Assessment of left ventricular systolic function in aortic stenosis and prognostic implications

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This editorial refers to ‘Global longitudinal strain is a strong independent predictor of all-cause mortality in patients with aortic stenosis’ by L.G. Kearney et al., on pages 827–833

Left ventricular (LV) ejection fraction, most commonly assessed with two-dimensional echocardiography, is an important prognostic determinant of many cardiovascular diseases. The decision of implanting specific cardiovascular devices, such as cardiac resynchronization therapy or implantable cardioverter defibrillator, recommending valvular surgery or chemotherapy relies on the LV ejection fraction. However, the accumulating evidence shows that LV ejection fraction is an imperfect measure of LV systolic function since it simply reflects the changes in the LV cavity volume and does not take into consideration the complex architecture of the LV.¹,²

The LV myocardial fibre changes the three-dimensional spatial orientation from a right-handed helix in the subendocardial region to a left-handed helix in the subepicardium.¹ This counter-clockwise and clockwise spiral muscle configuration results in a characteristic three-dimensional LV deformation with shortening in the longitudinal and circumferential directions, thickening in the radial direction, and twist in the circumferential-longitudinal plane and permits LV emptying and filling with optimal mechanical efficiency. Thus, 15% of myofibre shortening during systole results in 40% myocardial wall thickening and >60% change in the LV ejection fraction in the normal heart.³ In addition, the extracellular collagen matrix of the myocardium supporting this myofibre arrangement is key to maintain the LV shape and size. Any change in the myofibre alignment or extracellular matrix may lead to LV dysfunction.

Current imaging techniques, such as diffusion tensor and tagged magnetic resonance imaging and speckle tracking, permit non-invasive evaluation of the LV spiral muscle configuration and quantification of LV shortening, thickening, and twisting deformations. Particularly, speckle tracking echocardiography permits accurate assessment of multidirectional LV strain (longitudinal, circumferential, and radial) by tracking frame-to-frame natural acoustic markers equally distributed within the myocardium in two-dimensional grey-scale images.

A large body of evidence has demonstrated a close correlation between the LV ejection fraction and global LV longitudinal strain.⁴ However, this correlation is not perfect, suggesting that global LV longitudinal strain assessed with speckle tracking and LV ejection fraction measured with Simpson’s method on two-dimensional echocardiography do not reflect the same aspects of LV systolic function. The subendocardial myocardial fibres are the main determinants of LV longitudinal strain, whereas the mid-myocardial and epicardial fibres, with a circumferential and longitudinal three-dimensional disposition are the main determinants of the circumferential and rotational mechanics. At an early stage of myocardial disease, where the subendocardial layers may be affected by fibrosis or ischaemia and mid-myocardial and subepicardial layers may be unaffected, impaired longitudinal subendocardial shortening will be compensated by normal circumferential and rotational mechanics resulting in a preserved LV ejection fraction. Transmural myocardial injury or progression of the disease will impair myocardial circumferential and rotational mechanics leading to a reduced LV ejection fraction. Consequently, global LV longitudinal strain has been proposed as a more sensitive method than LV ejection fraction to detect subtle myocardial disease.

Numerous studies have reported a subtle LV systolic dysfunction assessed with global LV longitudinal strain in multiple clinical conditions where LV ejection fraction may be preserved (diabetes mellitus, hypertension, valvular heart disease and use of chemotherapy).⁵–⁷ In addition, the severity and extent of myocardial disease has been accurately evaluated with multidirectional LV strain speckle tracking echocardiography. For example, the magnitude of regional LV longitudinal, radial, and circumferential strain has been associated with myocardial scar transmurality and presence of viable myocardium in patients with ischemic heart disease.⁸ Furthermore, impaired global LV longitudinal strain has been independently associated with poor long-term outcome in...
patients with ischaemic heart disease or mitral regurgitation for example.1,10

Among these clinical applications, the detection of subtle heart disease with multidirectional LV strain speckle tracking has been one of the major areas of research. In the current issue of the Journal, Kearney et al.11 demonstrate the clinical implications of LV systolic dysfunction as assessed with global LV longitudinal strain speckle tracking in patients with aortic stenosis and preserved LV ejection fraction. In 120 patients with various degrees of aortic stenosis (26% mild, 21% moderate, and 53% severe) and the LV ejection fraction ≥50%, the assessment of global LV longitudinal strain with speckle tracking demonstrated the presence of LV systolic dysfunction in 17, 40, and 69% of patients with mild, moderate, and severe aortic stenosis, respectively. In addition, patients were followed-up for the occurrence of all-cause mortality or major cardiovascular events. During a median follow-up of 2.1 years, 20 patients died, including 11 patients who died of cardiac causes. Patients who died during the follow-up period showed significantly more impaired global LV longitudinal strain compared with patients who remained alive (−10±4% versus −16±3%, P < 0.001). On multivariate analysis, global LV longitudinal strain was an independent predictor of all-cause mortality (hazard ratio: 1.28, 95% confidence interval 1.09–1.49; P = 0.002) together with clinical symptoms and the age-adjusted Charlson comorbidity index. These results are in agreement with previous series reporting a progressive decay in multidirectional LV strains along with increasing severity of the aortic valve stenosis.6,12

In addition, Lancellotti et al.12 have recently demonstrated that the presence of impaired global LV longitudinal strain in patients with asymptomatic moderate-to-severe aortic stenosis is independently associated with the development of symptoms, occurrence of aortic valve replacement, and death at follow-up.

The pathophysiology underlying these findings has been demonstrated in several experimental and clinical studies.2 As LV myocardial wall stress increases due to the pressure overload caused by the stenotic aortic valve, the LV develops progressive concentric hypertrophy which will minimize the wall stress and maintain normal endocardial shortening at an early phase of the disease. Subsequent changes in the extracellular collagen matrix, with increasing replacement fibrosis, and the presence of subendocardial ischaemia will lead to impaired longitudinal shortening. At this stage, increasing LV hypertrophy will still compensate for this fall in LV longitudinal shortening and the LV ejection fraction will remain preserved. However, at more advanced stages of the disease, when LV hypertrophy cannot longer compensate a reduced LV longitudinal and mid-wall shortening, LV ejection fraction will decrease with subsequent development of symptoms. Aortic valve replacement and the relief of the pressure overload, before significant impairment in LV longitudinal shortening and progressive replacement fibrosis occur, has been associated with significant improvements in symptoms, recovery of LV longitudinal shortening, and improved long-term outcome.13 In contrast, patients with severe aortic stenosis, extensive replacement fibrosis, and reduced LV longitudinal shortening who undergo aortic valve replacement do not show clinical improvement despite having preserved LV ejection fraction prior to surgery.13 Therefore, early detection of impaired LV longitudinal shortening in patients with aortic stenosis may be the preferred method to identify the patients who will benefit from surgical aortic valve replacement. However, the incremental prognostic value of global LV longitudinal strain over well-known haemodynamic parameters of aortic stenosis severity and over LV ejection fraction has not been demonstrated in the study by Kearney et al.

Current American and European guidelines consider aortic valve replacement as class I indication in patients with severe symptomatic aortic stenosis and patients with severe aortic stenosis and reduced LV ejection fraction (<50%).14,15 Definition of severe aortic stenosis has been highly debated, and, indeed the cut-off values of several haemodynamic parameters to define severe aortic stenosis are controversial. While the American guidelines consider severe aortic stenosis when the mean transvalvular gradient is of >40 mmHg or the aortic valve area is <1.0 cm² (or <0.6 cm² if indexed), the European guidelines consider a mean transvalvular gradient of >50 mmHg as severe aortic stenosis. In the present study, the mean transvalvular gradient and aortic valve area among patients who died at follow-up were 44±23 mmHg and 0.8±0.4 cm², respectively, compared with 39±19 mmHg and 1.1±0.4 cm² in patients who remained alive.11 This suggests that many patients with aortic stenosis who do not fulfill current criteria for surgical aortic valve replacement have an increased mortality risk if left untreated. Whether global LV longitudinal strain would have been a better prognosticator than the mean transaortic valve gradient or aortic valve area remains unknown. Ongoing research evaluating the prognostic implications of impaired LV longitudinal strain in patients with aortic stenosis will elucidate the role of this parameter in the management of these patients.

Conflict of interests: Victoria Delgado received consulting fees from St. Jude Medical and Medtronic.

References

**IMAGE FOCUS**

**What went wrong and how it got right: heart team provides value in transcatheter aortic valve replacement**

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**Image description**

An 89-year-old woman deemed at extreme surgical risk underwent aortic CoreValve® (Medtronic Inc., Minneapolis, MN, USA) implantation. Her history was significant for hypertension and chronic lung disease. Work-up at admission revealed: blood pressure 96/43 mmHg, heart rate 80 bpm, soft second heart sound, and late-peaking systolic murmur (grade 3/6) in the precordium with radiation to the neck.

Transoesophageal echocardiography (TEE) immediately after implantation showed the CoreValve in situ and an echodense mobile structure adherent to the posterior surface of the valve (arrow) (Panel A, Supplemental online data, Video S1). Aortic root angiography showed a radiopaque mobile structure at the proximal edge of the valve (Supplemental online data, Video S2). Colour-flow TEE showed severe aortic regurgitation across a flail leaflet of the CoreValve (Panel B, Supplemental online data, Video S3). This was confirmed by haemodynamics, as blood pressure dropped to 52/26 mmHg and left ventricular end-diastolic pressure increased to 40 mmHg.

The decision to implant a CoreValve within the previous one was promptly made, with resultant deployment in <5 min. The patient became stable; TEE and aortic root angiography confirmed mild paravalvular regurgitation. Follow-up TEE on day 30 showed stable valve position and normal haemodynamics.

So far, reported mechanisms of intraprocedural severe aortic regurgitation are malpositioning, undersizing, or underexpansion of the valve. This case highlights the pivotal role of echocardiographic guidance during transcatheter aortic valve implantation in identifying unexpected but potentially life-threatening complications. It also highlights the need for a ‘heart team’ of experienced cardiologists, cardiac surgeons, and anaesthesiologists.

Supplementary material is available at EJCTS online.

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