IS DOPPLER TISSUE EARLY LEFT VENTRICULAR FILLING VELOCITY PRELOAD INDEPENDENT OF PRELOAD ALTERING MANEUVERS?

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SUMMARY

Objective. Transmitral Doppler flow indices are used to evaluate diastolic function. Recently, Doppler tissue velocities have been used as an index of left ventricular relaxation. The aim of this study was to determine whether Doppler tissue velocities are influenced by preload alterations.

Methods. We altered left ventricular preloads in 17 patients (all men, 49±8 years) while recording echocardiographic measurements of left ventricular end-diastolic volume, left atrial maximal area, peak early Doppler filling velocity and left ventricular myocardial velocities during early filling. Preload altering maneuvers included Trendelenburg (Stage 1), reverse Trendelenburg (Stage 2) and amyl nitrate (Stage 3). Systolic blood pressures were taken at every stage.

Results. Compared to baseline left ventricular end diastolic volume (p=0,001), left atrial area (p=0,003), peak early mitral Doppler filling velocity (p=0,01) and systolic blood pressures (p=0,001) were changed as a result of preload altering maneuvers. Only left ventricular myocardial velocities during early filling were significantly unaffected by preload altering maneuvers.

Conclusion. In contrast to standard transmitral Doppler filling indices, Doppler tissue early diastolic velocities are not significantly affected by physiological preload altering maneuvers. Thus, Doppler tissue velocities during early left ventricular diastole may be more useful as an index of diastolic function by providing a preload-independent assessment of left ventricular filling.

Key Words: *Doppler Tissue Echocardiography, Preload Alterations*

ÖZET

DOPPLER DOKU SOL VENTRİKÜL ERKEN DOLMA HIZI ARDYÜK DEĞİŞTİRİCİ MANEVRALAR KULLANILDIĞINDA ARDYÜKTEN ETKİLENİR Mİ?

Amaç: *Transmitral Doppler akım verileri diyastolik fonksiyonu değerlendirmek için kullanılmıştır. Son zamanlarda, Doppler doku hızları sol ventrikül gevşemesinin bir göstergesi gibi kullanılmıştır. Bu çalışmada Doppler doku hızlarının ön yük değiştirici manevralardan etkilenip etkilenmediğinin saptanması amaçlandı.*

Yöntem: *17 hastada (tümü erkek, 49 ± 8) ekokardiyografik sol ventrikül miyokardiyum hızları ölçümlerini yaparken sol ventrikül ön yükünü değiştirdik Trendelenburg (1. basamak), ters Trendelenburg (2. basamak) and amil nitrat (3. basamak) ön yük değiştirici manevralar olarak kullanıldı. Her basamak için sistolik kan basıncı ölçüldü.*

Sonuçlar: *Başlangıç ile karşılaştırılınca, sol ventrikül diyastol hacmi (p=0,001), sol atriyum alanı (p=0,003), pik erken mitral Doppler dolum hızı (p=0,001) ve sistolik kan basınçları (p=0,001) ön yük değiştirici manevralar ile değişti, ancak sol ventrikül miyokardı hızı erken dolumda ön yük değiştirici manevralar ile anlamlı değişmedi.*

Yorum: *Mitral seviyeden Doppler dolum verilerinin tersine, Doppler doku erken diyastol hızları fizyolojik ön yük değiştirici manevralardan önemli derecede etkilenmez. Böylece erken sol ventrikül diyastolu sırasında Doppler doku hızları sol ventrikül diyastolu sırasında Doppler doku hızları sol ventrikül dolumunun ön yükden bağımsız değerlendirilmesini sağlayan daha yararlı bir gösterge olabilir.*

Anahtar Kelimeler: *Doppler Doku Ekokardiyografi, Ön Yük Değiştirme*

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Diastolic dysfunction is the primary mechanism responsible for dyspnea in patients with heart failure, irrespective of the presence or severity of systolic dysfunction (1-3). Left ventricular (LV) diastolic dysfunction usually precedes systolic dysfunction (4,5) and abnormal relaxation is observed at its earliest stage (2-6). Conventional clinical evaluation of LV relaxation involves determining the time constant of pressure decay during isovolumic diastole as calculated from the LV pressure curve (7). Doppler echocardiography has become the noninvasive technique of choice for the evaluation of diastolic function (8,9). LV filling and, more recently, pulmonary venous Doppler flow indices have been used to evaluate different parameters of diastolic function, including LV filling, pressure, relaxation and stiffness (8,10-12). Unfortunately, because there are several physiologic variables - including volume status, left atrial pressure and rate of myocardial relaxation (13-15) - it is often difficult to determine which individual variable is responsible for a specific Doppler pattern unless other relevant clinical and/or invasive information is available (6,16-18).

Doppler tissue imaging (DTI) is a new ultrasound modality that records systolic and diastolic velocities within the myocardium (19-23) and at the corner of the annulus (24-26). Recently, the early diastolic velocity recorded at the lateral corner of the annulus (EDTV) has been demonstrated to decline progressively with age and to be reduced in pathologic LV hypertrophy (25) as well as in patients with restrictive cardiomyopathy (26). These findings suggest that EDTV is an index of LV relaxation that may not be influenced by left atrial pressure. Therefore, this study was designed to assess whether EDTV as recorded by DTI is a preload-independent index of LV relaxation that will differentiate pseudonormalized mitral flow from a normal pattern.

Methods

PATIENTS

The study group consisted of 17 patients (all men, 49±8 years of age) with stable forms of chronic ischemic syndrome. All patients underwent echocardiographic evaluation in our laboratory for assessment of cardiac structure and function. Criteria for inclusion were presence of sinus rhythm and absence of any congestive heart failure, valvular heart disease, primary myocardial heart disease, secondary hypertrophy (hypertension, aortic stenosis, etc.) or endocrinological and renal diseases. All subjects gave written informed consent before participation.

ECHOCARDIOGRAPHY

Subjects studied in the echocardiography laboratory were first imaged with a commercially available echocardiography machine (Acuson model 128, Mt. View, California, or Hewlett-Packard model 72020A, Andover, Maryland) equipped with a multifrequency transducer as well as the DTI program. Images were taken in the left lateral decubitus position, and complete echocardiographic studies were performed using standard views and techniques. Two-dimensional studies were recorded from the parasternal long and short axis and the apical four- and two-chamber views. End-diastolic volumes and left atrial area were obtained from the apical four-chamber view. All Doppler echocardiographic and DTI recordings were obtained during normal respiration.

PULSED DOPPPLER ECHOCARDIOGRAPHY

The sample volume was set at the mitral valve orifice in the long axis view of the left ventricle or the four-chamber view recorded from the cardiac apex, and transmitral flow velocity patterns were recorded. Early diastolic wave velocity was then obtained.

Doppler Tissue Imaging: In the apical view of the left ventricle, sample volumes were set at the lateral portion of the mitral annulus. Motion velocity patterns for each patient were recorded using the pulsed Doppler method. After baseline parameters were obtained, the studies were repeated on the same subjects using the preload-altering maneuvers. These stages were defined as Baseline, Stage 1 (Trendelenburg position), Stage 2 (reverse Trendelenburg position) and Stage 3

Table 1: Changes in Echocardiographic Measurements with Preload Altering Maneuvers

Variables	Baseline	Stage 1	Stage 2	Stage 3
LVEDV (ml)*	199 ± 132	242 ± 186	212 ± 163	188 ± 133
LA Area (mm2)**	22 ± 9	24 ± 10	22 ± 10	20 ± 8
E Wave (cm/sec)¶	82 ± 33	85 ± 32	72 ± 26	73 ± 20
EDTV (cm/sec) #	10 ± 4	11 ± 3	11 ± 3	11 ± 4
BP*	126 ± 19	123 ± 17	118 ± 21	103 ± 22

*p=0,001; **p=0,003; ¶p=0,01; #p= NS (stage 1,2,3 parameters comparing baseline)

(amyl nitrate inhalation). Blood pressure was recorded continuously at all stages.

STATISTICAL ANALYSIS

Data was presented as mean value ± SD. Analysis of variance and t tests were used to compare differences between the stages, with a value of p< 0,05 considered significant.

Results

Normal values for left ventricular end diastolic volume (LVEDV), left atrial (LA) area, left ventricular early mitral flow velocity (E) and EDTV were obtained from the annulus for the Baseline (Table 1). In Stage 1, early diastolic mitral inflow velocity profile increased (p=0,01) with the Trendelenburg maneuver, which is known to increase preload. LVEDV (p=0,001) and LA (p=0,003) area increased significantly in Stage 1, but EDTV did not change significantly (p<0,05). In Stage 2 (reverse Trendelenburg) and Stage 3 (amyl nitrate inhalation), EDTV was unchanged, but other variables changed significantly (Table 1).

Discussion

The results of this study suggest that peak Doppler tissue early left ventricular velocities are not affected by varying preload conditions. In spite of the changes in hemodynamic parameters, EDTV did not change significantly.

Mitral flow variables are load-dependent, and patients with a relaxation abnormality may show a normal pattern with elevated atrial pressure. This pattern may occur because mitral flow variables are velocity data determined by the pressure difference between the left atrium and left ventricle during diastole. The effect of volume changes on Doppler tissue velocities has the theoretical advantage of being less preload-dependent than mitral flow variables. Garcia et al (26) observed that peak EDTV correlates poorly with peak E velocity, suggesting the relative preload-independence of peak EDTV. In this study, we demonstrated that peak early mitral annulus velocity, in contrast to mitral inflow velocity, did not change significantly after preload alteration by Trendelenburg or reverse Trendelenburg maneuvers or amyl nitrate inhalation. Some findings were previously demonstrated by Sohn et al (27) by alteration of the preload with infusion of saline or nitroglycerin. Aranda et al (28) also showed that during routine examination of heart transplant cases, peak EDTV did not change as a result of preload alteration with nitroglycerin.

In contrast to standard Doppler echocardiography, DTI is capable of measuring myocardial tissue velocity, which directly reflects the contractile and relaxation properties of the myocardium. All of our subjects had evidence of normal left ventricular systolic function, no evidence of coronary artery disease as detected by coronary angiography, and no pericardial effusion. Both Trendelenburg maneuvers and inhalation of amyl nitrate affected the blood pressure response (p=0,001), LVEDV (p=0,001) and LA area change (p=0,003). Changes in the hemodynamic profile such as increase in heart rate and decrease in blood pressure, LVEDV and LA area following inhalation of amyl nitrite are well known and probably mediated by venous and arterial dilatation via reflex sympathetic stimulation by baroreceptors (29). Relaxation velocities by Doppler tissue echo with different preload conditions did not change significantly, suggesting that myocardial relaxation is independent of preload. This observation is consistent with the findings of Stoddard et al (30). Impaired relaxation is a common denominator in patients with heart failure, with or without systolic dysfunction (1-3). During heart failure, left atrial pressure increases in response to a reduction in LV compliance. This increase masks the influence of impaired relaxation on the transmitral velocity, producing a pseudonormal pattern with an E/A ratio >1 and shortening the isovolemic relaxation time and deceleration time (9, 10, 31). However, abnormal myocardial relaxation still exists in these patients and can be demonstrated with invasive measurements of the time constant of relaxation and with the flow propagation velocity of LV inflow assessed by color M-mode echocardiography (32-34).

EDTV as a preload-independent index of LV relaxation is significant in that it may permit differentiation between pseudonormal mitral flow patterns and normal patterns. Diagnosis and management of this group of patients seem to be more confidently carried out by a combination of clinical and echocardiographic variables of the pulmonary vein velocity as well as EDTV as a new high technologic tool. Recently, greater emphasis has been given to the possibility of using EDTV as a pre-load independent method of detecting left ventricular relaxation abnormalities in practical cardiology.

In conclusion, in contrast to standard diastolic transmitral Doppler filling indices, Doppler tissue early diastolic velocities are not significantly affected by physiological preload altering maneuvers. Thus, EDTV during early LV diastole may be a more useful index of diastolic function by providing preload independent assessment of LV filling.

REFERENCES

1. Grossman W, Mc Laurin LP, Rolett EL, et al. Alterations in left ventricular relaxation and diastolic compliance in congestive cardiomyopathy. Cardiovasc Res 1979; 13:514-22.

2. Dougherty AH, Nacarelli GV, Gray EL, et al. Congestive heart failure with normal systolic function. Am J Cardiol 1984; 54:778-82.

3. Grossman W. Diastolic dysfunction and congestive heart failure. Circulation 1990; 81 Suppl III:III-1-7.

4. Grossman W, Mc Laurin LP. Diastolic properties of the left ventricle. Ann Intern Med 1976; 84:316-26.

5. Bonow RO, Bacharach SL, Green MV, et al. Impaired left ventricular diastolic filling in patients with coronary artery disease: assessment with radionuclide angiography. Circulation 1981; 64:315-23.

6. Ishiada Y, Meisner JS, Tsujioka K, et al. Left ventricular filling dynamics: influence of left ventricular relaxation and left atrial pressure. Circulation 1986; 74:187-96.

7. Weiss JL, Fredriksen JW, Weisfeldt ML. Hemodynamic determinants of the time-course of fall in canine left ventricular pressure. J Clin Invest 1976; 58:751-61.

8. Nishimura RA, Abel MD, Hatle LK, et al. Assessment of diastolic function of the heart: background and current applications of Doppler echocardiography. Part II. Clinical studies Mayo Clin Proc 1989; 64:181-204.

9. Thomas JD, Weyman AE. Echo Doppler evaluation of left ventricular diastolic function: Physics and Physiology, Circulation 1991; 84:990-97.

10. Appleton CP, Hatle LK, Pop RL. Relation of transmitral flow velocity patterns to left ventricular diastolic function: new insights from a combined hemodynamic and Doppler echocardio-

graphic study. J Am Coll Cardiol 1988; 12:426-40.

11. Hoit BD, Walsh RA. Diastolic function in hypertensive heart disease. In: Gaasch WH, Le Winter M, editors. Left Ventricular Diastolic Dysfunction and Heart Failure. Philadelphia: Lea and Febiger 1994; 354-72.
12. Labowitz AJ, Pearson AC. Evaluation of left ventricular diastolic function: clinical relevance and recent Doppler echocardiographic insights. Am Heart J 1987; 114:836-51.
13. Choong CY, Hermann HC, Weyman AE, et al. Preload dependence of Doppler derived indexes of left ventricular diastolic function in humans. J Am Coll Cardiol 1987; 10:800-08.
14. Gardin JM, Rohan MK, Davidson DM. Doppler transmitral flow velocity parameters: relation between age, body surface area, blood pressure and gender in normal subjects. Am J Noninvasive Cardiol 1987; 1:3-10.
15. Kuo LC, Quinones MA, Rokey R, et al. Quantification of atrial contribution to left ventricular filling by pulsed Doppler echocardiography and the effect of age in normal and diseased hearts. Am J Cardiol 1987; 59:1174-78.
16. Appleton CP, Hatle LK. The natural history of left ventricular filling abnormalities: assessment by two dimensional and Doppler echocardiography. Echocardiography 1992; 9:437-45.
17. Choong CY, Abascal VM, Thomas JD, et al. Combined influence of ventricular loading and relaxation on the transmitral flow velocity profile in dogs measured by Doppler echocardiography. Circulation 1988; 78:672-83.
18. Colan SD, Borrow KM, Neumann A. Effects of loading conditions and contractile state (methoxamine and dobutamine) on left ventricular early diastolic function in normal subjects. Am J Cardiol 1985; 55:790-96.
19. Sutherland GR, Stewart MJ, Groundstroem KWE, et al. Color Doppler myocardial imaging: a new technique for the assessment of myocardial function . J Am Soc Echocardiography 1994; 7:441-58.
20. Miyatake K, Yamagishi M, Tanaka N, et al. New method for evaluating left ventricular wall motion by color-coded tissue Doppler imaging: in vitro and in vivo studies. J Am Coll Cardiol 1995; 25:717-24.
21. Donovan CL, Armstrong wf, Bach DS. Quantitative Doppler tissue imaging of the left ventricular myocardium: validation in normal subjects. Am Heart J 1995; 130:100-04.
22. Uematsu M, Miyatake K, Tanaka N, et al. Myocardial velocity gradient as a new indicator of regional left ventricular contraction: detection by a two dimensional tissue Doppler imaging technique. J Am Cardiol 1995; 26:217-23.
23. Gorscan J 3d, Gulati VK, Mandarino WA, et al. Color coded measures of myocardial velocity throughout the cardiac cycle by tissue Doppler imaging to quantify regional left ventricular function. Am Heart J 1996; 131:1202-13.
24. Isaaz K, Munoz del Romeral L, et al. Quantification of the motion of the cardiac base in normal subjects by Doppler echocardiography. J Am Soc Echocardiography 1993; 6:166-76.
25. Rodriguez L, Garcia MG, Ares M, et al. Assessment of mitral annular dynamics during diastole by Doppler tissue imaging: Comparison with mitral Doppler inflow in subjects without heart disease and in patients with left ventricular hypertrophy. Am Heart J 1996; 131:982-87.
26. Garcia MG, Rodriguez L, Ares M, et al. Differentiation of constrictive pericarditis from restrictive cardiomyopathy: assessment of left ventricular diastolic velocities in longitudinal axis by Doppler tissue imaging. J Am Coll Cardiol 1996; 27:108-14.
27. Sohn DW, Chai IH, Lee DJ, et al. Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function . J Am Coll Cardiol 1997; 30:474-80.
28. Aranda JM, Weston MW, Puleo JA, et al. Effect of loading conditions on myocardial relaxation velocities determined by Doppler tissue imaging in Heart Transplant recipients. J Heart Lung Transplant 1998; 17:693-97.
29. Lundbrook P, Byrne J, Jurnik R, et al. Influence of reduction of preload and afterload by nitroglycerin on left ventricular diastolic pressure-volume relations and relaxation in man. Circulation 1977; 56:937-43.

30. Stoddard M, Pearson A, Kern M, et al. Influence of alteration in preload on the pattern of left ventricular diastolic filling as assessed by Doppler echocardiography in humans. Circulation 1989; 79:1226-36.

31. Thomas JD, Choong CYP, Flachskampf FA, et al. Analyşis of the early transmitral Doppler velocity curve: effects of primary physiologic changes and compensatory preload adjustment. J Am Coll Cardiol 1990; 16:644-55.

32. Brun P, Tribwilly C, Duval AM. Left ventricular flow propagation during early filling is related to wall relaxation: a colour M-mode Doppler analysis. J Am Coll Cardiol 1992; 20:420-32.

33. Stügaard M, Smseth OA, Risoe C, et al. Intraventricular early diastolic filling during acute myocardial ischemia, assessment by multigated color M-mode Doppler echocardiography. Circulation 1993; 88:2705-13.

34. Takatsuji H, Mikami T, Urasawa K, et al. A new approach for evaluation of left ventricular diastolic function: spatial and temporal analysis of left ventricular filling flow propagation by color M-mode Doppler echocardiography. J Am Coll Cardiol 1996; 27:365-71.