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Review

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Diastolic Dysfunction: Pathogenesis, Therapy and the Importance of Doppler Echocardiography

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Abstract: Diastolic dysfunction is characterized by increased resistance to ventricular filling, inappropriate upward shift of the diastolic pressure-volume relationship and exercise intolerance. Inappropriate tachycardia, decreased diastolic compliance and impaired systolic relaxation lead to diastolic dysfunction. Optimal therapy will depend on the type and pathophysiologic phase of disease. Doppler echocardiography is a valuable tool to diagnose diastolic dysfunction and therapeutic effects of drugs on diastolic function in different groups of patients. Recently a lot of studies have been going on this subject.

Key Words: *Diastolic dysfunction, Doppler echocardiography.*

Pathogenesis

Diastolic dysfunction is an abnormality that causes impaired left ventricular filling by different reasons. This abnormality usually can be described during very early stages of many cardiac and noncardiac diseases. Increased left ventricular enddiastolic pressure (LVEDP) may cause subendocardial ischemia; also in the chronic situations, may cause hypertrophy and remodelling. The increase of Pyressure/Volume ratio due to the increased resistance of left ventricle preload and exercise intolerance are the main signs of diastolic dysfunction. Tachycardia leads to decrease on compliance and systolic relaxation which plays an important role in the arise of diastolic physiologic control from the relaxation abnormality. The proper treatment must be chosen according to the type of pathogenesis.

It has been suggested by some extreme optimists, that LVEDP may be calculated from the ratio of the E and A waves of the mitral velocity waveform (figure 1). Unfortunately this measurement does not allow reliable noninvasive measurement of LVEDP and publications claiming such possibilities do not bear up to scientific scrutiny. Abnormalities of the E:A ratio do, however, provide some qualitative information on ventricular diastolic function.

As in the case of Congestive Heart Failure, it can either develope as a secondary decrease on diastolic performance or be together with normal systolic dysfunction at rest(1, 2). The mortality of this type of isolated diastolic dysfunction is rather low incidance (3). The exercise intolerance is usually the first sign (4). Dyspnea is a manifestation as a result of exercise is very widespread and can be seen in a large amount of diseases such as hypertrophic cardiomyopathy, aort stenosis, hypertension, ischemic cardiomyopathy. In most of the clinic cases, it is stated that contraction and relaxation are effected as a part of ongoing spectrum in the situation of existence of systolic abnormalities (5). The increase of endsystolic pressure effects the early diastolic preload negatively. In addition to relationship of relaxation and sytolic parameters, primary abnormal relaxation which may be described as impaired compliance is more complicated and discussions are still being published (10).

On the other hand, according to the quite a large number of clinical treatment specialists opinion, a large portion of ventricular relaxation is a part of diastole (6, 9). It has been devised that relaxation is impaired earlier than contraction in most of cases on the basis of physiologic mechanisms. It can be found out typically in the Ca++ coupling abnormalities. In the case that earliest period of relaxation is distorted (such as abnormal relationship of contractile protein), measurements like ejection fraction, endsystolic P/V ratio, dp/dt may present abnormality, even in some situations with normal late phase of relaxation.

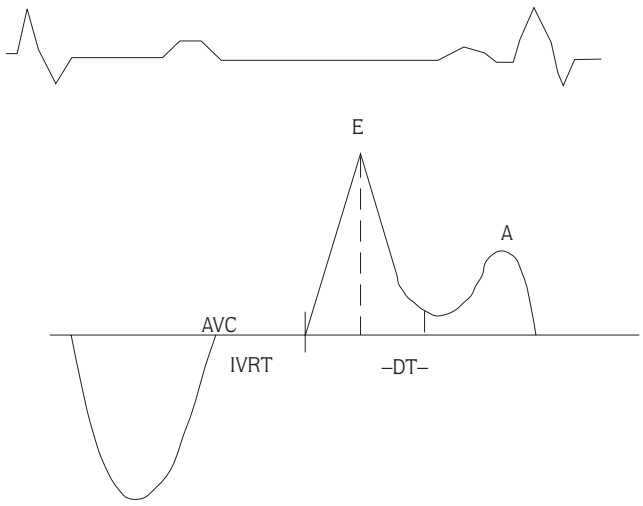

Figure 1. Diastolic Parameters (Mayo Clinic Doppler Criterias) Doppler Mitral Inflow Velocity Patterns.

Label	Denfinition	Normal Range
E	peak early filling velocity	0.8±0.2 m/s
A	peak atrial filling velocity	0.5±0.2 m/s
E/A	ratio	≤1.5
DT	deceleration time (time from the peak E velocity to baseline)	190±20 msec
IVRT	isovolumic relaxation time (time from aortic valve closure (AVC) to onset of mitral flow)	70-90 msec

Normal values are age-dependent. These values represent normals for age group (20-50 yrs.) DT and IVRT values are normal less in those < 20 yrs and greater in those > 50 yrs.

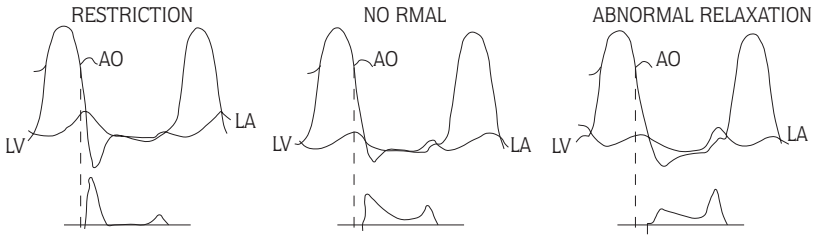

Figure 2. LV, aortic pressures and diastolic waves of myocardial restriction and impaired relaxation compared with normal according to hemodynamic criterias of Mayo Clinic.

Systolic relaxation and pressure reduction are closely related with volume increase during early rapidly inflow and preload have been considered as a part of systolic relaxation (5). On the other hand, in the case of physiologic compensatuar contraction prolongation, P/V ratio is not increased and diastolic preload is not affected. On the time being not only the treatment against etiopathogenesis, but also treatments way to increase the myocardial compliance and it's effects on echocardiographic measurements are being investigated.

Diastolic function is being primarily affected by geometrical alterations of ventricular wall (structural changes of myofibril and extracellular matrix). Together with primary diastolic dysfunction due to reduction of compliance, extraventricular compression (such as pericardial diseases) and external mechanical obstruction of the patients with ventricular dilatation are other reasons of diastolic dysfunction (5, 11, 13). Even a minor increase in pressure or volume of right ventricle shall increases septal distortion (echocardiographic paradox septum) and pericardial pressure increase together with diastolic P/V ratio without affecting the sistolic function (11). Pulmonary hypertension and emboli limit the pulmonary venous drenage and lead to decreased left ventricular filling.

Mitral valve flow is best seen apical position of echocardiography. The drop of the EF slope due to diastolic filling dysfunction can be seen not only mitral stenosis, but also reduction of myocardial compliance. Left ventricular filling abnormality can be detected in the patients having pulmonary hypertenison, right ventricular MI and failure, because of volume reduction. DE slope indicates acceleration which is early phase velocity of blood flow from left atrium to ventricle. It depends on the volume and therefore for the patients having normal enddiastolic pressure, reduction of volume causes DE shorter. In this case, atrial systol supports diastolic load more and a prominent A wave can be observed relative to reduced E poiht. DE shortens in the case of effects increasing the enddiastolic pressure such as aort regurgitation, the impative effect of regurgitated blood flor causes the left ventricular filling to be more distorted (18).

Echocardiologically, in addition to the finding out of left ventricular diastolic flow velocity, detection of the pulmoner venous flow velocity (PFV) has become more important. Systolic and diastolic flow (S_{PFv}-D_{PFV}) ratio is important particularly for the evaluation of premature diastolic dysfunction. Increase of S_{PFv}/D_{PFV} reduction associated with normal mitral E/A ratio is a sing of regressed left ventricular dysfunction in the heart failure (impaired relaxation and myocardial restriction, respectively). The regression of diastolic filling brings about the mitral E/A ratio reduction. For the diagnosis of diastolic dysfunction, it is found out higher predictive value of combined evaluation of mitral E/A ratio and pulmonary venous flow velocity (19). Pulmonary venous flow velocity is also shown by transeosophageal echocardiography, the increase of S_{PFv}-D_{PFV} ratio for elderly people is concluded as the diastolic dysfunction due to reduction of myocardial elasticity and it was stated that in this group, velocity of reversed a(ar) flow with atrial systol is manifested (20). In the situations of myocardial restriction "ar" is most prominent (figure 3).

At the Hammersmith Echocardiology Course that planned by British Postgraduate Medical Federation held in 1997, the echocardiographic evaluations of diastolic dysfunction caused by different reasons have been presented and discussed. Early diastolic septal distortion and diastolic dysfunction due to left ventricular preload reduction have been defined when pulmoner emboli, right ventricular MI and failure occur. For the patients whose right ventricle enddiastolic dimension is thicker then half of left ventricle, diastolic circular structure of left ventricle may be distorted, moreover it was stated that tricuspide regugitation should be searched by doppler.

It was pointed out that, for the patients having excessive regurgitation, preload is evidently limited (reduced E) at annulus level, there is limitation of mitral valve opening at aortic regurgitation and early and late flow waves of mitral valve when annulus levels are measured by doppler. It was stated that in this group compared to normal case, diastolic reverse flow evidently increases between posterobasal segment and mitral posterior leaflet.

It was indicated that in acute MI, although in the early period systolic functions are normal, diastolic dysfunction may occur and it is thought abnormal relaxation is the most often filling pattern. The left atrial emptying index which can be provided by diastolic slope of aortic posterior wall and enddiastolic LV pressure have been shown a high correlation in acute MI. Therefore, it was stated that intrensec aortic diseases must be ruled out such as aortic aneurism because these strongly effect on aortic wallmotion.

For coroner artery patients, after increasing the heart rate by transosephagial atrial pacing, deceleration slope increase during doppler examination. It was stated that these examination is more diagnostic than only E/A ratio. It was also stated that E, A ratio is impaired highest level in aortic stenosis, it is relatively lower in coronary artery disease (CAD). It has been demostrated that little E wave and usually prolonged deceleration time can be detected in hypertrophic cardiomyopathy. On the other hand, diastolic dysfunction have been detected 30% with Romatoid Artritis, 20% with Systemic Amyloidosis, 25% with Behçet Disease.

Bradicardic drugs must be used to increase exercise tolerance and decrease LV end-diastolic pressure in

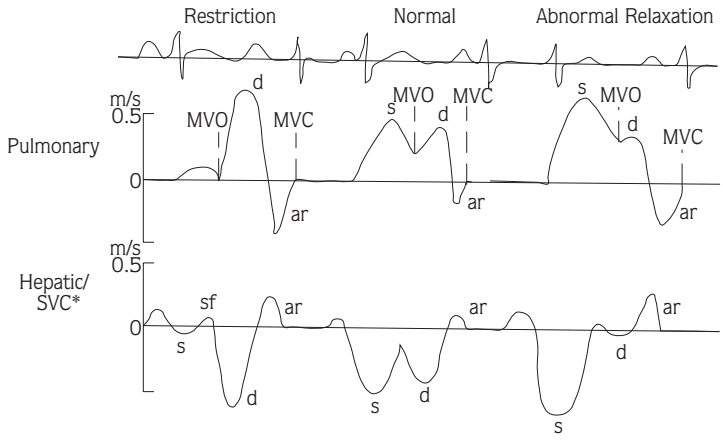

Figure 3. Pulmonary and hepatic venous flow velocities in myocardial restriction and impaired relaxation compared with normal according to hemodynamic criterias of Mayo Clinic.

diastolic dysfunction provocated by tachycardia. Myocardial compliance must be increased in myocardial hypertrophy and fibrosis. ACE inhibitor drugs, anti-aldesteron drugs which is still being developed be used for this purpose (14, 16). These drugs are known effective drugs on LV remodelling. Diuretics are effective to increase exercise tolerance wih minimal change in systolic performance and to decrease diastolic loading and pericardial restriction (17). Despite diastolic low atrial filling pressure, decreasing of myocardial mass appears very earlier than decreasing of collagen. Turn over duration of collagen is nearly 80-120 day, but proteins of myocyte are trunovered in approximately 5-10 days. Decreasing of LV mass can be provided by optimization of the ratio of myofibrilles, which are hypertrophied by Angiotensine and extracellulary matrix (collagen III), which are increased by aldosterone. Digital theraphy is intensively used to correct exercise intolerance in practise. The importance of echocardiology can be appraised especially in patients with normal systole but dysfunctioned diastole. On this point, the drug choice must be aimed to increase of myocardial compliance, not systolic function.

It has been known that the correction of diastolic dysfunction with therapy in hypertensive patients has a positive correlation with reducing of myocardial mass index detected by echocardiography. Isolated diastolic dysfunction better treats with ACE inhibitors than Ca^{++} channel blockers and this observation was stated during Hammersmith Echocardilogy Course. On the other hand, it was also stated that Ca^{++} channel blockers have been more effective on secondary diastolic dysfunction to impaired endsystolic relaxation caused by Ca++ coupling, sarcoplasmic reticulum pump and myofibrilles relationship abnormalities. These observations are obviously shown that rapidly inflow phase of diiastole has very close relationship with endsystolic relaxation.

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