Symposium: Review Article

Diastolic heart failure in the elderly

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Abstract Heart failure with preserved left ventricular function is a common problem among elderly patients. Given that diastolic heart failure (DHF) occurs in up to 50% of all heart failure admissions, and that incidence increases with age, knowledge of current recommendations for its diagnosis and treatment are extremely important for the elderly population. Causes of DHF include the aging process itself, hypertension, left ventricular hypertrophy, aortic stenosis, and hypertrophic obstructive cardiomyopathy. The patient with DHF may present with signs and symptoms similar to those observed in systolic heart failure. Treatment goals for the patient with DHF include achieving normal volume status, improving relaxation of the left ventricle, regression of hypertrophy if possible, and management of any co-morbidities that may aggravate the clinical status of patients with DHF. Hopefully, in the future, further data from randomized clinical trials will allow a more defined approach to care in these patients. (J Geriatr Cardiol 2006;3:210-221.)

Key Words diastolic dysfunction; elderly; heart failure; left ventricular hypertrophy; aging

Introduction

Heart failure with preserved left ventricular function is a common problem among elderly patients. The natural aging process of the heart results in a stiff, non-compliant left ventricle, which can in many cases cause symptoms of heart failure. Co-morbid conditions common in the elderly such as hypertension or coronary artery disease may accelerate the development of diastolic dysfunction. Diastolic heart failure (DHF) has always been a diagnostic dilemma for clinicians and there has been much debate on the exact definition of the disorder. Unfortunately, in contrast to systolic heart failure, less effort has been made to take an evidence-based approach to the study of DHF. Consequently, less data on which to base strategies for the management and diagnosis of this process are available.

Given that DHF occurs in up to 50% of all heart failure admissions, and that the incidence increases with age, knowledge of current recommendations for its diagnosis and treatment are extremely important for the elderly population.1,2 The American Heart Association states that "the diagnosis of diastolic heart failure is generally based on the finding of typical symptoms and signs of heart failure in a patient who is shown to have a normal left ventricular ejection fraction and no valvular abnormalities on echocardiography".3,4 Others argue that for a definite diagnosis of DHF, patients must have an ejection fraction above 50 percent within three days of an episode of congestion with evidence of diastolic dysfunction measured by cardiac catheterization.5,6

Although, cardiac catheterization remains the gold standard for the diagnosis of diastolic abnormalities, this is an invasive test that may not always be appropriate for all elderly patients. Furthermore, Zile et al. demonstrated that in 63 patients with clinical signs of heart failure with preserved LV function, 92% had elevated end-diastolic pressures in the cardiac catheterization laboratory, and 79% had an abnormal time constant of LV relaxation.7 The authors concluded that objective measurements of LV diastolic function were not required to establish the diagnosis of diastolic heart failure, but could support or confirm the diagnosis. Advances in the field of echocardiography, especially as it pertains to the study of diastolic dysfunction, have provided clinicians with a non-invasive means to evaluate for the presence of diastolic abnormalities. This reduces the risk of supporting or confirming the diagnosis of DHF.

The high prevalence of diastolic dysfunction as well as co-morbid conditions in the elderly make DHF commonly confused with other disease entities. For example, patients with renal failure, cirrhosis, or low albumin states may present with volume overload states independent of diastolic failure. Many of these patients have signs of diastolic dysfunction on imaging studies such as the echocardiogram. However, diastolic dysfunction may not be the main cause of the symptoms or volume overload in such patients.
Therefore, as in most aspects of clinical medicine, the history and physical examination remains paramount in the evaluation of patients with DHF.

Causes of DHF include the aging process itself, hypertension, left ventricular hypertrophy, aortic stenosis, and hypertrophic cardiomyopathy (see pathophysiology). Table 1 lists disorders that may cause restriction to diastolic filling including myocardial diseases, pericardial disorders, or endocardial causes. This review will focus on myocardial causes.

### Epidemiology

Overall, DHF is extremely common in the elderly population with a prevalence of 50% in patients over the age of 70. Among all patients with congestive heart failure, 50% have a normal ejection fraction. Elderly women are affected more than men in a 2:1 to 4:1 ratio. The annual mortality of 5-8% in patients with DHF is less than the rate of 10-15% generally found in patients with systolic heart failure. However, in elderly patients the mortalities for DHF and systolic heart failure (SHF) may be more similar. One large population-based study showed that patients discharged with the diagnosis of heart failure with preserved left ventricular function were more likely to be older and also have atrial fibrillation or hypertension. These patients had similar 30 day and one year mortality compared to patients with ejection fractions <40%. The rates of readmission for heart failure were also similar between groups. Another, large registry-based study suggests in-hospital mortality is lower in DHF than SHF. However, the length of stay appears to be similar for heart failure hospitalizations independent of ejection fraction. These data suggest that either DHF itself, or DHF combined with co-morbidities may be as dangerous an entity as SHF.

### Pathophysiology

In the normal heart, for contraction to occur, extracellular calcium enters the cytosol causing release of calcium from the sarcoplasmic reticulum (SR). Tropomyosin blocks the binding site where the interaction between myosin and actin occur. When calcium binds to Troponin C, a change in morphology occurs that displaces tropomyosin from this binding site allowing actin and myosin to interact. For normal relaxation to occur, the cytosol must be cleared of calcium so that it can dissociate from troponin C and the actin-myosin complex can disassociate. During this process, ATP is consumed which allows contraction and the dissociation of the actin-myosin complex. Calcium efflux from the cytosol is dependent upon two major mechanisms. First, the SR has an ATP-dependent calcium transporter that returns calcium into the SR. Second, a Ca-Na exchanger sends calcium back across the sarcolemma in exchange for sodium.

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<td>Constrictive pericarditis</td>
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Table 1. Causes of DHF
The Na-K ATPase on the sarcolemma pumps sodium out and potassium into the cytosol, thus maintaining a favor-
giotensin-renin system, sympathetic nervous system and several cytokines are activated by the pressure overloaded state. Activation of angiotensin II is known to have deleterious effects on afterload and cardiac remodeling. Hearts undergo unfavorable remodeling from neurohormonal activation and therefore may develop further diastolic dysfunction.31

Diagnosis

The patient with DHF may present with signs and symptoms similar to those observed in systolic heart failure. These include dyspnea on exertion, paroxysmal nocturnal dyspnea, orthopnea, chest tightness, edema, and ascites. Orthopnea is a very specific symptom, which when elicited with a careful history is very diagnostic of congestion and may as well be prognostic if it still exists at time of discharge.32,33 The physical exam may reveal jugular venous distension, rales, edema, and an S4. The non-specific nature of DHF symptoms may be easily confused by other disease states such as those caused by pulmonary and renal diseases. Care should also be taken to exclude non-cardiac diseases that may result in volume overload. These include conditions such as cirrhosis, nephrotic syndrome, and renal failure.

Patients presenting with these signs or symptoms should be further evaluated with an electrocardiogram to screen for ischemia, arrhythmias, and conduction delays.34 Laboratory evaluation of electrolytes including calcium, magnesium, and potassium should also be performed. Disturbances in these electrolytes may make patients prone to arrhythmias. Clinicians should also check serum creatinine, hematocrit, BNP, and thyroid stimulating hormone as all of these values may help to guide treatment.2,35,36 The chest x-ray may be normal, reveal cardiomegaly, pulmonary congestion, or pleural effusions. At initial diagnosis, we believe patients should be monitored on telemetry to screen for arrhythmias as potential exacerbating causes. Aggressive diuresis can promote volume and electrolyte shifts, which can also make abnormal hearts more prone to arrhythmias. An echocardiogram should be performed not only to evaluate the presence of diastolic dysfunction, but perhaps more importantly to rule out abnormalities such as valvular disease, right sided heart failure, systolic dysfunction and pericardial disease. A search for ischemia with a stress test or angiogram may also be warranted given the association between ischemia and diastolic dysfunction.34

BNP testing has been shown to be both sensitive and specific in the diagnosis of heart failure. BNP levels greater than 400 pg/ml have been shown to be diagnostic of heart failure and may correlate with elevated pulmonary capillary wedge pressure. BNP levels below 100 pg/ml are less frequently associated with a diagnosis of heart failure.37,38 In one study comparing BNP to echocardiographic findings in patients with preserved ejection fraction, a BNP over 62 pg/ml was found to be associated with 85% sensitivity and 83% specificity for the diagnosis of diastolic dysfunction.39 BNP cannot be used to distinguish between diastolic and systolic dysfunction.40 However, it is also important to consider that patients with DHF tend to have lower BNP levels than patients with systolic dysfunction when presenting with similar degrees of congestion.4 Although BNP is not a substitute for clinical judgment, a comprehensive history and physical exam should be combined with BNP results to adequately assess a patient for heart failure.41 It is important to keep in mind that an elevated BNP is not synonymous with fluid overload, and therefore an elevated BNP should not automatically lead to diuresis as a treatment strategy.

As for cardiac testing, some experts argue that diastolic dysfunction is a clinical diagnosis in which preserved LV systolic function is associated with clinical findings of heart failure, possibly making further testing (in addition to echocardiography) less crucial in diagnosis. Several modalities are available to demonstrate abnormalities that support or confirm the diagnosis of diastolic dysfunction. Traditionally, cardiac catheterization has been considered the gold standard for identifying the presence of diastolic dysfunction. In the cardiac catheterization laboratory, pressure-volume curves are shifted upward and to the left (Fig. 2). That is, for a given volume, pressures are higher, reflecting decreased compliance of the left ventricle. Additionally, micromanometer catheters may be used to measure peak negative dP/dt and δ (time constant of LV relaxation) to demonstrate impaired LV diastolic relaxation.2 Negative dP/dt evaluates changes in pressure over time whereby smaller changes in dP/dt reflect less relaxation of the left ventricle.

Although cardiac catheterization provides a reliable assessment of diastolic function, echocardiography gives the clinician a non-invasive method of evaluating a number of diastolic parameters. Echocardiography should be routinely performed to rule out concomitant valvular abnormalities, hypertrophy and to ensure preserved systolic function in patients who present with heart failure. This is often preferable, especially in the elderly patient. It must be noted, however, that echocardiography cannot give accurate measurements of filling pressures, but can suggest when filling pressures may be elevated and can evaluate for relaxation and compliance of the left ventricle. The principle way in which echocardiography evaluates diastolic function is by assessing blood flow during diastole. Pulsed Doppler measures velocity of mitral inflow which usually demonstrates a bimodal pattern. Early diastole is characterized by an E velocity, and later diastole is characterized by an A velocity (Fig. 3).42

After left ventricular contraction, the left ventricle begins to relax. When the left ventricular pressure decreases below the left atrial pressure, a pressure gradient develops that leads to acceleration of flow across the mitral valve.
into the left ventricle.\textsuperscript{43-47} This initial velocity is the E velocity. The rate of the decrease in the E wave velocity is referred to as the deceleration time. The deceleration time is a measure of chamber compliance of the left ventricle.\textsuperscript{52, 48, 49} Therefore, longer deceleration times indicate less compliance of the left ventricle.

As left ventricular pressures decrease, the initial E velocity decreases. The A wave follows as a result of atrial contraction. In a patient with sole diastolic dysfunction in the absence of significantly elevated left atrial filling pressures, the E velocity will be small relative to the A velocity. That is, the less compliant, less relaxed left ventricle prevents a high initial velocity of mitral inflow. This decrease in velocity and flow at the beginning of diastole results in higher left atrial filling pressures, which ultimately create a higher pressure gradient in later diastole, thereby leading to a higher A velocity.\textsuperscript{45} The E/A ratio lessens with age, and it is therefore critical to refer to a reference table of diastolic parameters when evaluating a patient for the presence of diastolic dysfunction.

Any physiologic condition that causes an elevation of left atrial pressure can lead to a higher E/A ratio. Higher left atrial pressure creates a gradient in early diastole that causes a higher than normal velocity. This abnormality is described as "restrictive" physiology. If diastolic dysfunction deteriorates enough in a specific patient, LA pressures rise, and the E/A ratio can revert back from a low E/A ratio to a higher ratio.

Therefore, despite having significant relaxation abnormalities, elevation filling pressures result in normal E/A ratios; a process referred to as "pseudonormalization" (Fig. 4).\textsuperscript{52} Additional information regarding left ventricular diastolic function can be obtained by placing a pulsed Doppler probe directed towards the pulmonary veins where they empty into the left atrium.\textsuperscript{52, 50-52} Diastolic pulmonary vein flow mirrors early diastolic mitral inflow (E wave velocity). Therefore, when early diastolic flow is impaired, such as from abnormalities in relaxation, the pulmonary diastolic flow is decreased resulting in a higher pulmonary vein systolic/diastolic ratio. If left atrial filling pressures are high, there will be a higher gradient across the mitral valve during diastole, leading to higher diastolic velocities, and therefore a low systolic/diastolic ratio in the pulmonary vein.

The preload dependent nature of the standard pulsed Doppler evaluation of blood flow velocity significantly limits its ability to differentiate normal flow patterns from pseudonormal patterns. A newer ultrasound modality, Doppler tissue imaging, measures velocities within the myocardium and at the mitral annulus.\textsuperscript{53, 54} Adjustments of the echocardiography equipment are required in order to detect the low velocity, high amplitude signal of myocardial tissue in contrast to the high velocity low flow signal of blood. This adjustment allows direct evaluation of left ventricular relaxation independent of the filling pressures.\textsuperscript{53} Although further study is required in the field of Doppler tissue imaging, its use represents a significant advancement in the evaluation of the patient with diastolic dysfunction which may aid not only in the diagnosis of diastolic dysfunction but also serve as a benchmark for assessing treatment modalities.

\textbf{Treatment}

Treatment goals for the patient with DHF include achieving normal volume status, improving relaxation of the
left ventricle, regression of hypertrophy if possible, and management of any co-morbidities that may aggravate the clinical status of patients with DHF. Guidelines for management of diastolic heart failure have been published by the American College of Cardiology/American Heart Association (Table 2).62 Despite data that suggest that diuretics increase serum creatinine, activate the renin-angiotensin system, and may be associated with a higher mortality, diuretics remain the first line of treatment in the volume overloaded patient with diastolic dysfunction because no other therapy to date has been shown as effective at relieving congestion.35,62-64 Several caveats may be helpful with regard to the use of diuretics in patients with diastolic dysfunction. In the elderly patient, following the glomerular filtration rate (GFR) may be more helpful than the serum creatinine level. Secondly, initial doses of loop diuretics may need to be higher in the elderly due to depressed renal function. Finally, careful attention should be paid to urine output after initial dosing so that the diuretics can be redosed at higher levels if needed. Because volume-pressure relationships in patients with DHF are shifted upward and to the left, higher filling pressures may be required for optimal performance of the left ventricle.4 Therefore, overdiuresis with excessive reduction in filling pressures may result in renal dysfunction and hypotension. The therapeutic margin of error for diuretics is very narrow.

Beta-blockers have many beneficial effects in DHF. However, as previously stated, cAMP activation causes

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<th>Table 2. ACC/AHA guidelines on management of chronic heart failure: recommendations in patients with preserved systolic function 62</th>
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<tr>
<td><strong>Class I</strong></td>
</tr>
<tr>
<td>1. Control systolic and diastolic hypertension in accordance with published guidelines (Level A evidence)</td>
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<td>2. Control of ventricular rate in patients with atrial fibrillation (Level C evidence)</td>
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<tr>
<td>3. Diuretics to control pulmonary congestion and peripheral edema (Level C evidence)</td>
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<td><strong>Class IIa</strong></td>
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<tr>
<td>Coronary revascularization in patients with coronary artery disease in whom symptomatic or demonstrable myocardial ischemia is judged to have an adverse effect on cardiac function (Level C evidence)</td>
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<td><strong>Class IIb</strong></td>
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<td>1. Restoration of sinus rhythm in patients with atrial fibrillation to improve symptoms. (Level C evidence)</td>
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<tr>
<td>2. Use of beta adrenergic blocking agents, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, or calcium antagonists in patients with controlled hypertension to minimize symptoms of heart failure (Level C evidence)</td>
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<td>3. Digitalis to minimize symptoms of HF (Level C evidence)</td>
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<td><strong>Classification:</strong></td>
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<td>Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective</td>
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<td>Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment</td>
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<td>Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy</td>
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<td>Class IIb: Usefulness/efficacy less well established by evidence/opinion</td>
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<tr>
<td>Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful and in some cases may be harmful</td>
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<td><strong>Level of Evidence:</strong></td>
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<td>Level A: Data derived from multiple randomized clinical trials.</td>
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<td>Level B: Data derived from a single randomized trial or multiple non randomized trials</td>
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<td>Level C: Consensus opinion of experts</td>
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increased lusitropy by enhancing SR calcium reuptake and increasing calcium availability.\textsuperscript{13} Given that beta agonists cause cAMP release, one might conclude that blocking this pathway might be detrimental in DHF.\textsuperscript{14} Nonetheless, beta blockers increase left ventricular filling time, coronary flow, and reduce oxygen demand.\textsuperscript{65} They also have been shown to control blood pressure and reduce LVH.\textsuperscript{66, 67} It has been theorized that slowing the heart rate may allow more time for calcium efflux from myocytes and thereby reverse the calcium overload seen in DHF.

Several multicenter, randomized clinical trials have evaluated beta-blockers in the treatment of DHF. In the SWEDIC trial, carvedilol was compared to placebo in patients with DHF. It showed that there was improvement in the E/A ratio echocardiographically, however there was no improvement in relaxation time.\textsuperscript{68} In another small study of 158 elderly patients with prior MI, and DHF, propranolol was shown to reduce mortality and LV mass.\textsuperscript{69} However, this might have been related to the beta-blocker effect post-MI that has previously been shown to reduce mortality. Finally, in the SENIORS trial, subgroup analysis of patients with HF treated with the beta blocker nebivolol who had a preserved EF>35\% showed a trend toward decreased composite endpoint of all cause mortality or cardiovascular hospital admission.\textsuperscript{70}

Non-dihydropyridine calcium channel blockers may be beneficial for their effects on increased relaxation through decreasing effects of calcium on the actin-myosin complex. One small study showed that verapamil significantly reduced symptoms of DHF and improved diastolic filling in contrast to placebo.\textsuperscript{71} Also, calcium channel blockers improve LV diastolic function in patients with hypertrophic cardiomyopathy, which has similar mechanisms to diastolic heart failure. LV diastolic filling rate increases with treatment and exercise tolerance improves.\textsuperscript{72, 73}

Control of hypertension in accordance with previously published guidelines is also a Class IA ACC/AHA guideline recommendation for DHF.\textsuperscript{80} This is important due to the worsening of diastolic failure with uncontrolled hypertension. A discussion of choice of agent to manage hypertension is beyond the scope of this review. However, use of medications that have previously been shown to decrease mortality are recommended.\textsuperscript{74}

The evaluation and treatment of ischemia is an ACC/AHA Class IIa, evidence C recommendation for DHF.\textsuperscript{82} Coronary artery disease is a potentially reversible cause of diastolic heart failure and may be subclinical.\textsuperscript{74} Invasive or non invasive testing is recommended depending on the clinical situation. Guidelines for cardiac catheterization and stress testing are published elsewhere.\textsuperscript{75, 76} Use of beta-blockers, and calcium channel blockers have been shown to decrease myocardial oxygen demand and increase exercise duration in patients with ischemic heart disease.\textsuperscript{77} Revascularization may be indicated in many patients. Other medications used to treat ischemia such as nitrates should be used with some degree of caution due to their propensity to reduce preload in a heart that already has a preload dependent state which may lead to hypotension.

Finally, the goal of therapy becomes reversal of the activated neurohormonal state. Traditionally this has been achieved with angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), and mineralocorticoid receptor blockers (MRB). ACE inhibitors have been shown to cause regression in left ventricular hypertrophy and improvement in diastolic dysfunction.\textsuperscript{78, 79} They have also been shown to prevent progression of diastolic dysfunction.\textsuperscript{80} ACE inhibitors and ARBs have been shown in trials to cause reduction in myocardial fibrosis and stiffness, both of which are mechanistic causes of DHF.\textsuperscript{81, 82} One registry of 2,906 consecutive patients admitted with heart failure who were admitted to 10 acute-care community hospitals, showed that patients with preserved ejection fractions that were treated with an ACE inhibitor had a significant improvement in NYHA functional class compared to those not treated with an ACE inhibitor.\textsuperscript{83} Another analysis from the Heart Outcomes Prevention Evaluation (HOPE) Investigators showed that the ACEI, ramipril, was associated with regression in ECG findings of left ventricular hypertrophy and these changes were associated with reduced risk of death, MI, stroke and heart failure.\textsuperscript{84} However, there is yet to be a randomized clinical trial evaluating the effects of ACEI on survival in patients with DHF. The Perindopril in Elderly People With Chronic HF (PEP-CHF) study attempted to look at mortality with ACEIs in patients with DHF. However, of the 850 patients randomized, several withdrew from the study and placebo group making the study insufficiently powered to detect mortality. Nonetheless, in the patients treated with perindopril there was an improvement in NYHA functional class, 6-minute walk distance, and fewer heart failure admissions.\textsuperscript{85}

Several studies have evaluated the effects of ARBs on diastolic dysfunction. Warner et al examined the effects of losartan on 20 patients with diastolic dysfunction on echocardiography, preserved left ventricular systolic function and a hypertensive response to exercise. Patients treated with losartan reported better quality of life and had increased exercise tolerance.\textsuperscript{86} The CHARM-Preserved Trial enrolled 3023 patients with symptomatic heart failure and preserved ejection fraction (>40\%). Patients were randomized to candesartan (ARB) or placebo. At 37 months there was a trend toward decreased cardiovascular death and hospitalization that nearly met statistical significance.\textsuperscript{87} Treatment with candesartan was associated with a reduction in heart failure hospitalizations (P=0.014).

Mineralocorticoid receptor blocker use has been evaluated in a small study of 30 patients with dyspnea on exertion, preserved ejection fraction and diastolic dysfunction. Patients who received spironolactone 25mg daily for six
months had improved echocardiographic indices of diastolic dysfunction.98

Digitalis blocks the Na-K ATPase on the sarcolemma. Blocking this receptor causes increased intracellular Na and therefore reduction of the Na-Ca exchange transport gradient. This results in higher cytosolic calcium and increased inotropy, however, with a reduction in diastolic function. The DIG Trial showed a reduction in hospitalizations in patients with diastolic dysfunction treated with digitalis. This may have been due to a reduction in heart rates given the AV nodal blockade caused by digitalis.99 In a follow up of 988 patients, a smaller group of patients than in the original DIG Trial, there were no differences in hospitalization rates or mortality in patients with diastolic heart failure treated with digoxin.90

Large-scale, randomized blinded placebo control trials are still needed to determine the optimal management of patients with DHF. Hopefully, these studies will help guide more formal definitions of how to classify this syndrome. The current ongoing trials assessing efficacy of ACEI/ARB include the Irbesartan in Heart Failure Preserved Systolic Function (I-PRESERVE) study and the Hong Kong Diastolic Heart Failure Study.90-92 The Trial of Aldosterone Antagonists Therapy in Adults with Preserved Ejection Fraction Congestive Heart Failure Study (TOPCAT) intends to assess efficacy of an aldosterone antagonist in DHF by mortality and hospitalization endpoints.93

In the hospitalized patient, there is no role for inotropic therapy in preserved left ventricular function. Few studies have evaluated the efficacy and safety of vasodilators in patients with heart failure. Nesiritide, (synthetic B-type natriuretic peptide), when used in FDA approved doses, has been shown to reduce pulmonary capillary wedge pressure and symptoms in patients with acute decompensated heart failure.94 However, a recent meta-analysis questioned the safety of this agent. The meta-analysis showed trends toward increased 30 day mortality and increased creatinine in patients using nesiritide.94,95 Further studies are required to evaluate the safety and efficacy of nesiritide.96-98

As with systolic heart failure we recommend the treatment of co-morbid conditions. Diabetes should be aggressively managed. Electrolytes should be aggressively repleted to avoid arrhythmias. Anemia should likely be treated with erythropoietin derivatives. Goals have not yet been well defined for the degree to which anemia should be treated.99 Immunosuppression for both influenza and pneumonia should be administered.99 Concurrent illness can precipitate heart failure exacerbations and add to mortality and morbidity. Therefore, diuretic doses may need to be adjusted during episodes of co-morbid illness such as infections. Drugs that promote fluid retention should be avoided, such as NSAIDs, corticosteroids, or thiazolidinediones.

Intracellular thiamine deficiency may be as high as three times more common in patients with heart failure.100 This may be related to poor nutrition in heart failure patients or chronic diuretic use.100,102 Given that thiamine deficiency is associated with worsened cardiac function, treatment of thiamine deficiency may be beneficial in this patient population. Further studies are needed to determine whether treatment with thiamine will improve heart failure.100,104

Another goal of treatment is to increase diastolic filling time and myocardial relaxation by controlling the heart rate and using agents that may improve relaxation. Control of atrial fibrillation and other tachyarrhythmias are of the utmost importance in this arena.92 Patients with diastolic dysfunction become more dependent on atrial contraction given the relative shifting of diastolic inflow of the left ventricle to late diastole. Reducing heart rates allow for longer filling times of the ventricle.2,8

Tachyarrhythmias such as atrial fibrillation need to be aggressively treated. First and foremost, the rate must be controlled to augment diastolic filling time. However, one needs to consider whether these patients might benefit from cardioversion as they can become quite dependent on the atrial contribution to diastolic filling. Although the AFFIRM trial showed increased morbidity in patients with rhythm control versus rate control, the study did not specifically study patients with DHF.105 Traditionally beta-blockers and non-dihydropyridine calcium channels blockers have been used for control of arrhythmias. Also, it has been thought that these agents increase lusitropy of the heart, therefore allowing better diastolic filling; however, there is a paucity of data. It is difficult to ascertain whether the observed benefit of calcium channel blockers is related to reduction in heart rate, reduction of ischemia, or an improvement in relaxation of the left ventricle.

Standard rules for dosing in the elderly should be followed. Drug clearance is significantly decreased with age and reduced renal function as well as hepatic metabolism.106 Elderly patients tend to be receiving multiple agents and drug-drug interactions are relevant.106 We recommend starting with one medication at a time and starting a low dose followed by a slow titration as tolerated. Medications may be added as tolerated while carefully monitoring for side effects.

Patients should be considered for enrollment in a cardiac rehabilitation program. Exercise has been shown to enhance diastolic function. Patients with diastolic dysfunction lose the mechanisms that enhance LV filling during exercise. Exercise training has been shown to enhance diastolic function in cardiac hypertrophy and might reverse the diastolic dysfunction of aging.107-109 Patients need to be properly selected for exercise programs taking into account other functional limitations.

Once congestion is relieved with the return to baseline of symptoms and signs of heart failure, we recommend a trial of ambulation to ensure that symptoms have resolved (possibly a six minute walk test) which may correlate with
prognosis as well.\textsuperscript{110-112} Certainly, other (neurologic, musculoskeletal, etc) functional limitations need to be considered. We also recommend discharge BNP testing. A BNP <230 pg/ml at time of discharge from hospitalization has been associated with decreased cumulative probability of heart failure visit, admission or death.\textsuperscript{113} BNP levels measured when a patient is euvo1emic may be helpful to follow that patient clinically, however, there are no studies available to confirm this. This baseline "dry BNP" may help guide subclinical heart failure especially in patients with obesity or pulmonary disease. As a rule, the BNP does not typically decrease by more than 30pg/ml per hour.\textsuperscript{114}

Summary

The high prevalence of DHF in the elderly population requires that clinicians are familiar with diagnostic and treatment modalities available for patients with this disorder. The physician should rule out diseases that may be confused with DHF. In addition to the history and physical exam, BNP levels, echocardiography and cardiac catheterization may be helpful in supporting the diagnosis of diastolic dysfunction. Diagnosis and treatment of arrhythmias, hypertension and coronary disease are important in the management of diastolic dysfunction. Although, the field of DHF is plagued by a lack of randomized controlled clinical trials, treatment with ACE inhibitors, angiotensin II receptor blockers, calcium channel blocker, and/or beta-blockers should be considered in the appropriate patients. Diuretics remain the cornerstone of therapy for relief of congestion. However, agents without the neurohormonal activation of diuretics need development. Care must be taken not to overdiurese this sensitive population with preexistent renal dysfunction. Special consideration of side effects of these medications should be taken in the elderly population. Hopefully, in the future, further data from randomized clinical trials will allow a more defined approach to care in these patients.

References


