



CASE REPORT

Dynamic left ventricular dyssynchrony: a potential cause of no contractile reserve in patients with low-gradient aortic stenosis

Patrizio Lancellotti^{1*}, Catherine Szymanski², Marie Moonen¹, Christophe Garweg¹, Kim O'Connor¹, Christophe Tribouilloy², and Luc A. Piérard¹

¹Department of Cardiology, University Hospital of Liège, B-4000 Liège, Belgium; and ²Department of Cardiology, University Hospital of Amiens, Picardie, France

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Dobutamine stress echocardiography (DSE) has the potential to stratify patients with low-gradient aortic stenosis (AS) but little is known about ventricular dyssynchrony associated with AS. We report the case of a patient who presented AS associated with left ventricular (LV) dyssynchrony. A DSE was performed, which showed no contractile reserve but an increase in LV dyssynchrony. In this patient, the reduced aortic valve area was probably because of the association of inadequate forward stroke volume due to ischaemic cardiomyopathy and fixed severe AS. The cause of LV dysfunction may include a certain degree of intrinsic myocardial dysfunction due to ischaemic cardiomyopathy and afterload mismatch associated with dynamic LV dyssynchrony, which could be a determinant of forward stroke volume response.

Introduction

The fortuitous association of aortic stenosis (AS) with the increase of left ventricular (LV) dyssynchrony is uncommon. We describe the case of a patient with AS with no significantly contractile reserve, associated with LV dyssynchrony, which increases on dobutamine stress echocardiography (DSE).

Case description

C.F., a 77-year-old man with AS, was referred to our stress echocardiography laboratory for contractile reserve evaluation. He had a chronic pulmonary disease. He also presented a prior history of anterior myocardial infarction 11 years ago that was medically treated, with recurrence of angina 3 years ago treated by elective angioplasty of the left anterior descending coronary artery and left main coronary artery with active stents implantation. At that time, the LV function was moderately altered (LV ejection fraction 42%), and moderate AS (valve area 1.2 cm²) was diagnosed. His evolution was marked by progressive clinical deterioration with the occurrence of dyspnoea (NYHA class III)

and the development of a significant LV systolic dysfunction. A recent coronary angiography showed a good permeability of the treated vessels and confirmed the depressed LV function. The AS was, however, evaluated as severe, and a pulmonary hypertension was noted. The calculated Euroscore was 23.72%. On the 12-lead electrocardiogram, a left bundle-branch block (QRS duration of 125 ms) was observed. As he remained symptomatic on optimal medical therapy including a diuretic, an angiotensin-converting enzyme-inhibitor, and a beta-blocker, a DSE was planned. The DSE was performed with an initial dobutamine infusion of 5 µg/kg/min for 3 min, followed by 2.5 µg/kg/min up to a maximal dose of 10 µg/kg/min. The beta-blocker, atenolol, was interrupted 48 h before the test. The patient remained asymptomatic during DSE. During the test, heart rate increased from 49 to 62 bpm, whereas there were no significant changes in systolic blood pressure (122 vs. 112 mmHg). On baseline transthoracic echocardiography, the LV ejection fraction was severely reduced (33%) and the LV was enlarged (end-diastolic diameter 64 mm) and globally hypokinetic. The aortic valve area was estimated at 0.93 cm² (0.52 cm²/m²) (outflow tract time velocity integral 20.5 cm) with a mean transvalvular pressure gradient of 26 mmHg (Figure 1, bottom). The systolic pulmonary artery pressure was 35 mmHg, and the E/E_a ratio was

* Corresponding author. Tel: +32 4 366 71 94; fax: +32 4 366 71 95.
E-mail address: plancellotti@chu.ulg.ac.be

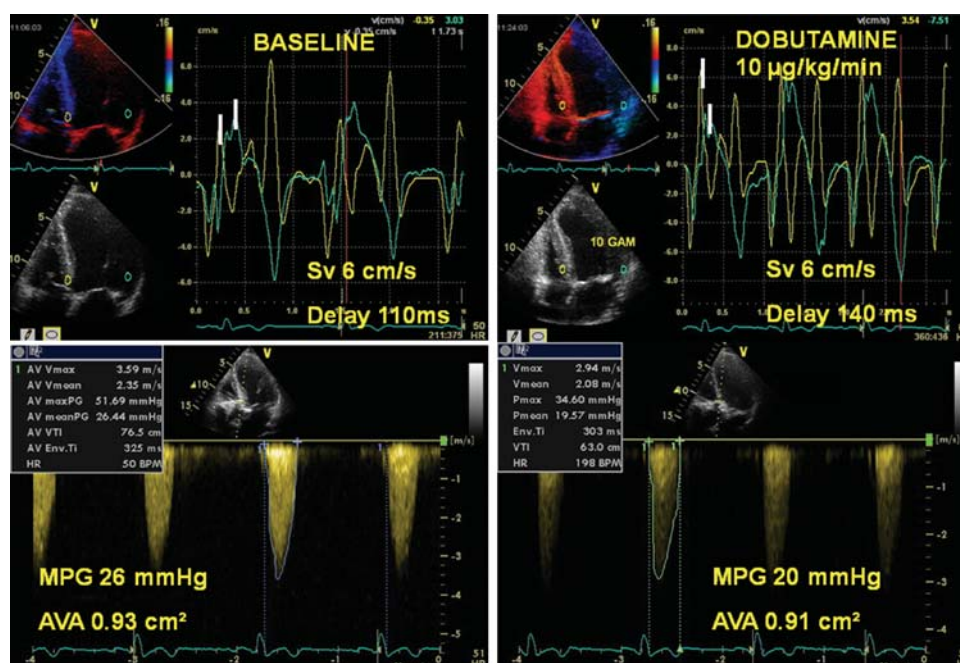


Figure 1 (Top) Tissue Doppler imaging echocardiograms depicting dobutamine-induced changes in left ventricular dyssynchrony as estimated by the difference in time-to-peak systolic velocity between the septum and the lateral wall. During test, the septal-to-lateral wall delay increased. The basal septal peak systolic velocity (Sv) was low (because of left ventricular dysfunction) and remained unchanged during dobutamine stress echocardiography. (Bottom) During dobutamine stress echocardiography, the mean transaortic pressure gradient (MPG) decreased, whereas the calculated aortic valve area (AVA) did not change.

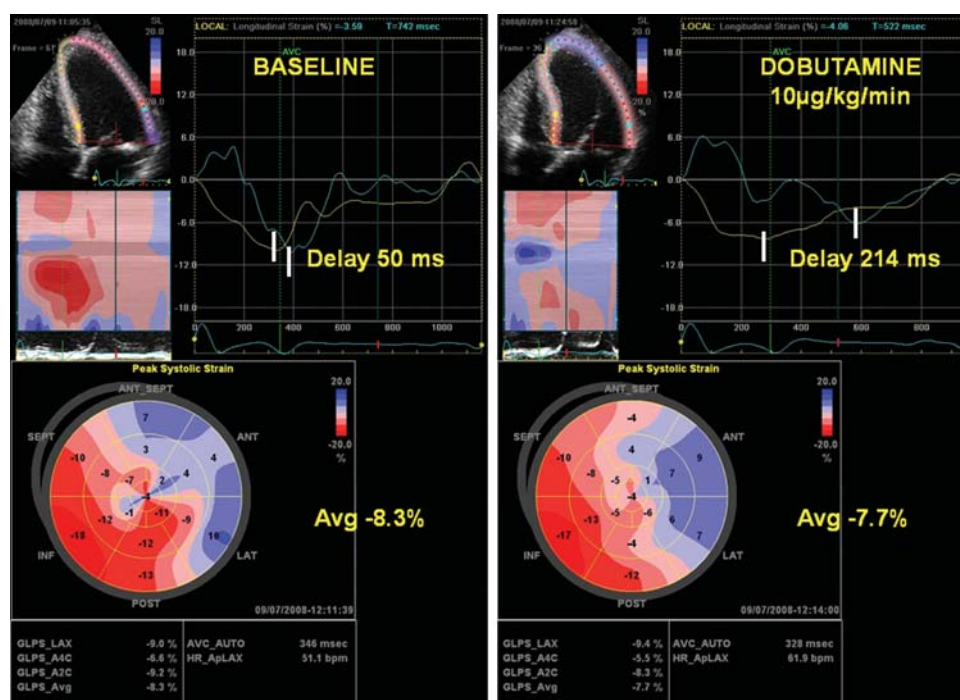


Figure 2 (Top) Apical four-chamber view showing peak longitudinal myocardial strain obtained in the septum and the lateral wall. During dobutamine stress echocardiography, the septal-to-lateral time-to-peak strain increased, indicating dynamic dyssynchrony. (Bottom) Bulls-eye figure of peak systolic strain values in the left ventricle. Red, normal strain values; pink, reduced values; light pink, severely reduced values. The global (Avg, average) myocardial deformation was significantly altered both at rest and during dobutamine stress echocardiography.

evaluated at 13 (E-wave velocity 52 cm/s, E_a mitral annulus velocity by pulsed wave tissue Doppler 4 cm/s). Colour-coded tissue Doppler analysis of basal myocardial velocities

(Figure 1, top) and 2D speckle tracking of myocardial deformation in the apical four-chamber view revealed a septo-lateral dyssynchrony (Figure 2, top). By using automated

function imaging (AFI), a significant impairment of the longitudinal function with a global peak-negative strain of -8.3% (Figure 2, bottom) was revealed. During graded dobutamine infusion, the aortic valve area remained fairly unchanged (0.91 cm^2 , $0.51 \text{ cm}^2/\text{m}^2$), whereas the outflow tract time velocity progressively decreased and reached 16.5 cm at peak dose (mean aortic pressure gradient 20 mmHg), indicating the absence of contractile reserve and the undetermined severity of AS. The global longitudinal strain by using the AFI declined during test, whereas E/E_a remained stable. Surprisingly, the basal septal-to-lateral delay increased significantly from rest to peak test, suggesting that dynamic dyssynchrony could potentially attenuate the stroke volume adaptation during DSE. Taking into account these data, the decision was to refer first the patient to a biventricular pacing implantation and reevaluate the AS severity under stimulation. However, the patient refused and left the hospital. A few weeks later, he came back for severe heart failure and an urgent surgery was performed. The hospital stay was quite long and complicated by acute renal failure and pulmonary sepsis. One month after surgery, he left the hospital alive. The LV ejection fraction was improved (42%). To date, he is in NYHA class II.

Discussion

This case revealed the paradigm in the assessment of low-flow, low-gradient AS by DSE. Indeed, the failure to elicit significant increase in forward stroke volume—absence of contractile reserve—during dobutamine infusion could be related to several findings such as the presence of dynamic LV dyssynchrony.

Low-flow, low-gradient aortic stenosis and stress testing

Patients with severe AS and reduced LV ejection fraction have a poor prognosis with medical treatment and a high operative risk.^{1–5} In this situation, DSE provides operative risk stratification and is a strong predictor of peri-operative mortality.^{2,6–8} Thus, it can determine the absence or the presence of contractile reserve.^{4,7,8} Patients with a contractile reserve have an acceptable operative risk (5%)⁶ with a good long-term prognosis, and valve replacement may improve long-term survival and functional status. Surgery may thus be recommended in most of these patients. Patients without contractile reserve have a high operative mortality (32%).^{5,6} These patients may have LV function irreversibly damaged by previous myocardial infarction and extensive myocardial fibrosis³; therefore, aortic valve replacement is less beneficial. However, surgery should not be denied solely on the absence of contractile reserve because such a DSE response does not predict the lack of LV ejection fraction improvement after operation.⁹ In a recent study of Quéré *et al.*,⁹ 65% of their patients without pre-operative contractile reserve on DSE and who survived after aortic valve replacement obtained $\geq 10\%$ improvement of LV ejection fraction during follow-up. Moreover, 90% of these patients obtained improved clinical status. Nevertheless, patients with LV dysfunction due to primary cardiomyopathy, with only moderate AS, may probably not benefit from valve surgery.^{1,4,5}

Dobutamine stress echocardiography and left ventricular dyssynchrony

Regional function and LV contractility can be evaluated non-invasively by measuring myocardial strain or deformation. The utility of stress echocardiography may be improved by tissue Doppler analysis.¹⁰ Changes in pre-load and afterload are important determinants of myocardial deformation. Chattopadhyay *et al.*¹¹ have shown that in patients with LV dysfunction, the prevalence and severity of dyssynchrony increases during pharmacological stress. Lancellotti *et al.*¹² have distinguished three groups of changes in dyssynchrony with exercise: patients without difference between rest and exercise, patients with dyssynchrony at rest that normalized at exercise, patients without dyssynchrony at rest that appeared at exercise. Cardiac resynchronization may not improve LV dyssynchrony in patients in whom LV dyssynchrony disappears at stress¹² in contrast to those in which stress increases LV dyssynchrony. Valzania *et al.*¹³ have shown that cardiac resynchronization-induced improvement of LV synchronicity is also maintained during stress in responders to resynchronization.

Relation between aortic stenosis and left ventricular dyssynchrony

A subset of patients with low-gradient AS and a small valve area may have not true severe, fixed AS but a concomitant cardiomyopathy associated with only mild-to-moderate AS.⁴ Dobutamine stress echocardiography is thus useful to distinguish between severe and relative AS.^{1,6,14} However, such a distinction is basically based upon the presence of a contractile reserve defined by a $>20\%$ dobutamine increase in forward stroke volume. Conversely, the absence of contractile flow recruitment characterized patients with an undetermined severity of AS. The failure to elicit significant increase in forward stroke volume during dobutamine infusion could be related to several findings: severely diseased LV, afterload mismatch, and (as demonstrated for the first time in our case) dynamic LV dyssynchrony. These factors may, however, interact to varying degrees. For instance, in this case, the global myocardial deformation was significantly altered both at rest and during DSE, suggesting that the cause of LV dysfunction was probably linked to irreversible myocardial dysfunction due to fibrosis and ischaemic cardiomyopathy. In this situation, although debated, it may have been possible that the presence of even moderate aortic valve obstruction may have created a certain degree of afterload mismatch sufficient to alter the LV function and preclude contractile recruitment during DSE.^{15,16} However, in the present case, the LV function improved significantly after aortic valve replacement, indicating the absence of an extensive myocardial fibrosis process. The explanted valve was severely calcified and the surgeon reported a severe AS. Furthermore, in the presence of fixed AS, the possibility offers to the LV to recruit function and increase transvalvular flow under dobutamine infusion may be exhausted by excessive afterload mismatch. Moreover, the dynamic increase in LV dyssynchrony—delayed electromechanical coupling of the LV walls—during DSE may also limit the pumping ability of the LV, resulting in a blunted rise in forward stroke volume and cardiac output.¹⁷ Such a dynamic LV dyssynchrony might thus be a marker of excessive afterload mismatch and additively attenuate the

extent of contractile reserve. In heart failure patients, dynamic LV dyssynchrony has been shown to be inversely correlated with stroke volumes changes during exercise and proportionally related to dynamic mitral regurgitation.¹² Unfortunately, such a dynamic behaviour of mitral regurgitation was not assessed in the present case.

Conclusion

In the presence of fixed AS, excessive afterload mismatch can be associated with dynamic increase in LV dyssynchrony, which in turn could attenuate the stroke volume response to dobutamine infusion. In other words, in patients with low-flow, low-gradient and an undetermined severity of AS, the presence of dynamic LV dyssynchrony could be a potential cause of no contractile reserve. As in the present case the LV function improved after aortic valve replacement, it might be argued that dynamic LV dyssynchrony might identify a subset of patients with low-gradient AS who might benefit from aortic valve surgery.

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