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Left ventricular systolic synchrony in dilated cardiomyopathy patients with normal QRS wave

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Abstract: **Objective** To evaluate the distribution characteristics of left ventricular systolic dyssynchrony (LV-SD) in dilated cardiomyopathy (DCM) patients with chronic heart failure (CHF) and normal QRS wave width, by pulsed-wave Doppler tissue imaging (PW-DTI), and study its relation with left ventricular systolic function, ventricular remodeling, and functional mitral regurgitation (FMR). **Methods** The time to peak systolic velocity (Ts) in 12 left ventricular segments was evaluated by PW-DTI, from which the standard deviation (SD) of Ts in the 12 segments (Ts-SD) and maximum Ts difference (Ts-maxD) were calculated. **Results** Ts-SD and Ts-maxD in the 12 LV segments of the DCM patients with CHF were significantly higher than those of the healthy controls ($P<0.01$). In DCM patients with CHF and normal QRS wave width, the incidence of LV-SD was 29.8% (14/47) and the inferior wall was the most frequent distribution site of contraction delay. Linear regression analysis revealed a negative correlation between Ts-SD, Ts-maxD, and left ventricular ejection fraction (LVEF) ($P<0.01$), but a positive correlation between Ts-SD, Ts-maxD and left ventricular end-diastolic volume (LVEDV), lefe ventricular end-systolic volume (LVESV), New York Heart Association (NYHA) cardiac function, FMR ($P<0.01$) in DCM patients with CHF. **Conclusion** LV-SD exists in DCM patients with normal QRS width. LV-SD aggravates the LV systolic function damage, which is closely associated with left ventricular remodeling. LV-SD may contribute to the FMR in DCM patients.

Key words: dilated cardiomyopathy; chronic heart failure; left ventricular systolic dyssynchrony; pulsed-wave Doppler tissue imaging

QRS 波宽度正常的扩张型心肌病左室收缩同步性研究

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[摘要] **目的**：运用脉冲多普勒组织成像(PW-DTI)技术评价 QRS 波宽度正常的扩张型心肌病(DCM)慢性心力衰竭患者左室收缩同步性的分布特征，及其与左室收缩功能、心室重构、功能性二尖瓣

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返流(FMR)的关系。**方法**:应用PW-DTI技术测量47例DCM慢性心力衰竭患者(DCM组)和40例正常人(正常对照组)左室壁12个节段的收缩达峰间期(Ts),计算Ts的极差(Ts-maxD)和标准差(Ts-SD)。**结果**:DCM组Ts-SD和Ts-maxD显著大于正常对照组($P<0.01$);DCM组中Ts-maxD大于100 ms或Ts-SD大于34.4 ms患者有14人,即不同步率为29.8%(14/47),收缩延迟的部位以左室下壁多见;DCM慢性心力衰竭患者Ts-SD,Ts-maxD与左室射血分数(LVEF)呈负相关($P<0.01$),与左室舒张末容积(LVEDV),左室收缩末容积(LVESV),功能性二尖瓣返流(FMR),纽约心脏协会(NYHA)心功能分级呈正相关($P<0.01$)。**结论**:部分QRS波宽度正常的DCM慢性心力衰竭患者左室存在机械收缩不同步;左室机械收缩不同步加重心功能损害,与左室重构亦有密切关系,并可能是DCM患者FMR的原因之一。

[**关键词**] 扩张型心肌病; 慢性心力衰竭; 左室收缩不同步; 脉冲多普勒组织成像

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Prolonged QRS duration (≥0.12 s) is considered to be the criterion of asynchronous contraction of left ventricular, as well as an indication for patients with heart failure (HF) to receive cardiac resynchronization therapy (CRT). However researches have shown that 20% – 30% of the patients with a wide QRS complex did not benefit from CRT[1], while some of the HF patients who have normal QRS duration were detected asynchronous left ventricular contraction and benefit from the CRT[2], indicating that the QRS duration can not precisely reflect the synchrony of mechanical movement of left ventricular[3-4]. In recent years, Doppler tissue imaging (DTI) technique was widely used in researches on synchrony of myocardial movements[5]. It provided electro-mechanical coupling information by determining the velocity and time of contraction contraction of different segment, and is more sensitive and accurate in reflecting the synchrony of myocardial movements.

At present, there are many researches on synchrony of left ventricular contraction in HF patients with wide QRS complex, while study in HF patients with normal QRS is few. In this article, using pulsed-wave Doppler tissue imaging (PW-DTI) technique, we assessed the synchrony of left ventricular contraction in dilated cardiomyopathy (DCM) patients with HF and normal QRS.

1 SUBJECTS AND METHODS

1.1 Subjects

We studied 47 patients diagnosed of DCM and HF (DCM group) including 31 males and 16 females [aged 16 – 68 (49 ± 13) years, QRS duration (97 ± 12) ms, heart rate (75 ± 10) bpm]. The stage of HF was New York Heart Association (NYHA) II-IV. Forty healthy subjects (control group) including 27 males and 13 females received the physical examination [aged 22 – 67 (48 ± 13) years, QRS duration (94 ± 10) ms, heart rate (72 ± 8) bpm]. The ages, gender ratio, QRS durations, and heart rates between the DCM group and the control group had no significant difference ($P > 0.05$). The patients were selected based on the DCM criteria defined by World Health Organization (WHO)/International Society and Federation of Cardiology (ISFC) in 1995, and they all satisfied the Framingham Criteria for HF. Patients with coronary atherosclerosis, cardiac valvular heart disease, congenital heart disease, chronic pulmonary heart disease, simple right heart failure, pericardial disease, acute left heart insufficiency, atrial fibrillation or flutter and those who had been implanted permanent cardiac pacemaker were excluded.

1.2 Methods

The patients were placed in left lateral position. Ultrasonic cardiogram equipment HP-5500 (USA), frequency of probe 2 – 4 MHz was used in the study. A total of 3 cardiac cycles was chosen to measure the indexes at the end of calm expiration, and the average values were calculated. The whole process was stored in read-write disk in the form of Loop for the future analysis.

1.2.1 General ultrasonic cardiography

We measured the area of left ventricular cavity's short-axis plane at the short axis view of mitral valve orifice and papillary muscle level, and the diameter of long-axis at the apical 4-chamber view. By using the modified Simpson formula, we calculated the left ventricular ejection fraction (LVEF), the left ventricular end-diastolic volume (LVEDV), and the left ventricular end-systolic volume (LVESV). We obtained the color Doppler image of the mitral valve regurgitation beam when it reached the maximum area at the apical 4-chamber view, traced the mitral regurgitation area (MRA) and left atrium area (LAA) and calculated the ratio of MRA and LAA (MRA/LAA).

1.2.2 PW-DTI

The system program was set on the DTI mode, using the optical gain (the velocity scale 10–20 cm/s, the scanning speed 100 mm/s). In apical 4- and 2-chamber, and the left ventricular long-axis views, the ultra sound beam issued by the probe paralled to left ventricular longitudinal motion with the angle between them smaller than 20°. We took 12 samples of the basal and middle segments of the 6 left ventricular walls, and measured the period from the beginning of QRS complex to the maximum contraction velocity (Ts). Fig. 1 showed the measuring mothod. The range (Ts-maxD) and standard deviation (Ts-SD) of Ts were calculated. Ts-maxD > 100 ms or Ts-SD > 34.4 ms was considered as contraction asynchrony[6].

1.3 Statistical analysis

Data were presented as mean ± standard deviation ($\bar{x} \pm s$). The statistical analyses were performed with SPSS13.0. The comparison of measurement data between the 2 groups was tested with t-test, and the comparison of gender ratio was tested with chi-square test. Linear correlation or Spearman rank correlation analysis was used to test the correlation. $P < 0.05$ was considered as statistical significance.

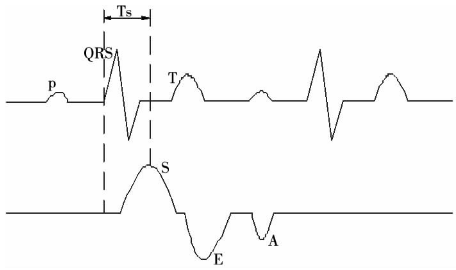

Fig. 1 Image and measurement method of PW-DTI of left ventricular wall.

2 RESULTS

2.1 Comparison of PW-DTI indexes between the 2 groups

The PW-DTI of healthy adults' left ventricular walls manifested as positive S wave in the systole, and reverse E and A wave in the diastole (Fig. 2). The PW-DTI of DCM heart failure patients' left ventricular walls was similar to that of the healthy subjects with a decreased amplitude. The value of Ts of the DCM group was significantly higher than that of the control group ($P < 0.01$, Fig. 2, Tab. 2). The values of Ts-SD and Ts-maxD of DCM group [(38.66 ± 12.71) ms and (119 ± 30) ms] were significantly higher than those of the control group [(22.98 ± 5.59) ms and (55 ± 15) ms, $P < 0.01$].

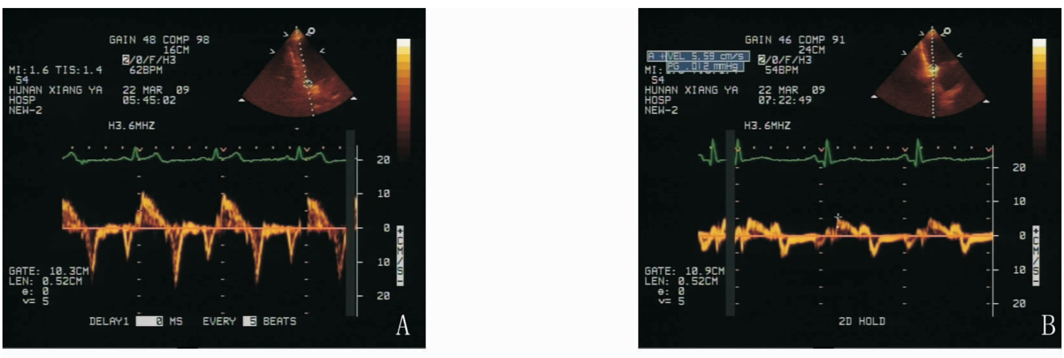

Fig. 2 PW-DTI curve of healthy adult (A) and patients with DCM heart failure (B).

Tab. 2 Comparison of Ts between the DCM group and the control group ($\bar{x} \pm s$, ms)

Groups	Segments	PSV	LW	AW	IW	ASV	PW
Control	Basal	233 ± 31	198 ± 27	200 ± 24	240 ± 30	231 ± 31	228 ± 37
	Middle section	239 ± 35	197 ± 27	202 ± 26	248 ± 30	232 ± 31	234 ± 37
DCM	Basal	335 ± 86**	332 ± 70**	306 ± 74**	354 ± 78**	340 ± 85**	349 ± 88**
	Middle section	341 ± 90**	341 ± 69**	313 ± 74**	366 ± 88**	346 ± 85**	341 ± 75**

PSV: Posterior septum wall; LW: Lateral wall; AW: Anterior wall; IW: Inferior wall; ASV: Anterior septum wall; PW: Posterior wall. Compared with the control group, ** $P < 0.01$.

2.2 Asynchronous rate and the distribution of contraction delay

There were 14 cases in the DCM heart failure group got Ts-maxD > 100 ms or Ts-SD > 34.4 ms, i.e., the asynchrony rate was 29.8% (14/47). Most of the patients (68%) had only 1 ventricular wall presented contraction delay, a small part of the patients (32%) had 2 or more. The parts that contraction delay occurred were mostly positioned in left ventricular lower wall (LVLW, 45%), then left ventricular posterior wall (LVPW, 28%), left ventricular lateral wall (LV-LW, 26%), anterior septum (19%), posterior septum and anterior wall (11%, 9%).

2.3 Correlation analysis

The Ts-maxD and Ts-SD was negatively correlated with LVEF ($r = -0.560$, -0.553; $P < 0.01$), and positively correlated with LVEDV, LVESV, NYHA cardiac function level, and functional mitral regurgitation (FMR) ($r = 0.629$, 0.557, $P < 0.01$; $r = 0.710$, 0.654, $P < 0.01$; $r = 0.549$, 0.590, $P < 0.01$; $r = 0.530$, 0.542, $P < 0.01$; Tab. 3).

Tab. 3 Correlation coefficients of Ts-maxD, Ts-SD and LVEF, LVEDV, LVESV, NYHA cardiac function, FMR

Indexes	LVEF	LVEDV	LVESV	NYHA cardiac function	FMR
Ts-maxD	−0.560	0.629	0.710	0.549	0.530
Ts-SD	−0.553	0.557	0.654	0.590	0.542

3 DISCUSSION

It was shown in research[7] that asynchrony of left ventricular contraction is an important factor of the decreased contraction function of chronic heart failure patients. Studies[8-9] have showed that CRT combined with ideal pharmacotherapy can reverse the cardiac remodeling and reduce the hospitalization rate of heart failure patients. Today the hotspots are to assess the asynchrony of left ventricular contraction, choosing suitable patients, and improve CRT's reactivity so as to best benefit heart failure patients. At present the main standard of asynchrony is QRS duration. However, studies[10-11] showed QRS duration beared weak correlation with synchrony of left ventricular contraction. Though it is found in clinical practice that 30% −40% of HF patients with a wide QRS complex (≥0.12 ms) have preferable synchrony of left ventricular contraction[12]. Further, for heart failure patients diagnosed of desynchronization of left ventricular contraction with normal QRS duration, CRT can effectively improve their symptoms and reverse the ventricular remodeling[2]. So it is necessary to study other technical indexes that may reflect the asynchrony of ventricular contraction. Owing to its high spatial and temporal resolution, DTI is capable of sensitively reflecting the synchrony of left ventricular contraction.

Ts is the period from the beginning of QRS complex to the point of maximal velocity of contraction (Vmax), and is also the period during which the excitation-contraction of the myocardium reaches the maximum. The larger the Ts-maxD and the Ts-SD is, the more discordant and dissymmetrical the left ventricular contraction will be. This study showed that, the Ts-maxD and the Ts-SD of left ventricle in the DCM heart failure group are obviously higher than those in the control group, suggesting the local myocardium contraction delay and the nonuniformity of left ventricular contraction. In this research, the QRS duration of DCM heart failure patients was normal, while 14 patients were detected asynchrony of left ventricle by DTI technique, the rate was 29.8% (14/47). This result is similar to the research performed by Sade, et al.[13]. In some researchers' opinion, pathologic myocardium has difficulty on electro-mechanical coupling. So although the electrocardiogram shows normal QRS duration, there still may be contraction delay and asynchrony in different sections of myocardium.

To obtain the most ideal synchronizing effect, the most delayed part is usually selected as the pace-making cite of left ventricle in CRT. It was found in this study that, in the DCM heart failure patients, the part that contraction delay occurred mostly is in LVLW, and relatively less is the anterior wall. This may represent the distributive characteristics of left ventricular contraction asynchrony in DCM heart failure patients. It was reported[14] that when placing the electrodes on positions selected according to the DTI technique, the therapeutic effect of CRT was much better than placing them on other places[15-16]. It is suggested that the DTI technique is practically valuable in deciding the part of delayed mechanical movement in the heart.

When the left ventricular contraction is not synchronous, the muscular tone of the part that contracts is earlier than that of the adjacent parts with delayed contraction, which causes the blood to flow to the delayed parts and sections, resulting in the distension and expension of the local myocardium. When the delayed section contracts, the muscular tone forces the blood to flow to the delayed ventricular wall and sections. The discordant contraction presented in different parts at different time may result in blood shunt and cause a decreased ejection fraction of the whole heart. It may also cause the redistribution of blood in different parts of the heart and metabolic nonuniformity, leading to the pathological and physiological alternations, accelerating the progress of ventricular remodeling, and further damaging the myocardial functions. It was showed in this research that the Ts-SD and Ts-maxD of the DCM group was negatively correlated to the LVEF, and was positively correlated to NYHA cardiac function, LVEDV and LVESV, indicating that the asynchrony of myocardial contraction in different sections might accelerate the progress of ventricular remodeling, and damage the cardiac functions. It is found in some CRT follow-up study[17] that when the synchronism of left ventricular contraction is improved, cardiac functions will be improved and the left ventricular remodeling will be obviously reversed.

FMR refers that the mitral valve regurgitation presents when the function of left ventricle decrease while the valve itself has no pathological change. It is common in patients with nonischemic cardiomyopathy or ischemic cardiomyopathy combined with chronic heart failure. In this research, the DCM heart failure patients has mild or moderate FMR. Ts-SD and Ts-maxD, the contractive asynchrony indexes, were positively correlate to the degree of FMR. Apart from mitral annulus dilation due to the alternations of left ventricular structure, limit of papillary muscle and mitral valve leaflets to shift towards the Apex of the heart and the outside, and decreased kinetic energy of mitral valve closure, FMR may also result from the asynchrony of the myocardial contraction in the papillary muscle in anterior-lateral and posterior-medial mitral valve[18-19]. In recent years, research[20] showed that CRT can promote the ventricular synchronization as well as alleviate mitral valve regurgitation, indicating that the asynchrony of cardiac contraction might relate to FMR. However, some researcheres believed that[21-22] FMR has close relation with asynchrony of cardial diastole. So, further researches are required to study the correlation between FRM and heart's mechanical movements.

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