Tissue Velocities and Myocardial Deformation in Asymptomatic and Symptomatic Aortic Stenosis

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Background: Assessment of myocardial longitudinal function has proved to be a sensitive marker of deteriorating myocardial function in aortic stenosis, demonstrated by both color Doppler tissue imaging and recently by two-dimensional speckle-tracking echocardiography. The aim of this study was to compare velocity (color Doppler tissue imaging) and deformation (two-dimensional speckle-tracking echocardiography) in relation to global and regional longitudinal function in asymptomatic and severe symptomatic aortic stenosis.

Methods: In a cross-sectional design, 231 patients with aortic stenosis were divided into four groups: asymptomatic moderate aortic stenosis (aortic valve area, 1.0–1.5 cm^2; $n = 38$), asymptomatic severe aortic stenosis (aortic valve area < 1.0 cm^2; $n = 66$), and symptomatic severe aortic stenosis with preserved ($n = 68$) and reduced (<50%) left ventricular ejection fraction ($n = 59$).

Results: Among all global (peak systolic s′, diastolic e′ and a′, longitudinal displacement, and global longitudinal strain and strain rate) and regional longitudinal (basal, middle, and apical longitudinal strain and strain rate) parameters, only diastolic e′, longitudinal displacement, and basal longitudinal strain (BLS) remained significantly associated with symptomatic status, independent of age, gender, heart rate, aortic valve area, stroke volume index, left ventricular mass index, left atrial volume index, and tricuspid annular systolic plane excursion. Furthermore, in a model with the aforementioned parameters, including e′, longitudinal displacement, and BLS, only BLS remained significantly associated with symptomatic status in the entire study population (BLS per one-unit decrease: odds ratio, 1.23; 95% CI, 1.04–1.46; $P = .017$). Furthermore, patients with BLS < 13% were more likely to be symptomatic (odds ratio, 4.97; 95% CI, 2.6–9.4; $P < .001$), and no patients with asymptomatic severe aortic stenosis with BLS ≥ 13% were admitted with myocardial infarction or heart failure during follow-up of 1,462 days.

Conclusions: Among the many echocardiographic measures of longitudinal velocity and deformation, BLS has the strongest association with symptomatic status in aortic stenosis, and BLS < 13% is related to adverse outcomes in severe asymptomatic aortic stenosis. (J Am Soc Echocardiogr 2015;■:■-■.)

Keywords: Aortic stenosis, Regional longitudinal function, Speckle-tracking, Tissue Doppler

Cardiac long-axis function has been intensively investigated over the more than three decades since the 1979 study by Dumesnil *et al.*[1] demonstrated that longitudinal shortening, measured by M-mode echocardiography, was reduced in patients with aortic stenosis compared with normal subjects and patients with aortic or mitral regurgitation. Since the era of M-mode echocardiography, many new methods have been added to the echocardiographic toolbox, and today we can assess myocardial performance with both tissue Doppler velocities[2] and two-dimensional (2D) speckle-tracking echocardiography[3] in relation to systolic and diastolic function and global, regional, and multidirectional performance.[4]

In severe asymptomatic aortic stenosis, the single echocardiographic parameter included in the guidelines is left ventricular ejection fraction (LVEF), which when <50% provides a clear indication for aortic valve replacement.[5] However, because of progressive changes and myocardial hypertrophy in aortic stenosis, LVEF may be preserved until late in the disease despite decreasing stroke volumes and impaired contractility.[6,7] It seems intuitively correct to monitor cardiac function to identify patients with worsening aortic stenosis, and measures of longitudinal cardiac function, evaluated by color Doppler tissue imaging (DTI) and 2D STE, seem especially appealing. In contrast to conventional echocardiographic measures

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Abbreviations

BLS = Basal longitudinal strain

CV = Coefficient of variation

DTI = Doppler tissue imaging

GLS = Global longitudinal strain

LVEF = Left ventricular ejection fraction

OR = Odds ratio

STE = Speckle-tracking echocardiography

2D = Two-dimensional

of systolic function, global and regional longitudinal function have proved to be sensitive markers of deteriorating myocardial function in various heart diseases,[8-10] including aortic stenosis.[4,11-15]

In previous studies, tissue velocities measured by color DTI have proved to be more robust measures of longitudinal function compared with the newer technique with 2D STE,[16] but regional function may not be reflected accurately with color DTI, because of tethering.[17] In contrast, 2D STE is angle independent, and regional function is not influenced by adjacent segments (tethering).[18,19] Thus, the aim of this study was to compare global and regional velocity and deformation in patients with asymptomatic and symptomatic aortic stenosis, divided into four groups according to severity (aortic valve area), symptomatic status, and LVEF.

METHODS

Study Population

The study population of 231 patients with aortic stenosis was recruited from March 2008 to January 2012 from two parallel studies investigating the use of multidetector computed tomography and echocardiography in asymptomatic patients ($n = 104$) and symptomatic patients scheduled for aortic valve replacement, with or without coronary bypass grafting ($n = 127$).

Inclusion criteria for both studies were aortic valve stenosis and an echocardiographic peak velocity by continuous-wave Doppler of >2.5 m/sec, and patients with phosphocreatinine > 130 mmol/L, allergies to iodine contrast media, and other severe heart valve disease were excluded.

Group 1: Asymptomatic Cohort. The patients in the asymptomatic cohort were recruited from six hospitals in the greater Copenhagen area by screening for patients with the diagnosis registry code for aortic stenosis (DI35.0) in clinical records, hospital registries, and echocardiographic databases. One hundred twenty-four patients with asymptomatic aortic stenosis and peak velocities > 2.5 m/sec and none of the aforementioned exclusion criteria gave informed consent to participate in the study. At the time of inclusion at the University Hospital of Copenhagen, Rigshospitalet, all patients underwent transthoracic echocardiographic examinations, and asymptomatic status was confirmed by obtaining their medical histories. Twenty patients were excluded from this study because of atrial fibrillation ($n = 9$), reduced LVEF (<50%; $n = 4$), poor image quality ($n = 5$), mild aortic stenosis with aortic valve area > 1.5 cm^2 ($n = 1$), and symptomatic status at the time of examination at Rigshospitalet ($n = 1$). One hundred four patients with moderate to severe asymptomatic aortic stenosis, defined as an aortic valve area ≤ 1.5 cm^2, were ultimately included in this study.

Group 2: Symptomatic Cohort. The symptomatic cohort was recruited by screening all patients referred for elective aortic valve replacement, with or without concomitant coronary bypass grafting, at University Hospital of Copenhagen, Rigshospitalet, from March 2008 to March 2010. The treating physician was blinded to the results of the echocardiographic examination, and referral for aortic valve replacement was performed independently by the clinical heart team.

One hundred eighty-five patients had data sets available for 2D speckle-tracking echocardiographic and color DTI analysis. Patients with atrial fibrillation ($n = 31$), ventricular arrhythmias ($n = 5$), aortic valve area ≥ 1.0 cm^2 ($n = 14$), or poor image quality ($n = 8$) were excluded. Ultimately, 127 patients were included in the study.

The entire study cohort of 231 patients with aortic stenosis consisted of 104 patients from the asymptomatic cohort (moderate, $n = 38$; severe, $n = 66$) and 127 patients from the symptomatic cohort (severe with preserved LVEF, $n = 68$; severe with reduced LVEF [<50%], $n = 59$).

The study was approved by the local research and ethics committee (H-B-2009-027), and all patients gave individual informed consent. Data from the two cohorts concerning measurement of aortic valve area by multidetector computed tomography have been published.[20]

Echocardiography

Examinations that took place from March 2008 to July 2009 ($n = 66$) were performed using a Vivid 7 Dimension system (GE Vingmed Ultrasound AS, Horten, Norway) with a 3.5-MHz transducer. From August 2009 to January 2012, examinations ($n = 165$) were performed using a Vivid E9 ultrasound system (GE Vingmed Ultrasound AS), with a 3.5-MHz transducer. All participants were examined with conventional 2D echocardiography and pulsed-wave and color DTI. Echocardiographic cine loops were obtained by recording three consecutive heart cycles. All examinations were performed by two experienced operators. Offline analyses were performed by a single experienced operator, who was blinded to all other patient data, using EchoPAC BT version 11.1.0 (GE Vingmed Ultrasound AS).

Conventional Echocardiography. Left ventricular diameters, wall thicknesses, relative wall thickness, and tricuspid annular plane systolic excursion were assessed and calculated as recommended. Left ventricular mass was calculated from left ventricular linear dimensions using the Devereux formula and divided by body surface area (calculated using the Du Bois formula) to obtain left ventricular mass index.[21] Left ventricular hypertrophy was defined as a left ventricular mass index > 115 g/m^2 for men and > 95 g/m^2 for women. Left ventricular geometry (normal, concentric remodeling, or eccentric and concentric hypertrophy) was assessed according to relative wall thickness (increased if ≥0.43) and left ventricular mass index.[21] Left ventricular volumes and left atrial volume index were estimated using the biplane method of disks (modified Simpson's rule).[21] LVEF was considered reduced when <50%. Stroke volume was calculated with the Doppler method; stroke volume = cross-sectional area in left ventricular outflow tract × velocity-time integral in left ventricular outflow tract.

Left ventricular outflow tract diameter was measured in midsystole in the parasternal long-axis view.

Pulsed Doppler recordings were performed in the apical three- and five-chamber views by placing the sample volume 0.5 to 1.0 cm below the aortic valve, where a clear and smooth signal could be obtained. Peak flow velocity across the aortic valve was determined in the three- or five-chamber view, where the highest velocity could be obtained. To avoid underestimation, caution was made to align the continuous-wave curser parallel with the stenotic jet. The flow signal was traced to obtain peak velocity, velocity-time integral, and