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ORIGINAL ARTICLE

Differential Myocardial Fibre Involvement by Strain Analysis in Patients With Aortic Stenosis

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Background Aortic stenosis (AS) is the most common valvular heart disease and can result in left ventricular (LV) systolic impairment. LV myocardial fibres are organised in layers: the subendocardial layer is orientated longitudinally and the subepicardial layer circumferentially. We hypothesised that there is differential involvement of myocardial fibres in patients with aortic stenosis.

Methods We performed multi-directional, multi-layered systolic strain analysis in 70 patients (aged 72 ± 10.7 years) with varying grades of AS severity (mean gradient 32.3 ± 20 mmHg, aortic valve area 1.1 ± 0.6 cm^2) and in Q5 30 controls. Clinical, demographic and resting echocardiographic data were recorded. Left ventricular subendocardial and subepicardial systolic strains were measured in the longitudinal, radial and circumferential axes.

Results Systolic subendocardial strain was significantly higher than subepicardial strain in all three axes in patients and in controls. There were significant differences in longitudinal, but not in circumferential and radial Q6 strain, or left ventricular ejection fraction (LVEF), between patient groups. Aortic valve mean gradient (MG) and valve area (AVA) correlated better with subendocardial longitudinal strain ($r = 0.548$, $p < 0.001$; $r = -0.54$, $p < 0.001$ respectively) than with subepicardial longitudinal strain ($r = 0.496$, $p < 0.001$, $r = -0.544$, $p < 0.001$ respectively). Correlations between circumferential and radial strain and MG or AVA were poor.

Conclusions There was differential impairment in LV systolic strain in all three cardiac axes in patients with AS. Left ventricular longitudinal strain impairment was proportional to AS severity. Subendocardial longitudinal strain correlated better with AS severity than subepicardial longitudinal strain while correlations between circumferential and radial strain and AS severity were weak.

Keywords Aortic stenosis • Echocardiography • Ventricular function • Longitudinal strain

Introduction

Q7 Aortic stenosis (AS) is the most common presentation of valvular heart disease. Left ventricular (LV) systolic impairment is a well-known complication of AS and portends worse prognosis [1]. LV ejection fraction (LVEF) often remains within normal limits until more advanced stages of AS. Recent studies have shown LVEF to be insensitive in detecting early subclinical myocardial dysfunction [2]. In contrast, LV strain and strain rate analysis are more

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sensitive indices of subclinical myocardial involvement. Recent studies have shown abnormal LV strain mechanics despite preserved LVEF in patients with AS [3,4].

Myocardial architecture is a complex array of longitudinally and circumferentially orientated fibres, predominantly organised in subendocardial and subepicardial layers, respectively [5]. Subendocardial longitudinal fibres are more susceptible to increased wall stress and reduced myocardial perfusion [6]. It has been suggested that fibrotic changes induced consequent to AS may start in the subendocardium, and gradually progress to involve the entire myocardium [7]. Multi-directional strain analysis along longitudinal, circumferential and radial axes would provide important insights into the pathophysiological changes within the myocardium in AS. Whilst a recent study suggested that the myocardial dysfunction begins in the subendocardium and subsequently progresses to transmural involvement [2], there is currently very limited data on the changes in multi-directional systolic strain in the different myocardial layers (i.e. subendocardial versus subepicardial) and how this correlates with AS severity.

The aims of this study were to examine if there was differential involvement of myocardial fibres in patients with AS and to determine whether this differential involvement correlates with AS severity.

Methods

Patient Groups

Patients with AS who underwent transthoracic echocardiography in the Department of Cardiology at Liverpool Hospital from 2008 to December 2014 were identified retrospectively from a departmental database and included in this study. Only those patients who also had an invasive coronary angiogram at our hospital within 5 years of the echocardiogram demonstrating non-obstructive coronary artery disease, defined as less than 50% stenosis in the major epicardial coronary arteries and its major branches, were included. Other exclusion criteria included rhythm other than sinus rhythm, left bundle branch block, co-existing significant left sided valvular heart disease (defined as more than mild aortic or mitral regurgitation or mitral stenosis), previous myocardial infarction or coronary revascularisation. Patients with suboptimal echocardiographic images were also excluded. A total of 70 patients with AS were included in this study. Thirty patients, randomly identified, with no AS or other valvular diseases or LV dysfunction were included as controls. The study was approved by the Human Research Ethics Committee of the South Western Sydney Local Health District and informed consent was waived given the retrospective nature of the study.

Echocardiography

A comprehensive transthoracic echocardiogram was performed with appropriate two-dimensional, colour and Doppler imaging performed from standard transthoracic imaging windows (parasternal, apical and subcostal). Left ventricular wall thickness and biplane LV ejection fraction were measured using standard recommendations for LV chamber quantification [8]. All valves were evaluated with colour and Doppler interrogation.

Aortic valve area (AVA) was calculated by the continuity equation using velocity time integrals of the aortic and LV outflow tract. Peak and mean transaortic valve gradients were calculated using the modified Bernoulli equation. Assessment and classifications of the AS severity were based on transaortic valve peak velocity, mean gradient, and AVA according to the guidelines of the American Society of Echocardiography [9]. Mitral inflow velocities were measured from pulsed-wave Doppler echocardiographic image in the apical four-chamber view. Transmitral early diastolic (E wave) and late diastolic (A wave) velocities, the E/A ratio, as well as deceleration time of the E wave were measured. Peak myocardial velocity of mitral annular contraction, with the sample volume placed at the base of the septum during early diastole (e'), was measured using tissue Doppler imaging. Three cardiac cycles were measured with the results averaged for all measurements.

Two-Dimensional Strain and Strain Rate Analysis

Two dimensional strain and strain rate analyses were performed on grey scale images of the left ventricle using Velocity Vector Imaging (Syngo VVI, Siemens Medical Solutions). Mean peak systolic longitudinal strain and strain rate were averaged from the 18 segments measurements (six segments from each of the apical four-, two-, and three-chamber views) (Figure 1A-D). Peak systolic circumferential and radial strain and strain rate were measured and averaged from the six segments in the short-axis view of the LV at the papillary muscle level (Figure 1E-J).

The myocardial wall was divided into two layers – the subendocardial and subepicardial layers. During analysis of the subendocardial layer, the endocardial border was manually traced at end-systole and the width of the region of interest manually adjusted to include the inner half of the myocardial wall (i.e. the subendocardial layer) only. The analysis was then repeated for the subepicardial layer, with the region of interest manually adjusted to cover the subepicardial layer – from mid-myocardial wall to the epicardial border – at end-systole (Figure 1). The software then automatically tracks and accepts segments of good tracking quality and rejects poorly tracked segments. The operator was able to manually override computer-generated tracking and accept or reject individual segments based on visual assessments of the tracking quality. Three cardiac cycles were analysed and the measurements averaged.

Statistical Analysis

All continuous variables are reported as the mean ± 1 SD unless otherwise stated. Categorical variables are presented

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