GAS* global area strain, *GCS* global circumferential strain, *GLS* global longitudinal strain, *GRS* global radial strain

parameters are within normal limits. Mori et al. [9] used tissue Doppler to demonstrate a decrease in peak systolic radial strain in the posterior wall in DMD patients with preserved shortening fractional. Yamamoto et al. [15] used tissue Doppler radial strain in the posterior wall, which was assessed from the mid-LV short-axis view, to obtain the transmural strain profile and found it could predict future LV dysfunction in DMD patients with preserved EF. Tissue Doppler-derived strain and strain rate were used as a method to quantify myocardial deformation; however, because of the influence of the angle between the direction of ultrasound beam and the wall motion, tissue Doppler imaging in quantitative analysis of myocardial strain of different directions is restricted, mainly used for accessing longitudinal strain in the direction along the long axis of the heart, not for the apex segment and in the direction of the short axis, which have a large angle between acoustic beam and myocardial. In addition to this, it has several drawbacks that include noise interference and confounding of interpretation by tethering of adjacent myocardium and cardiac translational movements [21]. The application of 2D STE, which is angle independent, overcomes the limitations of tissue Doppler imaging [22, 23]. Ryan TD et al. [10] showed that 2D speckle tracking detected abnormal circumferential strain in young DMD children before standard measures of detecting global dysfunction.

The recently developed 3D STE is a novel noninvasive method to quantify LV function and dyssynchrony [14]. Compared with 2D STE, 3D STE can track speckles in three dimensions, overcoming the limitation of 2D out-of-plane speckle motion and allowing efficient single acquisition with simultaneous assessment of all LV segments in the same 3D data set. 3D STE has been used to assess LV function in plenty of heart diseases, such as cardiomyopathy, congenital heart disease, and congestive heart failure [12–14]. 3D strain is based on speckle tracking and tracks all points of the region of interest, from the endocardium to epicardium, frame by frame. The 3D strain acquires longitudinal, circumferential, radial, and area strain in the same cardiac cycle with good accuracy and reproducibility [21]. We and others have recently shown potential advantages of 3D STE in unveiling subclinical deformation impairment of the LV myocardium [24–26]. To our knowledge, this is the first study to adopt 3D STE to assess LV myocardial deformation for detection of subclinical dysfunction in children with DMD.

In our study, we demonstrated that 3D GLS, GCS, GRS, and GAS were all significantly decreased in DMD patients. However, there was no difference in LVEF and 3D LVEF between the patients and control subjects. Our findings are consistent with a recent multicenter and prospective study in DMD patients with 2D strain [27]. In their study, Spurney CF et al. [27] found that the average circumferential and longitudinal strain in DMD children with normal shortening fractions was significantly decreased, and they considered that the 2D strain was feasible and reproducible to detect subclinical cardiac disease in the DMD patients. Unlike LVEF, which derived from both M-mode and 3D echocardiography need to calculate ventricular volume based on geometric assumption, myocardial strain assesses the change in myocardial fiber length compared with its original length in the plane in which it is measured [28]. Strain enables the direct assessment of myocardial deformation for evaluating global and regional myocardial function, so it is more sensitive in reflecting LV function. Moreover, in our study, we used 3D STE, which can overcome the limitation of failure

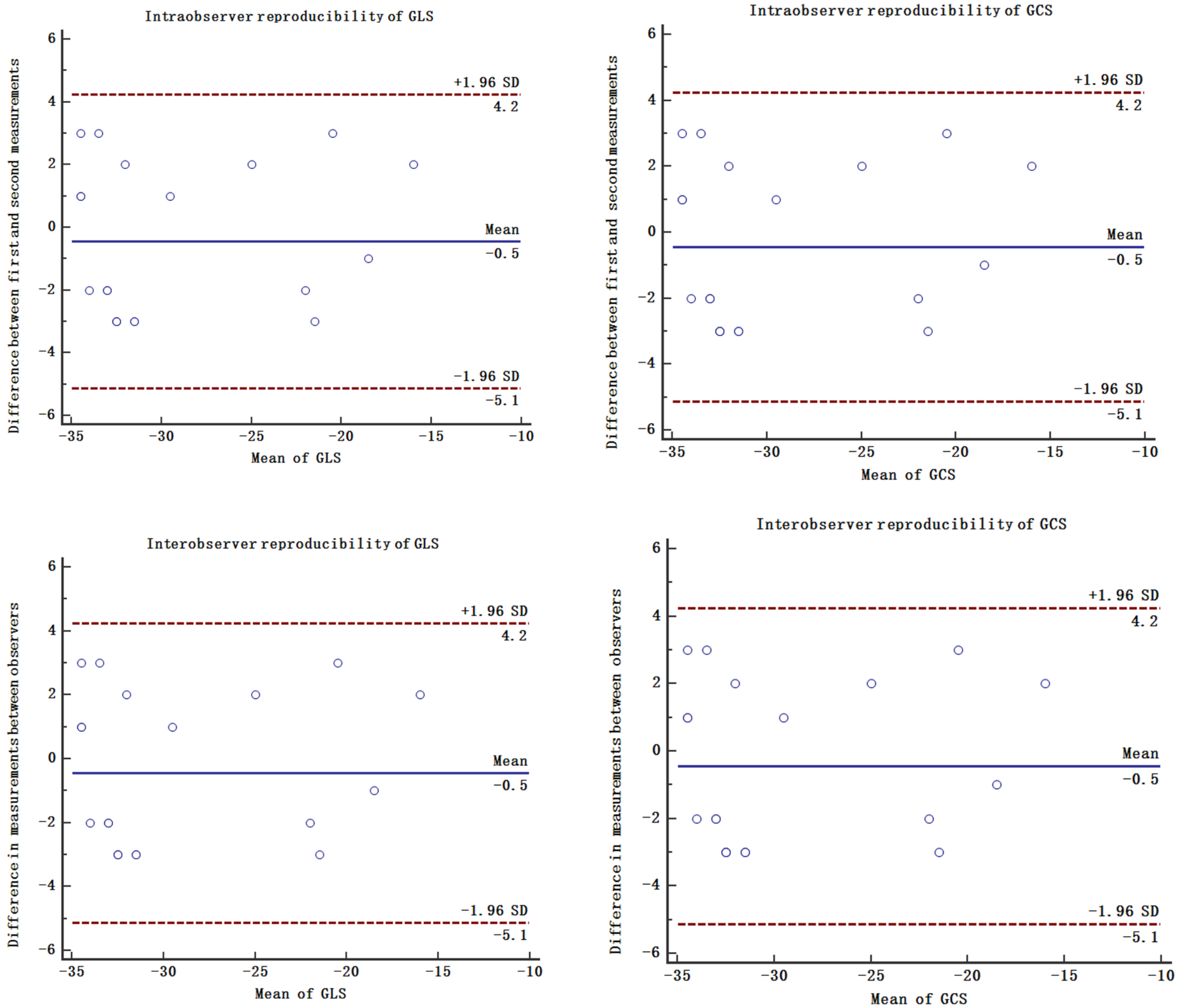

Fig. 4 Bland–Altman analysis of intra- and inter-observer variability for left ventricular three-dimensional (3D) strain indices of GLS, GCS, GRS, and GAS. The blue thick lines represent the mean difference, the red dashed lines represent the mean bias ± 2 SD. The value of the x-axis represents the mean of two measurements in intraobserver variability and two observers in interobserver variability. *GAS* global area strain, *GCS* global circumferential strain, *GLS* global longitudinal strain, *GRS* global radial strain

of 2D STE to track out-of-plane speckle motion and allow efficient single acquisition with simultaneous assessment of all LV segments in the same 3D data set. In addition to high sensibility, 3D STE also had great reproducibility for high inter- and intra-observer interclass correlation coefficient values of 3D global strain in our study, which are consistent with other previous studies of 3D LV strain [12–14].

We also observed that older children (> 8 years) with DMD had lower 3D strain values than younger patients, which concurred with our speculation and previous research [11]. In a cardiac magnetic resonance tagging study, Kan et al. [11] found that myocardial strain decrease was prevalent in young DMD patients despite normal EF, and these strain values continued to decline with advancing age (> 10 years). According to our finding, we confirmed that cardiac dysfunction became more progressive with age, and the deterioration could be detected at earlier ages by 3D strain. Unsurprisingly, there was no difference in LVEF between young and older DMD children. Therefore, 3D strain is more sensible than conventional echocardiography to detect myocardial impairment and can be used to identify strata of cardiomyopathy in patients with DMD.

3D GAS is a new parameter derived from 3D STE. Area strain reflects a combination of longitudinal and circumferential strain, thus assessing the percentage change in mid-myocardium from its original dimensions, and providing a

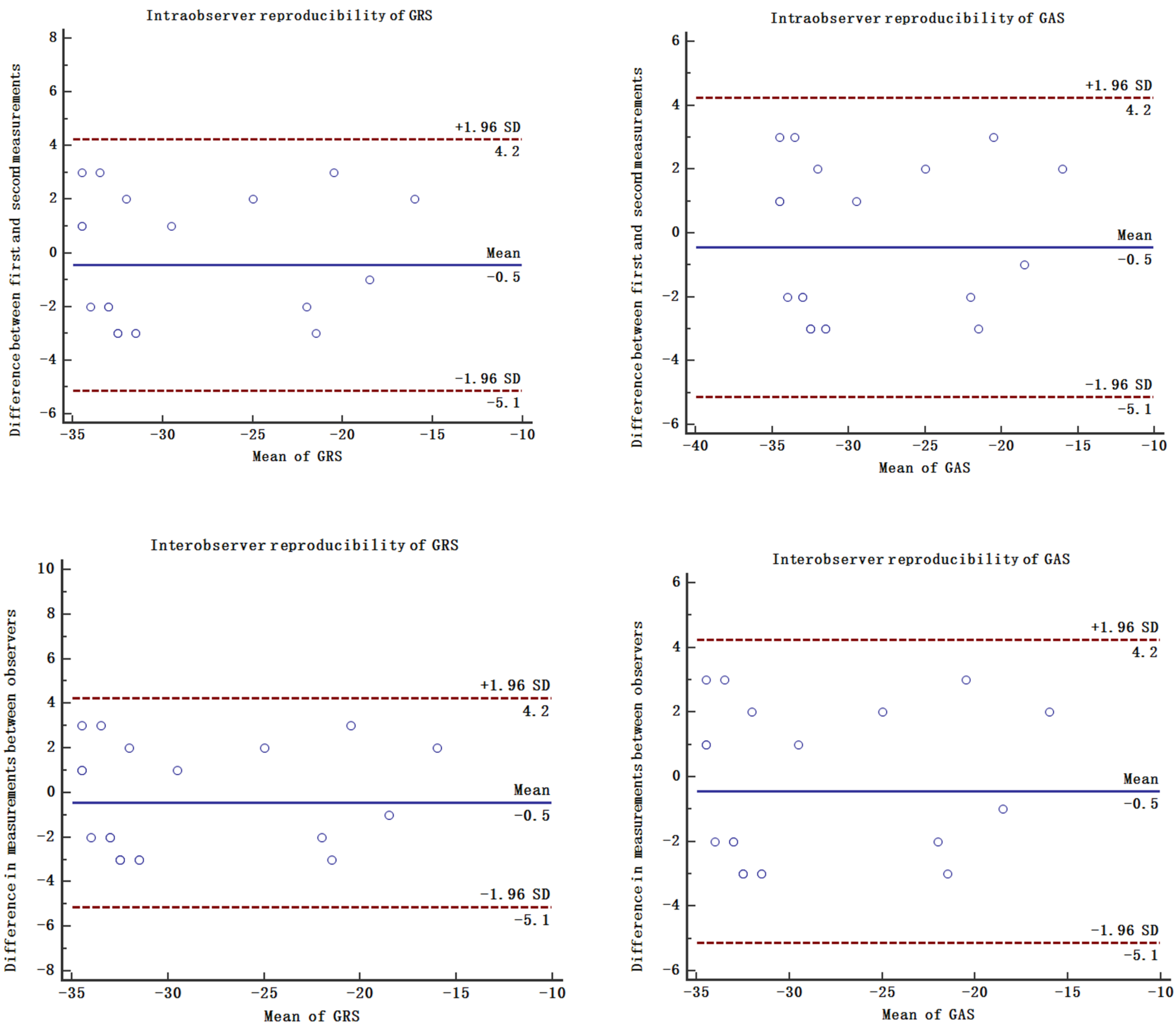

Fig. 4 (continued)

comprehensive measure of LV myocardial deformation [21]. Previous investigators [13, 14] observed that GAS was sensitive and reproducible to discover early and subtle LV systolic dysfunction with greater feasibility than other strain parameters (GLS, GCS, and GRS). In the present study, 3D GAS was significantly decreased in DMD patients compared with control subjects. The ROC curve analysis further showed that the 3D GAS had the largest area in differentiating between children with DMD and control subjects compared with the other strain parameters and LVEF. Our findings agree with those of Li et al. [13], who used 3D area strain to assess global LV performance after repair of tetralogy of Fallot (TOF). They found that 3D GAS could detect impairment of LV global performance in patients with repaired TOF and differentiate patients from healthy subjects. In addition, Huang et al. [29] demonstrated that 3D GAS is a new modality to identify early myocardial abnormalities in patients with systemic lupus erythematosus who may have normal LV systolic function with 2D echocardiography. In our study, GRS performed equally well with GAS based on the AUC curves; therefore, we considered that 3D global strains can detect subclinical impairment of myocardial function and may be a marker index of myocardial dysfunction in children with DMD.

Early detection of subclinical LV myocardial dysfunction in patients with DMD who have preserved LVEF is important because early medical treatment can reverse the symptoms and signs of congestive heart failure and help prevent the development of myocardial fibrosis. Recent studies showed that patients with DMD obtain a better cardiac outcome with early detection of latent myocardial involvement and early medical treatment for myocardial deterioration [30]. Duboc et al. found that in children with DMD, treatment with angiotensin-converting enzyme inhibitors (ACEi) resulted in a reduction in the number of patients with worsening myocardial function 3 and 5 years later, even among those with a normal EF [31, 32]. Jefferies et al. suggested that as soon as echocardiography abnormalities are found, ACEi and/or beta-blocker treatment is recommended, which they demonstrated to be effective to improve LV function [8]. The benefit of early detection of cardiac involvement can also be supported by observations in murine models. In a DMD mouse model, those treated earlier with lisinopril and spironolactone demonstrated less cardiomyocyte damage and improved myocardial strain [33]. According to our findings, the early detection of abnormal 3D strains could make early identification of patients with DMD and with preserved LVEF who are at risk of irreversible myocardial dysfunction possible so that medical treatment can be administered earlier for preventing the development of congestive heart failure.

Several limitations of this study need to be addressed. First, this was a single-center cross-sectional study and the sample size was relatively small. Although the largest area under the ROC curve for the 3D GAS implies a high discriminative ability to separate patients from control subjects, larger-scale studies are needed to verify these findings. Second, the 3D STE technique is focused primarily on the assessment of systolic function at present. Although diastolic dysfunction has been reported in children with DMD [27], we focused on 3D systolic myocardial deformation in the present study. Third, the accuracy of 3D STE measurement depends on the quality of images, but acoustic windows tend to be limited because of altered body habits, including scoliosis and significant chest wall adiposity. If the image quality is poor, it is difficult to establish the full-volume database. In our study, we studied a young cohort (average age 8.8 years) for the purpose of confirming whether 3D STE can detect myocardial damage as early as possible; therefore, we chose the children with DMD at a relatively young age. The youngest child in our study was 5 years old, and the oldest was 14 years 1 month. According to our experience, children older than 12 years have notoriously poor acoustic windows because of adiposity and scoliosis. There were only 6 children who were older than 12 years in our study. However, we could still obtain the 3D volume data of their LV with the chest deformity by swinging the probe or letting the children change their posture and hold their breath.

Conclusions

3D STE can detect early preclinical myocardial dysfunction in children with DMD by decreased global strain despite having normal conventional echocardiographic LV function and no overt heart failure symptoms. 3D GAS might be a valuable marker to distinguish DMD patients from those control subjects and stratify cardiomyopathy in young DMD patients with normal LVEF.

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Compliance with ethical standards

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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