

UPDATE

Clínical Decision Making Based on Cardiac Diagnostic Imaging Techniques (III)

Diagnosis and Therapeutic Guidance of Diastolic Heart Failure

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Despite diastolic dysfunction is recognized to play a major role in the pathophysiology of heart failure, the importance of an accurate diagnosis and treatment of this syndrome in clinical practice is poorly established. Recent publications suggest that diastolic dysfunction is the primary cause of heart failure in 30-50% of patients. Several studies also show that, in a significant number of patients with systolic dysfunction, diastolic function is the major determinant of their symptomatic status, their response to treatment and their outcome. Other preliminary data suggest that diastolic dysfunction is an important cause of exercise intolerance in patients with chronic hypertension. This paper discusses the most recent concepts related to the mechanisms, the diagnosis and the treatment of diastolic dysfunction based on diagnostic imaging techniques.

Key words: *Diastole. Congestive heart failure. Echocardiography. Doppler.*

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Diagnóstico y guía terapéutica de la insuficiencia cardíaca diastólica

A pesar de la importancia de la disfunción diastólica en la fisiopatología de la insuficiencia cardíaca, la relevancia del diagnóstico y tratamiento de este síndrome está poco reconocida en la práctica clínica. Publicaciones recientes sugieren que en un 30-50% de pacientes con insuficiencia cardíaca la causa primaria es una disfunción diastólica. Varios estudios también demuestran que en un número importante de pacientes con insuficiencia cardíaca sistólica la función diastólica suele determinar la sintomatología, el pronóstico y la respuesta al tratamiento. Otros datos preliminares sugieren que la disfunción diastólica es una causa importante de intolerancia al esfuerzo en pacientes con hipertensión arterial crónica. En este artículo se discutirán los conceptos más actuales en relación con los mecanismos, el diagnóstico y el tratamiento de la disfunción diastólica.

Palabras clave: *Diástole. Insuficiencia cardíaca. Ecografía. Doppler.*

INTRODUCTION

In spite of therapeutic advances over the last 2 decades, heart failure continues to be one of the most prevalent syndromes, with a mortality of 50% at 5 years and at a cost of more than 10 000 million dollars annually in the United States.¹ Epidemiological studies

predict a significant increase in the prevalence of heart failure in the future, because of the increase in the life expectancy of the general population,² and to the prevention of sudden death by use of the implantable defibrillator.³ It has been determined that 30% to 50% of patients who present with the diagnosis of heart failure have a normal ejection fraction.⁴ It is currently recognized that diastolic dysfunction plays an important role in the symptomatology of cardiomyopathy, valve disease, ischemic disease, and arterial hypertension.⁵ In spite of the fact that life expectancy rate in diastolic heart failure is better than with systolic dysfunction in heart failure, recent studies have shown that this rate is reduced in the normal population.⁴

Diastolic dysfunction can be defined as a condition in which the filling pressure is found to be increased in order to maintain normal cardiac output. Therefore, patients with diastolic dysfunction can have a variety

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ABBREVIATIONS

(-) dP/dt : velocity of maximum decline in ventricular pressure.
 τ : isometric relaxation time constant.
 A: atrial contraction wave in mitral flow derived Doppler.
 Am: diastolic velocity of the myocardium obtained by tissue Doppler during atrial contraction.
 AR: reverse flow toward the pulmonary veins during atrial contraction.
 $AR_{dur} - A_{dur}$: difference between the length of the retrograde atrial contraction wave of pulmonary venous flow and the anterograde atrial contraction wave in ventricular filling.
 ATP: adenosine triphosphate.
 BNP: brain natriuretic peptide.
 CV: ventricular relaxation.
 Ca^{++} : calcium.
 D: atrial filling wave during the early filling phase in pulmonary venous flow.
 dp: pressure change.
 dV: volume change.
 El: tissue elasticity.
 E: protodiastolic filling wave in mitral flow derived Doppler.
 E_{DT} : deceleration time of protodiastolic filling.
 Em: myocardium diastolic velocity obtained via tissue Doppler during early filling phase.
 h: thickness of the ventricular wall.
 p_a : atrial pressure.
 p_v : ventricular pressure.
 Sm: myocardium systolic velocity obtained by means of tissue Doppler.
 S: atrial filling wave during ventricular systole in pulmonary venous flow.
 v: velocity.
 vp: ventricular flow propagation velocity gradient according to M-mode color Doppler.

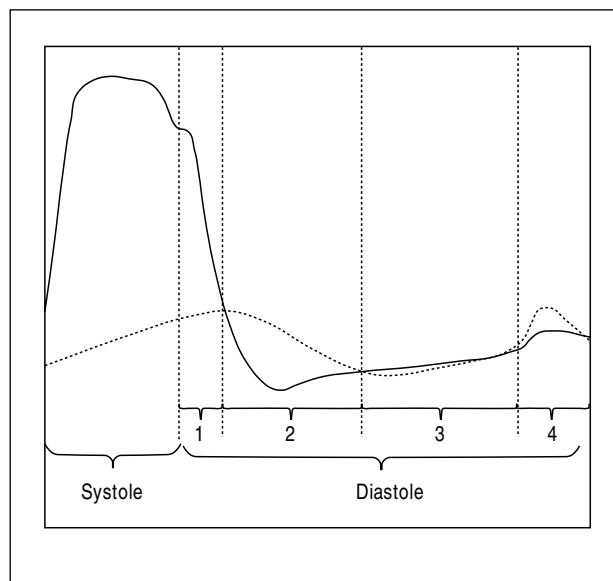


Fig. 1. Phases of the cardiac cycle. The continuous line represents ventricular pressure. The dotted line represents simultaneous atrial pressure. Phase 1: isovolumetric relaxation; phase 2: early filling; phase 3: diastasis; phase 4: atrial contraction.

traventricular pressure decreases rapidly before ventricular filling begins. This involves 3 phases in patients with sinus rhythm. The early filling phase begins with the opening of the mitral valve, when the decrease in intraventricular pressure is less than the value of the atrial pressure. The second, or equilibrium, phase is seen in patients with normal diastolic function and low cardiac frequency. During this phase, ventricular volume is maintained constant due to the equalizing of the atrioventricular pressure. Finally, the filling phase by atrial contraction depends, as its name indicates, on the increase in pressure by atrial pressure. Several physiological variables interact during ventricular diastole⁶⁻⁸ (Table 1). Among these, the most fundamental are ventricular relaxation and distensibility, and atrial contraction.

of symptoms, from exertional dyspnea to advanced heart failure.

PHYSIOPATHOLOGY

Conventionally, left ventricular diastole lasts from the moment the aortic valve closes until the closing of the mitral valve, and its duration tends to be two-thirds of the cardiac cycle at rest (Figure 1). During exercise, the duration of diastole is shortened, proportionately, more than that of systole, lasting 50% of the total duration. The first diastolic phase, from the closure of the aortic valve to the opening of the mitral valve, is the isovolumetric relaxation period. During this period, in-

TABLE 1. Factors that contribute to diastole

Ventricular relaxation
Ventricular distensibility
Atrial contractility
Filling pressure and volume (pre-load)
Arterial pressure (afterload)
Pericardial distensibility
Interventricular dependence
Intra-aortic pressure
Neurohormonal activation
Cardiac frequency
Atrioventricular electrical conduction interval
Intraventricular electrical conduction

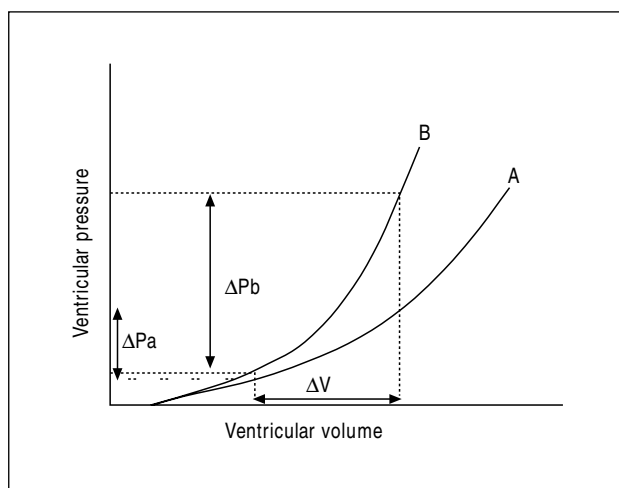


Fig. 2. Ventricular distensibility in a normal subject (A) compared with a subject with diastolic dysfunction (B). Given the same increase in ventricular volume (ΔV), the increase in pressure is greater in the subject with diastolic dysfunction (ΔP_B).

Ventricular relaxation

Relaxation (lusitropism) of cardiac muscle fibers is an active property that uses energy in the form of adenosine triphosphate (ATP). This energy is required to transfer the calcium (Ca^{++}) from the cytoplasm back to the sarcomatous reticulum, reactivating the inhibitory effect of the troponin-tropomyosin⁹ complex and allowing, in turn, the dissociation of the actin and myosin filaments. Relaxation does not only depend on the availability of energy, but also on the abundance of Ca^{++} ion in the cytoplasm.¹⁰ The effect of the relaxation of cardiac muscle fibers causes a sudden decrease in the pressure of the left ventricle. The speed at which the pressure decreases during the isovolumetric relaxation period directly reflects the relaxation speed of the muscle fibers. This speed can be measured with invasive techniques and tends to be defined as the velocity of maximum decline in ventricular pressure ($-dP/dt$) or the isometric relaxation time constant (τ).^{11,12} Several studies have shown that in the left ventricle the apex normally relaxes more quickly and before the middle and basal segments, causing a suction effect. This suction has been quantified invasively by the simultaneous measurement of pressure gradients in different areas of the ventricular cavity, and in normal ventricles an apicobasal difference of 1 mm Hg to 3 mm Hg has been noted. Preliminary data indicate that in normal subjects the suction increases during exercise, and in patients with cardiac failure this increase directly affects aerobic capacity.¹³ It is important to note that ventricular relaxation is directly related to contractility. Studies performed by Torrent-Guasp¹⁴ even suggest that apical suction is caused by the contraction

of certain muscle fascicles, given the spiral form of the left ventricle.

Ventricular distensibility

Ventricular distensibility depends on the relaxation between the «strain» of the myocardial fibers and the «stress» (applied surface force). This association is affected by the active relaxation of the sarcomeres and by the relative content of elastic and collagen fibers in the connective tissue. These fibers determine the size and anatomical form of the left ventricle, and form the matrix that allows conversion of the shortening and lengthening of muscle fibers during changes in pressure.¹⁵⁻¹⁷ The relationship between «strain» and «stress» of the collagen fibers is initially low, but increases structurally as the fibers are stretched.¹⁸ This phenomenon explains why, even in normal subjects, excessive volume overload may result in the development of cardiac failure. The distensibility of the left ventricle (C_v) can decrease: *a*) upon reduction of tissue elasticity (E_t) due to the increase in the density of the collagen fibers in response to humoral factors (angiotensin, noradrenaline, etc.), and *b*) upon an increase in wall thickness, which occurs commonly in response to a chronic elevation of arterial pressure, or both. Ventricular wall thickness is an important parameter in the study of diastolic function. In general, this is found to be abnormally increased in hypertrophic and restrictive cardiomyopathy. Given the relationship between ventricular distensibility (C_v) and the thickness of the ventricular wall (h), in ventricles with a normal diameter and increased thickness, distensibility decreases even when tissue elasticity (E_t) is normal, since:

$$C_v \propto \frac{E_t}{h}$$

Hemodynamically, C_v can be defined as the relationship between the change in volume and the change in pressure (dV/dp), or as the constant of ventricular volume (volume required to increase ventricular pressure by a factor of e , 2.718, $V_v k$). Given the same filling volume, in a ventricle with normal C_v the increase in pressure is less than a ventricle with a reduced C_v (Figure 2).

Atrial contractility

Left ventricular function depends on its preloading, afterload, and contractility.¹⁹ Atrial preloading (atrial volume at the end of the early ventricular filling phase) directly affects the strength of atrial contraction, in accordance with the Starling law: the volume determines the strain of muscle fibers which, in turn, directly determines shortening and, therefore, the volume of atrial ejection. In patients with abnormal or

TABLE 2. Causes of diastolic dysfunction

Arterial hypertension
Senility
Ischemic heart disease
Diabetes
Dilated cardiopathy
Hypertrophic cardiopathy
Restrictive cardiopathy*
Constrictive pericarditis

*Amyloidosis, post-irradiation, Fabry disease, glycogen deposit disease, and others.

incomplete ventricular relaxation due to elevated cardiac frequency or a first degree block, the atrial pre-load volume is increased, which entails greater atrial ejection volume. This mechanism maintains of the cardiac output in patients with changes in ventricular relaxation, especially during exercise. Therefore, the development of atrial fibrillation may entail a decrease in cardiac output and the appearance of congestive symptoms in these patients. Ventricular distensibility constitutes the postload of the left atrium. Atrial contraction is ineffective when the C_v is reduced, due to the fact that part of the atrial ejection volume travels in a retrograde direction since there are no valves in the pulmonary veins. Various factors that affect ventricular contractility, such as chronic volume and pressure overload, can also affect atrial contractility which also tends to diminish, in infiltrative cardiomyopathy and in patients with atrial fibrillation, immediately after cardioversion.²⁰

The combination of all of these processes allows for maintenance of an ejection volume and cardiac output that are adequate under normal filling pressure. Patients with diastolic dysfunction may present with different degrees of change in one or more of these processes, as well as manifest symptoms ranging from slight exertional dyspnea to pulmonary and peripheral edema.

ETIOLOGY

Arterial hypertension, heart disease, and senility are the most common causes of diastolic dysfunction (Table 2). Hypertensive cardiomyopathy is responsible for a third of hospitalizations due to heart failure²¹ and half of cases of acute pulmonary edema without hypertension that present to emergency departments.²² Chronic arterial hypertension increases wall stress and at the same time induces hypertrophy of the sarcomeres, increasing wall thickness.²³ Humoral factors, such as the increase in angiotensin II and in circulating concentrations of insulin, have been linked to the development of myocardial hypertrophy and to an increase in the expression of type II collagen in the extracellular matrix. Muscle hypertrophy and the increase in the co-

llagen matrix thickness prevent progressive dilation and keep wall stress stable but, at the same time, cause a decrease in distensibility. Experimental studies in humans have also shown that in these patients both the presence of acute ischemia and the abrupt increase in arterial pressure can cause an even greater increase in ventricular rigidity and in filling pressures, contributing to the development of acute pulmonary edema syndrome.

The prevalence of diastolic heart failure increases with the aging of the population. Between the third and ninth decades it is estimated that ventricular mass increases 1g to 1.5g for every year of life.²⁴ Pathology studies on normal individuals of advanced age have shown an increase in the thickness of muscle fibers and in type II collagen content and, therefore, a reduction in ventricular distensibility.²⁵ These anomalies may result in a decrease in aerobic capacity during exercise, as well as the development of symptoms of dyspnea and low cardiac output in many people of advanced age who develop atrial fibrillation.

Heart disease can affect relaxation by limiting the energetic substrate during episodes of acute ischemia. In patients with a previous infarct or chronic arterial hypertension, or both, in the setting of interstitial fibrosis that affects ventricular distensibility,²⁶ the ischemic episodes may cause pulmonary edema to develop.

Restrictive cardiopathy comprises a group of cardiac changes characterized by reduced ventricular volume and decreased distensibility.²⁷ The increase in the thickness of the ventricular wall in these patients is caused by interstitial infiltration with no muscle hypertrophy. Therefore, the diagnosis tends to be established when there is a disparity between low voltage electrocardiographic results and the presence of an increase in the thickness of the ventricular wall on echocardiogram. The ejection fraction may be reduced in patients with severe restrictive cardiomyopathy, although the left ventricle volume may remain low. The atria are characteristically dilated. The most common causes of restrictive cardiopathy include, among others, amyloidosis, post-irradiation cardiopathy, muscular dystrophy, and changes in glycogen deposit.

Diastolic function is frequently altered in primary hypertrophic cardiomyopathy. The disruption of muscle fiber organization, with an increase in ventricular wall thickness,²⁸ and abnormal electrical conduction tend to cause changes in ventricular relaxation and distensibility.²⁹

In dilated idiopathic cardiomyopathy there are also changes in relaxation, distensibility, and atrial function. Several studies have shown that diastolic function is directly related to the symptomatology and prognosis of these patients.³⁰

In constrictive pericarditis, the thickening of the pericardium causes a decrease in distensibility, with an increase in the interdependence between both ventri-

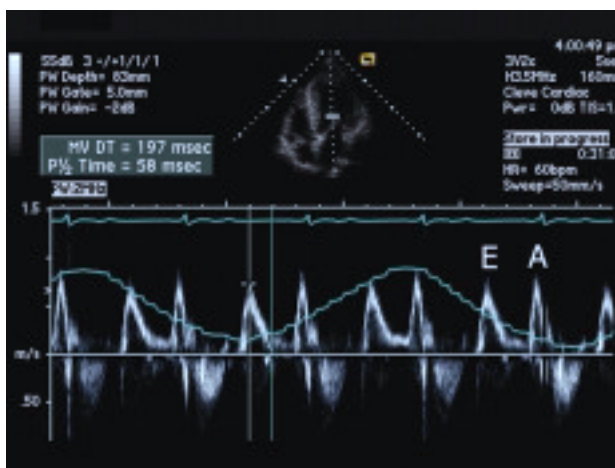


Fig. 4. Pulsed transmitral Doppler indicating early ventricular filling wave (E) and atrial contraction (A). Measured from the time of deceleration (DT) of the early filling wave.

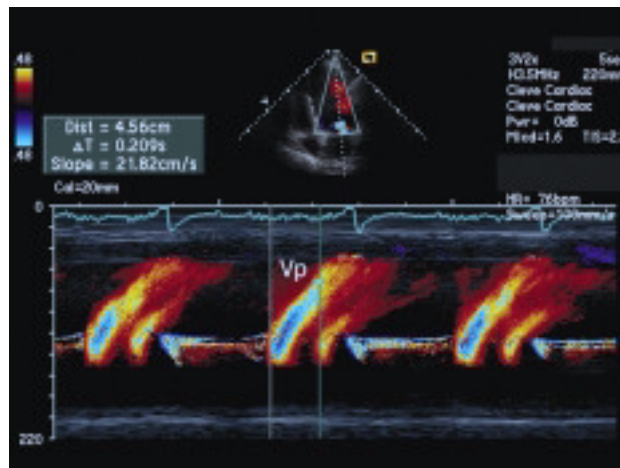


Fig. 6. M-mode color Doppler indicating the ventricular flow propagation gradient (v_p).

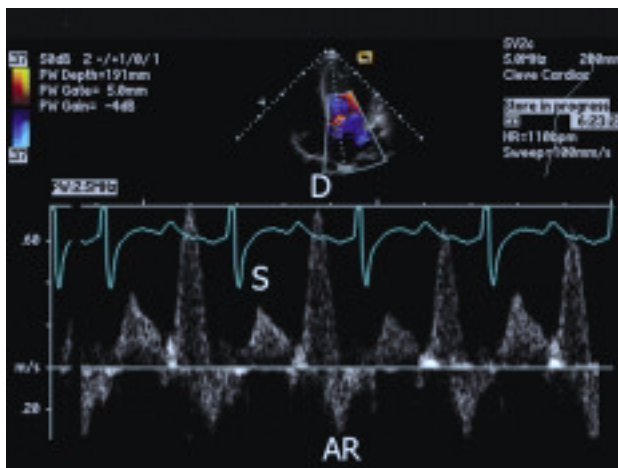


Fig. 5. Pulsed Doppler that indicates the systolic (S), diastolic (D) and retrograde flow waves of atrial contraction (AR) in pulmonary venous flow.

axation velocity of the left ventricle ($1/\tau$).³⁷ At the end of the early filling stage, the decrease in atrial pressure and the simultaneous increase in intraventricular pressure reduce the pressure gradient, causing deceleration of early filling flow. The distensibility of the left ventricle (C_v) is the principal determinant of deceleration of the early filling velocity (E_{FV}). In rigid ventricles, the deceleration time is reduced, as the filling volume causes a sudden increase in intraventricular pressure, equalizing this pressure with the atrial pressure and causing the rapid cessation of early filling flow $E_{FV}=70/2 C_v$. The physical determinants of the ventricular filling wave during atrial contraction (A) are the same as those that determine the E wave.^{38,39} Muscular contraction of the left atrium increases atrial pressure and, therefore, the atrioventricular gradient, causing acceleration of the A-wave

flow. The relaxation of the left atrium and the simultaneous increase in ventricular pressure cause deceleration of A. The left atrial function and ventricular distensibility are the factors that fundamentally contribute to the occurrence of these events. The E/A relationship is the basis for the interpretation of diastolic function on Doppler echography (Table 3). Nevertheless, since interpretation depends on various factors, its correct interpretation tends to require complementary information.

Doppler study of pulmonary venous flow

A Doppler study of pulmonary venous flow complements the interpretation of ventricular filling flow, particularly in the study of atrial function. Pulmonary venous flow in patients in sinus rhythm has 3 characteristic waves: *a*) the S wave, which represents filling of the atrium during ventricular systole; *b*) the D wave, which represents a second filling phase during ventricular diastole, and *c*) the AR wave, which represents the reserve flow toward the pulmonary veins during atrial contraction (Figure 5). Since there are no valves that impede the backward movement of flow from the left atrium to the pulmonary veins, the relation between the amplitude and the duration of the A filling wave of the left ventricle and the AR wave in the pulmonary veins depends on the distensibility of the left ventricle:⁴⁰

$$CV \propto A_{dur} - AR_{dur}$$

Doppler study of ventricular flow propagation

Several studies have shown that the filling velocities of the left ventricle vary depending on spatial lo-

cation. The maximum velocity E changes as the flow is displaced from the mitral orifice toward the apex. In ventricles functioning normally, E is rapidly displaced and reaches higher amplitude near the apex, probably due to the suction caused by the apical relaxation accelerating the flow.⁴¹ In patients with abnormal relaxation, E is greater near the mitral orifice, decreasing in amplitude and displacing itself more slowly toward the ventricular apex. This information can be easily obtained by means of an M-mode color Doppler imaging study. The propagation velocity (v_p) of the early filling wave on M-mode color Doppler allows qualitative estimation of left ventricular relaxation^{42,43} (Figure 6). In contrast with the E wave on pulsed Doppler, v_p is relatively independent of atrial pressure,⁴⁴ so that the pattern of normal filling can be distinguished from that of pseudonormal filling.⁴⁵ The digital information obtained on M-mode color Doppler imaging can also be quantitatively analyzed. Using a simplified form of the Euler differential equation, the spatial-temporal distribution of the velocities can be applied to calculate the pressure intraventricular pressure gradients:

$$\rho \left[\frac{\delta v}{\delta t} + \frac{\delta v}{\delta e} \right] = - \frac{\delta p}{\delta e}$$

These pressure gradients physiologically generate the ventricular filling suction.^{46,47} M-mode color Doppler can also be useful to estimate atrial pressure, in combination with pulsed Doppler imaging of ventricular filling. The propagation velocity (v_p) from M-mode color Doppler imaging of ventricular filling is inversely related to the isovolumetric relaxation constant (τ), and is relatively independent of atrial pressure. On the other hand, the E wave filling on ventricular Doppler imaging is determined by atrial pressure and relaxation:⁴⁸⁻⁵⁰

$$(E \propto \frac{P}{\tau})$$

Therefore, atrial pressure can be non-invasively⁵¹ estimated as:

$$Pa = k \times \frac{E}{v_p}$$

Tissue Doppler studies

Applying the same physical principle used to analyze blood flow, Doppler studies can be adapted to obtain the velocity of myocardial movement.⁵² In normal subjects, tissue Doppler allows determination of a systolic velocity (S_m) and a diastolic velocity during early filling (E_m) and atrial contraction (A_m) (Figure 7). Several studies have shown a direct relationship between

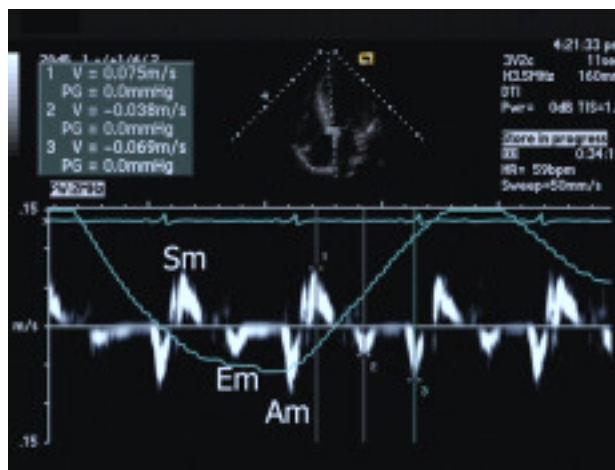


Fig. 7. Tissue Doppler showing systolic myocardial velocity (S_m) and diastolic myocardial velocity during early filling (E_m) and atrial contraction (A_m).

ventricular relaxation and E_m ,⁵³ which also appears to be less influenced by atrial pressure. This method has proven to be useful for differentiating restrictive cardiomyopathy from constrictive pericarditis.⁵⁴ Similar to the application of M-mode color Doppler imaging, the E_m wave of tissue Doppler can be used in combination with transmitral E wave Doppler imaging to estimate atrial pressure⁵⁵

Normal filling pattern

The normal Doppler pattern for ventricular filling is characterized by a prominent E, with rapid acceleration and gradual deceleration. The E wave amplitude is determined by rapid relaxation. The A wave is of lesser proportion due to the low atrial volume at the end of the early filling phase and, therefore, $E/A > 1$. M-mode color Doppler imaging shows a propagation velocity (v_p) > 45 cm/s, and tissue Doppler shows $E_m > 8$ cm/s.

Slow filling pattern

Upon diminishing the relaxation velocity of the myocardial fibers, the E amplitude is reduced. Given that atrial contraction begins before ventricular relaxation is complete, the volume in the atrium at the end of early filling increases, which in turn increases the atrial ejection volume and therefore the A amplitude. A slow relaxation pattern is characterized by an $E/A < 1$ and an EDT > 240 ms.^{56,57} A slow relaxation pattern is common in normal individuals of advanced age and in patients with hypertensive,⁵⁸ hypertrophic,⁵⁹ and ischemic cardiomyopathy.⁶⁰ These patients frequently present with few symptoms, but tend to have reduced cardiac output during exercise. The slow relaxation pattern tends to be associated with the presence on

auscultation of an S4 atrial gallop. M-mode color Doppler shown a propagation velocity (vp)<45 cm/s, and on tissue Doppler Em<8 cm/s.

Pseudonormal filling pattern

As diastolic dysfunction advances, cardiac output diminishes, which in turn causes a reduction in renal excretion of sodium and water and the elevation of left atrial pressure. This elevated pressure, in turn, produces changes in the mitral flow pattern in the opposite manner to those changes caused by abnormal relaxation. The isovolumetric relaxation time is shortened, as atrial pressure advances the moment of mitral opening. The E amplitude is increased, while the A decreases due to the reduction in ventricular distensibility. This pattern is indistinguishable from a normal filling pattern, and is frequently observed in patients with dilated, hypertrophic, and restrictive cardiomyopathy. Certain clinical and echographic characteristics help distinguish a pseudonormal filling pattern from a normal filling pattern. These include the presence of systolic dysfunction or other echocardiographic findings suggestive of heart disease, such as dilation of the left atrium. Pulmonary vein flow tends to demonstrate a reverse atrial contraction wave (AR)>35 cm/s and $AR_{dur} > A_{dur}$. M-mode color Doppler shows a propagation velocity (v_p)<45 cm/s, and on tissue Doppler $E_m < 8$ cm/s. These allow a normal filling pattern to be distinguished from a pseudonormal filling pattern.

Restrictive filling pattern

An excessive increase in atrial pressure ultimately causes a marked shortening in isovolumetric relaxation time. In this filling pattern, the early filling deceleration time (EDT) is also shortened due to low ventricular distensibility. The amplitude and duration of A are reduced significantly. Thus, the filling pattern cannot be detected in spite of there being evidence of atrial activity on electrocardiogram and in pulmonary vein flow on Doppler. The restrictive filling pattern is related to the presence of advanced congestive symptoms, with auscultatory detection of an S3 ventricular

gallop,⁶¹ as well as with an elevated cardiac mortality rate. The restrictive filling pattern is characterized by an E/A ratio >2 and an EDT<150 milliseconds. The reverse atrial contraction wave (AR) is prominent, unless atrial function has deteriorated. M-mode color Doppler shows a propagation velocity (vp)<45 cm/second, and on tissue Doppler Em<8 cm/second

TREATMENT

In spite of the prevalence of diastolic heart failure, to date no randomized studies have been performed to determine the effect of specific therapeutic agents for the treatment of this syndrome. Nevertheless, evidence available at present suggests that most drugs that are used today for the treatment of systolic heart failure are also effective in the management of diastolic heart failure (Table 4).

Diuretics are useful in patients with diastolic dysfunction who show signs of volume overload (edema, pulmonary congestion). Nevertheless, it must be taken into account that these patients have a tendency to easily develop pre-renal azotemia, since when the filling pressure decreases the ejection volume also decreases. In the SHEP study, patients of advanced age with ventricular dysfunction who received antihypertension treatment with hydrochlorothiazide showed a reduction in the incidence of heart failure.⁶² This suggests that the chronic use of diuretics in hypertensive patients can also cause an improvement in distensibility by reducing the thickness of the ventricular wall.

The decrease in arterial pressure with the use of angiotensin converting enzyme inhibitors (ACEI) and calcium channel blockers in patients with hypertensive cardiopathy are effective, causing remodeling by reducing ventricular wall thickness and mass and, therefore, causing an increase in distensibility. In certain patients with hypertrophic cardiopathy, verapamil has been shown to increase ventricular relaxation.⁶³ Nevertheless, in patients with dilated and restrictive cardiopathy, the effect of verapamil tends to be the opposite, causing a deterioration in diastolic function and an increase in filling pressures.⁶⁴

In contrast, ACEIs tend to improve relaxation and distensibility in patients with diastolic dysfunction, independently of the ejection fraction.⁶⁵ Treatment of hypertension with these agents causes a reduction in ventricular mass, a decrease in atrial volume, normalization of ventricular filling Doppler parameters, and a reduction in circulating values of atrial natriuretic peptides (ANP).⁶⁶ Recent studies have shown similar effects with use of angiotensin II inhibitors.⁶⁷

In patients with diastolic dysfunction, control of cardiac frequency and maintenance of sinus rhythm allow optimization of ventricular filling. Treatment with beta-blockers is effective not only due to these mecha-

TABLE 4. General therapeutic recommendations in accordance with phases of diastolic dysfunction^a

Phase	
Slow relaxation	Reduction in cardiac frequency, prevention of arrhythmias, control of hypertension ^b
Pseudonormal	Vasodilators, diuretics, beta blockers
Restrictive	Diuretics and vasodilators ^c

^aBased on expert opinion, without prospective validation.

^bTaking into account the pressure response during stress test.

^cTaking into account the administration of beta blockers following the appropriate use of diuretics and in the absence of pulmonary congestion.

nisms,⁶⁸ but also because of their neurohormonal inhibitory effect. Chronic stimulation by catecholamines entails the development of interstitial fibrosis and, therefore, the long-term use of beta blockers causes an increase in distensibility.⁶⁹

The vast majority of patients with diastolic dysfunction are asymptomatic or paucisymptomatic at rest, but tend to show exercise intolerance. During exercise, the duration of filling time diminishes at a higher rate than the ejection time. In normal subjects, relaxation velocity increases, increasing filling due to suction and allowing an increase in the ejection volume. In patients with diastolic dysfunction, the increase in relaxation proportionate to cardiac frequency is limited. The increase in venous return results in an proportionately greater increase in pressure than in filling volume, due to a reduction in distensibility, also limiting aerobic capacity.¹³ Recent studies have shown that betablockers and angiotensin II receptor antagonists may improve exercise tolerance in patients with diastolic dysfunction,⁷⁰ although it is not known if this occurs by some direct mechanism or indirectly by reducing arterial pressure.

CONCLUSIONS

Diastolic dysfunction not only is important in the development of symptoms and the response to treatment in patients with a normal ejection fraction, but also has prognostic and therapeutic implications in systolic heart failure. Echography allows the establishment of a diagnosis, the severity of the condition, and the specific mechanism in the majority of patients. Therefore, command of these techniques is important for the clinical cardiologist and the echography technician. Future studies are needed to determine the usefulness of the study of diastolic function during exercise and the application of echography studies as therapeutic guidelines.

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