☆ CME PAPER ☆

Primary Diastolic Heart Failure

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Diastolic heart failure is defined clinically when signs and symptoms of heart failure are present in the presence of preserved left ventricular systolic function (ejection fraction >45%). The incidence and prevalence of primary diastolic heart failure increases with age and it may be as high as 50% in the elderly. Age, female gender, hypertension, coronary artery disease, diabetes and increased body mass index are risk factors for diastolic heart failure. Hemodynamic consequences such as increased pulmonary venous pressure, post-capillary pulmonary hypertension, and secondary right heart failure as well as decreased cardiac output are similar to those of systolic left ventricular failure, although the nature of primary left ventricular dysfunction is different. Diagnosis of primary diastolic heart failure depends on the presence of preserved left ventricular ejection fraction. Assessment of diastolic dysfunction is preferable but not mandatory. It is to be noted that increased levels of B-type natriuretic peptide does not distinguish between diastolic and systolic heart failure. Echocardiographic studies are recommended to exclude hypertrophic cardiomyopathy, infiltrative heart disease, primary valvular heart disease, and constrictive pericarditis. Myocardial stress imaging is frequently required to exclude ischemic heart disease. The prognosis of diastolic heart failure is variable; it is related to age, severity of heart failure, and associated comorbid diseases such as coronary artery disease. The prognosis of severe diastolic heart failure is similar to that of systolic heart failure. However, cautious use of diuretics and/or nitrates may cause hypotension and low output state. Heart rate control is essential to improving ventricular filling. Pharmacologic agents such as angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, and calcium channel blockers are used in selected patients to decrease left ventricular hypertrophy. To decrease myocardial fibrosis, aldosterone antagonists have a potential therapeutic role. However, prospective controlled studies will be required to establish their efficacy in primary diastolic heart failure. (AJGC. 2002;11:178–189)

It is well established that the syndrome of heart failure can occur in the presence of both preserved and depressed ventricular systolic function.[1,2] Primary diastolic heart failure is diagnosed when left ventricular (LV) ejection fraction is normal or near normal and primary systolic heart failure is diagnosed when there is a decrease in LV ejection fraction. It should be appreciated, however, that abnormalities of diastolic or systolic function do not always cause clinical heart failure. Furthermore, in both primary systolic and diastolic heart failure, some indices of systolic and diastolic function may be abnormal. For example, in dilated cardiomyopathy with a marked increase in ventricular diastolic pressure, a restrictive transmitral flow pattern (diastolic dysfunction) is frequently present. Similarly, in primary diastolic heart failure, although the ejection fraction is normal, myocardial contractile function may be depressed. It is also recognized that the phase of systole following completion of ejection until the closure of the semilunar valves (hang-out time) is related to myocardial relaxation. The isovolumic relaxation and rapid filling phases are also markedly influenced by systolic function.[3] Thus, systolic and diastolic phases and function are interdependent.

The clinical manifestations and hemodynamic consequences of diastolic and systolic heart failure may be similar, although the primary pathophysiologic mechanisms are different. Decreased ventricular compliance (increased stiffness) and abnormal diastolic filling are the principal functional abnormalities in patients with diastolic heart failure.[4,5] Decreased LV compliance is associated with a disproportionate elevation of its diastolic pressure,

which causes a passive increase in left atrial and pulmonary venous pressures, which produces symptoms of pulmonary venous congestion. Passive increase in pulmonary artery pressure (post-capillary pulmonary hypertension), when severe, is the mechanism of secondary right ventricular failure associated with increased right ventricular diastolic and right atrial pressure and signs and symptoms of systemic venous hypertension. With a marked restriction in ventricular filling stroke volume may decline due to decreased preload associated with signs and symptoms of low cardiac output.

In primary systolic failure, a reduced LV ejection fraction is the initial functional derangement, which is associated with a disproportionate increase in end-systolic and end-diastolic volumes and pressures and a passive increase in left atrial and pulmonary venous pressures—the hemodynamic mechanism of signs and symptoms of pulmonary venous congestion. Post-capillary pulmonary hypertension and right heart failure is associated with signs and symptoms of systemic venous hypertension. A decrease in forward stroke volume and cardiac output may also occur due to reduced ejection fraction. The mechanism of hemodynamic consequences in primary diastolic heart failure is summarized in Table I. It is apparent that it is difficult to distinguish between diastolic and systolic heart failure by clinical and hemodynamic profiles.

DEFINITION AND DIAGNOSIS OF PRIMARY DIASTOLIC HEART FAILURE

As the principal functional derangement in diastolic heart failure is decreased compliance (increased stiffness),[5] which is associated with an upward shift of the LV diastolic pressure volume curve, a pathophysiologic definition has been proposed based on these functional abnormalities. The proposed pathophysiologic definition is "a condition resulting from an increased resistance to filling of one or both ventricles, leading to symptoms of congestion due to an inappropriate upward shift of the diastolic pressure-volume relation (that is, during the terminal phase of the cardiac cycle)."[3] Although this definition describes the principal pathophysiologic mechanism of primary diastolic heart failure, it is not clinically applicable, as it is difficult to determine the pressure-volume curves in routine clinical practice. A more practical definition that can be easily applied in clinical practice is "a condition with classic findings of congestive failure, with abnormal diastolic and normal systolic function at rest." The proposed diagnostic criteria, which can be applied in most clinical circumstances, are 1) definitive evidence of congestive heart failure; 2) objective evidence of normal LV systolic function; and 3) objective evidence of LV diastolic dysfunction (relaxation, filling, distensibility).[6,7]

Diagnosis of congestive heart failure can be made clinically in the vast majority of patients if the symptoms of pulmonary venous hypertension (paroxysmal nocturnal dyspnea, orthopnea) and/or systemic venous hypertension (dependent edema) are present, along with clinical and radiologic findings of increased LV diastolic pressure (S_4, S_3 gallops), pulmonary venous pressure (chest x-ray), pulmonary artery pressure (increased pulmonic component of the second heart sound), and right ventricular failure (S_3 gallop, elevated jugular venous pressure, hepatomegaly, peripheral edema). It should be appreciated that it is not necessary for all the symptoms and signs to be present in individual patients for the diagnosis of heart failure. Indeed, in some patients with suspected heart failure, many or all the physical findings may be lacking. In occasional patients, cardiopulmonary exercise testing, pulmonary function tests, exercise echo-Doppler studies, and determination of hemodynamics at rest and during exercise are necessary to distinguish between symptoms of cardiac and noncardiac origin.

A few recent studies have also suggested that higher than normal plasma levels of atrial and brain natriuretic peptide indicate heart failure. Clinical diagnosis of heart failure is often based on physicians' subjective impressions. To overcome the subjectivity, various criteria have been proposed in various studies. The cri-

Table I. Mechanisms of Hemodynamic Consequences in Primary Diastolic Heart Failure

Decreased LV compliance→disproportionate increase in LVDP→passive increase in LAP→PVP (signs and symptoms of pulmonary venous congestion) →post capillary pulmonary hypertension→secondary RV failure (signs and symptoms of systemic venous hypertension)
Restriction of ventricular filling→decreased preload→decreased stroke volume and cardiac output (signs and symptoms of low cardiac output)

LV=left ventricular; DP=diastolic pressure; LAP=left atrial pressure; PVP=pulmonary venous pressure; RV=right ventricular

Table II. Criteria for Congestive Heart Failure Used in the Framingham Study*

MAJOR CRITERIA	MINOR CRITERIA	MAJOR OR MINOR CRITERIA
Paroxysmal nocturnal dyspnea or orthopnea	Ankle edema	Weight loss >4.5 kg in 5 days in response to treatment
Neck vein distention	Night cough	
Rales	Dyspnea on exertion	
Cardiomegaly	Hepatomegaly	
Acute pulmonary edema	Pleural effusion	
S_3 gallop	Vital capacity decreased one half from maximal capacity	
Increased venous pressure >6 cm of water	Tachycardia (rate of >120/min)	
Circulation time >25 sec		
Hepatojugular reflux		

*For a definite diagnosis of congestive heart failure in this study, two major or one major and two minor criteria had to be present concurrently. Reprinted with permission from *N Engl J Med*. 1971;285:1441–1446.[8]

teria used in the Framingham study, initially proposed for the diagnosis of congestive heart failure, have been used for the diagnosis of diastolic heart failure in some studies (Table II).[8] For establishing a definite diagnosis of congestive heart failure in this study, two major or one major and two minor criteria had to be present concurrently. When these diagnostic criteria are used, it is likely that more symptomatic patients with moderate and severe heart failure will be identified and patients with milder heart failure may be missed.

The objective evidence of normal LV systolic function is more frequently established in clinical practice by determining the ejection fraction, by echocardiography or radionuclide ventriculography. At the bedside, although a normal LV apical impulse usually indicates a normal LV ejection fraction, a sustained LV impulse, which is most frequently associated with a reduced ejection fraction, may also be present in patients with marked LV hypertrophy with normal ejection fractions. Thus, for clinical purposes, echocardiographic or radionuclide ventriculographic evaluation of LV systolic function should be considered in all patients with clinically confirmed or suspected heart failure.

During initial evaluation, echocardiography and Doppler studies are preferable, as additional information regarding valvular heart disease, wall thickness, mass atrial enlargement, and LV diastolic, right ventricular systolic, and systemic venous pressures can be obtained.

There is controversy regarding the definition of preserved ejection fraction; in some studies, 50% or higher[9] and in others, 45% or higher[10] has been regarded as normal and has been used for the diagnosis of diastolic heart failure. In clinical practice, most frequently, a minimum ejection fraction of 45%, estimated by echocardiography, is used to define preserved LV systolic function.

Assessment of the neurohormonal profile has been suggested to distinguish between preserved and depressed LV ejection fraction. Increased levels of N-terminal atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) have been shown to indicate reduced ejection fraction.[11] However, recent studies have also reported that in patients with clinical heart failure and a normal ejection fraction, endothelin-1, norepinephrine, ANP, and BNP levels are increased.[12] Furthermore, higher BNP levels have been reported to indicate a poorer prognosis in patients with primary diastolic heart failure.[12] Thus, estimation of BNP may be useful for the diagnosis of clinical LV failure, rather than for estimation of the ejection fraction.[13]

After establishing the presence of preserved LV systolic function, it is desirable to assess LV diastolic function; however, it is not mandatory to document the type and/or severity of diastolic dysfunction in patients with overt clinical heart failure.[1,2] Various indices of diastolic function—relaxation, chamber and myocardial stiffness, diastolic pressure-volume curves, and diastolic filling characteristics—can be assessed by either invasive or noninvasive techniques.[14] In clinical practice, echo-Doppler studies are preferable and can provide information regarding relaxation (e.g., isovolumic relaxation time), abnormalities of filling (e.g.,

abnormal early filling/atrial filling velocity ratio), and changes in LV diastolic pressure (e.g., restrictive transmitral filling pattern, abnormal pulmonary venous flow patterns). During radionuclide ventriculographic study to measure the LV ejection fraction, it is also possible to assess diastolic function by determining the peak filling rate and time to peak filling.

It should be appreciated that clinical heart failure with preserved systolic function (diastolic heart failure) can be caused by heterogeneous pathophysiologic conditions. Hypertrophic cardiomyopathy, infiltrative cardiomyopathies such as amyloidosis, valvular heart diseases, constrictive pericarditis, endocardial fibroelastosis, and other forms of restrictive cardiomyopathy can cause similar clinical syndromes and may need to be excluded by specific investigations before the diagnosis of "primary" diastolic heart failure is established. The diagnostic steps that can be used in clinical practice are summarized in Table III.

PREVALENCE OF PRIMARY DIASTOLIC HEART FAILURE AND ASSOCIATED PATHOPHYSIOLOGIC DISORDERS

The true incidence and prevalence of primary diastolic heart failure is difficult to estimate, as most studies are not prospective and have been performed in referral institutions. In the Study of LV Dysfunction (SOLVD) registry, approximately 30% of patients with the diagnosis of heart failure had preserved LV systolic function.[15–19] In a number of retrospective studies, the reported incidence of diastolic heart failure varied between 20%–40%.[15] The community studies reported an incidence as high as 50%.[18] In all studies, however, it has been observed that the incidence increases with age. In patients less than 60 years old, the incidence is about 15%–25%; between 60–70 years old, it is 35%–40%; and in patients 70 years old or older, approximately a 50% incidence of diastolic heart failure has been observed. The incidence is also higher in elderly women. The reasons for a higher incidence in females than in males are not entirely clear. Why primary diastolic failure is more common in the elderly is also not clear. Age-related changes in the myocardial structure and function and changes in the neuroendocrine profile have been suggested as contributing factors.[20]

In animal studies, it has been observed that myocardial cell size increases with age. The collagen content of the myocardium also increases. The sar-

Table III. Suggested Approaches in the Diagnosis of Primary Diastolic Heart Failure

EVIDENCE OF CONGESTIVE HEART FAILURE
Clinical evaluation
Cardiopulmonary exercise test along with pulmonary function tests in selected patients
Exercise hemodynamics in selected patients
Determination of brain natriuretic peptides in selected patients
EVIDENCE OF PRESERVED LEFT VENTRICULAR SYSTOLIC FUNCTION
Echocardiography (preferable)
Radionuclide ventriculography in selected patients
Contrast ventriculography in selected patients when cardiac catheterization is performed for other clinical indications
EVIDENCE OF DIASTOLIC DYSFUNCTION (NOT MANDATORY)
Echo-Doppler studies (preferable)
Radionuclide ventriculography in selected patients
Cardiac catheterization in selected patients
TO EXCLUDE SPECIFIC PATHOPHYSIOLOGIC CONDITIONS
Examples:
Hypertrophic cardiomyopathy: echocardiography
Constrictive pericarditis: cardiac catheterization, magnetic resonance angiography
Amyloidosis: cardiac biopsy
Restrictive cardiomyopathy: cardiac catheterization

coplasmic reticular calcium ATPase activity (SERCA), which is necessary for appropriate calcium reuptake and initiation of myocardial relaxation, has been found to be decreased in senescent hearts. The overexpression of SERCA in senescent hearts in transgenic animals has been shown to enhance myocardial relaxation and contractile function. The neuroendocrine changes with aging, such as decreased β-adrenergic receptor density, decreased β-adrenergic inotropic response, and increased angiotensinogen and angiotensin-converting enzyme (ACE) concentrations and angiotensin receptors, may be contributing factors for myocyte hypertrophy and increased myocardial collagen content.

Age-related changes in vascular and cardiac function might also be contributing factors in the higher incidence of diastolic heart failure in the elderly population. The compliance of the aorta and of large- and medium-size arteries is substantially decreased. The reflected waves in arterial pulsation may be accentuated and may occur during systole, which increases the resistance to LV ejection, and may contribute to LV hypertrophy, which is associated with impaired diastolic function. Calculated LV mass is usually increased, but the contractile function and ejection function remain unchanged. With aging, the early filling rate is decreased, which is compensated by increased late filling, as is evident from the decreased E/A ratio in the transmitral flow pattern. In the elderly population, the incidence of systolic hypertension increases, which may be associated with LV hypertrophy, an important contributing factor to diastolic heart failure. Furthermore, in the elderly, the incidence of coronary artery disease (CAD) also increases, which may produce ischemia-induced LV diastolic dysfunction. The age-related contributing factors in the genesis of diastolic heart failure are summarized in Table IV.

"Primary diastolic heart failure" appears to be a "clinical syndrome" of the elderly. The most frequent etiologic association, particularly in the elderly population, is hypertension with or without CAD (Table V).[21] However, the incidence of clinically silent, significant CAD is considerable in diastolic heart failure.[22] Diabetes is also a relatively frequent pathophysiologic association. In African Americans, diabetes, obesity, and increased body mass index appear to be more important associations than in Caucasians (Table VI).[23] Thus, the assessment of clinical profile may aid in the diagnosis of primary diastolic heart failure. Furthermore, it is relevant to the therapeutic interventions for prevention of this syndrome. It should be emphasized that irrespective of race and gender, hypertension is the most frequent etiologic association of primary diastolic heart failure and adequate control of hypertension is necessary to decrease its incidence.

PROGNOSIS OF PRIMARY DIASTOLIC HEART FAILURE

Prospective and controlled studies to assess prognosis and the natural history are lacking, and a

Table IV. Age-Related Changes in Myocardial Structure and Neuroendocrine, Vascular, and Cardiac Function

CHANGES IN MYOCARDIAL STRUCTURE
Myocardial cell size: increased
Collagen content: increased
Sarcoplasmic reticular calcium ATPase (SERCA) activity: decreased
CHANGES IN NEUROENDOCRINE FUNCTION
Decreased β-adrenergic receptor and β-androgenic inotropic response
Increased angiotensinogen
Increased angiotensin-converting enzyme and angiotensin receptors
CHANGES IN VASCULAR AND CARDIAC FUNCTION
Decreased arterial compliance
Accentuated reflected or tidal aortic waves
Increased left ventricular mass
Unchanged contractility and ejection fraction
Decreased early filling and increased late filling

Table V. Diastolic Heart Failure in the Community: Underlying Cardiovascular Diseases, Olmsted County, MN (1996–1997)

Left ventricular ejection fraction >45%
Females, 79.6±13.6 years
Males, 75.9±8.7 years
Hypertension without coronary artery disease: 28%
Hypertension with coronary artery disease: 36%
Hypertension with valvular heart disease: 15%
Diabetes: 18%
Hypertrophic/restrictive cardiomyopathy: 3%

Adapted with permission from *Circulation.* 2000;102:II-780[21]

Table VI. Heart Failure With Preserved Systolic Function in African Americans: The Role of Diabetes Mellitus and Obesity

	CAUCASIANS	AFRICAN AMERICANS
Age (years)	71.8±12.9	69.6±12.8
Body surface area (m^2)	1.87±0.29	1.97±0.26*
Body mass index (kg/m^2)	28.7±7.4	31.8±9.3*
Severe obesity (%)	36	57*
Diabetes (%)	24	37*
Coronary artery disease (%)	31	24
Hypertension (%)	57	66

*Statistically significant difference
Adapted from *Circulation*. 2000;102:II-781[23]

wide range of mortality and morbidity has been observed.[1,15] In some studies, a 5-year mortality of 50% was observed and was similar to that of primary systolic heart failure.[18] The similar mortality rates in patients with diastolic and systolic heart failure in this study were independent of the incidence of hypertension or CAD. In a community-based study, 1-, 2-,and 3-year mortality of 29%, 39%, and 60%, respectively, were reported.[24] In contrast, in a study of patients with new-onset heart failure in the outpatient setting, 2-year mortality of patients with preserved LV systolic function was only 8%, and significantly less than the 2-year mortality of patients with systolic heart failure (19%).[25] The hospitalization rates were also lower in patients with diastolic heart failure. The explanation for these wide differences in the observed incidences of mortality and morbidity in these studies is not apparent. There are no obvious differences in race, gender, or age of the population studied, and the incidences of a history of hypertension, diabetes, or CAD were also similar. The severity of clinical heart failure of patients in these studies might have been different, which might explain, to some extent, the differences in the observed incidences of mortality and morbidity of primary diastolic heart failure in these studies.

The presence of CAD is associated with poor prognosis, particularly in the elderly. Aronow et al.[26] reported 1-, 2-, 3-, and 4-year mortality rates of 22%, 38%, 46%, and 56%, respectively, in 166 patients with an average age of 82 years, all with CAD. In the absence of documented CAD, the prognosis appears more favorable. Zile et al.[27] reported annual mortality of approximately 2% in patients without CAD but with LV hypertrophy. Brogan et al.[28] studied 53 patients without coronary artery and valvular heart disease, confirmed by cardiac catheterization. A history of hypertension was present in 83%, and diabetes in 30% of patients. In 15% of patients, LV hypertrophy was

documented. During the average follow-up of 68 months, there was only one cardiac death. Thus, it appears that in the absence of significant LV hypertrophy and myocardial ischemia (idiopathic primary diastolic heart failure), the overall prognosis may not be as unfavorable as has been observed in some studies. However, controlled, prospective studies will be necessary for appropriate assessment of the prognosis of patients with primary diastolic heart failure. Age, clinical severity of heart failure, degree of LV hypertrophy, myocardial ischemia resulting from CAD, diabetes, and other comorbid conditions, such as renal failure, will remain important determinants of long-term prognosis of primary diastolic heart failure.

THERAPEUTIC APPROACHES

The objectives and the potential therapeutic approaches for primary diastolic heart failure are outlined in Table VII. Most patients present with symptoms related to pulmonary and systemic venous hypertension. Diuretics, nitrates, ACE inhibitors, and angiotensin II subtype 1 (AT_1) receptor blocking agents decrease right atrial and pulmonary capillary wedge pressures and are useful in relieving congestive symptoms. Indeed, diuretic therapy is required in almost all symptomatic patients. However, diuretics and nitrates should be used cautiously, as excessive diuretics and nitrates may decrease cardiac output and induce hypotension and renal failure. The doses of diuretics and nitrates should be adjusted according to improvement in symptoms and changes in weight. Although ACE inhibitors and AT_1 blockers decrease pulmonary and systemic venous pressures, they may also induce hypotension and renal failure and therefore should be used cautiously.

Several drugs have the potential to improve ventricular relaxation (lusitropic effect). The drugs that increase myocardial cyclic adenosine monophosphate concentrations, such as β-adrenergic agonists and cardiac-specific phosphodiesterase inhibitors, may also enhance myocardial relaxation.[29] Clinically available β adrenergic agonists and phosphodiesterase inhibitors can be administered only intravenously and therefore can be used for short-term treatment only. Furthermore, these agents can also induce malignant ventricular arrhythmias. Thus, the clinical usefulness of these drugs is limited.

Phospholamban inhibition and enhanced SERCA are associated with increased myocardial relaxation; however, drugs targeted to achieve these objectives are not available. Nitric oxide promoters also have the potential to improve relaxation and diastolic function. The beneficial effect of nitrates may be partly mediated by nitric oxide.

Controversy exists about the potential role of digitalis therapy in patients with preserved systolic function in sinus rhythm. In the Digitalis Investigation Group (DIG) trials,[30] 988 patients with congestive heart failure had LV ejection fractions greater than 45%. The clinical benefits, i.e., the combined incidence of death and hospitalization for treatment of heart failure, were similar to those in patients with reduced LV ejection fractions.[15,30] However, digitalis therapy presently should be considered only in patients with atrial fibrillation, to control ventricular response, and not in patients in sinus rhythm.

In approximately 30% of patients, overt heart failure is precipitated by the onset of atrial fibrillation and in such patients, adequate control of heart rate and maintenance of sinus rhythm are beneficial. Pharmacotherapy with β blockers and amiodarone may be effective. In refractory patients, atrioventricular modal ablation and pacemaker therapy should be considered.

In patients with sinus rhythm and relative tachycardia, a reduction in heart rate may be associated with improved ventricular filling and hemodynamics, and β blocker therapy may be useful in such patients.

LV hypertrophy and increased LV mass are major pathophysiologic determinants of primary diastolic heart failure. Therapeutic interventions to decrease LV hypertrophy and mass have potential benefits in the management of this syndrome. ACE inhibitors and AT_1 receptor blockers decrease LV wall thickness and mass and improve diastolic function in patients with hypertension. In some patients with diastolic heart failure, ACE inhibitors may decrease rehospitalization rates. In experimental studies, ACE inhibitors and AT_1 blockers have been shown to enhance myocardial relaxation. Angiotensin I receptor blocking agents can improve exercise performance in patients with diastolic dysfunction and a hypertensive response to exercise.[31] A decrease in systemic arterial pressure in hypertensive or normotensive patients is associated with an improvement in diastolic function. Thus, some reduction of arterial pressure with ACE inhibitors, AT_1 blockers, β blockers, nitrates, or calcium channel blockers is desirable.

Calcium channel blocking agents also can decrease LV hypertrophy ad mass and improve diastolic function.[32] However, long-term clinical benefits of such therapy need to be determined. Heart rate-regulating calcium channel blocking agents, such as verapamil or diltiazem, may improve symptoms and LV diastolic function in some patients with hypertrophic cardiomyopathy.[33]

Table VII. Therapeutic Objectives and Potential Therapies for Primary Diastolic Heart Failure

To Relieve Congestive Symptoms
Diuretics, nitrates, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II subtype 1 receptor blocking agents (AT_1 blockers)
To Improve Myocardial Relaxation (Lusitropic Agents)
Drugs with positive inotropic effects Beta-adrenergic agonists Phosphodiesterase inhibitors ACE inhibitors, AT_1 blockers
To Decrease Heart Rate and Improve Diastolic Filling
Beta blockers Heart rate-regulating calcium channel blockers
To Control Ventricular Response and/or Maintain Sinus Rhythm in Atrial Fibrillation
Beta blockers Amiodarone Heart rate-regulating calcium channel blockers Atrioventricular nodal ablation and pacemaker therapy
To Decrease Left Ventricular Hypertrophy and Mass
ACE inhibitors, AT_1 blockers Beta blockers Calcium channel blockers Any drug effective for adequate control of hypertension
To Decrease Myocardial Fibrosis and Collagen Content
ACE inhibitors, AT_1 blockers Aldosterone antagonists
To Decrease Myocardial Ischemia
To decrease myocardial oxygen demand: beta blockers, nitrates, calcium channel blockers To improve myocardial perfusion: revascularization therapy
To Prevent Primary Diastolic Heart Failure
Adequate treatment of hypertension, diabetes, and obesity and modification of other risk factors for coronary artery disease

Interstitial fibrosis and increased myocardial collagen content are pathophysiologic contributing factors in primary diastolic heart failure. Therapies with potential to decrease myocardial fibrosis and collagen content may be useful in the management of this syndrome. In experimental studies, angiotensin inhibitors and aldosterone antagonists have been shown to decrease myocardial fibrosis and collagen content.[34] However, clinical studies are lacking to demonstrate such benefits of these drugs in patients with established diastolic heart failure.

Myocardial ischemia resulting from atherosclerotic CAD is a major mechanism of diastolic heart failure. Therapies to relieve myocardial ischemia, either by decreasing myocardial oxygen demand (β blockers, nitrates, and calcium channel blockers) or by increasing myocardial perfusion (revascularization), are likely to be beneficial. However, improved outcome of such therapy needs to be demonstrated by appropriate clinical studies.

As the long-term prognosis of patients with overt and severe diastolic heart failure is poor, preventive therapy should be considered in patients at high risk of developing diastolic heart failure. Adequate treatment of hypertension, diabetes, and obesity and modification of other risk factors for CAD should be and can be employed in clinical practice to prevent primary diastolic heart failure.

CONCLUSION

Primary diastolic heart failure is more prevalent in the elderly and is associated with variable mortality and morbidity. Hypertension, with or

without CAD, is the most frequent pathophysiologic association. CAD and increasing age are adverse prognostic factors. Treatments, at present, are largely symptomatic. There is a need for prospective, controlled studies to assess the usefulness of various therapeutic intervenes that are employed empirically. Preventive treatment should also be considered.

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CME Questions

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INSTRUCTIONS FOR COMPLETING THIS FORM

Read the selected paper and answer *all* the questions that follow. After each question there is a series of possibly correct answers. Please select the one best answer for each and place your selection on the answer grid. **YOU MUST ALSO COMPLETE THE CME EVALUATION SECTION** and return the form within 6 months of the paper's publication to receive credit. Letters of credit will be mailed to participants biannually.

ACCREDITATION STATEMENT

Winthrop-University Hospital (WUH) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians. WUH designates this Continuing Medical Education activity for up to one (1) credit hour in Category 1 credit towards the AMA Physicians' Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

The authors and editors of this educational activity have indicated that the information discussed is as objective and free from bias as possible. They have indicated that there is no commercial relationship that may be perceived as a real or apparent conflict of interest.

OBJECTIVE AND TARGET AUDIENCE

All physicians who care for geriatric patients are eligible to receive credit. At the conclusion of this activity, participants should be able to: 1) summarize the important points discussed in the paper reviewed; 2) identify patients to whom the paper is relevant; 3) modify management practices as new information is learned; and 4) identify deficiencies in their knowledge base.

QUESTIONS: PLEASE SELECT THE ONE BEST ANSWER FOR EACH AND PLACE YOUR SELECTION ON THE ANSWER GRID.

1. All of the following statements regarding clinical manifestations of diastolic heart failure are true except:

A _____Clinical manifestations may be very similar to manifestations due to systolic heart failure.
B _____Pulmonary venous congestion is often present.
C _____Peripheral swelling of the ankles is distinctly absent in diastolic heart failure.
D _____Hemodynamic profiles obtained in patients with diastolic heart failure may be similar to those obtained in systolic heart failure.

2. With regard to the pathophysiologic derangements in diastolic heart failure, which of the following sequences is false?

A _____Decreased left ventricular compliance leads to a disproportionate increase in left ventricular diastolic pressure leads to passive increases in left atrial pressure.
B _____Restriction of ventricular filling leads to decreased preload leads to decreased stroke volume and cardiac output.
C _____Increased post-capillary pulmonary hypertension leads to secondary right ventricular failure leads to increased jugular venous pressure.
D _____Myocardial damage from loss of myocytes leads to increased left ventricular filling pressure leads to pulmonary edema.

3. With regard to prevalence of primary diastolic heart failure, which of the following statements is false?

A _____ In patients less than 60 years old, the incidence ranges from 15%-25%.
B _____ The incidence of diastolic heart failure decreases with advancing age.
C _____Hypertension is the most frequent etiologic association of primary diastolic heart failure.
D _____Secondary causes of diastolic heart failure include infiltrative cardiomyopathies, endocardial fibroelastosis, and forms of restrictive cardiomyopathy.

4. With regard to prognosis of primary diastolic heart failure, which of the following statements is true?

A _____In some observational studies, the 5-year mortality was as high as 50%-60%, similar to that of primary systolic heart failure.
B _____Most studies have demonstrated clear differences between race and gender in patients dying from diastolic heart failure.
C _____The presence of coronary artery disease is associated with improved prognosis, particularly in elderly patients with diastolic heart failure.
D _____Long-term prognosis of patients with diastolic heart failure is distinctly unrelated to comorbid conditions, such as diabetes, renal failure, or myocardial ischemia.

5. With regard to therapy for diastolic heart failure, which of the following statements is false?

A _____Diuretic therapy should be used in most patients.
B _____Digitalis therapy is considered the primary form of therapy, regardless of the presence of dysrhythmia.
C _____Myocardial ischemia has been found to be a major mechanism resulting in diastolic heart failure, but improved outcomes with revascularization therapy have not yet been definitively demonstrated.
D _____Calcium channel blockers may improve symptoms and left ventricular diastolic dysfunction in some patients with hypertrophic cardiomyopathy, but long-term clinical benefits have yet to be determined.

CME Answers

Answer the questions from the previous page by selecting the best choice of A, B, C, or D

Questions: 1.__ 2.__ 3.__ 4.__ 5.__

CME Evaluation

	Agree				Disagree
1. My knowledge was enhanced by this activity.	1.__	2.__	3.__	4.__	5.__
2. The activity helped to clarify issues specific to geriatric patients.	1.__	2.__	3.__	4.__	5.__
3. The information obtained from this exercise will have an impact on my care of patients.	1.__	2.__	3.__	4.__	5.__
4. The format of the exercise was useful.	1.__	2.__	3.__	4.__	5.__

5. Suggestions for future topics:

WHERE TO SEND THE COMPLETED CME FORM

Please print all information.
There is no charge to members of the Society of Geriatric Cardiology.
Nonmembers please submit a $3.00 administrative fee in the form of a check made out to the Office of Academic Affairs-WUH.

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