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REVIEW ARTICLE

Assessment of mechanical dyssynchrony during patient's selection for cardiac resynchronization therapy by speckle tracking echocardiography

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Abstract. *Myocardial strain is the degree of myocardial segment thickness or length from final diastolic to final systolic value that is assessed using speckle tracking echocardiography (STE). We analyzed forty-three scientific publications available in the PubMed search system from 2001 to 2019 years.*

Interventricular dyssynchrony is more common in patients with left bundle branch block. Early transseptal activation lead to pressure gradient change and septal flash (SF). SF is a presystolic abnormal contraction of interventricular septum basal segments before left ventricular (LV) walls contraction. It is possible to identify SF during all strain types — longitudinal, radial and circumflex.

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Intraventricular dyssynchrony is associated with the change of LV segments stimulation sequence. Strain delay index (SDI) is calculated as the ratio of systolic to maximum strain peak delays. Longitudinal Dyssynchrony Index — maximum difference among final systolic strain peaks of 12 myocardial segments.

Key words: *speckle tracking echocardiography; mechanical dyssynchrony; cardiac resynchronization therapy; congestive heart failure.*

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Myocardial morphology and kinetics

Heart contraction is a complex physiological process due to its anatomical and morphological features. The wall of the left ventricle (LV) has three layers. Middle layer consists of circular muscles. The muscles of subendocardial and subepicardial myocardium are longitudinal, have spiral orientation, and rotate orthogonally (multidirectional): the subendocardial part rotates in clockwise direction (a right-handed helix), and subepicardial part — in counterclockwise direction (a left-handed helix). Global rotation at the basal segments level, papillary muscles and LV apex is the ratio of presented layers rotation and is measured in degrees. The severity strictly decreases from apex to basal segments to middle segments [1,2]. Such architectonics provides homogeneity of cardiac contraction and LV twist and untwist — important cardiac biomechanical processes. This twist is a mutual rotation of LV apex and base and is also measured in degrees. Base usually rotates in clockwise direction, and apex — in counterclockwise [3,4].

Methodology

Speckle Tracking Echocardiography (STE) estimates myocardial strain — the degree of myocardial segment thickness or length from final diastolic to final systolic value (in percent). Its derivative — strain rate shows the speed of shortening or thickening [5]. The method is based on a semi-automatic analysis of the speckle movement — group of points ranging in size from 20 to 40 pixels and form unique acoustic patterns [6]. STE is registered in the mode of a gray-scaled two-dimensional ultrasound image, so it does not depend on the scanning angle. This makes it possible to assess myocardial segments deformation in three directions: longitudinal, circular and radial, that makes it superior to tissue doppler imaging (TDI) [7]. STE also highly correlate with magnetic resonance imaging [8].

On the other hand, there are several potential limitations of this method. Firstly, it strictly depends on the optimal frame rate — 35–70 per minute. Secondly, it requires extremely high quality of two-dimensional ultrasound images in order to visualize blood-endocardial border, epicardial and pericardial cavities. Recording should also be done during breath holding in order to avoid acoustic patterns drift with stable electrocardiographic picture — heart sinus rhythm [7,8].

Normative values

The results of resent studies on the assessment of myocardial deformation using STE, are reflected in modern recommendations. Only Global Longitudinal Strain (GLS) was reliable and reproducible indicator for LV systolic function assessment. Thus, the meta-analysis of 24 studies from 2009 to 2011 (2597 healthy volunteers, average age 47 years, 51% — men), the average GLS was 19.7% [9]. According to the JUSTICE study (817 healthy volunteers, average age 36 years, 61% — men), average GLS value differed for devices companies: 21.3±2.1% for General Electric; 18.9±2.5% for Phillips and 19.9±2.4% for Toshiba [10]. The intra- and inter-research variability was low: 5.2% and 6.5%, for General Electric; 5.1% and 6.2% for Philips; 6.2% and 5.4% for Toshiba, respectively [11]. The HUNT study revealed gender differences in GLS values: 15.9% for men; 17.4% for women [12]. It is also remarkable that the severity of GLS decreases with age: 22.2±2.2% for patients under 20 years; 20.9±1.9% for patients over 60 years [13].

Therefore, current guidelines published by EACVI / ASE in 2015 propose using the GLS value above 20% as a normal [14]. The 2011 ASE / EAE recommendations suggested using 18±2% as the lower limit of the normal value [15].

Average rates of global radial LV deformation in adults were 54.6±12.6% and 42±7%, global circular deformation 22.8±2.9% and 23.3±3% according to different studies [10.16]. The severity of circular deformation decreases or remains unchanged, radial — always remains the same [13,16].

The results of studies on the rotation and twisting reveal extremely large interval of average values. It is also remarkable that according to Yi Zhang, the apical rotation increases with age — from 2.19±1.27 ° to 10.34±1.54 °, and basal decreases — from 1.13±0.39 ° to 7.21±2.19 ° [17].

Thus, large variability of values that determine lower limit of deformation, rotation and twisting of the myocardium, shows that each laboratory using the STE method to assess myocardial function need to determine its own normative values.

Chronic heart failure and cardiac resynchronization therapy

Global longitudinal strain (GLS) decreases in all three directions in patients with chronic heart failure (CHF). Moreover, the severity GLS reduction correlates with NYHA functional class (FC) of CHF, that is due to change in myocardial fibers orientation due to cardiac remodeling [18]. Moreover, GLS is a promising indicator for patients with mild systolic dysfunction with preserved LV ejection fraction (EF), and can be useful for patients with unexplained symptoms of heart failure [19]. Some authors claim that 16% of GLS is associated with CHF with preserved LV EF, and 12% with severe systolic dysfunction [20].

Cardiac resynchronization therapy (CRT) improves LV contractility and leads to cardiac reverse remodeling. Numerous randomized clinical trials demonstrated that NYHA FC of CHF, the number of admissions due to CHF progression and CHF and all-cause mortality decreases due to CRT [21].

Nowadays, combination of parameters is used in order to select patients for CRT: FC of CHF, duration of QRS complex, left bundle branch block (LBBB), LV EF. Thus, myocardial electrical dysynchrony is emphasized. But about 30% of patients do not respond to therapy [21].

A number of studies have shown that the criteria of clinical response to CRT in patients with intraventricular and interventricular mechanical dyssynchrony in combination with the selection criteria used in the national guidelines are superior to existing criteria alone [22].

Mechanical dyssynchrony and speckle tracking echocardiography method

Dyssynchrony is the pathological contraction or relaxation of individual heart chambers or myocardium segments due to electrical conductivity impairment [23]. When assessing mechanical dyssynchrony in patients with heart failure using STE method, it is important to remember that electrical impulses (EI) propagate faster in the longitudinal direction of cardiomyocyte (CM) — 0.50–0.98 m/s than in the transverse — 0.19–0, 26 m/s [24,25]. The coincidence between CM position and EI direction is physiological and is called isotropic conduction. Under certain conditions, the CMs may underwent "functional dissociation", therefore, the speed of EI in the longitudinal direction can decrease [24]. Since the direction and orientation of the myocardial layers changes in patients with CHF, it seems relevant to use the STE method to study myocardial deformation in three directions: longitudinal, circular and radial.

The following types of mechanical dyssynchrony are distinguished: atrioventricular, interventricular and intraventricular. Atrioventricular dyssynchrony is premature left atrium contraction before venous return during LV filling phase and the reduction of LV filling time. Due to the reduction of LV preload, the Frank-Starling mechanism is lower that compromises the stroke volume [26]. However, the STE method is potential assessment method of only the types of mechanical dyssynchrony described below.

Interventricular dyssynchrony: left bundle branch block and septal flush

Interventricular dyssynchrony is seen in patients with EI impairment with block of one of His bundle branches, most often LBBB. The anterolateral segment of the right ventricle is excited earlier due to an electrical impulse propagation through the intact right branch of His bundle. Distribution has the following sequence: interventricular septum (IVS), LV anterior wall, vertically through the anterolateral LV segment, heart apex. Subsequently, excitation changes direction from LV apex downward, — reaches the lateral and posterolateral LV segments close to the mitral annulus (MA) and forms U-shaped conduction pattern [27,28].

Despite obvious conduction impairment, LBBB is a complex heterogeneous disorder at several anatomical levels. The transseptal activation front subsequently propagates along preserved Purkinje fibers or CMs with significantly lower speed compared with specialized cells. The line of functional conduction block is usually parallel to the septum, directed from LV base to its apex in patients with LBBB. Its location can be front, lateral or lower (low septal) [27].

Not only the location of conduction block line, but also the place of EI conduction through IVS and transseptal conduction time are the factors determining QRS complex duration. According to Auricchio A. et al. patients with septal apical EI conduction showed longer transseptal conduction time, and patients with over 40 ms had QRS complex duration significantly higher (197±28 ms and 154±21 ms; p=0.001). Patients with lateral functional block line had lower duration of the QRS complex (156±19 ms and 194±32 ms; p=0.003) and shorter transseptal conduction (18±21 ms and 61±22 ms; p=0.001) [27]. This explains why, in a number of studies, the response to CRT was associated not only with QRS complex duration and its morphology — complete LBBB, but also with mechanical myocardial dyssynchrony.

It is also remarkable that early transseptal activation — less than 20 ms — is accompanied by transeptal pressure gradient change and abnormal presystolic basal IVS segment displacement into LV cavity (pre-ejection septal shortening) before heart walls movement, since there is no LV resistance [29]. Septal shortening stops due to late LV wall contraction and is called septal rebound stretch [30]. This phenomenon was first described in 1982 as septal flash (SF) and can be determined using STE (Figure 1) [31,32]. As a result, posterior papillary muscle can move towards the MA and lead to early systolic mitral regurgitation [26]. Identification of SF is possible during the assessment of all deformation types: longitudinal, radial, circular [32–34]. According to several authors, SF is a consequence of LBBB, and is the best predictor of the response to CRT [32,33]. The START study evaluated circular deformation of six LV myocardial segments at papillary muscles level. The results of the study showed that standard deviation increase of the intervals between the circular deformation peaks in the curves with several peaks (T first-SD of CS> 116 ms) and the beginning of QRS complex is more reliable approach to identify the response to CRT compared with echocardiography (OR 9.83; 95 % CI 3.78–25.6; p<0.001) [32].

Moreover, SF may be associated with expanded response to CPT [35]. Several myocardial deformation models were revealed in patients with SF and varying degree of response to CPT [36].

Intraventricular dyssynchrony

Intraventricular dyssynchrony is associated with the change of LV segments stimulation sequence. Local stretching of uncoordinated segments of the myocardium occurs during isovolumetric contraction. The systole effectiveness decreases, and metabolic needs of contracting part of the myocardium subsequently increase. Asynchronous contraction of the papillary muscles, as well its tightening due to the asynchronous contraction of other LV myocardium segments can lead to excessive tendinous cords tension, displacement and incomplete closure of the mitral valve and regurgitation [37].

Intraventricular myocardial dyssynchrony assessment using STE is based on measuring delays be-

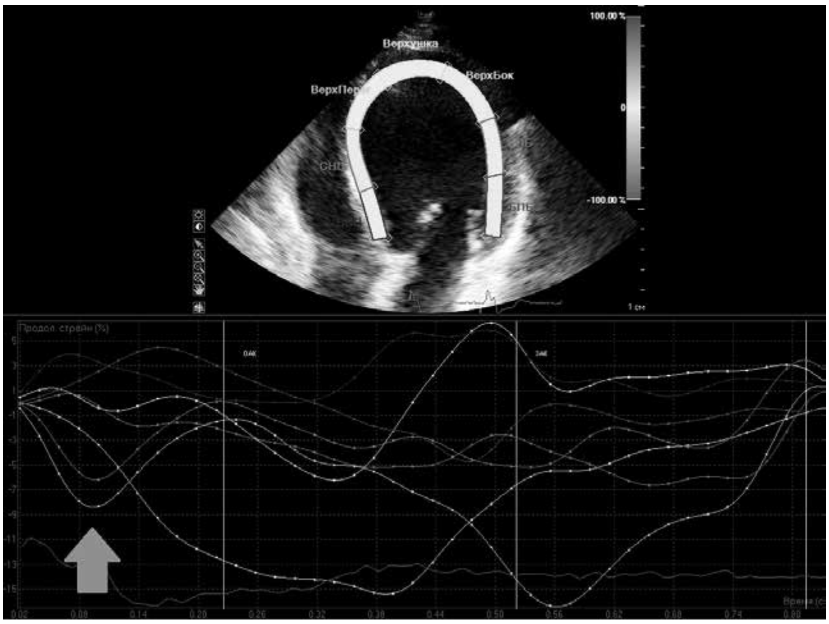

Figure 1. Early presystolic LS peak in basal and middle IVS segments in patient with SF (indicated by an arrow).

tween deformation peaks. Thus, only mechanical dyssynchrony is estimated.

The Strain Delay Index (SDI) — wasted energy of sixteen LV myocardial segments is commonly used. SDI is maximum and final systolic deformation peaks delay ratio [38]. The authors of the MUSIC study demonstrated that longitudinal SDI correlated with reverse LV remodeling (r=0.61; p<0.01) in patients with wide and narrow QRS complexes. SDI over than 25% predicted the response to CPT with positive and negative predicted 80 and 84% values, respectively (AUC=0.88; p<0.001) [38].

Researchers also use traditional for two-dimensional echocardiography and simpler in calculation method — the determination of the interval between the deformation peaks of the middle segments of opposite LV walls — the posterior and anterior-septal (opposing wall delay) [39]. Thus, according to STAR study, it was found that pronounced radial deformation dyssynchrony with 130 ms cut-off value of response to CRT with 87% sensitivity and 67% specificity (AUC=0.71; p<0.001) [40]. It is important to note that the results of several studies with long observation period showed higher survival rate of patients with initial pronounced radial deformation dysynchrony compared with patients without dysynchrony [39].

The CARDIA study showed that the longitudinal strain estimation is more reproducible compared with radial and circular strains [41]. It was also noted that combined dyssynchrony index of all three strain types has better prognostic value compared with using each parameter separately [42].

Longitudinal Dyssynchrony Index, 12SD-ε is evaluated using STE and TDI and is also remarkable [38, 39]. Standard deviation of the intervals between deformation peaks of 12 myocardial segments (basal and middle LV levels) and the beginning of the QRS complex were determined. 12SD-ε value over 60 ms according to TDI predicts the response to CRT with a 79% sensitivity and a 92% specificity (AUC=0.852; p<0.001) [39]. Therefore, complex approach — the use of STE and TDI together — improves the assessment of the global systolic LV function and also increases the ability to predict the response to CRT (table 1) [43].

Table 1. **Predictors of the CRT effectiveness according to STE and TDI**

Parameters	Method	Cut-off value	Strain type
T first-SD, ms	STE	>116	Circular
SDI, %	STE	>25	Longitudinal
Opposing wall delay, ms	STE	>130	Radial
12SD-ε, ms	TDI	>130	Longitudinal

Comment: T first-SD — standard deviation of the intervals between the peaks of circular deformation of curves with several peaks; SDI –Strain Delay Index; 12SD-ε — Longitudinal Dyssynchrony Index; STE — Speckle Tracking Echocardiography; TDI — Tissue Doppler Imaging.

Conclusion

The assessment of interventricular dysynchrony — the search of interventricular septum movement impairments — and intraventricular mechanical dysynchrony in order to predict the response to CRT using the STE method is a promising section of modern ultrasound diagnostics.

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