Are the Latest International Recommendations Sufficient for Diastolic Function Analysis?

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The physiology of diastolic function is complex. It results from the interaction of a number of factors involving ventricular elasticity and restorative forces that, when dysfunctional, lead to increased filling pressure.

Echocardiography is the best noninvasive tool for evaluating diastolic function. It allows to evaluate of different parameters to analyze different variables and their combinations. However, it is precisely in the wealth of information it offers that lie its complexity and difficulty of approach.

In the vast majority of cases, diastolic function changes slowly, and its recovery, when possible, is also slow. For this reason, it is usually assumed that diastolic function is quite stable, and that its modifications will occur chronically.

However, diastolic function may change acutely, in a matter of seconds or minutes, as in acute myocardial ischemia, arrhythmias, or pacemaker adjustment.

It may remain abnormal for as long as the dysfunction generating factor persists, as in prolonged ischemia and volume overload, with rapid recovery after correction of the underlying disorder.

The recognition of acute variations in diastolic function is a tool of great clinical utility, particularly in emergencies, and is an indicator of the therapeutic response or worsening of the condition.

Note that diastolic dysfunction is the earliest conventional echocardiographic sign of ischemia, following the ischemic cascade.

Diastolic dysfunction varies from the incipient form with minimal abnormalities to the more advanced form with a restrictive pattern characterized by a high increase in filling pressure. The restrictive stage indicates exhaustion or tolerance limit of adaptation mechanisms, be it specifically due to primary diastolic dysfunction, as in restrictive diseases, or as the end result of severe systolic dysfunction.

Diastolic dysfunction is currently classified into three progressive degrees of severity.

This classification is very useful and necessary, but we must remember that not all the parameters that we use in the evaluation behave in the same way, nor do they behave in a uniform way.

On top of that, pharmacological intervention, which is highly beneficial for the patient, is an important complicator in the interpretation of results, as it accentuates the heterogeneous behavior of the different parameters used. While some go normal, others remain abnormal or are not reversible in some cases, particularly in older patients.

These aspects reach major relevance in the severe forms of diastolic or systolic and diastolic dysfunction, which require, in the treatment, careful approach and the use of drugs, with frequent therapeutic adjustments. In these situations, the recognition of subtle differences in the variables that quantify diastolic function elucidates the clinical condition and guides the medical treatment with safety, including with prognostic value.

The Guideline on Diastolic Dysfunction of the American Society of Echocardiography (ASE), published in 2009[1], was characterized by a large number of variables, making the diagnosis of diastolic dysfunction quite complicated.

The 2016 Guideline of the ASE,[2] was apparently intended to streamline the analysis. It established new cutoff points on some variables, increasing specificity in the recognition of high filling pressures. On the other hand, it decreased sensitivity and increased indefiniteness in milder forms of dysfunction.

This Guideline proposes an algorithm to evaluate diastolic function in patients with normal ejection fraction, which has a Portuguese version, published by the DIC (Department of Cardiovascular Image) on a poster.[3]

This algorithm uses the concept of "indeterminate condition," for the situation in which the parameters are not sufficiently abnormal in number or intensity, for classification in grade I or II, according to the proposed cut-off points. This definition generated controversies that have not yet been resolved two years after the publication. Probably, defining this condition as "intermediate or transition degree" would have generated less controversy. On the other hand, only in the case of patients with diminished ejection fraction, the algorithm proposes to add another variable that is the pulmonary vein flow.

Worthy of note is that said algorithm does not consider the age of the patient and defines the septal E′ wave velocity < 7 cm/s, or lateral E′ wave < 10 cm/s as the cutoff point. These limits are not applicable to elderly patients, who present progressively lower values than normal, as the age increases.

Evolution does not stop. After two years, a number of publications address the theme.

Mitter et al.[4] suggest an algorithm in which the patient's age is first considered, in order to define the reference values that will be used. The presence of factors that may compromise the interpretation of diastolic function, such as arrhythmias,

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valvular heart diseases, mitral annular calcification, valvular prosthesis, etc., are evaluated. Only then is the evaluation of the diastolic function itself performed. The authors adopt cutoff values that had been modified by the ASE-2016 Guideline,[2] propose the use of a better targeted nomenclature, with words like "suggests..." for non-conclusive situations that, nevertheless, may support the clinical approach in a broader context.

Another useful tool is the evaluation of left ventricular global longitudinal strain (GLS) that has its applicability recognized and recommended in the evaluation of systolic function. However, GLS is also involved in diastolic dysfunction. Circumferential and radial strain also support the diagnosis. In the early stages of diastolic dysfunction, they are increased to compensate for a decrease in longitudinal strain, thus preserving ejection fraction. In advanced dysfunction, the three forms of strain are reduced, as described by Hortegal and Abenzur[5] in a recent review. However, with regard to diastolic function, the greatest contribution is given by strain rate analysis. Del Castillo et al.[6] found that, in indeterminate forms, left ventricular strain rate allows reclassifying dysfunction in the vast majority of cases, leaving only a small percentage of the total initial dysfunction in an indeterminate condition.

In the same direction, Singh et al.[7] have shown that left atrial longitudinal strain significantly contributes to the classification of different degrees of diastolic dysfunction, suggesting greater sensitivity and specificity than conventional parameters, particularly in degree I and II dysfunction.

In 2015, Selmery et al.[8] published a meta-analysis of 60 articles that used the ASE-2009 Guideline[1] as a reference for the diagnosis of diastolic dysfunction. They observed wide heterogeneity in the use of parameters and in the criteria to define diastolic dysfunction. In a group of 730 different patients, with low and high risk and normal controls, the variables were grouped in several combinations following these criteria. The final results showed that the prevalence of diastolic dysfunction ranged from 12 to 84%, according to the variable combination criteria used for diagnosis.

The ASE-2016 Guideline[2] should have contributed to improving the situation, however, we are certainly far from desirable.

For patients with decreased ejection fraction, the optimal number of parameters to be used has not yet been defined, nor has a sequence or stratification been recommended according to the underlying disorder. Therefore, the variables to be used are at the echocardiographer's discretion. Such facts probably maintain the heterogeneity of approach and results noted above.

In summary, evidence indicates that the diagnosis of diastolic dysfunction should result from a broad analysis that considers the patient's age and the clinical context. The interpretation of the information obtained varies widely according to whether it is a young or an elderly patient. What we consider a normal mitral flow pattern at 20 years of age would suggest a restrictive pattern at 70 years of age. Adding to that, assistance to octogenarians, nonagenarians and centenarians is becoming more frequent and, at these ages, defining what is normal is still a challenge.

The clinical and care context guides the approach and the way forward. It may be a patient with acute or chronic disorders, with normal or decreased ejection fraction, pressure or volume overload, with valvular heart diseases or prosthetic valves, arrhythmias, signs of desynchrony, or with pacemaker. Each situation will require a different approach, choosing the most appropriate parameters for each case, according to the resources available, going from the simplest to the most complex ones. It should address the low-complexity diagnostic needs or support high complexity, which addresses the critical patients.

In the light of the above information, we can conclude that the latest international recommendations contributed substantially to the evaluation of diastolic function; however, there are still many questions in the diagnosis of this complex dysfunction.

Because of all this, a new guideline that considers the latest resources and available evidence, guiding its applicability in a broad and comprehensive way, would be very welcome.

Furthermore, it is advisable and necessary that specialized scientific societies keep disseminating and updating the knowledge about evaluation and interpretation of diastolic function.

Both initiatives, i.e., editing a new guideline and widely disseminating knowledge, would certainly be of great help both for the doctors who daily deal with this important and complex dysfunction and for the patients who suffer from it.

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