

Stress echocardiography in valvular heart disease: indications and results

Echocardiographie de stress dans les valvulopathies: indications et résultats

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SUMMARY

Introduction: Valvulopathies represent one of the main cardiac diseases around the world. It can present with diagnostic challenges due to their dynamic nature. Stress echocardiography has emerged as a valuable imaging tool in the evaluation of valvular heart diseases, giving insight into the dynamic changes of valvular function and hemodynamics. The aim of our study was to describe the indications and results of stress echocardiography in valvular heart disease.

Methods: We conducted a monocentric retrospective descriptive study including patients with valvular heart disease who underwent stress echocardiography between 2004 and 2022 at the cardiology department of Habib Thameur Hospital.

Results: Our study included 39 patients with a mean age was of $56 \pm 9,5$ years with a gender ratio of 0,69. Hypertension was the most frequently associated cardiovascular risk factors observed in 8 patients (32,1%). Rheumatic fever was observed in 5 patients 3 of which had mitral stenosis.

Exercise echocardiography was done in 20 patients (51,3%) and Dobutamine stress echo in 19 (48,7%). Exercise echocardiography was indicated in 15 patients (75%) with mitral stenosis. Dobutamine stress echocardiography was done in 16 patients (84%) with aortic stenosis. Mean Dobutamine dose used during stress echocardiography was $13,5 \pm 8$ gamma/kg/min. Stress echocardiography was indicated in 16 patients (41%) with low flow low gradient aortic stenosis followed by 15 patients (38%) presenting with an asymptomatic severe mitral stenosis. Exercise echocardiography was positive in 56% of patients with mitral stenosis with a mean increase in mean mitral valve gradient of 9,5 mmHg and SAP of 21 mmHg. Dobutamine stress echocardiography was positive in 50% of cases, revealing a true severe aortic stenosis, with a mean increase in mean aortic valve gradient of 11 mmHg moving from 33 to 44 mmHg after the test.

Conclusion: Stress echocardiography is a helpful tool complementing resting echocardiography in valvular heart disease.

KEYWORDS

stress echocardiography; valvular heart disease

RÉSUMÉ

Introduction : Les valvulopathies représentent l'une des principales maladies cardiaques dans le monde. Elles peuvent présenter des défis de diagnostic en raison de leur nature dynamique. L'échocardiographie de stress est devenue un outil d'imagerie précieuse dans l'évaluation des valvulopathies.

Objectif : Le but de notre étude était de décrire les indications et les résultats de l'échocardiographie de stress dans les valvulopathies.

Méthodes : Nous avons mené une étude descriptive rétrospective monocentrique incluant des patients atteints de valvulopathies ayant bénéficié d'une échocardiographie de stress entre 2004 et 2022 au service de cardiologie de l'hôpital Habib Thameur.

Résultats : Notre étude a inclus 39 patients d'un âge moyen de $56 \pm 9,5$ ans avec un sex-ratio de 0,69. L'hypertension était le facteur de risque cardiovasculaire le plus fréquemment retrouvé (32,1 %). Un rhumatisme articulaire aigu a été observé chez 5 patients dont 3 avaient une sténose mitrale.

Une échocardiographie d'effort a été réalisée chez 51,3 % et une échocardiographie d'effort à la Dobutamine chez 48,7 %. L'échocardiographie d'effort était indiquée chez 15 patients (75 %) présentant une sténose mitrale. Une échocardiographie à la dobutamine a été réalisée chez 16 patients (84 %) présentant une sténose aortique. La dose moyenne de dobutamine utilisée était de $13,5 \pm 8$ gamma/kg/min. L'échocardiographie d'effort a été indiquée chez 16 patients (41 %) présentant une sténose aortique à bas débit bas gradient, suivie de 15 patients (38 %) présentant une sténose mitrale sévère asymptomatique. L'échocardiographie d'effort était positive chez 56 % des patients présentant une sténose mitrale avec une augmentation moyenne du gradient valvulaire mitral moyen de 9,5 mmHg et du SAP de 21 mmHg. L'échocardiographie d'effort à la dobutamine était positive dans 50 % des cas, révélant une véritable sténose aortique sévère, avec une augmentation moyenne du gradient valvulaire aortique moyen de 11 mmHg passant de 33 à 44 mmHg après l'examen.

Conclusion : L'échocardiographie de stress est un outil complémentaire utile en complément de l'échocardiographie de repos dans les cardiopathies valvulaires

MOTS-CLÉS

Échocardiographie de Stress — Valvulopathie

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INTRODUCTION

Valvular heart disease (VHD) is an increasing problem both as a consequence of the aging population and as the result of other heart diseases. Resting Doppler echocardiography is the first step in diagnosing VHD and assessing its severity. However, there is growing recognition that assessment of heart valve disease in a resting state provides an incomplete evaluation of valve hemodynamics as the severity of valve obstruction and regurgitation is dynamic(1).

Stress echocardiography is a valuable tool in the assessment of patients with valvular heart disease(2–4). It provides a quantitative assessment to help guide clinical decision-making when there is a mismatch between symptoms and severity of valve disease. Stress echocardiography can be especially helpful in patients with slowly progressive valvular heart disease, which can result in gradual unintentional adaptations including reduction in functional capacity and a sedentary lifestyle. In this context, stress echocardiography can objectively assess exercise capacity and determine whether reported dyspnea and reduced exercise tolerance are related to valvular heart disease(5). The aim of this article was to study the indications and results of stress echocardiography in valvular heart disease.

METHODS

Study population

This was a retrospective, descriptive, monocentric study, conducted between 2004 and 2022 in the Cardiology Department of Habib Thameur Hospital, Tunis, Tunisia.

We included all patients who had stress echocardiography in the context of a valvular heart disease.

Patients who underwent stress echocardiography for other indications were not included. We excluded patients whose stress echocardiography reports were not exploitable.

Data retrieval

Data were collected from inpatient and outpatient medical files:

Clinical data: Age, gender, cardiovascular risk factors,

medical history, indication for stress echocardiography.

Stress echocardiography related data: Beta blocker discontinuation, resting heart frequency, heart frequency at peak exercise, symptoms, Dobutamine dose, Atropine injection, mean mitral valve gradients, mean aortic valve gradients, systolic pulmonary artery pressure (SAP), aortic valve orifice surface, mitral valve orifice surface, tricuspid regurgitation, left ventricular ejection fraction (LVEF).

Echocardiographic evaluation

Two dimensional transthoracic echocardiographic and Doppler studies were performed by qualified experienced operators using an ALT HDI between 2004 and 2012 and a Vivid E9 starting from 2013.

Patients were monitored for blood pressure, heart frequency and had EKG at the start and end of the test.

Stress echocardiography was done using either a bicycle ergometer or Dobutamine infusion.

During bicycle ergometer exercise echocardiography, the patient pedals against an increasing workload at a constant cadence. Each load takes 2 to 3 minutes before a 25 watts increase.

Dobutamine stress echocardiography requires the continuous administration of dobutamine through a peripheral venous access starting at low doses (5 gamma/kg/min) with an increment of 5 gamma each 3 minutes.

In the absence of chronotropic response despite reaching full doses of Dobutamine (generally at 40 gamma/kg/min), coadministration of atropine is indicated.

Positivity criteria

They were analyzed based on the VHD and the 2021 ESC recommendations on valvular heart disease and the 2017 guidelines issued by the American society of echocardiography (6,7).

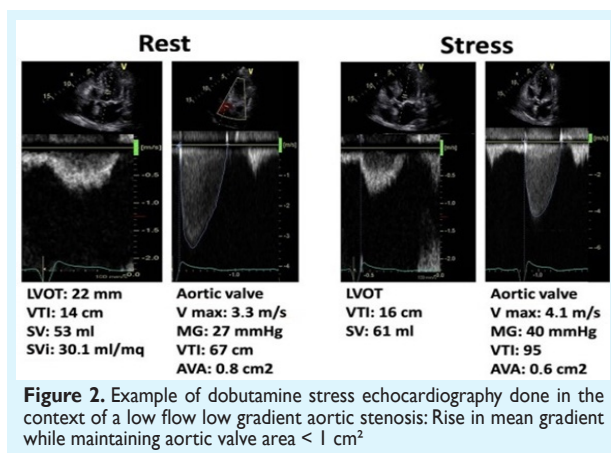
Aortic stenosis

In asymptomatic patients with severe aortic stenosis, exercise echocardiography is recommended to unmask symptoms in these patients who tend to limit their level of activity to adapt to the progression of valve disease. A fall in systolic blood pressure (≥ 20 mmHg in ACC/AHA and > 20 mmHg in ESC) and decreased exercise tolerance should also be noted.

In patients with low flow low gradient severe aortic stenosis with reduced ejection fraction (mean gradient < 40 mmHg, valve area ≤ 1 cm², LVEF $< 50\%$, stroke volume index ≤ 35 mL/m²), low dose dobutamine stress echocardiography is indicated to distinguish between true severe aortic stenosis, that caused the LV dysfunction, and pseudo-severe aortic stenosis (increase in valve area with the increased flow)(6,7).

Degree of stenosis	Contractile reserve	Mean gradient	Area valve evolution
Severe	Present	Increase	Stable
Pseudo-severe	Present	Stable	Increase
Indeterminate	Absent	Stable	Non modified

Figure 1. Results of dobutamine stress echocardiography in low flow low gradient aortic stenosis



Mitral stenosis

In cases when there is a discrepancy between resting echo results and clinical symptoms, exercise stress echocardiography is recommended to evaluate symptomatic response, exercise capacity, and the evolution of the mean mitral valve gradient and pulmonary artery pressure. The test is considered positive when there is an increase in mean mitral valve gradient ≥ 15 mmHg or SAP ≥ 60 mmHg. In patients unable to conduct an exercise, high dose dobutamine stress echocardiography is an alternative. The test is positive if there is an increase in mean mitral valve gradient ≥ 18 mmHg.

In symptomatic patients with moderate mitral stenosis ($\geq 1,5$ cm²), exercise stress echocardiography is also indicated. The positivity criteria are the same(6,7).

Aortic regurgitation

Exercise stress echocardiography in the context of aortic regurgitation is proposed as an aiding tool in 2 specific situations: Severe AR with no symptoms and non-severe AR with symptoms.

The aim of the test is to reveal symptoms during exercise. It also provides LV contractile reserve assessment (7).

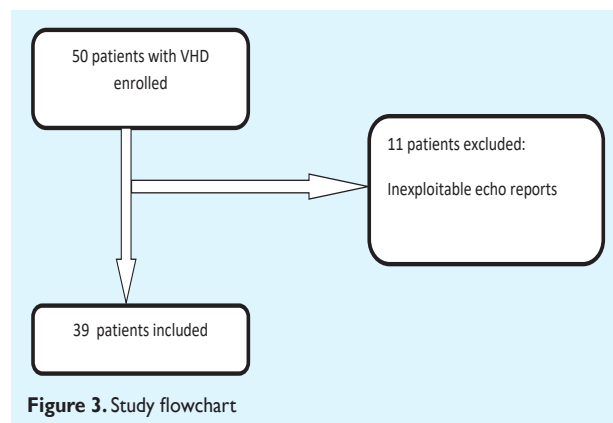
Mitral regurgitation

In asymptomatic patients with severe mitral regurgitation, exercise stress echocardiography is used to provoke symptoms.

In non-severe mitral regurgitation symptomatic patients, the test is considered positive if there is an increase in MR severity (≥ 1 grade), dynamic pulmonary hypertension (SAP ≥ 60 mmHg) and the absence of contractile reserve ($< 5\%$ increase in LVEF or $< 2\%$ increment in global longitudinal strain).

In secondary mitral regurgitation, an increase in effective regurgitant orifice area ≥ 13 mm² and SAP ≥ 60 mmHg conclude to the positivity of the test (7).

A total of 39 patients were included in this study as shown in figure 3.



The mean age of the study population was $56,4 \pm 9,5$ years old [38-75 years old]. The population was predominantly female representing 59% with a gender ratio of 0,69. Fifty percent had no cardiovascular risk factors whereas 22% had 2 and more.

Arterial hypertension was the most frequent cardiovascular risk factor observed in 8 patients (32,1%), followed by smoking (29,6%), diabetes mellitus (21,4%) and coronary artery disease (7,1%)

Five patients had a history of rheumatic fever; of which 3 had mitral stenosis.

Exercise echocardiography was done in 20 patients (51,3%) and Dobutamine stress echo was done in 19 (48,7%).

The repartition of valvulopathies according to the type of stress echo performed is shown in figure 4.

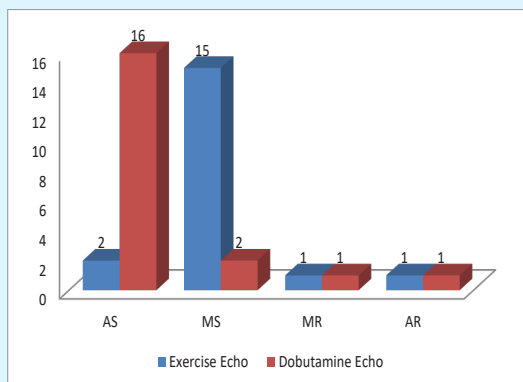


Figure 3. The repartition of valvulopathies according to the type of stress echocardiography performed

(AS: Aortic stenosis; MS: Mitral stenosis; MR: Mitral regurgitation; AR: Aortic regurgitation)

The main indication for SE was low flow low gradient aortic stenosis followed by discrepancies in clinical and echocardiographic findings.

The distribution is shown in the figure 5.

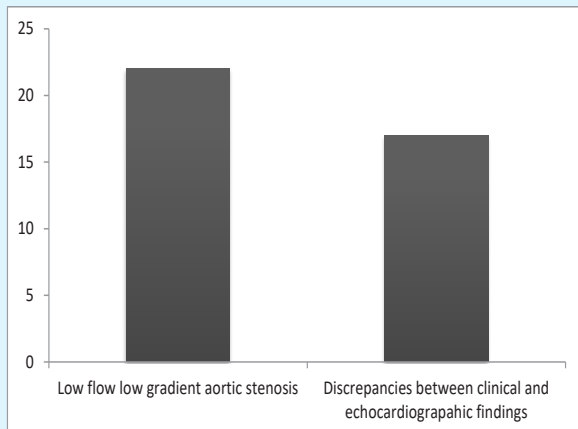


Figure 3. Indications for stress echocardiography

Mean Dobutamine dose used during stress echocardiography was $13,5 \pm 8$ gamma/kg/min with a minimum of 5 and a maximum of 30 leading to a mean heart rhythm of $102 \pm 26,8$ bpm [67-165].

Atropine was used in 25% of Dobutamine stress echocardiography in cases when wanted chronotropic response was not reached after high doses of Dobutamine.

Mitral stenosis

Seventeen patients with MS underwent SE. Mean age was $49 \pm 5,6$ years. The mean SAP before exercise was $34 \pm 9,1$ mmHg with a minimum of 15 and a maximum of 50 mmHg and the mean SAP during the stress test was $57 \pm 8,9$ mmHg [30 – 79 mmHg].

Mean mitral valve area was $1,6 \pm 0,3$ cm² with a minimum of 1,1 and a maximum of 2,4 cm²

Mitral valve mean gradient before exercise was $7,1 \pm 2,4$ mmHg [4-11]. After exercise mean gradient increased to $16,6 \pm 5,6$ mmHg with a minimum of 8 and a maximum of 26 mmHg.

There was a mean increase in SAP of 21 mmHg and 9,5 mmHg in mean mitral valve gradient.

Exercise echocardiography was considered positive in 9 patients (56%), negative in 4 patients (25%) and not conclusive in 4 patients.

A total of 6 patients had Mitral Balloon Commissurotomy (MBV). Two patients had implantation of mechanical valve. The other was treated medically with annual echocardiographic control.

Aortic stenosis

Eighteen patients with AS underwent SE. The mean age was $63 \pm 6,9$ years old.

Stress echocardiography was indicated in low flow low gradient state in 14 cases (77%) and in 4 cases of asymptomatic severe aortic stenosis.

Mean LVEF was $34,3\% \pm 9,7$ [20-60%].

Mean aortic valve gradient before the test was $33 \pm 7,3$ mmHg with a minimum of 20 and a maximum of 50 mmHg, while, after the test, it was $44,8 \pm 9,6$ [30-69 mmHg].

Mean aortic valve area was $0,73$ cm² $\pm 0,2$ with a minimum of 0,35 and a maximum of 1 cm²

There was a mean increase in mean aortic valve gradient of 11 mmHg.

In cases when Dobutamine stress echocardiography was indicated in low flow low gradient cases, contractile reserve was found in 13 cases (81%): True severe aortic stenosis was found in 8 cases (50%), pseudo-severe AS in 3 cases (19%) and indeterminate low flow low gradient AS in 5 cases (31%)

Exercise echocardiography was performed in 2 cases of asymptomatic severe AS; One patient developed symptoms and the other remained symptom free.

Surgical aortic valve replacement was performed in 8 patients (89%). The other case was treated medically due to high surgical risk.

Aortic regurgitation

Two patients with aortic regurgitation were referred for stress echocardiography. Their mean age was 41,5 years old [38-45 years old].

The first patient had an asymptomatic severe aortic regurgitation and LVEF of 60%. There was an increase in SAP from 15 mmHg before exercise to 45 at peak exercise. Patient developed shortness of breath and the exam was considered positive. The patient was referred for surgical repair.

The second had a severe aortic regurgitation with LVEF of 20% and had Dobutamine stress echocardiography in search of contractile reserve. SE found no contractile reserve.

Mitral regurgitation

Two patients with mitral regurgitation had a stress echocardiography. Their mean age was 61,5 years old [59-64 years old].

The first patient had an asymptomatic severe mitral regurgitation, a LVEF of 64% and a moderate tricuspid regurgitation estimating base SAP at 30 mmHg. The exam was positive: patient developed symptoms and there was an increase in SAP at peak exercise (70 mmHg).

The other patient had a reduced LVEF at 35%. He had akinesia in inferior walls and severe eccentric ischemic mitral regurgitation. The exam was performed in search of viability in inferior walls in view of revascularization. The test came negative.

DISCUSSION

Stress echocardiography has been shown to increase diagnostic accuracy in several valvulopathies and helps determine the opportune moment of intervention and predicts the post operative outcome in valvular heart disease.

The aim of this article was to study the indications and results of stress echocardiography in valvular heart disease.

We conducted a retrospective, descriptive, monocentric study, between 2004 and 2022 in the Cardiology Department of Habib Thameur Hospital, Tunis, Tunisia that included 39 patients with valvular heart disease.

The study showed that our population was predominantly females, having a mean age of 56 years old.

Mitral and aortic stenosis were the main valvulopathies explored by stress echocardiography.

In case of mitral stenosis, exercise echocardiography was the method of choice. Discrepancies between clinical and resting echocardiographic data were the main indication for stress echocardiography.

The exam was positive in 56% of cases; There was a mean increase of 21 mmHg in SAP and 9,5 mmHg in mean mitral valve gradient.

In case of aortic stenosis, Dobutamine stress echocardiography was the preferred method. The exam was done mainly in low flow low gradient states (77%). Mean LVEF was 34%

The exam was positive in half of the cases. There was a mean increase in mean aortic valve gradient of 11 mmHg.

RESULTS

The average age of our population was 63 ± 10 years with extremes of 41 to 88 years. A male predominance was noted: 49 male patients (87.5%) and 7 female patients (12.5%), with a sex ratio of 7. Diabetes and smoking were the most common risk factors (71% and 70%, respectively). Ischemic heart disease was the most frequent underlying heart disease (43%) while 21% of heart diseases were of undetermined origin.

The baseline characteristics of the study population are reported in (Table I).

Mitral stenosis

Stress echocardiography in the context of mitral stenosis is usually done when there is a discordance between clinical symptoms and the degree of MS at resting echocardiography.(8)

This was the case in our study.

The mitral valve and the transmitral gradient are dynamic. Exercise, by increasing the heart rate, leads to a shortening of the diastolic filling time, which increases the transmitral gradient and consequently leads to an increase in left atrial pressure and pulmonary capillary pressure.

These changes explain why symptoms may occur during exercise in cases of moderate mitral stenosis.

These data align with our study that showed an increase in mean mitral valve gradient and development of dyspnea at peak exercise.

Another hemodynamic reason for the onset of symptoms at exercise is the development of pulmonary hypertension leading to secondary afterload on the right ventricle. In most patients, the increase in pulmonary artery pressure is passive, secondary to left atrial elevated pressure without a change in pulmonary vascular resistance. In 10% to 15% of patients with severe mitral stenosis, there is an increase in pulmonary arteriolar resistance and pulmonary artery pressure. This rise in pulmonary artery pressure creates a burden on the right ventricle, resulting in right ventricular hypertrophy, dilation, and eventually failure. Thus, the patient develops shortness of breath and complains of decreased exercise tolerance.(9)

Our study showed an increase in SAP at peak exercise comparing to resting values.

Grimaldi et al(10) demonstrated the usefulness of exercise stress echocardiography in patients with moderate mitral stenosis. In symptomatic patients with moderate stenosis, 35 (76%) had dyspnoea. This was associated with an increase in mean transmitral gradient above 15 mmHg or systolic pulmonary artery pressures above 60 mmHg.

Aortic stenosis

Aortic stenosis is a disease that affects older patients comparing to mitral stenosis. One study showed that aortic sclerosis is a progressive state that starts at the 60s and become clinically relevant at the 70s.

Our study showed a mean age of 68 years in patients with aortic stenosis.

Forty per cent of patients with severe aortic stenosis are asymptomatic at the time of diagnosis, but the majority of these patients are elderly subjects who tend to limit their activity. The role of DSE is to reveal this limitation.

Exercise stress echocardiography is more physiological. In asymptomatic severe AS patients, exercise stress echocardiography is recommended, whereas Dobutamine echocardiography is the test of choice in patients with low-gradient with reduced ejection fraction.(11)

In asymptomatic patients with moderate or severe AS, a significant exercise-induced rise in mean aortic valve gradient can result in an elevated risk of unfavorable

events (including development of symptoms, cardiac death or necessity of aortic valve replacement). An increase >20 mmHg is considered pathological.(12,13)

The timing of intervention in asymptomatic severe aortic stenosis is controversial. The natural history is highly variable, with an estimated risk of sudden death of 1-1.5% per year (14-16). Regular clinical and echographic monitoring every 6 months is currently recommended.

Studies have shown that stress echocardiography is safe in this population and provides prognostic information.(17-19)

Lancelotti et al (20) found an increase in pulmonary artery pressure during exercise in 55% of patients with severe asymptomatic aortic stenosis. This association increases the risk of cardiac events by a factor of 2.

An inadequate response of the LV to exercise (a fall and/or modest rise in LVEF during exercise) is associated with a progression towards the development of symptoms in the short and midterm, with a greater risk of major cardiac events than those with an adequate response(13).

Low flow low gradient aortic stenosis: when the EF is low, it is important to distinguish between true aortic stenosis with low flow and pseudo-severe aortic stenosis (moderate aortic stenosis with low flow related to a myocardium disease responsible for incomplete opening of the aortic sigmoid)(21,22)

There is a third outcome of dobutamine stress echocardiography: Stable mean gradient with a stable aortic valve area. A new parameter, deduced from the dobutamine test, has recently been described to best assess the degree of these low-gradient aortic stenoses called projected valve area: extrapolating the area for a normal level of transvalvular flow (250 mL/s). Studies have shown a good correlation with the degree of severity of aortic stenosis and an indicator of prognosis(23).

In a multicentre French study (24) of 217 patients with severe aortic stenosis, LVEF < 35% and low gradient (< 30 mmHg) who underwent aortic valve replacement, mortality was 16% overall. The absence of contractile reserve at dobutamine stress echocardiography was a strong predictor of perioperative mortality, reaching 30%. In contrast, in patients with contractile reserve, perioperative mortality was only 5-8%.

Aortic regurgitation

Stress echocardiography has no role in assessing the severity of an aortic regurgitation, but it does provide information on the contractile reserve and functional tolerance of patients. It is even debatable whether this test should be performed in search of contractile reserve.

The absence of contractile reserve was predictive of the development of LV dysfunction in medically treated patients and in postoperative patients who had undergone valve replacement (25).

The absence of an increase in LVEF during exercise is associated with an increased risk of LV dysfunction, onset of symptoms and sudden death(26). The search for contractile reserve can therefore determine the ideal time for intervention in asymptomatic patients with severe aortic leakage.

In our study, the test was done to detect contractile reserve in order to guide treatment strategy.

Mitral regurgitation

Stress echocardiography, ideally during exercise, can be indicated in patients with chronic MR with clinical and echocardiographic discrepancy. Studies have shown that 20 to 30% of pauci-symptomatic patients with significant MR have reduced functional capacity. These patients are at increased risk of cardiovascular events and mortality in the absence of early surgical intervention(27–29).

The ESC and ACC/AHA recommend the use of stress echocardiography when there is a clinico-echographic discordance in class IIa. The ESC also recommends its use to quantify changes in the grade of mitral regurgitation, pulmonary pressures and LV function during exercise. A stress SAP >60 mm Hg has a prognostic value and predicts necessity of intervention in asymptomatic patients with severe MR(6).

For patients who do not meet the operability criteria, the ACC/AHA recommend stress echocardiography to assess exercise tolerance in these patients and to serve as a reference for future assessments(30).

VD function has also gained in interest in MR and has a prognostic impact. A reduction in exercise TAPSE (<19 mm) was correlated with early surgical intervention in patients with severe asymptomatic MR(31).

Secondary MR is a dynamic condition in which

the degree of mitral regurgitation at rest does not necessarily reflect it during exercise.

The exercise-induced increase or decrease in MR grade appears to be related to local LV remodelling and mitral valve deformation and not to changes in overall left ventricular function. Similarly, changes in regurgitant orifice area were not related to the severity of ischaemic MR at rest or to the severity of left ventricular dysfunction.

Dobutamine stress echocardiography studies myocardial viability and helps estimate contractile reserve in patients with ischemic MR, the presence of which indicates a benefit of myocardial revascularization therapy(28).

CONCLUSION

Stress echocardiography remains one of the established diagnostic tools for the assessment of valvular heart disease. Our study showed that the main two indications for stress echocardiography in valvular heart disease are low flow low gradient aortic stenosis and asymptomatic severe mitral stenosis; Stress echocardiography helps guide the optimal treatment strategy in both cases. However, in regurgitant valvulopathies, its role is questionable and more studies involving larger populations are necessary to help understand their utility in these cases.

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