

Editorial

Refining Determination of Cardiac Involvement in Amyloidosis With Three-dimensional Speckle Tracking Echocardiography

Perfeccionamiento de la determinación de la afectación cardiaca en la amiloidosis mediante ecocardiografía *speckle tracking* (rastreo de marcas) tridimensional

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Amyloidosis is a severe disease that often has devastating clinical consequences. Determination of cardiac involvement is of great importance. In the article published in *Revista Española de Cardiología*, Urbano-Moral et al¹ investigated 40 patients with light chain amyloidosis to extend the diagnostic utility of echocardiography by applying the exciting new technique of 3-dimensional (3D) speckle tracking echocardiography. Because amyloidosis is uncommon, echocardiography has traditionally played a critically important diagnostic role in identifying features consistent with cardiac amyloidosis.² These echocardiographic features may frequently alert clinicians to pursue appropriate diagnostic testing, such as biopsy, or suggest cardiac involvement in patients with laboratory evidence of systemic amyloidosis. Importantly, over half of patients affected by this condition show cardiac involvement at diagnosis, which is the most important prognostic factor.

Amyloidosis is an unusual disease of unknown cause with a variable clinical course and limited treatment options. Establishing the diagnosis may be complex, requiring positive amyloid Congo red staining by fat aspirate, bone marrow biopsy, or cardiac biopsy. In addition, immunohistochemical staining or immunofluorescence microscopy may detect evidence of light chain-related amyloid, while serum or urine immunofixation may detect a monoclonal plasma cell proliferative disorder using serum- or bone marrow-free light chain ratio analysis. Systemic amyloidosis often results in deposition of amyloid substance in the heart, which affects myocardial function in unique and interesting ways. Determination of cardiac involvement may vary among different subtypes of amyloid disease, and diagnostic information in addition to echocardiography may be obtained from the standard 12-lead electrocardiogram, serum biomarkers, cardiac magnetic resonance imaging, and nuclear techniques.³ Echocardiographic criteria have been most commonly used for clinical diagnosis, including the simple observation of increased wall thickness that is not left ventricular (LV) hypertrophy. Shortened deceleration time by

pulsed Doppler of the mitral inflow velocity was introduced by Klein et al,⁴ and reduced early diastolic tissue Doppler mitral annular velocity by Garcia et al.⁵ These Doppler criteria remain an established part of the diagnostic approach to amyloidosis.

Speckle tracking echocardiography, also known as deformation imaging, has had a major impact on the quantification of myocardial mechanics and has established clinical utility.⁶⁻⁸ An exciting observation was made by Phelan et al⁹ using speckle-tracking longitudinal strain segmental analysis to demonstrate relative apical sparing to differentiate wall thickening from cardiac amyloidosis from other more common causes of LV wall thickening, such as hypertensive heart disease or aortic stenosis. These authors showed that the segmental longitudinal strain ratio of average apical strain/average mid- and basal strain with a value more than 1.0 indicated apical sparing consistent with amyloidosis, with 93% sensitivity and 82% specificity. A recent study by Baccouche et al¹⁰ used the same vendor to analyze and compare 2-dimensional (2D) and 3D assessment in 24 participants, 12 with cardiac amyloid and 12 with hypertrophic cardiomyopathy. These authors described similar relative longitudinal and circumferential apical sparing, showing an “inverse pattern” of radial strain with higher values in apical segments, which progressively decreased toward the base. In contrast, healthy controls showed a normal radial strain gradient of basal to apical decreasing radial strain. As expected, hypertrophic cardiomyopathy patients showed significantly lower values than healthy participants. Using cardiac magnetic resonance imaging with late gadolinium enhancement, the authors demonstrated a basal to apical gradient in hypertrophic cardiomyopathy diseases, although it was much more pronounced in cardiac amyloid.¹⁰

More recently, Quarta et al¹¹ reported 2D speckle tracking echocardiographic data from a large series of 172 patients with cardiac amyloidosis. These authors included 80 patients with amyloid light-chain amyloidosis, 56 patients with nonmutant transthyretin-related amyloidosis, and 36 patients with transthyretin-related mutant-form amyloidosis. They observed that 100% of patients with cardiac amyloidosis had abnormal radial strain and 93% had abnormal longitudinal strain, reporting that strain performed better than routine pulsed Doppler or tissue Doppler in detecting cardiac involvement.

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The present study by Urbano-Moral et al¹ builds on these previous studies by adding evaluation of cardiac amyloidosis by the newer technology of 3D speckle tracking echocardiography. Three-dimensional strain techniques continue to develop quickly and have been shown to be useful in accurately measuring cardiac chamber volumes, segmental and global function, and intraventricular dyssynchrony.¹² The present report confirms previous observations by 2D speckle tracking of greater involvement of the basal segments than the apical segments. Furthermore, the authors associated the degree of abnormalities in 3D speckle tracking strain with the degree of elevation in the serum biomarker, brain natriuretic peptide, an established marker of disease extent and prognosis in heart failure. They showed that LV longitudinal and circumferential strain were reduced in patients with cardiac involvement (-9 ± 4 vs -16 ± 2 ; $P < .001$, and -24 ± 6 vs -29 ± 4 ; $P = .01$, respectively), with the most prominent impairment at the basal segments. They introduced the assessment of right ventricular (RV) 3D strain and showed that the reduced RV strain measurements were correlated to changes in LV strain in cardiac amyloidosis; however, they could not apply RV strain to many patients, and RV strain assessment appears to be currently limited in their experience. Most importantly, they used a multivariable analysis to demonstrate that 3D LV longitudinal strain was associated with the presence of cardiac involvement (odds ratio = 1.6; 95% confidence interval, 1.04-2.37; $P = .03$), independently of the presence of brain natriuretic peptide and troponin I criteria for cardiac amyloidosis.

The limitations of 3D speckle tracking include the need for adequate image quality, with 9% being excluded for 3D LV strain analysis and 41% being excluded for 3D RV strain analysis. In addition, there are marked differences in acquisition rates compared with 2D speckle tracking, with 3D technique having lower volume rates.¹³ Other limitations include the need for user training to limit interobserver variability in the placement of regions of interest affecting data output and variability reported from different vendors.^{14,15}

In conclusion, the study by Urbano-Moral et al¹ extends the diagnostic utility of echocardiography in detecting and quantifying cardiac involvement in amyloidosis. This new information builds on previous clinical information obtained from a low voltage electrocardiogram, shortened mitral inflow deceleration time by pulsed Doppler, and reduced tissue Doppler mitral early diastolic velocity. Speckle tracking strain echocardiography in terms of global longitudinal strain appears to be a highly sensitive indicator of cardiac amyloidosis that may be superior to previous approaches and at least deserves clinical attention. These enhancements in the diagnosis of cardiac amyloidosis are accompanied by exciting recent advances in treatment options, which all result in improvements in patient care.

CONFLICTS OF INTEREST

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REFERENCES

1. Urbano-Moral JA, Gangadharamurthy D, Comenzo RL, Pandian NG, Patel AR. Ecocardiografía *speckle tracking* (rastreo de marcas) tridimensional en la amiloidosis cardiaca de cadenas ligeras: estudio de los parámetros de mecánica miocárdica ventricular izquierda y derecha. *Rev Esp Cardiol*. 2015;68:657-64.
2. Gertz MA, Comenzo R, Falk RH, Fermand JP, Hazenberg BP, Hawkins PN, et al. Definition of organ involvement and treatment response in immunoglobulin light chain amyloidosis (AL): a consensus opinion from the 10th International Symposium on Amyloid and Amyloidosis, Tours, France 18-22 April 2004. *Am J Hematol*. 2005;79:319-28.
3. Mohty D, Damy T, Cosnay P, Echahidi N, Casset-Senon D, Virot P, et al. Cardiac amyloidosis: updates in diagnosis and management. *Arch Cardiovasc Dis*. 2013;106:528-40.
4. Klein AL, Hatle LK, Burstow DJ, Seward JB, Kyle RA, Bailey KR, et al. Doppler characterization of left ventricular diastolic function in cardiac amyloidosis. *J Am Coll Cardiol*. 1989;13:1017-26.
5. Garcia MJ, Rodriguez L, Ares M, Griffin BP, Thomas JD, Klein AL. Differentiation of constrictive pericarditis from restrictive cardiomyopathy: assessment of left ventricular diastolic velocities in longitudinal axis by Doppler tissue imaging. *J Am Coll Cardiol*. 1996;27:108-14.
6. Suffoletto MS, Dohi K, Cannesson M, Saba S, Gorcsan 3rd J. Novel speckle-tracking radial strain from routine black-and-white echocardiographic images to quantify dyssynchrony and predict response to cardiac resynchronization therapy. *Circulation*. 2006;113:960-8.
7. Gorcsan 3rd J, Tanaka H. Echocardiographic assessment of myocardial strain. *J Am Coll Cardiol*. 2011;58:1401-13.
8. Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. *Heart*. 2014;100:1673-80.
9. Phelan D, Collier P, Thavendiranathan P, Popovic ZB, Hanna M, Plana JC, et al. Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis. *Heart*. 2012;98:1442-8.
10. Baccouche H, Maunz M, Beck T, Gaa E, Banzhaf M, Knayer U, et al. Differentiating cardiac amyloidosis and hypertrophic cardiomyopathy by use of three-dimensional speckle tracking echocardiography. *Echocardiography*. 2012;29:668-77.
11. Quarta CC, Solomon SD, Uraizee I, Kruger J, Longhi S, Ferlito M, et al. Left ventricular structure and function in transthyretin-related versus light-chain cardiac amyloidosis. *Circulation*. 2014;129:1840-9.
12. Tanaka H, Hara H, Saba S, Gorcsan 3rd J. Usefulness of three-dimensional speckle tracking strain to quantify dyssynchrony and the site of latest mechanical activation. *Am J Cardiol*. 2010;105:235-42.
13. Negishi K, Negishi T, Agler DA, Plana JC, Marwick TH. Role of temporal resolution in selection of the appropriate strain technique for evaluation of subclinical myocardial dysfunction. *Echocardiography*. 2012;29:334-9.
14. Pérez de Isla L, Balcones DV, Fernández-Golfín C, Marcos-Alberca P, Almería C, Rodrigo JL, et al. Three-dimensional-wall motion tracking: a new and faster tool for myocardial strain assessment: comparison with two-dimensional-wall motion tracking. *J Am Soc Echocardiogr*. 2009;22:325-30.
15. Badano LP, Cucchini U, Muraru D, Al Nono O, Sarais C, Iliceto S. Use of three-dimensional speckle tracking to assess left ventricular myocardial mechanics: inter-vendor consistency and reproducibility of strain measurements. *Eur Heart J Cardiovasc Imaging*. 2013;14:285-93.