ABSTRACT

Diastolic dysfunction, which is increasingly seen as being influential in precipitating heart failure and determining prognosis, is often unrecognized. In elderly patients with high rates of comorbidities, determining whether symptoms are attributable to cardiac conditions or other coexisting comorbidities can be clinically challenging. Moreover, in hemodynamically unstable patients, real-time decisions regarding fluid status are critically important. With better understanding and assessment of diastolic function, physicians should be in a better position not only to diagnose diastolic dysfunction or heart failure, but also to manage it more effectively. To optimize this approach, assessing diastolic function at the time of hemodynamic compromise or symptomatic deterioration is essential. In this review, clinical implications of assessing left ventricular diastolic function and filling pressures in critically ill patients will be reviewed with case-based discussions to emphasize how information regarding left ventricular diastolic function and filling pressure can be used for correct diagnosis and proper management of these patients.

Keywords: Diastolic function; Echocardiography; Hemodynamics

INTRODUCTION

Patients older than 80 years of age continue to be the fastest growing segment in the United States. The aging population rate in Korea is also rising steeply, and the percentage of the population aged 60 years and above is predicted to increase from 13.7% in 2015 to 28.6% by 2050. Cardiovascular disease is the most common cause of morbidity and mortality in the elderly, and heart failure is the most common hospital discharge diagnosis in this population and is still increasing. It also has been shown that heart failure with preserved ejection fraction increases in incidence with age. However, investigators have traditionally focused on abnormalities of systolic function to explain the signs and symptoms of heart failure despite the fact that many of the changes that occur in the cardiovascular system as a result of aging have a greater impact on diastolic function than on systolic function. It also has become increasingly evident that abnormalities of diastolic function play a major role in precipitating heart failure and determining prognosis.
Diastolic dysfunction is also a common feature in patients admitted to the intensive care unit (ICU). On the one hand, diastolic dysfunction could be the underlying condition resulting in ICU admission due to acute pulmonary edema, or be a breakthrough complication of another process. On the other hand, although elevation of filling pressure is the most important hemodynamic consequence of diastolic dysfunction, it is also important to avoid hypovolemia in elderly critically ill patients admitted to the ICU. Therefore, management of ICU patients with symptomatic left ventricular diastolic dysfunction currently relies on maintaining a delicate hemodynamic balance between excessive filling pressure with associated pulmonary venous congestion and inadequate preload resulting in low cardiac output. Invasive hemodynamic monitoring with Swan-Ganz catheter had been used for this purpose, but echocardiography has replaced invasive cardiac catheterization for various hemodynamic assessments because it is easy to use at the bedside and repeated measures can be obtained. Of all of the hemodynamic measurements used in daily clinical practice, left ventricular filling pressure is one of the most important. Thus, reliable non-invasive estimation of filling pressure is the most useful information that can be obtained from echocardiographic assessment of diastolic function in critically ill patients because it provides an opportunity to better understand the pathophysiology and hemodynamic status of these patients. Despite the importance of assessing left ventricular diastolic function and filling pressure, these assessments are frequently ignored and under-appreciated. Furthermore, inaccuracy of echocardiographic parameters for estimating left ventricular filling pressure is often criticized despite the echocardiographic assessment is not usually performed at the time of hemodynamic compromise or symptomatic deterioration. Because many therapeutic interventions may rapidly decrease left ventricular filling pressure and potentially alter diastolic properties (e.g. diuretics, control of hypertension, positive-pressure ventilation, correction of hypoxemia), echocardiographic assessment should be performed as soon as possible to when the acute insult occurred. In this review, we will discuss the clinical implications of assessing left ventricular diastolic function and filling pressure in critically ill patients based on case studies and highlight how information regarding left ventricular diastolic function and filling pressure can be used to correctly diagnose and manage these patients.

**CASE 1**

An 82-year-old man was admitted to the hospital due to chest pain and dyspnea and was subsequently diagnosed with non-ST elevation myocardial infarction. Chest X-ray showed bilateral pleural effusion with pulmonary edema. Echocardiography showed akinesia at the posterior wall of the left ventricle, and left ventricular ejection fraction was 55%. However, mitral inflow pattern showed a restrictive physiology, suggesting significant diastolic dysfunction with elevated left ventricular filling pressure. At the time of discharge, the patient’s symptom of dyspnea was relieved and chest X-ray showed the disappearance of bilateral pleural effusion and pulmonary congestion (Figure 1). Despite the patient’s symptomatic and radiological improvement, however, global left ventricular systolic function and ejection fraction were similar to those at admission. In contrast, mitral inflow pattern had changed from a restrictive physiology to a relaxation abnormality, suggesting significant improvement in left ventricular filling pressure and diastolic function (Figure 2).

**Comment**

Abnormalities of systolic function are commonly used to explain the signs and symptoms of heart failure. However, diastolic dysfunction has a greater impact on precipitating heart failure.
failure and determining symptomatic status and prognosis. Despite this, the importance of diastolic dysfunction is often unrecognized. This case underscores the importance of left ventricular diastolic function in heart failure and ischemic heart disease. Restrictive filling pattern at the time of admission with pulmonary edema and bilateral pleural effusion characterized by a tall E velocity, shortened deceleration time, and small A velocity are indicative of severe diastolic dysfunction with elevated filling pressure. Abnormal relaxation pattern at the time of discharge identifies a patient with minimal or no symptoms of heart failure at rest because left ventricular filling pressure is usually not elevated. Although various echocardiographic parameters for assessing left ventricular diastolic function are available, mitral flow pattern is the single most important parameter to assess in patients with suspected heart failure.

**CASE 2**

A 69-year-old man presented with severe chest pain and was subsequently diagnosed with extensive anterior wall myocardial infarction. Echocardiography showed akinesia of the...
anterior septum and anterior wall, and left ventricular ejection fraction was 35%. During admission to the coronary care unit, his blood pressure and urine output were noted to be decreased. Despite inotropic administration, the patient's condition did not improve. Bedside portable echocardiography showed low mitral E velocity and reversed E/A ratio, suggesting volume depletion or dehydration (Figure 3). Based on Doppler echocardiographic findings, fluid was administered rather than diuretics or volume restriction. After hydration, the patient's condition improved and blood pressure and urine output increased.

Comment

Volume expansion is the first therapeutic measure when a patient presents with hemodynamic instability. However, when the preload of the heart is already high, volume expansion can be hazardous, especially in elderly patients with decreased left ventricular compliance. Because of this concern, despite the need for adequate fluid balance, dehydration in elderly critically ill patients who are admitted to the ICU is not uncommon but usually unrecognized. It is important to avoid hypovolemia in these patients because it can lead to subsequent unexpected complications, such as hypotension and renal failure. Close monitoring is needed in patients being treated with volume expansion because of the delicate balance between excessive pulmonary congestion and reduced preload. Although diuretics are appropriate for the relief of congestion and edema, they are most effective in patients with evidence of fluid retention. In addition, caution should be taken to avoid overdiuresis, which may result in intravascular volume depletion and resultant hypotension or prerenal azotemia. Unlike in patients with grade 2 or 3 diastolic dysfunction (with elevated filling pressures) in whom the addition of diuretics should be considered due to elevated filling pressures, patients with grade 1 diastolic dysfunction (abnormal relaxation) will not benefit from diuretic therapy because their filling pressure is usually not elevated at rest (Figure 4). Echocardiographic evaluation can identify those patients who would benefit from diuresis. If there is no overt evidence of volume overload, then diuretics should not be used.
CASE 3

A 74-year-old woman presented with severe dyspnea (NYHA 4). She had had an anterior wall myocardial infarction several years ago and at that time, she was diagnosed as having three-vessel disease with left ventricular aneurysm. Subsequently, an implantable cardioverter defibrillator (ICD) was inserted due to ventricular tachycardia. She also had chronic kidney disease and diabetes mellitus and her left ventricular ejection fraction was 28%. Chest X-ray showed increased vascular markings suspicious of pulmonary edema. Chest computed tomography was performed and pulmonary edema was diagnosed (Figure 5). Mitral flow showed a relaxation abnormality pattern with a prominent L wave, and estimated right ventricular systolic pressure was 51 mmHg. Interestingly, echocardiographic examination 5 months previously when she was admitted to the hospital due to milder symptom of dyspnea (NYHA 2) showed a restrictive physiology (Figure 6) and more advanced diastolic dysfunction. Despite efforts to reduce pulmonary edema by administering diuretics, the patient’s symptom did not improve and in fact became further aggravated. Chest X-ray showed an increase in pulmonary vascular markings and consolidation despite intensive diuretic therapy (Figure 7). Subsequently, a sputum culture revealed Klebsiella pneumoniae. After intensive antibiotic therapy rather than diuretics, the patient’s symptoms improved.

Figure 4. Changes after diuretic therapy in patients with abnormal relaxation. Patients with grade 1 diastolic dysfunction (abnormal relaxation) will not benefit from diuretic therapy because their filling pressure is usually not elevated.

Figure 5. Chest X-ray (A) and chest CT (B) interpreted as pulmonary edema.
Diastolic Function in Critically Ill Patients

Figure 6. Mitral inflow and tricuspid regurgitation velocity pattern 5 months prior (A) and on admission (B).

Figure 7. Chest X-ray on admission (A) and 4 days after intensive diuretic therapy (B). Despite intensive diuretic therapy, pulmonary vascular markings and consolidation did not improve.
Comment
Dyspnea is defined as difficult or labored breathing and occurs whenever the work of breathing is excessive. It is a common symptom in a variety of cardiac and noncardiac diseases, emphasizing the need for a thorough differential diagnosis. A comprehensive history, physical examination, and basic laboratory tests are important in the initial assessment; however, the diagnosis may depend on specialized testing. Cardiac causes of dyspnea include right, left, or biventricular congestive heart failure with systolic dysfunction, coronary artery disease, recent or remote myocardial infarction, hypertension with left ventricular hypertrophy, cardiomyopathy, valvular dysfunction, pericardial diseases, arrhythmia, congenital heart disease, and primary diastolic dysfunction. In an elderly population with high rates of comorbidities, determining whether symptoms are attributable to cardiac conditions or to other coexisting comorbidities can be challenging. In this case, despite the presence of significant diastolic dysfunction with elevated filling pressure, the severity of the patient’s dyspnea and the degree of diastolic dysfunction and filling pressure elevation did not correlate well when compared with serial echocardiographic examination. Thus, a discordant relationship between echocardiographic parameters of diastolic dysfunction and filling pressure elevation and the severity of the symptom of dyspnea can provide insight into the cause of the dyspnea in the presence of multiple comorbidities.

CASE 4
A 27-year-old man was transferred from another hospital due to acutely decompensated heart failure. He was diagnosed with dilated cardiomyopathy and his condition was stable with medical therapy. After administration of a beta blocker, his condition deteriorated. At the time of admission, mitral inflow showed a restrictive physiology, suggesting significant diastolic dysfunction with elevated left ventricular filling pressure. Subsequently, heart transplantation was performed because of intractable severe heart failure despite optimal medical therapy.

Comment
Beta-blockers have been shown to reduce mortality and improve quality-of-life in patients with heart failure. However, the individual response to beta-blocker therapy is highly variable in terms of tolerance and efficacy. A previous study showed that mitral flow pattern and its changes after loading manipulations can identify patients that require different clinical management during beta-blocker titration. Management of beta-blocker titration is more complex in patients with a restrictive physiology than in patients with a non-restrictive pattern (Figure 8). In patients with a restrictive physiology, because most of the filling of the left ventricle occurs in early diastole, prolonging the diastolic filling time would not be beneficial and may even be harmful due to the decrease in cardiac output as a result of the decrease in heart rate. Therefore, prolonging the diastolic filling time with a beta blocker in the presence of restrictive physiology would not be beneficial and could even be harmful (Figure 9). An individualized approach is needed in patients with heart failure who are under consideration for initiation of beta blocker therapy. In this regard, the severity of diastolic dysfunction and the pattern of mitral inflow provide important information when considering the initiation or titration of beta blockers in patients with heart failure.
CONCLUSIONS

Diastolic dysfunction, which can precipitate heart failure and determine prognosis, is often unrecognized and has therapeutic implications distinct from those associated with systolic dysfunction. Determination of diastolic function is an integral part of an echocardiographic examination, especially in patients with symptoms of heart failure. In an aging society, elderly...
patients with high rates of comorbidities are common, but determining which symptoms are attributable to cardiac conditions versus other coexisting comorbidities can be clinically challenging. Performing echocardiography in all hemodynamically unstable patients can help to guide real-time decisions regarding fluids status and evaluate treatable underlying causes of shock. Therefore, echocardiography should be performed in patients with hemodynamic instability to identify underlying treatable causes and to help guide fluid resuscitation. In this regard, understanding the mechanism and hemodynamics of diastolic dysfunction in critically ill patients is crucial. Increased understanding and assessment of diastolic function will put physicians in a better position not only to diagnose diastolic dysfunction or heart failure, but also to manage it more effectively. To optimize this approach, assessing diastolic function at the time of hemodynamic compromise or symptomatic deterioration is essential.

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