2D sledenje ultrazvočnega vzorca deformacije miokarda pri otrocih s hipertrofično kardiomiopatijo

2D speckle-tracking in assessment of myocardial strain in children with hypertrophic cardiomyopathy

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Ključne besede:
2D sledenje ultrazvočnega vzorca, deformacija miokarda, ehokardiografija, hipertrofična kardiomiopatija, zgodnja diagnoza, zdravljenje, otrok.

Key words:
2D speckle tracking, strain, echocardiography, hypertrophic cardiomyopathy, early diagnosis, treatment, children.

Članek prispel / Received
8. 6. 2018

Članek sprejet / Accepted
9. 6. 2021

Izvleček

Namen: *Ocena deformacije (strain) miokarda pri otrocih s hipertrofično kardiomiopatijo (HKMP).*

Metode: *61 otrokom starosti med 7 in 17 let z asimetrično obliko smo z 2D sledenjem ultrazvočnega vzorca (2D speckle-tracking imarging) deformacije miokarda ocenili sistolično funkcijo levega ventrikla. V analizi smo uporabili globalno in segmentno longitudinalno, cirkumferenčno in radialno deformacijo. Pridobili smo podatke o deformaciji slojev endokarda in epikarda, glede na določen segment levega ventrikla, kot tudi skupne vrednosti deformacije.*

Rezultati: *PGlobalna longitudinalna deformacija in longitudinalna stopnja deformacije sta se zmanjšali zaradi motenega krčenja hipertrofiranih segmentov v 100% primerov neobstruktivnih*

Abstract

Purpose: *To assess the myocardial strain in children with hypertrophic cardiomyopathy (HCM).*

Methods: *A total of 61 patients aged between 7 and 17 years with an asymmetric form of HCM underwent an ultrasound examination of the heart using standard techniques. An assessment of the left ventricular systolic function was performed using the two-dimensional (2D) speckle-tracking mode with analysis parameters that included global and segmental longitudinal, circumferential, and radial myocardial strains. Strain data for the subendocardial and subepicardial layers for each segment of the left ventricle, as well as their total values, were determined.*

Results: *Global longitudinal strain and longitudinal strain rate were dec-*

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in obstruktivnih oblik HKMP. Zmanjšanje parametrov globalne, radialne in cirkularne deformacije smo opazili pri vseh bolnikih z obstruktivno obliko HKMP in pri 39 (86,6%) bolnikih z neobstruktivno obliko bolezni. Obenem smo ugotovili statistično pomembno razliko med deformacijo in stopnjo deformacije pri bolnikih z neobstruktivno obliko bolezni v primerjavi z obstruktivno obliko HKMP.

Zaključek: *Spremembe deformacije miokarda pri otrocih s HKMP z 2D sledenjem ultrazvočnega vzorca nakazujejo zgodnjo sistolično disfunkcijo levega ventrikla. Longitudinalna deformacija miokarda se je v primerjavi z radialno in cirkumferenčnno, izkazala za najbolj občutljivi parameter. Ta kaže statistično pomembno razliko pri otrocih z obstruktivno obliko HKMP v primerjavi z bolniki z neobstruktivno obliko bolezni. Izsledki, pridobljeni v tej raziskavi, so pomembni v okviru t.i. terapije zgodnjega začetka HKMP in so lahko pomembni pri izboljšanju prognoze otrok s HKMP.*

reased due to the impaired contractility of hypertrophied myocardial segments in 100% of cases of non-obstructive and obstructive HCM forms. A decrease in global, radial, and circumferential strain parameters and their rates has been observed in all children with an obstructive form of HCM and 39 (86.6%) patients with non-obstructive form. At the same time, there was a statistically significant difference between strains and strain rates in children with a non-obstructive form of HCM in comparison to those with an obstructive form of the disease.

Conclusion: *Changes in myocardial strains observed using the 2D speckle-tracking mode in children with HCM indicate early systolic dysfunction of the left ventricle. Longitudinal strain was the most sensitive compared to radial and circumferential types. It was statistically significantly different in children with an obstructive form of HCM compared to those with non-obstructive form of the disease. These results are important for early therapy initiation and, therefore, may improve prognosis in children with HCM.*

INTRODUCTION

Two-dimensional (2D) speckle-tracking is a noninvasive ultrasonic method of heart visualization that allows to evaluate the kinetics of the myocardium. This method is based on the ultrasound tracking of the "spot" or speckle in the myocardial tissue, which results in the formation of a spectral pattern. Speckle is unique for each part of the myocardium. It reflects the movement of myocardial tissue. The operating system follows the speckle in the 2D plane, defining its movement trajectory or tracking. Then, myocardial segments are isolated and their kinetics assessed. The displacement of the myocardium or strain is the main parameter in this method. Using 2D speckle-tracking, it becomes possible to define the longitudinal, radial, and circumferential myocardial strains and to estimate their rates (1, 2). This method has several advantages. First, it does not depend on the scanning angle in a way that tissue Doppler examination does. Second, any parameters can be calculated and analyzed in different parts of the myocardium in the off-line mode. It is also necessary to take into account the limitations of this method. The optimal frame rate should be 60–100 frames/min. It also depends on the heart and respiratory rates (3, 4). In addition, the operating system does not perform an integral analysis of strain in tachycardia and tachypnea (5). Finally, it is difficult to assess strain due to many artifacts in the extracted image when performed on a non-compact myocardium (6). It is necessary to consider different accuracy levels when assessing data in the longitudinal and cross directions.

The 2D speckle tracking allows to assess the local systolic function of the myocardium (5,7). The method has found wide application in the adult cohort of patients in assessing the local contractility of the ischemic site after a previous myocardial infarction (8). In addition, many publications on the use of 2D speckle-tracking in oncology and nephrology are devoted to evaluating the local myocardial contractility in patients taking cardiotoxic drugs (9,10).

The use of a 2D speckle-tracking method is limited in children due to their high heart and respiration rates. The global longitudinal strain of the myocardium is well studied. Radial and circular strains have been studied much less due to the small myocardial wall thickness (on average up to 6 mm) and a large number of artifacts (11). The 2D speckle-tracking method is very important for children with hypertrophic cardiomyopathy (HCM) (12). HCM is the second most common disease of the myocardium in children. Most commonly, it is identified by an asymmetrical interventricular septum with a predominant lesion. For these children, the assessment of local left ventricular systolic function is critical (13). However, the values of global systolic function (ejection and shortening fractions) lie within the relevant values over a long period of time (14). Assessment of myocardial strain changes is a promising and topical direction in the definition of early disruptions of local contractility in the left ventricular myocardium. This technique helps to define observation tactics and to correct the treatment strategy for children with HCM.

The purpose of the study: to assess myocardial strain in children with HCM.

MATERIALS AND METHODS

A total of 61 patients (14 girls, 47 boys, age range: 7–17 years, mean age: 12 years) with an asymmetric form of HCM underwent a comprehensive clinical, laboratory, and instrumental examination and received treatment in the cardio-rheumatology department of the Academician Yu. E. Veltishchev Research Clinical Institute of Pediatrics in 2014–2018 in Moscow, Russia. A total of 45 (73.8%) children had the non-obstructive form of HCM, and 16 (26.2%) children had the obstructive form of HCM. Obstruction was determined at the level of the left ventricular output tract. The pressure gradient was 30–50 mm Hg both at rest and during the stress test. Latent forms of obstruction were not revealed. A total of 21 (34.4%) children had their disease diagnosed before the age of seven. In addition, there were 34 (55.7%) children who were diagnosed at age 7–12 years and only six (9.9%) at 13–17 years. The disease exposure at the time of examination was ≤1 year for six (9.9%) children, 1–5 years for 40 (65.6%) children, and >5 years for 15 (24.5%) children.

The ultrasound heart examination was carried out in accordance with the standard technique on a Toshiba Artida ultrasound machine (Japan) using a matrix sensor with a frequency range of 4–6 MHz. Parameter assessment of the global left ventricular systolic function was performed in 2D mode to obtain an ejection fraction (EF, %) measured using the Simpson's method and a shortening fraction (FS, %) (15). Local systolic function assessment was performed in off-line 2D speckle-tracking mode. Global and segmental longitudinal, circumferential, and radial myocardial strain and strain rate in 12 segments of the basal and median left ventricular departments were measured. The software provided the strains for the subendocardial and subepicardial myocardial layers in each segment and their total values.

Apical positions (two- and four-chamber) on the long axis of the left ventricle were used to measure the longitudinal strain. To assess the radial and circumferential strains, parasternal positions along the short axis of the left ventricle at the mitral valve level and the papillary muscles were used (Fig. 1). In addition, the electrocardiogram was recorded in parallel. All children's heart and respiratory rates were within the relevant values. The software carried out the analysis of integral myocardial strain curves at the time of systole COR in the automatic and semi-automatic modes from the R wave on an electrocardiogram during three cardiac cycles and obtained the average values. To compare the myocardial wall thickness and strain parameters in 2D mode, the thickness was measured in the same segments where the myocardial strain assessment was

carried out. A 16-segment left ventricular division was used to assess the local myocardial contractility (4).
Statistical analysis of the results was carried out using STATISTICA 10.0 software (StatSoft, Tulsa, OK, USA). The quantitative data provided the mean (M), standard deviation (σ), median, minimum, and maximum values. The Kruskal–Wallis (ANOVA) tests were performed to assess the significance of differences in quantitative variables in the small groups. The χ^2 criteria were used for the assessment of reliability of qualitative variable differences.
Studies were conducted in accordance with ethical principles and legislation. All of the children and their parents signed the informed consent form to participate in the study.

RESULTS

The EF and FS of the left ventricle were lower than the relevant values in five (11.1%) children with the non-obstructive form of HCM and in all patients with obstructive form of HCM (p=0.0001). Five children with the non-obstructive HCM and decreased EF and FS had a noticeable degree of hypertrophy in three myocardial segments of the left ventricle (myocardial thickness: ≥25 mm; *z*-score: >4.24; Fig. 1).
Global longitudinal strain and longitudinal strain rate decreased in both groups in 100% of cases. A decrease in global, radial, and circumferential strain parameters and their rates was observed in every child with an obstructive form of HCM and in 39 (86.6%) children with a non-obstructive form. At the same time, there was a statistically significant difference in the strain rate parameters in children with a non-obstructive form of HCM compared to those with an obstructive form of the disease (Table 1).
A total of 40 (65.6%) children had mild hypertrophy of 2–3 myocardial segments of the left ventricle (myocardial thickness of up to 20 mm; *z*-score: ≤4.24). In addition, 21 (34.4%) children had expressed hypertrophy of 3–7 segments (myocardial thickness

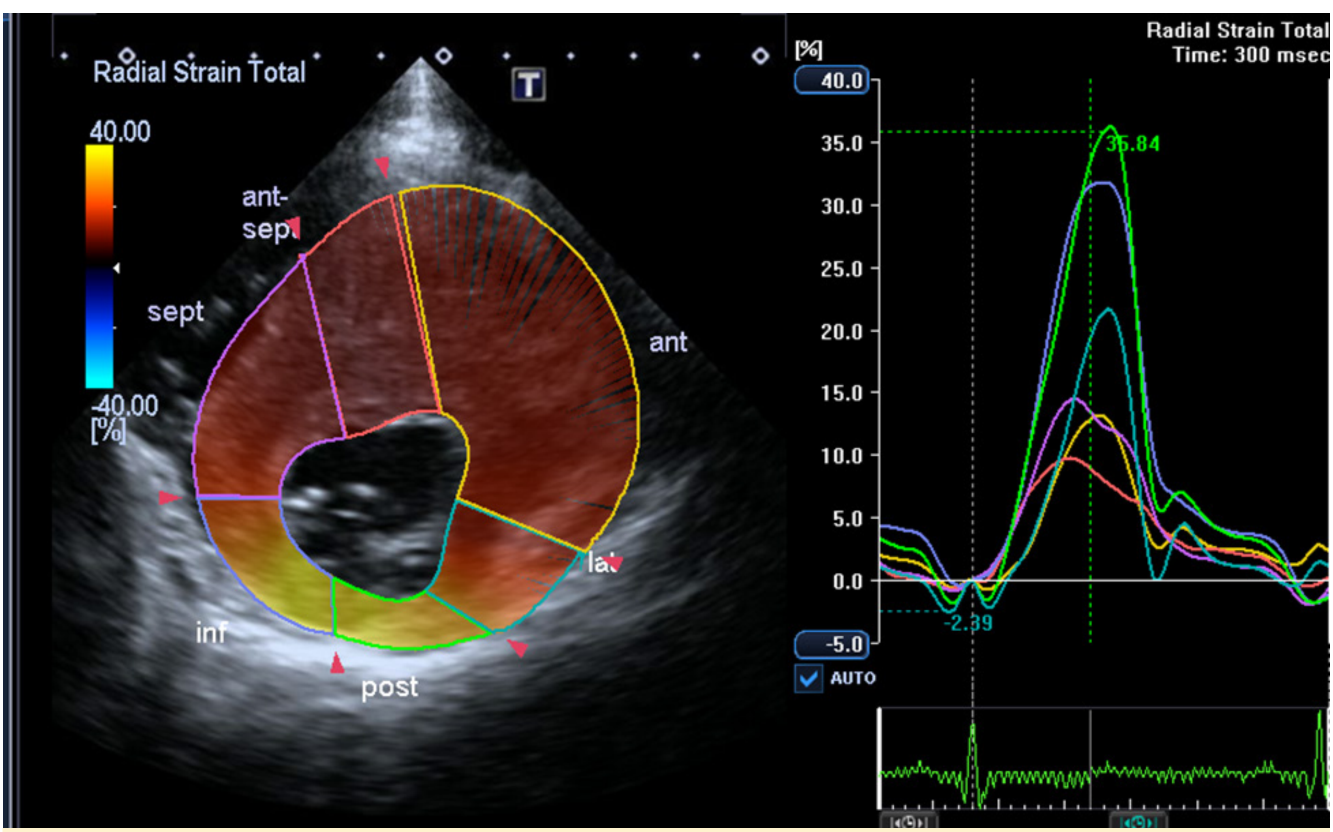

Figure 1. *Measurement of left ventricular radial strain in 2D speckle tracking mode. Parasternal position along the short axis of the left ventricle in the papillary muscle level of the mitral valve.*

>25 mm; *z*-score: >4.24). In the analysis of the degree of hypertrophy expression, the hypertrophy prevailed in the anteroseptal, anterior, and anterolateral segments, which corresponded to the topographical level of the interventricular septum (Fig. 2). The strain indicators in these segments were below the corresponding relevant values (20%). In addition, there was an increase in the strain indicators in the contralateral segments (Fig. 3). When assessing the myocardial layer strain, higher strain indicator values in the subendocardial layer of the myocardium were observed compared to those in the subepicardial layer (Fig. 4).

An analysis of the relationship between the strain indicators, EF, and FS showed that children with an obstructive form of HCM had "mean" feedback (statistically significant) between the longitudinal strain, EF, and FS. Direct correlations between radial and circular strain and EF and FS were noted. Similar correlation relationships were obtained when assessing the left myocardial ventricle (Table 2).

DISCUSSION

The study data confirmed the higher parameter sensitivity in the strain indicators used for the assessment of systolic function of the left ventricle compared to the EF and FS, which is in accordance with previously reported results (16). Changes in the

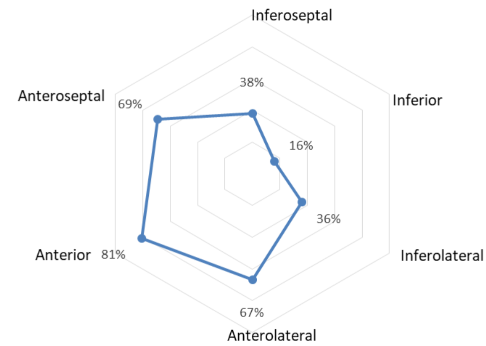

Figure 2. *Frequency of hypertrophied segments in children with HCM.*

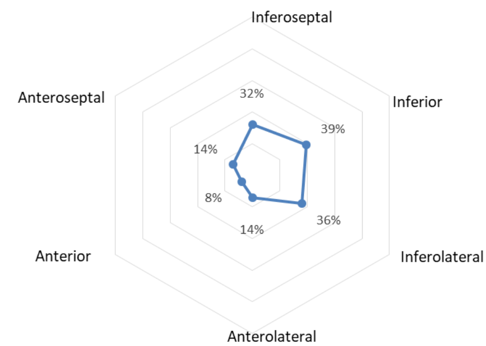

Figure 3. *Mean values of strain parameters (longitudinal, radial, and circular) in each segment in children with HCM.*

Table 1. *Left ventricular parameters of systolic function in children with HCM (N=61) .*

PARAMETERS (relevant values)	Non-obstructive form HCM (n=45)			Obstructive form HCM (n=16)			Reliability of distinctions, p
	M±σ	Median	Min. - max. values.	M±σ	Median	Min. - max. values.	
Longitudinal strain (20%)	-11.06±6.4	-10.44*	-9.33-18.4	-10.13±6.07	-8,24	-0.49-14.42	0.002
Longitudinal strain rate (0,68 s-1)	-0.59±0.13	-0.61*	-0.46-0.66	-0.36±0.23	-0.35	-0.22-0.61	0.0025
Radial strain (20%)	19.44±14.5	19.14*	8.44-39.6	15.10±11.2	13.42	0.89-18.1	0.003
Radial strain rate (1,08 s^{-1})	1.01±0.11	1.02*	0.82-2.77	0.94±0.41	0.87	0.65-1.02	0.002
Circular strain (20%)	-17.25±13.4	-18.11*	-8.9±33.5	-11.62±9.11	-12.29	-0.69±16.2	0.016
Circular strain rate (0,74 s-1)	-0.65±0.14	-0.56*	-0.12±-1.4	-0.51±0.21	-0.48	-0.32-0.71	0.011
Fractional shortening (30-45%)	28.44±1.99	30*	26-36	25.4±2.89	22	20-26	0.003
Ejection Fraction (60-75%))	62.14±2.34	66*	58-68	52.12±2.98	52	48-58	0.002

Note: * – *reliability of distinctions at p≤0,05.*

Table 2. *Coefficients of correlation (r) between left ventricular parameters of systolic function in children with HCM.*

PARAMETERS	Non-obstructive form		Obstructive form	
	EF	FS	EF	FS
Longitudinal strain (%)	r=-0,34	r=-0,34	r=0,50*	r=-0,53*
Longitudinal strain rate (s-1)	r=-0,39	r=-0,39	r=0,50*	r=-0,51*
Radial strain (%)	r=-0,31	r=-0,31	r=0,32*	r=-0,34*
Radial strain rate (s^{-1})(s)	r=-0,36	r=-0,36	r=0,39*	r=-0,39*
Circular strain (%)	r=-0,32	r=-0,32	r=0,42*	r=-0,41*
Circular strain rate (s^{-1})	r=-0,34	r=-0,34	r=0,37*	r=0,37*

*Note: * – reliability of distinctions at p≤0,05. EF – Ejection Fraction; FS – Fraction shortening.*

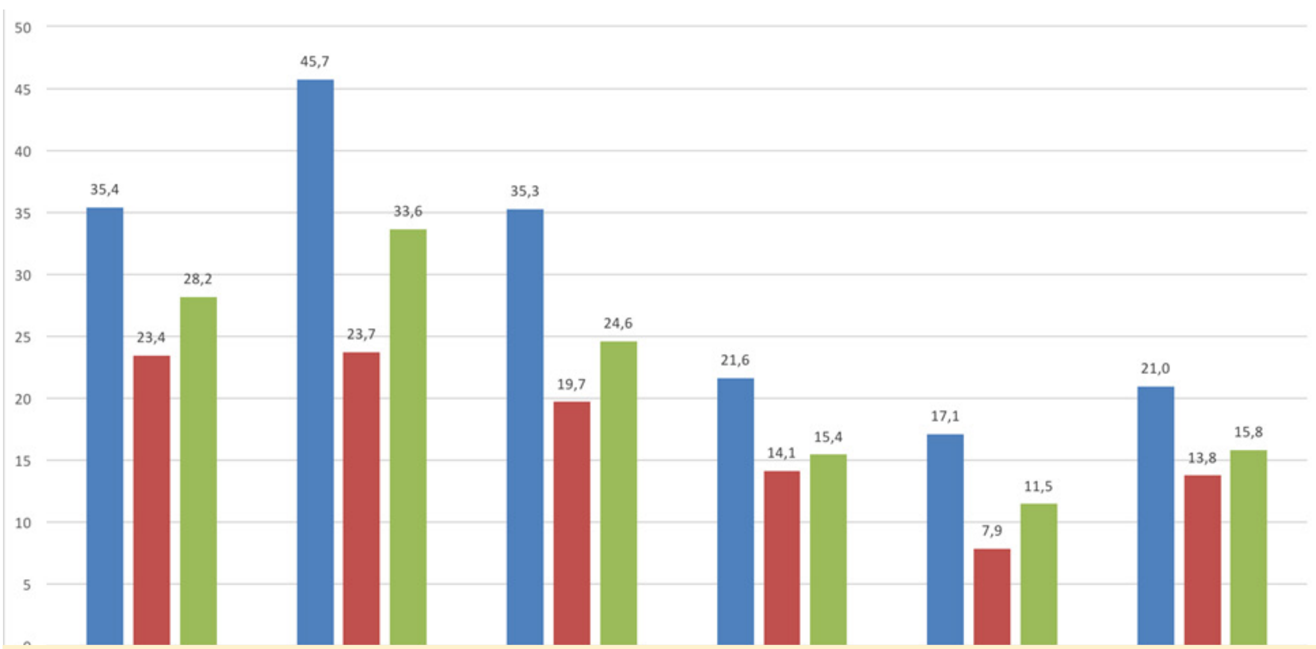

Figure 4. *Mean values of segmental strain parameters (subendocardial and subepicardial layers) in left ventricular myocardium in children with HCM.*

segmental and global longitudinal myocardial strains begin early. Changes in the traditional EF and FS start much later (17). These findings have been confirmed in the present research. Parameters of global and segmental longitudinal strain and their rates were reduced in 100% of cases. However, more than half of the children had intact EF and FS.

The analysis showed a decreased strain in more hypertrophied segments and increased strain in contralateral segments for children with HCM. This reveals how the compensatory mechanisms of the myocardium act. It also explains why the disease is not clinically apparent for a long time until it is exposed during a routine screening. Strain is a dynamic indicator reflecting well-expressed compensatory mechanisms in children with HCM.

The higher values of the myocardial strain parameters in the subepicardial layer compared to the subendocardial layer have been confirmed by prior studies (4,18). In the subendocardial layers of healthy cohort patients, strain values were higher than those in the subepicardial layers. This is apparently connected to the mechanical properties of the heart. The myocardial movement during systole begins in the subendocardial layers and progressively terminates in the pericardium.

The latest European guidelines for the diagnosis and treatment of HCM (13) recommend using 2D speckle-tracking to detect early signs of systolic dysfunction in this group of patients. The results of the present study have shown that the strain indicators obtained using 2D speckle-tracking can be useful for planning further diagnostic studies and developing treatment tactics not only in adults with HCM, but also in children. The assessment of strain indicators is the most significant when evaluating the segmental systolic function of the heart in children with HCM.

CONCLUSION

Changes in myocardial strain noticeable in the 2D speckle-tracking mode in children with HCM indicate early disruptions in the systolic function of the left ventricle. Among them, the longitudinal strain was the most statistically significantly different compared to the radial and circumferential strains in children with an obstructive form of HCM compared to non-obstructive form of the disease. The obtained results are essential for initiating appropriate therapy and improving HCM prognosis in children.

CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest associated with this study.

REFERENCES

1. Mondillo S, Galderisi M, Mele D, Cameli M, Lomoriello VS, Zacà V et al. Echocardiography Study Group Of The Italian Society Of Cardiology (Rome, Italy). Speckle-tracking echocardiography: a new technique for assessing myocardial function. J Ultrasound Med 2011; 30: 71–83.
2. Feigenbaum H, Mastouri R, Sawada S. A practical approach to using strain echocardiography to evaluate the left ventricle. Circ J 2012; 76: 1550–5.
3. Bansal M, Kasliwal RR. How do I do it? Speckle-tracking echocardiography. Indian Heart J. 2013; 65: 117–23.
4. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann P et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardizede formation imaging. Eur Heart J Cardiovasc Imaging 2015; 16: 1–11.
5. Mor-Avi V, Lang RM, Badano LP, Belohlavek M, Cardim NM, Derumeaux G et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. Eur J Echocardiogr 2011; 12: 167–205.
6. Bennett CE, Freudenberger R. The Current Approach to Diagnosis and Management of Left Ventricular Noncompaction Cardiomyopathy: Review of the Literature. Card Res and Pract 2016;

2016: e5172308.
7. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Amstrong A, Ernande L 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.
8. Ersboll M, Valeur N, Mogensen UM, Andersen MJ, Moller JE, Hassager Ch et al. Relationship between left ventricular longitudinal deformation and clinical heart failure during admission for acute myocardial infarction: a two-dimensional speckle-tracking study. J Am Soc Echocardiogr 2012; 25: 1280–89.
9. Yu AF, Raikhelkar J, Zabor EC, Tonorezos ES, Moskowitz CS, Adsuar R et al. Two-dimensional speckle tracking echocardiography detects subclinical left ventricular systolic dysfunction among adult survivors of childhood, adolescent, and young adult. Cancer Biomed Res Int 2016; 2016: e9363951.
10. Stefani L, Pedrizzetti G, Galanti G. Clinical Application of 2D Speckle Tracking Strain for Assessing Cardio-Toxicity in Oncology. J Funct Morphol Kinesiol 2016; 1: 343–54.
11. Levy PT, Machefsky A, Sanchez AA, Petel MD, Rogal S, Fowler S et al. Reference Ranges of Left Ventricular Strain Measures by Two-Dimensional Speckle-Tracking Echocardiography in Children: A Systematic Review and Meta-Analysis. J Am Soc Echocardiogr 2016; 29: 209–25.
12. Chernykh NYu, Groznova OS, Dovgan MI, Podolsky VA. A change in myocardial deformity as an early marker for myocardial dysfunction in children with hypertrophic cardiomyopathy. J Ros. Vestn. Perinatol i Pediatr 2016; 61: 70–4.
13. Elliott PM, Anastasakis A, Borger M A, Borggrefe M, Cecchi F, Charon P et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy. The Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J 2014; 36: 2735–9.
14. Ganame J, Mertens L, Eidem BW, Claus P, D'hooge J, Havemann LM et al. Regional myocardial deformation in children with hypertrophic cardiomyopathy: morphological and clinical correlations. Eur Heart J 2007; 28: 2886–94.
15. Lai WW, Geva T, Shirali GS, Frommelt PC, Humes RA, Brook MM et al. Task Force of the Pediatric Council of the American Society of Echocardiography; Pediatric Council of the American Society of Echocardiography. Guidelines and standards for performance of a pediatric echocardiogram: a report from the Task Force of the Pediatric Council of the American Society of Echocardiography. J Am Soc Echocardiogr 2006; 19: 1413–30.
16. Saito M, Okayama H, Yoshii T, Higashi H, Hagashi H, Marioka H et al. Clinical significance of global two-dimensional strain as a surrogate parameter of myocardial fibrosis and cardiac events in patients with hypertrophic cardiomyopathy. Eur Heart J Cardiovasc Imaging 2012; 13: 617–23.
17. Lai D, Hu K, Nordbeck P, Ertl G, Stork S, Weidemann F. Longitudinal strain bull's eye plot patterns in patients with cardiomyopathy and concentric left ventricular hypertrophy. Eur J Med Res 2016; 21: e4862218.
18. Chernykh NYu, Tarasova AA, Groznova OS. Assessment of left ventricular myocardial deformation by 2D speckle-tracking in healthy children and adolescents. Medical Council 2020; 18: 152–161.