Review Article

Role of Shear Wave Elastography in the Assessment of Myocardial Stiffness in Various Cardiomyopathies

Fabio Fernandes,[1] Nathalia Conci Santorio,[1] Natália de Melo Pereira,[1] Caio Rebouças Fonseca Cafezeiro,[1] Aristóteles Comte de Alencar Neto,[1] Bruno Vaz Kerges Bueno,[1] Fernando Linhares Pereira,[2] Maria Cristina Chammas[2]

Instituto do Coração (InCor), Faculdade de Medicina, Universidade de São Paulo,[1] São Paulo, SP – Brazil

Hospital das Clínicas (HC), Faculdade de Medicina, Universidade de São Paulo, [2] São Paulo, SP – Brazil

Abstract

Echocardiography is essential for the diagnosis and treatment of cardiovascular disease. Assessing left ventricle diastolic function is a major challenge, and several well-known ultrasound techniques, such as pulsed Doppler for mitral flow, tissue Doppler, and myocardial strain, are used to non-invasively estimate left atrial filling pressure. Although widely available, this approach has several limitations and does not truly represent the intrinsic properties of the cardiac muscle. However, cardiac elastography can be studied non-invasively by estimating myocardial stiffness through shear wave propagation speed in cardiac tissue. Elastography is already widely used to assess stiffness in other tissue types, such as thyroid, liver, and breast. In the context of cardiological assessment, this technique has already been successfully used in diseases such as cardiac amyloidosis and hypertrophic cardiomyopathy. This article aims to review the main concepts of this promising technique and present the published experiences of national and international services.

Introduction

Heart failure is defined as the heart's inability to pump a sufficient quantity of blood to meet the body's metabolic needs, or to do so at the expense of increased filling pressures.[1] This concept is extremely important, since approximately 50% of heart failure cases are classified as having preserved left ventricular ejection fraction,[1] in which increased filling pressure appears to be the predominant mechanism.

Classically, cardiac catheterization, an invasive technique, is used to directly measure intracavitary filling pressures, allowing construction of the pressure-volume curve. This approach characterizes the intrinsic properties of ventricular pump function throughout the cardiac cycle, in addition to hemodynamic variables, which clarifies the pathophysiology of heart diseases and contributes to their diagnosis.

One important property, a concept applied to different materials, is stiffness, ie, the extent to which an object resists deformation in response to an applied force.[2] Compliance, the opposite of stiffness, quantifies a material's deformability.[2] Thus, myocardial stiffness represents resistance to stretching when the myocardium is subjected to stress, corresponding to the slope of the stress vs deformation curve.[3] Left ventricular compliance is the variation in pressure in relation to variation in volume, and left ventricular stiffness can be measured by the slope of the pressure-volume curve in final diastole.[4]

Normal diastolic function is characterized by a normal left ventricular relaxation rate, with myocardial and left ventricular stiffness parameters within normal limits, resulting in low filling pressures.[5] During diastole, both active relaxation and myocardial stiffness, an intrinsic property associated with sarcomere proteins (such as titin) and the extracellular matrix, simultaneously determine the filling pattern of the left ventricle.[6] However, active relaxation is more predominant in early diastole, while passive myocardial stiffness is more predominant at end-diastole.[6] This implies that myocardial stiffness has a greater influence on the slope of the pressure-volume curve during end-diastole[6].

In most cases, diastolic function is determined through routine echocardiographic techniques, such as pulsed Doppler analysis of mitral flow, tissue Doppler and, more recently, myocardial strain, which allows non-invasive estimation of left atrial filling pressure. Despite their wide availability, these techniques have several limitations and do not, in fact, represent the intrinsic properties of the cardiac muscle.

Shear wave elastography represents a paradigm shift in echocardiography by non-invasively measuring myocardial stiffness, which can add important information to diastolic function assessment. In this article, we will discuss the fundamentals of its use and its main clinical applications.

Physical properties and methodology of shear wave elastography

Shear wave elastography is widely used for non-invasive assessment of liver and breast nodules, in addition to other applications, such as the characterization of kidney, prostate, and thyroid lesions.[7]

This technique involves measuring shear wave propagation speed in different tissues, which is directly proportional to their stiffness. It is important to conceptually differentiate between shear waves and compressive waves, which are

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Correspondência: Fábio Fernandes •
Av. Dr. Enéas Carvalho de Aguiar, 44. Postal code: 05403-900. Cerqueira César, São Paulo, SP – Brazil
E-mail: fabio.fernandes@incor.usp.br
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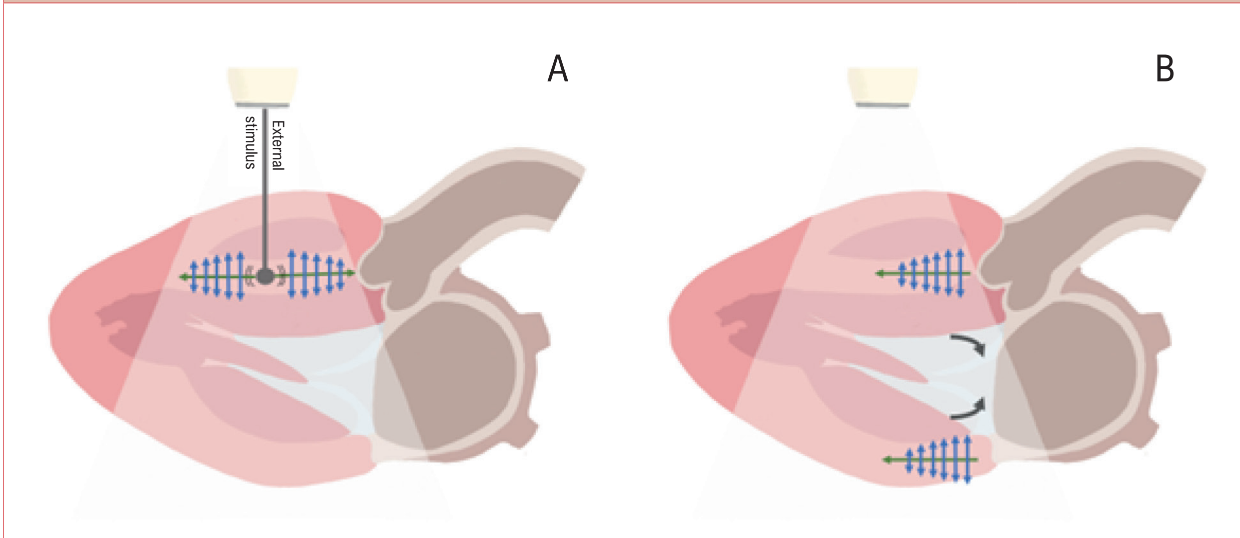
Central Illustration: Role of Shear Wave Elastography in the Assessment of Myocardial Stiffness in Various Cardiomyopathies



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Myocardial elastography methods. In A, shear waves are generated through impulses emitted by the transducer itself. In B, shear waves are generated naturally by mitral valve closure. The blue arrows represent tissue displacement, while the green arrows indicate the direction of shear wave propagation.

used in conventional ultrasound to produce images. In compressive waves, the particles move in parallel with the propagation direction, while in shear waves they move perpendicularly to it.[8] Additionally, shear waves have a propagation speed of around 1-10 m/s, which is much lower than compressive acoustic waves (around 1450-1550 m/s in soft tissue).[7] To evaluate shear waves with reasonable precision, specific transducers and equipment with a frame rate between 1000 and 10,000 frames/second are required.[9]

The lower propagation speed of shear waves make them essential for tissue characterization. It has been demonstrated that pathological tissue changes lead to increased propagation speed.[10] The evolution of ultrasound devices has made it possible to track such waves and differentiate small variations that occur during their journey through unhealthy tissue.

Cardiac elastography can be performed in different ways, depending on how the waves are generated, which is illustrated in the Central Figure. One way is through short, high intensity acoustic radiation pulses emitted by the transducer itself, which form shear waves that displace tissue (Central Figure A). To properly perform this technique, the targeted cardiac wall must be oriented parallel to the transducer, which emits the impulse and determines the speed at which the waves propagate through the tissue.[9]

In the context of cardiac physiology, the closing of the atrioventricular and semilunar valves generates shear waves of itself. Another technique is based on assessing the intrinsic movement of these naturally generated waves (Central Figure B). This analysis is more feasible and can be performed with more conventional equipment. Furthermore, such waves do not depend on an acoustic window for generation, allowing broader application in clinical practice. However, while transducer-generated waves can be controlled in time and space by an ultrasound device, naturally-generated waves appear at specific locations and periods during the cardiac cycle, requiring propagation velocity analysis at specific points.

Considering an isotropic medium with uniform density, stiffness can be estimated from the shear wave propagation speed according to the equation: $\mu = \rho c^2$, where "μ" represents myocardial stiffness (kPa), "ρ" tissue density, and "c" the shear wave propagation speed.[9]

A recently published Brazilian study was conducted at the Heart Institute of the University of São Paulo School of Medicine (InCor), in partnership with the Radiology Institute of the University of São Paulo University Hospital (InRad).[11] In this study, assessments were performed with a device already used by the service, an APLIO i800 (Canon Inc., Tokyo, Japan), with small adjustments made for the elastographic study and images obtained from a multifrequency convex probe (fundamental frequency 3.5 MHz). Shear wave propagation speed was measured at end-diastole, when the heart moves the least. Long-axis parasternal windows were used to assess the basal segment of the septum, while short-axis parasternal windows were used to assess the basal segment of the septum and the basal, middle and, apical segments of the septum, plus the right ventricle free wall, as shown in Figure 1.

Clinical applications of shear wave elastography

Several studies have shown promising results with this technique. In 2019, Petrescu et al. found higher propagation velocities in patients with cardiac amyloidosis and older adults, which suggested a correlation between propagation velocities and myocardial stiffness.[12] In 2020, the same group evaluated propagation speed in heart transplant patients, finding a good correlation with invasive measurement (right catheterization) of pulmonary capillary pressure and a diffuse pattern of myocardial injury assessed by cardiac magnetic resonance imaging.[13]

Based on shear wave propagation speed, Villemain et al. found greater myocardial stiffness in patients with hypertrophic cardiomyopathy than healthy controls, in addition to a significant correlation between fibrosis assessed by delayed enhancement cardiac magnetic resonance imaging and diastolic dysfunction parameters assessed by conventional echocardiography.[14]

Cvijic et al. used the method to evaluate hypertensive patients, finding that patients with advanced disease and concentric remodeling or concentric hypertrophy had greater stiffness than healthy controls.[15]

Alencar Neto et al. found greater myocardial stiffness in patients with transthyretin cardiac amyloidosis than healthy controls.[11] A decreasing pattern of stiffness towards the apex was described,[11] suggesting a pattern of apical sparing, which is compatible with the pathophysiology of the disease.

Although these are initial studies, they show that the technique is feasible and has potential clinical application. Considering that several diseases present with a hypertrophic phenotype, such as amyloidosis and hypertrophic cardiomyopathy, additional and more expensive diagnostic resources are required; a non-invasive technique associated with echocardiography can improve diagnosis and may add prognostic value for these diseases. Furthermore, it may revolutionize the assessment and understanding of diastolic function in general.

Challenges to using shear wave elastography

In addition to the difficulties inherent to new diagnostic techniques, such as different acquisition protocols and equipment, being an ultrasound technique, it is consequently operator-dependent and angle-dependent.[16]

Associated with such technical factors, cardiac tissue is essentially anisotropic, with different layers, thin walls, and its own movement patterns,[17] variables that can influence shear wave propagation speed. Furthermore, it has been shown that both geometric changes[18] and increased preload[17] affect

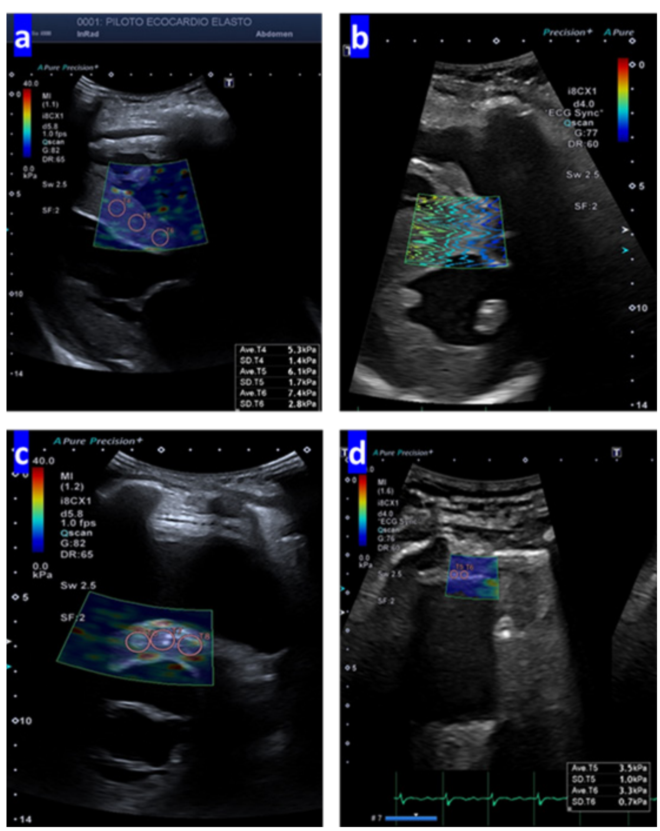

Figure 1 – *Myocardial elastography. In A, the basal segment of the interventricular septum is assessed in a long-axis parasternal window. In B and C, the middle and basal segments of the septum, respectively, are assessed in a short-axis parasternal window. In D, the right ventricle free wall is assessed in a short-axis parasternal window.*

these measurements. These mechanical factors limit the use of Young's modulus to determine myocardial stiffness, since they are not considered in this equation. Given that propagation speed is influenced by these variables, they should ideally be determined at the time of evaluation for correct interpretation of the results.

Other limitations include definitions of the ideal echocardiographic window and the number of myocardial segments to be analyzed. Significantly higher propagation velocities were obtained in an apical window than a parasternal window in healthy volunteers, with no significant correlation between the measured values.[19] It is worth mentioning that the directions in which the natural valve-generated shear waves propagate within the myocardium are unknown, which impairs accurate velocity estimation.[20]

It is also important to consider that elastography assessment depends on the phase of the cardiac cycle, with the impulse activated according to electrical heartbeat monitoring. However, there is no impediment to using the method in irregular heart rhythms, which limits conventional diastolic function assessment.

Future perspectives for shear wave elastography

Elastography may prove useful in other heart diseases, improving diagnostic and, possibly, prognostic and therapeutic response assessment. Since it is a non-invasive, accessible, and low-cost technique, it can be incorporated into traditional echocardiogram, a daily component of the clinical practice of cardiologists.

As interest in the technique has grown, the number of studies on cardiac elastography has increased. However, different impulse emission techniques, ultrasound devices, and configurations make it difficult to understand the data and standardize the results. The technique's standardization is fundamental and must be achieved in the future. Likewise, different result metrics can be found in the literature. There is a greater tendency to use wave propagation speed, rather than elasticity, thus avoiding equations that depend on mechanical factors inapplicable to the myocardium.

Tissue dispersion and anisotropy data can also be obtained through elastography, allowing for more advanced tissue characterization. Furthermore, most studies typically report shear wave speed in the interventricular septum using a long-axis parasternal window, due to the almost orthogonal relationship between the position of the ultrasound beam and the cardiac tissue required to induce the shear waves. However, other echocardiographic windows and regions of the myocardium may be used for other assessments, commensurate with advances in device quality.

Conclusions

Cardiac elastography has shown good accuracy in evaluating shear wave propagation speed, allowing myocardial stiffness estimation despite limitations, as well as a non-invasive and inexpensive detailed assessment of diastolic function. The method is still being tested and is the subject of growing interest in the national and international scientific community. The method may provide unique additional information to conventional echocardiography and add important diagnostic value for a variety of heart diseases.

Author Contributions

Conception and design of the research: Fernandes F; acquisition of data and analysis and interpretation of the data: Santorio NC, Pereira NM; writing of the manuscript: Santorio NC, Pereira NM, Cafezeiro CRF; critical revision of the manuscript for intellectual content: Fernandes F, Santorio NC, Cafezeiro CRF, Alencar Neto AC, Bueno BVK, Pereira FL, Chammas MC.

Potential Conflict of Interest

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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