Clinical Investigations

Evaluation of Biventricular Functions With Tissue Doppler Imaging in Patients With Myotonic Dystrophy

Address for correspondence:
Beste Ozben, MD
Yildiz Caddesi Konak Apartmani
No: 43/24 Besiktas
Istanbul, Turkey 34353
besteozben@yahoo.com

Tolga Ozyigit, MD; Beste Ozben, MD; Huseyin Oflaz, MD; Piraye Serdaroglu, MD
American Hospital, Department of Cardiology, Istanbul, Turkey (Ozyigit); Marmara University Faculty of Medicine, Department of Cardiology, Istanbul, Turkey (Ozben); Istanbul University Istanbul Faculty of Medicine, Department of Cardiology, Istanbul, Turkey (Oflaz); Istanbul University Istanbul Faculty of Medicine, Department of Neurology, Istanbul, Turkey (Serdaroglu)

ABSTRACT

Background: Myotonic dystrophy (MD) is characterized by myotonia with dystrophic involvement of the muscles. Cardiac involvement is usually not evident in the early stages of MD.
Hypothesis: We investigated biventricular functions by tissue Doppler imaging (TDI) in MD patients with no overt cardiac involvement to explore the value of TDI in the early detection of myocardial dysfunction.
Methods: A total of 21 MD patients (15 male, age: 32.2 ± 12.3 yrs) and 21 healthy controls (13 male, age: 32.2 ± 7.8 yrs) were included. In addition to conventional echocardiography, pulsed Doppler and TDI were performed including measurement of myocardial performance index (MPI); peak systolic (Sm) and early (Em) and atrial (Am) diastolic myocardial velocities at the basal mitral and tricuspid annulus.
Results: All patients and controls had normal ejection fraction. Transmitral E peak velocity was significantly lower while both deceleration time of E velocity and isovolumic relaxation time were significantly longer in MD patients ($P = 0.007$, $P = 0.001$, and $P < 0.001$, respectively). Sm, Em and Am peak velocities were significantly lower in MD patients in all segments except for Em of the mitral anterior annulus and Am of the tricuspid lateral annulus. Both left and right ventricular MPI were significantly higher in MD patients ($P < 0.001$ and $P = 0.013$, respectively).
Conclusion: There are changes in myocardial systolic and diastolic functions in MD patients although they have no overt heart failure. Myocardial tissue velocities and MPI are useful in identifying subclinical biventricular involvement in these patients.

Introduction

Myotonic dystrophy (MD), described by Steinert in 1909, is an inherited disorder transmitted in an autosomal dominant fashion and characterized by myotonia with dystrophic involvement of muscles and other multisystemic manifestations.[1,2] It is the most common type of myopathy in adults, occurring in 1 in 8000 births.[1–3]

Cardiac involvement is particularly frequent in patients with MD, being present in up to 89% of patients in the advanced stages of the disease.[4,5] Myocardial fibrosis is implied in the pathogenesis of cardiac involvement.[6–8] It is usually characterized by conduction system abnormalities with prolonged PR interval, bifascicular block, frequent bradyarrhythmias, and increased risk of sudden death.[1,4,5] The myocardium may also be affected in the form of a specific cardiomyopathy (myotonic heart disease) and patients may develop symptoms of heart failure.[3,9] Cardiovascular mortality is 30%, due to a combination of progressive left ventricular (LV) dysfunction, myocardial infarction, pulmonary embolism, or sudden death caused by either ventricular asystole, degeneration of ventricular tachycardia, ventricular fibrillation or electromechanical dissociation.[1,3]

Cardiac involvement is usually not evident in the early stages and global ventricular function may remain normal until late in the disease process. However, subclinical LV diastolic dysfunction has been detected in some cases in the early stages of the disease.[10–12] These diastolic abnormalities suggest an intrinsic myocardial abnormality in patients with MD and may represent a preclinical phase of myocardial involvement. The detection of early markers of cardiac involvement may be crucial for the appropriate management of these patients.

The diagnosis of cardiac involvement is usually based on echocardiography. However, conventional echocardiography reveals no pathology in half of the patients who have abnormal endomyocardial biopsy.[13] Tissue Doppler imaging (TDI) is much more sensitive than standard

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echocardiography in the quantitative assessment of biventricular functions; it is useful in detecting subclinical myocardial dysfunction.[14] This technique allows the evaluation of myocardial systolic and diastolic properties, as well as the estimation of LV and right ventricular (RV) filling pressure by adjusting Doppler transvalvular inflow early (E) diastolic velocities for myocardial early (Em) diastolic velocities of mitral or tricuspid annulus, which are independent of preload effect.

In the present study, we investigated LV and RV systolic and diastolic functions, by using both conventional echocardiographic and TDI parameters, in MD patients with no overt cardiac involvement. Our aim was to explore the value of the TDI technique in the early detection of myocardial dysfunction in these patients.

Patients and Methods

This investigation conforms to the principles outlined in the Declaration of Helsinki. The study was approved by the local ethical committee. All participants gave written informed consent.

A total of 21 patients with MD were recruited consecutively from the Neurophysiopathology Department of Istanbul University Faculty of Medicine. In 13 patients, the diagnosis of MD was made by genetic confirmation of CTG expansion in the 3′ untranslated region of the dystrophia myotonica-protein kinase (DMPK) gene on chromosome 19q13.3, which has been associated with the disorder.[15] In the remaining 8 patients, the diagnosis was based on neurological examination, medical history, and electromyography, which shows a typical myotonic discharge. Exclusion criteria were symptoms or signs of any previous heart disease including coronary artery disease, systemic arterial hypertension, arrhythmias, conduction abnormalities or pacemaker implantation, hemodynamically significant valvular heart disease, congestive heart failure, and pericardial disease. None of the patients were taking any cardiovascular medicine. Patients with other systemic disease such as diabetes mellitus, renal failure, or thyroid disorders were also excluded from the study.

A total of 21 healthy subjects of similar sex and age distribution were included into the study as a control group.

Echocardiographic Examination

All patients and controls underwent echocardiographic examination by an echocardiography device equipped with a 2.5 MHz phased-array transducer with harmonic capability (System Five, General Electric/Vingmed Ultrasound, Horten, Norway). Echocardiographic examinations were evaluated by a single blinded cardiologist. Two-dimensional echocardiography (2DE), pulsed and continuous wave Doppler, and color flow Doppler studies were performed using standard techniques on each patient. All patients were in sinus rhythm at the time of examination and none of the patients had any conduction abnormality including long or short PR interval, bundle branch blocks, or atrioventricular block. Measurements were performed on 3 consecutive heart beats and an average of the 3 measurements was taken.

As for the conventional echocardiographic parameters, aortic root diameter, left atrial diameter (LA), LV end-diastolic and end-systolic diameters (LVED and LVES), diastolic interventricular septal thickness (IVS), diastolic posterior wall thickness (PW), LV ejection fraction (LVEF; calculated by Teichholz method), and RV diameter were measured. Endocardial fractional shortening was calculated as the percentage change of LV internal dimension between systole and diastole. LV mass (LVM) was calculated as $0.8\ (1.04\ [\{LVED + PW + IVS\}^3 - \{LVIDD\}^3]) + 0.6$ g. Left ventricular mass index (LVMi) was calculated as LVM/body surface area. Systolic pulmonary artery pressure was calculated by adding RV systolic pressure determined from peak tricuspid regurgitant velocity to estimated right atrial pressure.

Conventional pulsed Doppler imaging of mitral and tricuspid inflow was recorded in the apical 4-chamber view. Early (E) and atrial (A) peak velocities of mitral and tricuspid valves, their ratio (E/A), E velocity deceleration time (DT), and isovolumic relaxation time (IVRT) were measured.

Pulsed TDI was performed to assess RV and LV longitudinal functions. In apical 4-chamber view, a 5 mm pulsed Doppler sample volume was placed at the level of the basal portion of RV lateral tricuspid annulus and LV septal and lateral mitral annulus. Apical 2-chamber view was also used to obtain the velocities of mitral annular segments of LV inferior and anterior walls. Care was taken to obtain an ultrasound beam parallel to the direction of mitral and tricuspid annulus motions. The pulsed TDI pattern is characterized by a positive myocardial systolic velocity (Sm) and 2 negative diastolic velocities, early (Em) and atrial (Am). Sm velocity is a good indicator of myocardial systolic function. Em and Am velocities and Em/Am ratio are valuable for assessment of myocardial diastolic function. The ratios of standard Doppler transmitral E peak velocity to Em peak velocity of mitral and tricuspid annulus (E/Em ratio) were determined as indexes of LV and RV filling pressure, respectively.[16–19]

The myocardial performance index (MPI), a Doppler index of combined systolic and diastolic myocardial performance, was determined by using the following equation: MPI = (isovolumetric contraction time + IVRT)/ejection time. From the TDI recordings, the time interval from the end to the onset of the mitral annular velocity pattern during diastole (a) was measured. The duration of the Sm (b) was measured from the onset to the end of the Sm. The LV MPI was calculated as (a−b)/b.[20] The RV MPI was calculated in the same way (as the difference between time interval from the end to the onset of the tricuspid annular velocity

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pattern and duration of tricuspid Sm divided by tricuspid Sm duration).

Statistical Analysis

All statistical analyses were performed by statistical software (SPSS 11.0 for Windows, Chicago, IL). Continuous variables were expressed as mean ± standard deviation. A Student t test was used for comparison of parametric values while a Mann-Whitney test was used for comparison of nonparametric data. A χ^2 test was used to compare qualitative data. A P value <0.05 was considered statistically significant.

Results

The clinical characteristics of the patients with MD and healthy controls are shown in Table 1. Age, gender distribution, body mass index, heart rate, systolic and diastolic blood pressure were similar.

M-mode and standard pulsed Doppler echocardiographic data are shown in Table 2 and Table 3, respectively. M-mode measurements did not differ significantly between the 2 groups. All patients had normal LVEF (61% ± 6%) and none of the patients had any wall motion abnormality. Transmitral E peak velocity was significantly lower while both DT of E velocity and IVRT were significantly longer in patients compared to controls ($P = 0.007$, $P = 0.001$ and $P < 0.001$, respectively). Transmitral E/A ratio was not significantly different between the 2 groups. Among tricuspid inflow measurements, there were not any significant differences in E peak velocity, A peak velocity, or tricuspid E/A ratio between groups. However, DT of E velocity was significantly longer in MD patients ($P < 0.001$).

Tissue Doppler imaging data of LV and RV are presented in Table 4. Sm peak values and Em and Am peak velocities were significantly lower in patients compared to controls in all segments except for Em of mitral anterior annulus and Am of tricuspid lateral annulus. There were no significant

Table 1. Clinical Characteristics of the Patients and Controls

	Patients (n = 21)	Controls (n = 21)	P
Age (yrs)	32.2 ± 12.3	32.2 ± 7.8	0.988
Sex (female/male) (n)	6/15	8/13	0.513
Body mass index (kg/m²)	21.00 ± 4.22	22.90 ± 2.64	0.087
Systolic blood pressure (mm Hg)	124.6 ± 14.8	128.2 ± 10.6	0.876
Diastolic blood pressure (mm Hg)	75.5 ± 8.2	76.2 ± 7.4	0.623
Heart rate (beats/min)	82 ± 10	80 ± 11	0.724

Table 2. Standard M-mode Echocardiographic Data

	Patients	Controls	P
Aortic root diameter (cm)	2.78 ± 0.21	2.90 ± 0.32	0.068
LA diameter (cm)	3.04 ± 0.29	3.24 ± 0.36	0.060
LVED (cm)	4.50 ± 0.52	4.73 ± 0.31	0.081
LVES (cm)	2.82 ± 0.48	2.96 ± 0.25	0.235
IVS (cm)	0.90 ± 0.13	0.90 ± 0.11	1.00
PW (cm)	0.84 ± 0.12	0.83 ± 0.08	0.768
LVMi (g/m²)	98.96 ± 21.82	96.88 ± 12.79	0.708
LVEF (%)	61 ± 6	60 ± 4	0.680
Endocardial fractional shortening (%)	37.6 ± 4.7	37.4 ± 3.4	0.909
RV (cm)	2.28 ± 0.23	2.38 ± 0.24	0.205
Systolic pulmonary artery pressure (mm Hg)	24 ± 4	24 ± 3	0.937

Abbreviations: IVS, diastolic interventricular septal thickness; LA, left atrial diameter; LVED, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVES, left ventricular end-systolic diameter; LVMi, left ventricular mass index; PW, diastolic posterior wall thickness; RV, right ventricular diameter.

Table 3. Standard Doppler Analysis of Transmitral and Tricuspid Inflow and Myocardial Performance Index of Both Ventricles

	Patients	Controls	P
Mitral			
E peak velocity (m/s)	0.77 ± 0.17	0.91 ± 0.16	0.007
A peak velocity (m/s)	0.55 ± 0.19	0.60 ± 0.11	0.252
Peak velocity E/A ratio	1.50 ± 0.46	1.54 ± 0.37	0.727
E velocity DT (ms)	185.48 ± 42.19	153.81 ± 22.36	0.001
IVRT (ms)	107.86 ± 15.11	85.00 ± 9.49	<0.001
Tricuspid			
E peak velocity (m/s)	0.58 ± 0.12	0.60 ± 0.09	0.535
A peak velocity (m/s)	0.41 ± 0.11	0.39 ± 0.06	0.530
Peak velocity E/A ratio	1.51 ± 0.52	1.56 ± 0.29	0.741
E velocity DT (ms)	220.76 ± 57.50	144.76 ± 28.87	<0.001

Abbreviations: A, atrial peak velocity; DT, E velocity deceleration time; E, early peak velocity; IVRT, isovolumic relaxation time.

Table 4. Pulsed Tissue Doppler Analysis of the Patients and Controls

	Patients	Controls	*P*
Mitral lateral annulus			
Sm peak (cm/s)	9.72 ± 2.47	11.64 ± 2.16	0.011
Em peak velocity (cm/s)	14.64 ± 4.65	18.68 ± 4.01	0.004
Am peak velocity (cm/s)	7.30 ± 1.93	11.14 ± 2.35	<0.001
Em/Am ratio	2.12 ± 0.73	1.78 ± 0.61	0.103
LV E/Em ratio	5.69 ± 1.95	5.00 ± 0.98	0.158
Mitral septal annulus			
Sm peak (cm/s)	7.84 ± 1.56	9.46 ± 0.72	<0.001
Em peak velocity (cm/s)	10.64 ± 3.54	12.73 ± 2.80	0.041
Am peak velocity (cm/s)	7.34 ± 1.63	10.83 ± 2.22	<0.001
Em/Am ratio	1.49 ± 0.44	1.25 ± 0.44	0.078
LV E/Em ratio	7.79 ± 2.60	7.40 ± 1.77	0.571
Mitral inferior annulus			
Sm peak (cm/s)	8.94 ± 1.81	11.44 ± 1.91	<0.001
Em peak velocity (cm/s)	13.31 ± 5.00	17.72 ± 4.55	0.005
Am peak velocity (cm/s)	9.13 ± 2.28	11.72 ± 2.65	0.002
Em/Am ratio	1.51 ± 0.52	1.63 ± 0.68	0.511
LV E/Em ratio	6.64 ± 3.19	5.43 ± 1.57	0.132
Mitral anterior annulus			
Sm peak (cm/s)	8.62 ± 1.74	10.35 ± 1.99	0.005
Em peak velocity (cm/s)	11.75 ± 4.34	13.87 ± 2.86	0.069
Am peak velocity (cm/s)	6.82 ± 1.63	10.29 ± 3.14	<0.001
Em/Am ratio	1.78 ± 0.63	1.45 ± 0.52	0.074
LV E/Em ratio	7.06 ± 2.18	6.76 ± 1.64	0.619
Tricuspid lateral annulus			
Sm peak (cm/s)	12.38 ± 2.91	14.40 ± 2.25	0.016
Em peak velocity (cm/s)	11.91 ± 3.54	14.39 ± 3.87	0.037
Am peak velocity (cm/s)	11.09 ± 3.84	12.30 ± 2.95	0.256
Em/Am ratio	1.20 ± 0.54	1.28 ± 0.62	0.656
RV E/Em ratio	5.29 ± 1.77	4.46 ± 1.27	0.090

Abbreviations: Am, atrial myocardial diastolic velocity; Em, early myocardial diastolic velocity; E: early peak velocity; LV, left ventricle; RV, right ventricle; Sm, myocardial systolic velocity.

differences in Em/Am ratio and E/Em ratio between the 2 groups.

In patients with MD, LV MPI was 0.73 ± 0.17 and RV MPI was 0.40 ± 0.15, while controls had a LV MPI of 0.37 ± 0.08 and RV MPI of 0.27 ± 0.17. Both LV and RV MPI were significantly higher in MD patients than in controls ($P < 0.001$ and $P = 0.013$, respectively).

Discussion

The detection of early markers of cardiac involvement may be crucial for appropriate management of patients with MD, but cardiac involvement is usually not evident in early stages of the disease. The novel finding of this study was the demonstration of significant changes in systolic and diastolic functions of both ventricles in patients with MD. Although all MD patients had normal LVEF, biventricular longitudinal functions and MPI of patients were significantly different than in the healthy subjects. Our findings suggest that myocardial function is affected even in the early stages of this disease when no overt heart failure is present.

Since skeletal muscle relaxation is a major clinical feature of MD, a parallel worsening of cardiac muscle diastolic relaxation is anticipated in these patients. Subclinical LV diastolic dysfunction has been detected in some cases in the early stages of this disease.[10–12] Vinereanu et al[21] explored subclinical cardiac involvement in 14 MD patients and found that early diastolic myocardial velocities were lower in patients with MD. In our study, both Em and Am peak velocities of mitral annulus were significantly lower in MD patients, which further confirmed the presence of diastolic dysfunction we detected by conventional pulsed Doppler imaging (significantly lower transmitral E peak velocity, longer DT of E velocity, and IVRT). Mitral anterior annulus Em of the patients was also lower than that of controls, but the difference was not significant, which might be due to small sample size. Parisi et al[12] reported that diastolic dysfunction also involved the RV in MD patients. In parallel to their study, we also found a lower tricuspid annular Em and a longer DT of E velocity in comparison with healthy controls.

Systolic functions may also be impaired in MD patients. De Ambroggi et al[22] detected wall motion abnormalities in MD patients. Tokgozoglu et al[23] reported that LVEF and stroke volume were reduced in patients with MD compared with age and heart rate matched controls. However, MD patients with normal LV regional wall motion at rest and LVEF were also shown to have reduced longitudinal systolic function.[24] Vinereanu et al[21] found that 10 of the 14 patients with MD had reduced longitudinal systolic function. Fung et al[24] prospectively evaluated 22 patients with MD without known heart failure and found that MD patients had reduced myocardial Sm velocities, correlating with their neurologic severity. Similarly, we also detected lower biventricular myocardial Sm velocities in MD patients. In our study, we evaluated Sm values of not only basal septal

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and lateral mitral annulus, but also basal anterior and inferior walls and demonstrated cardiac involvement in all walls of LV. In accordance with the studies pointing out peak Sm velocity as a more sensitive parameter than LVEF in detecting impairment of myocardial contractility,[25,26] we also suggest the use of TDI in early detection of the patients with subclinical cardiac dysfunction.

The peculiar finding of the present study is the use of MPI in patients with MD. We found significantly increased LV MPI in patients with MD. Right ventricular MPI was also significantly higher in patients with MD compared to controls. Myocardial performance index is a simple Doppler index of combined systolic and diastolic myocardial performance.[27,28] It is shown to be significantly more sensitive than the ejection fraction in the prediction of LV dysfunction based on the clinical development of congestive heart failure.[29] There is only 1 recently published study which demonstrated higher LV MPI in these patients.[30] To our knowledge, our study is the first that also demonstrated significantly higher RV MPI in MD patients. Since the MPI does not depend on ventricular geometry and incorporates diastolic function in addition to systolic function, we suggest the use of MPI in addition to myocardial tissue velocities for detection of biventricular involvement in MD patients.

Conclusion

Although conduction disturbances are the major cardiac abnormalities seen in patients with MD, biventricular systolic and diastolic functions may also be impaired in these patients. Although conventional echocardiography parameters are within normal limits, TDI is able to unmask early LV systolic and diastolic dysfunction as well as RV dysfunction. Myocardial performance index is more sensitive than LVEF in detecting subclinical dysfunction and may help elucidate myocardial pathophysiology in these patients. We suggest that TDI is a useful preclinical screening of heart disease in patients with MD and should be performed in all patients with suspected myocardial involvement. Future prospective studies with modern imaging modalities such as TDI and 2DE strain are needed to clarify the risk of developing overt cardiac disease in these patients and to define prognostic factors and treatment strategies.

References

1. Mathieu J, Allard P, Potvin L, et al. A 10-year study of mortality in a cohort of patients with myotonic dystrophy. *Neurology*. 1999;52:1658–1662.
2. New nomenclature and DNA testing guidelines for myotonic dystrophy type 1 (DM1). The International Myotonic Dystrophy Consortium (IDMC). *Neurology*. 2000;54:1218–1221.
3. Pelargonio G, Dello Russo A, Sanna T, et al. Myotonic dystrophy and the heart. *Heart*. 2002;88:665–670.
4. Rakocević-Stojanović V, Grujić M, Seferović P, et al. Myotonic dystrophy and cardiac disorders. *Panminerva Med*. 2000;42:257–261.
5. Mammarella A, Paradiso M, Antonini G, et al. Natural history of cardiac involvement in myotonic dystrophy (Steinert's disease): a 13-year follow-up study. *Adv Ther*. 2000;17:238–251.
6. Kennel AJ, Titus JL, Merideth J. Pathologic findings in the atrioventricular conduction system in myotonic dystrophy. *Mayo Clin Proc*. 1974;49:838–842.
7. Nguyen HH, Wolfe JT III, Holmes DR Jr, et al. Pathology of the cardiac conduction system in myotonic dystrophy: a study of 12 cases. *J Am Coll Cardiol*. 1988;11:662–671.
8. Thornton C. The myotonic dystrophies. *Semin Neurol*. 1999;19:25–33.
9. Sonaglioni G, Curatola L, Bollettini G, et al. Echocardiographic findings in dystrophia myotonica (Steinert's disease). *G Ital Cardiol*. 1984;14:551–556.
10. Fragola PV, Caló L, Luzi M, et al. Doppler echocardiographic assessment of left ventricular diastolic function in myotonic dystrophy. *Cardiology*. 1997;88:498–502.
11. Bu'Lock FA, Sood M, De Giovanni JV, et al. Left ventricular diastolic function in congenital myotonic dystrophy. *Arch Dis Child*. 1999;80:267–270.
12. Parisi M, Galderisi M, Sidiropulos M, et al. Early detection of biventricular involvement in myotonic dystrophy by tissue Doppler. *Int J Cardiol*. 2007;118:227–232.
13. Rakocević-Stojanović V, Pavlović S, Seferović P, et al. Pathohistological changes in endomyocardial biopsy specimens in patients with myotonic dystrophy. *Panminerva Med*. 1999;41:27–30.
14. Sutherland GR, Bijnens B, McDicken WN. Tissue Doppler echocardiography: historical perspective and technological considerations. *Echocardiography*. 1999;16:445–453.
15. Brook JD, McCurrach ME, Harley HG, et al. Molecular basis of myotonic dystrophy: expansion of a trinucleotide (CTG) repeat at the 3′ end of a transcript encoding a protein kinase family member. *Cell*. 1992;68:799–808.
16. Nagueh SF, Middleton KJ, Kopelen HA, et al. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. *J Am Coll Cardiol*. 1997;30:1527–1533.
17. Nagueh SF, Mikati I, Kopelen HA, et al. Doppler estimation of left ventricular filling pressure in sinus tachycardia. A new application of tissue Doppler imaging. *Circulation*. 1998;98:1644–1650.
18. Garcia MJ, Thomas JD, Klein AL. New Doppler echocardiographic applications for the study of diastolic function. *J Am Coll Cardiol*. 1998;32:865–875.
19. Sundereswaran L, Nagueh SF, Vardan S, et al. Estimation of left and right ventricular filling pressures after heart transplantation by tissue Doppler imaging. *Am J Cardiol*. 1998;82:352–357.
20. Tekten T, Onbasili AO, Ceyhan C, et al. Novel approach to measure myocardial performance index: pulsed-wave tissue Doppler echocardiography. *Echocardiography*. 2003;20:503–510.
21. Vinereanu D, Bajaj BP, Fenton-May J, et al. Subclinical cardiac involvement in myotonic dystrophy manifesting as decreased myocardial Doppler velocities. *Neuromuscul Disord*. 2004;14:188–194.
22. De Ambroggi L, Raisaro A, Marchianó V, et al. Cardiac involvement in patients with myotonic dystrophy: characteristic features of magnetic resonance imaging. *Eur Heart J*. 1995;16:1007–1010.
23. Tokgozoglu LS, Ashizawa T, Pacifico A, et al. Cardiac involvement in a large kindred with myotonic dystrophy. Quantitative assessment and relation to size of CTG repeat expansion. *JAMA*. 1995;274:813–819.
24. Fung KC, Corbett A, Kritharides L. Myocardial tissue velocity reduction is correlated with clinical neurologic severity in myotonic dystrophy. *Am J Cardiol*. 2003;92:177–181.

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25. Gorcsan J III, Deswal A, Mankad S, et al. Quantification of the myocardial response to low-dose dobutamine using tissue Doppler echocardiographic measures of velocity and velocity gradient. *Am J Cardiol*. 1998;81:615–623.
26. Nagueh SF, Bachinski LL, Meyer D, et al. Tissue Doppler imaging consistently detects myocardial abnormalities in patients with hypertrophic cardiomyopathy and provides a novel means for an early diagnosis before and independently of hypertrophy. *Circulation*. 2001;104:128–130.
27. Tei C. New non-invasive index for combined systolic and diastolic ventricular function. *J Cardiol*. 1995;26:135–136.
28. Tei C, Ling LH, Hodge DO, et al. New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function—a study in normals and dilated cardiomyopathy. *J Cardiol*. 1995;26:357–366.
29. Poulsen SH, Jensen SE, Nielsen JC, et al. Serial changes and prognostic implications of a Doppler-derived index of combined left ventricular systolic and diastolic myocardial performance in acute myocardial infarction. *Am J Cardiol*. 2000;85:19–25.
30. Lindqvist P, Mörner S, Olofsson BO, et al. Ventricular dysfunction in type 1 myotonic dystrophy: Electrical, mechanical, or both? *Int J Cardiol*. 2009; doi:10.1016/j.ijcard.2009.03.084.