Diastolic function in Steinert's disease

Abdallah Fayssoil, Olivier Nardi, Djillali Annane, David Orlikowski

Critical Care Unit, Raymond Poincaré Hospital, University of Versailles SQY, Garches, France

Abstract

Myotonic dystrophy type 1 (MD) is the most common autosomal dominant muscular dystrophy in adults. Cardiac involvement is mainly characterized by conduction abnormalities and arrhythmias. We sought to assess diastolic function in MD patients. Echocardiography-Doppler was performed in Steinert's patients and in a control group completed by tissue Doppler imaging (TDI). Twenty-six patients with Steinert's disease were included in the study and were compared to a control group. Mean age was similar in the 2 groups (45.1 years ±10.9 in Steinert's patients *vs* 42.1 years ±11 in control group p 0.4). 6 /26 patients with Steinert's disease disclosed a left ventricular (LV) ejection fraction <50%. Mean left atrial (LA) diameter was statistically different between Steinert's patients and patients in group control (27.8 mm ±8.5 *vs* 19.7 mm ±4; P=0.0018). Mean peak E/A mitral ratio was 1.29±0.45 in Steinert's patients *vs* 1.36±0.4 in control group (P=0.6). We found an increase of the mitral E deceleration time in Steinert's patients in comparison with patients in control group (219 ms ±53 *vs* 176 ms ±29; P=0.013). Mean peak lateral early diastolic velocity Ea was similar in the 2 groups (12.3 cm/s ±3 *vs* 13.1 cm/s ±3.8; P=0.50). Mean peak septal early diastolic velocity was similar in the 2 groups (11.2 cm/s ±2 *vs* 10.4±2; P=0.51). We found an increase of the LA diameter and an increase of the mitral deceleration time in Steinert's patients that suggest diastolic abnormalities.

Introduction

Myotonic dystrophy type 1 (MD), also known as Steinert's disease, is the most common autosomal dominant muscular dystrophy in adults.[1] This disease is characterized by multisystem disorder that affects the skeletal muscle, the eye, the endocrine system, the central nervous system and the heart. MD is caused by an abnormal expansion of a CTG trinucleotide repeat on chromosome 19q21. In MD, RNA sequesters splicing regulators of genes. Cardiovascular disease is one of the most prevalent causes of death in this disease. Cardiac involvement is mainly characterized by conduction abnormalities and arrhythmias.[1] Less commonly, cardiomyopathy may occur with LV dysfunction.[2] Echocardiography-Doppler is a simple and reproducible ultrasound imaging for the assessment of cardiac function. Moreover, tissue Doppler imaging (TDI) is an interesting tool for the analysis of sub clinical ventricular function and diastolic function.[3] Skeletal muscle myotonia is a clinical feature of MD. We sought to assess diastolic function in MD patients using TDI.

Materials and Methods

A total of 26 MD patients followed in our institution for annual respiratory function evaluation were included retrospectively in our study. The study was approved by our local clinical investigation center. Echocardiography was performed with a Siemens CV70 (Siemens, Munich, Germany). All the exams were realized for the follow- up of patients and were performed during the annual multidisciplinary consultation. Patients were examined in the left lateral decubitus position. A M-mode was performed from the parasternal long axis for the analysis of the following parameters: LV end-diastolic septal thickness, end-diastolic posterior wall thickness and LV end-diastolic diameter. LV ejection fraction (LVEF) was calculated from LV volumes using Teicholtz's method from the para-sternal long axis view and /or from the 4 chamber apical view using Simpson method. From the 4 apical chamber view, a pulsed-wave Doppler of trans-mitral flow was performed to assess mitral inflow velocities. The sample volume was placed at the tip of mitral leaflets from the apical 4-chamber view. Doppler indices were measured: peak early velocity (E), peak atrial velocity (A), E-wave deceleration time (EDT) and the peak E/A ratio was calculated. From the 4 chamber apical view, for TDI analysis, the sample volume was positioned within the lateral and the septal insertion site of the mitral leaflet. During the procedure, the angle between the Doppler beam and the longitudinal motion of the investigated structure was adjusted to a minimal level. The pulsed tissue Doppler pattern is characterized by a positive myocardial systolic velocity (Sm) and 2 negative diastolic velocities (early, Em and late, Aa). Myocardial E wave velocity (Ea) was defined as the maximal negative velocity during early diastole (cm/s).

Statistical analysis

Data are presented as mean value ±SD (standard deviation). A Student t test was used for statistical analysis. A P<0.05 was considered significant.

Correspondence: Abdallah Fayssoil, Critical Care Unit, hospital Raymond Poincare (AP-HP), University of Versailles SQY, 104 boulevard Raymond Poincare, 92380 Garches, France.
Tel. +33.014.710.77778 - Fax: +33.014.710.7783
E-mail: fayssoil2000@yahoo.fr

Key words: myotonic dystrophy, echocardiography-Doppler, diastolic function.

Key words: myotonic dystrophy, echocardiography-Doppler, diastolic function.

Contributions: the authors contributed equally.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 21 October 2013.
Revision received: 24 February 2014.
Accepted for publication: 3 March 2014.

Neurology International 2014; 6:5140
doi:10.4081/ni.2014.5140

Results

Twenty-six patients with Steinert's disease were included in our study (12 female and 14 male) and compared to a control group (n=13) (Table 1). Mean age was similar in the groups (45.1 years ±10.9 in Steinert's patients *vs* 42.1 years ±11 in control group, P=0.4). Nine patients benefited from pacemaker implantation because of conduction abnormities and 1 patient had implantable defibrillator. All patients with MD were asymptomatic and did not disclose any signs of heart failure. Mean vital capacity (VC) was 43.5% ±16 in MD patients. 6 patients/23 disclosed left ventricular dysfunction with LVEF <50%. LV end diastolic diameter (LVEDD) was not statistically different in Steinert's patients in comparison with the control group (42.6 mm ±8 *vs* 46.6 mm ±4, P=0.09). LVEF was statistically different between Steinert's patients and control group (58% ±13 *vs* 66% ±4.7, P=0.03). Mean left atrial (LA) diameter was statistically different between Steinert's patients and group control (27.8 mm ±8.5 *vs* 19.7 mm ±4, P=0.0018).

Mean peak E/A mitral ratio was 1.29±0.45 in Steinert's patients *vs* 1.36±0.4 in control group P=0.6). We found an increase of the mitral E deceleration time in Steinert's patients in comparison with control group (219 ms ±53 *vs* 176 ms ±29, P=0.013).

Table 1. Comparison of echocardiographic parameters between Steinert's patients and control group.

	Steinert's patients	Control group	P
Age (years)	45.1 (10.9)	42.1 (11)	0.46
LVEDD (mm)	42.6 (8)	46.6 (4)	0.09
IVSd (mm)	9.6 (1.8)	9.8 (1.28)	0.7
PWd (mm)	9.9 (1.6)	9.8 (1.2)	0.9
LVEF (%)	58 (13)	66.2 (4.7)	0.03
Mitral E/A ratio	1.29 (0.45)	1.36 (0.4)	0.6
EDT (ms)	219 (53)	176 (29)	0.013
LA diameter (mm)	27.8 (8.5)	19.7 (4)	0.0018
Peak Ea septal (cm/s)	11 (2)	10.4 (2)	0.51
Peak Ea lateral (cm/s)	12.3 (3)	13.15 (3.8)	0.50

Data are expressed as mean (standard deviation). LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic diameter; IVS, inter-ventricular septal; PW, posterior wall of the left ventricle; EDT, wave E deceleration time (ms); LA, left atrial.

Mean peak lateral early diastolic velocity Ea was similar in the 2 groups (12.3 cm/s ±3 *vs* 13.1 cm/s ±3.8, P=0.50). Mean peak septal early diastolic velocity was similar in the 2 groups (11.2 cm/s ±2 *vs* 10.4±2, P=0.51).

Discussion

We found LV dysfunction in MD patients (6 patients/26). Also, we found diastolic abnormalities in DM patients with a significant increase of the LA diameter in Steinert's patients (27.8 mm ±8.5 *vs* 19.7 mm ±4, P=0.0018) and a significant increase of the mitral E deceleration time in Steinert's patients in comparison with control group (219 ms ±53 *vs* 176 ms ±29, P=0.013). Peak lateral and peak septal early diastolic velocity Ea was similar in the 2 groups. Cardiac involvement in myotonic dystrophy had been assessed using Doppler-echocardiography by *others*.[4-7] Cardiac involvement in MD is characterized by conduction system abnormalities, supra-ventricular and ventricular arrhythmias and less frequently by myocardial dysfunction. MD is an inherited autosomal dominant muscular dystrophy due to expansion of a trinucleotide sequence on chromosome 19. RNA expression of the repeat expansion is involved in the physiopathology. RNA sequesters splicing regulators of genes. Perturbation of splicing and expression of troponine T seems imputable in the patho-physiology of cardiac dysfunction in MD.[8] Skeletal muscle relaxation abnormality, related to myotonia, is a clinical feature in MD. The same phenomenon seems present in cardiac muscle. Myocardial relaxation during diastolic process includes calcium extrusion from the cytosol and cross-bridge detachment. This phenomenon is affected by a number of proteins that regulate calcium homeostasis,[9] cross-bridge cycling, and energetics. Diastolic dysfunction may also be attributed to ischemia phenomena. Endomyocardial biopsies of patients with Steinert's disease disclosed subendocardial fibrosis, fatty infiltration, focal myocarditis and variable degree of fibre disarray in MD patients.[10] TDI provides analysis of regional motion of the heart by assessing systolic and diastolic velocities. TDI is less preload dependent, compared to traditional pulsed Doppler technique.[11]

Limits of our study

TDI is limited by angle dependence that can affects data. 2D stain is more suitable for the analysis. We did not assess LA volume that is a more pertinent parameter for diastolic abnormalities rather than LA diameter.

Conclusions

We found an increase of LA diameter and an increase of the mitral deceleration in Steinert's patients that suggest diastolic abnormalities.

References

1. Pelargonio G, Dello Russo A, Sanna T, et al. Myotonic dystrophy and the heart. Heart 2002;88:665-70.
2. Moorman JR, Coleman RE, Packer DL, et al. Cardiac involvement in myotonic muscular dystrophy. Medicine (Baltimore) 1985;64:371-87.
3. Alam M, Wardell J, Andersson E, et al. Characteristics of mitral and tricuspid annular velocities determined by pulsed wave Doppler tissue imaging in healthy subjects. J Am Soc Echocardiogr 1999;12: 618-28.
4. Fragola PV, Caló L, Luzi M, et al. Doppler echocardiographic assessment of left ventricular diastolic function in myotonic dys trophy. Cardiology 1997;88:498-502.
5. Bulock FA, Sood M, De Giovanni JV, Green SH. Left ventricular diastolic function in congenital myotonic dystrophy. Arch Dis Child 1999;80:267-70.
6. Fung KC, Corbett A, Kritharides L. Myocardial tissue velocity reduction is correlated with clinical neurologic severity in myotonic dystrophy. Am J Cardiol 2003; 92:177-81.
7. Lindqvist P, Mörner S, Olofsson BO, et al. Ventricular dysfunction in type 1 myotonic dystrophy: electrical, mechanical, or both? Int J Cardiol 2010;143:378-84.
8. McNally EM, Sparano D. Mechanisms and management of the heart in myotonic dystrophy. Heart 2011;97:1094-100.
9. Leite-Moreira AF. Current perspectives in diastolic dysfunction and diastolic heart failure. Heart 2006;92:712-8.
10. Phillips MF, Harper PS. Cardiac disease in myotonic dystrophy. Cardiovasc Res 1997;33:13-22.
11. Nagueh SF, Appleton CP, Gillebert TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009;22:107-33.