CASE PRESENTATION

Secondary ischemic mitral regurgitation in a young patient – therapeutic approach

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Abstract: Secondary ischemic mitral regurgitation (MR) is becoming increasingly frequent nowadays, as ischemic heart disease is more prevalent than before, even at young ages. We present the case of a 33-year-old patient with ischemic heart disease and secondary ischemic MR, whose management plan was established by a Heart Team including cardiologists, interventional cardiologist and cardiac surgeon. Optimal medical therapy and percutaneous myocardial revascularization were the chosen treatment options, with relief of symptoms and mild improvement of MR. Taking into consideration that there is no clear evidence of a certain advantage from a mitral valve intervention in this setting, the chosen strategy in this case was close follow-up of the patient. In conclusion, secondary MR needs to be carefully evaluated; until new studies and evidences emerge regarding the optimal treatment, every case requires a personalized plan of management.
Keywords: ischemic mitral regurgitation, ischemic heart disease.

Rezumat: Regurgitarea mitrală secundară ischemică devine din ce în ce mai frecventă în prezent, în condițiile în care boala cardiacă ischemică este din ce în ce mai des întâlnită, chiar și la pacienți tineri. Prezentăm cazul unui pacient în vârstă de 33 ani, cu boală cardiacă ischemică și regurgitare mitrală secundară ischemică, al cărui plan terapeutic a fost stabilit de către o echipă multidisciplinară, formată din cardiologi, cardiologi intervenționiști și chirurgi cardiovasculari. Terapia medicamentoasă optimă și revascularizarea micocardică percutană au fost opțiunile terapeutice alese, cu ameliorarea simptomatologiei și scăderea ușoară a gradului regurgitării mitrale. Luând în considerare faptul că nu există la momentul actual dovezi clare referitoare la beneficiul adus de corecția regurgitării mitrale secundare, strategia terapeutică aleasă a fost, în acest caz, monitorizarea atentă a pacientului. În concluzie, regurgitarea mitrală secundară ischemică necesită o evaluare comprehensivă; până la apariția unor noi studii și dovezi privind managementul optim, fiecare caz necesită un plan terapeutic personalizat.
Cuvinte cheie: regurgitare mitrală secundară, boală cardiacă ischemică.

INTRODUCTION

Mitral valve regurgitation (MR) represents nowadays almost one third of the acquired left-sided valve pathology in developed countries. The main classification of MR is primary and secondary[1]. Secondary MR, also known as functional MR, occurs when the valve leaflets and chordae are structurally normal, but leaflet coaptation is restricted by abnormal alterations in left ventricle (LV) geometry[2]. An increasingly frequent cause of secondary MR is ischemic heart disease; chronic functional ischemic MR represents a true challenge concerning diagnosis and management.[3]

CASE PRESENTATION

A 33-year-old male presented with progressively aggravated dyspnea and unproductive cough on moderate exertion within the last 6 months. He had relevant family history (his father died of myocardial infarction at the age of 51) and his own medical history revealed recently diagnosed arterial hypertension stage II and type 1 insulin-dependent diabetes mellitus with multiple microvascular complications (macroalbuminuria, distal sensory polyneuropathy).

Upon current admission, the clinical examination revealed no pathological signs, except for a grade III/VI

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systolic murmur that was heard with maximum intensity in the mitral area and radiated over the entire precordium. Resting ECG showed sinus rhythm and left ventricular (LV) hypertrophy with left ventricular strain. Laboratory studies revealed mild fasting hyperglycemia, hypertriglyceridemia and a NT-proBNP value of 240 pg/ml. Transthoracic echocardiography showed left ventricular hypertrophy with normal diameters and volumes, with hypokinesia of basal-inferolateral, basal and mid-anterolateral segments and akinesia of basal-inferior interventricular septum and basal- inferior segments. The LV ejection fraction was within normal limits, with longitudinal systolic LV dysfunction and LV diastolic dysfunction (pseudonormal mitral flow). Moderate MR was noted, with posterior mitral leaflet restriction and an eccentric regurgitant jet towards the left atrium posterior wall (Figure 1, Figure 2, Figure 3). The estimated pulmonary artery systolic pressure was 58 mmHg. Coronary angiography was performed, revealing a 40% stenosis of the proximal left anterior descending artery (LAD), 50-60% stenosis of the mid LAD, 80% stenosis of the second obtuse marginal branch (OM2) and hypoplastic, diffusely infiltrated right coronary artery (RCA) (Figure 4). Taking into consideration the LV hypertrophy and the presence of systemic hypertension in a young patient, an abdominal aorta angiography was also performed, including the renal arteries, with no significant lesions found. Stress echocardiography was performed to assess the indication of myocardial revascularization in a patient without angina. It showed worsening of the wall motion abnormalities in the inferior, inferolateral and inferior interventricular septum segments and worsening of MR, with severe MR during exercise. There was also an increase in pulmonary artery systolic pressure, reaching 70 mmHg during the test. Thus, the LAD stenoses were interpreted as haemodynamically nonsignificant and myocardial revascularization was indicated only for the marginal branch. After a Heart Team discussion of the case the first option was percutaneous coronary intervention (PCI) of the OM2. This was performed with a drug-eluting stent

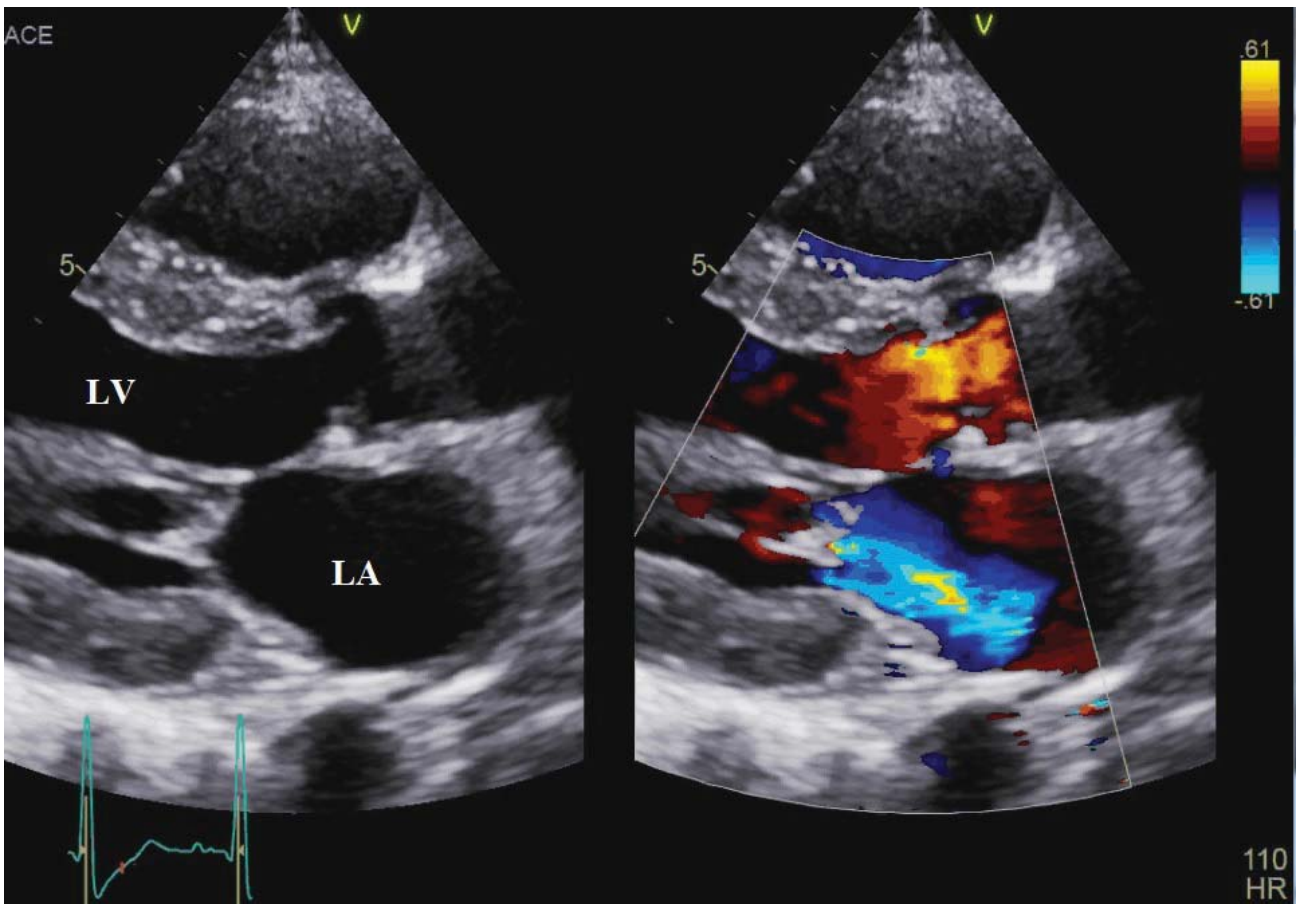

Figure 1. Transthoracic echocardiography, parasternal long axis view, 2D and color Doppler: moderate MR is visible, with posterior mitral cusp restriction and an eccentric regurgitation jet to left atrium posterior wall.

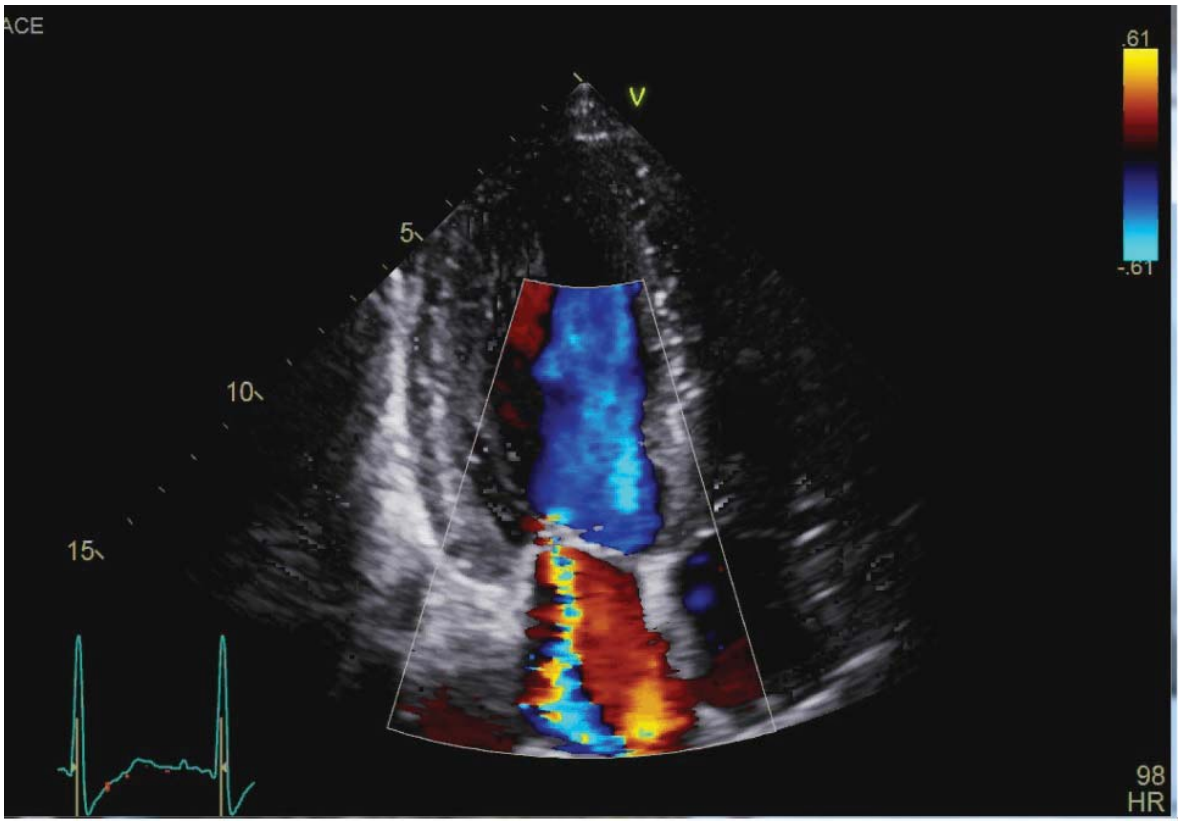

Figure 2. Transthoracic echocardiography, apical four chamber view, color Doppler: visualization of moderate MR with vena contracta of 4 mm.

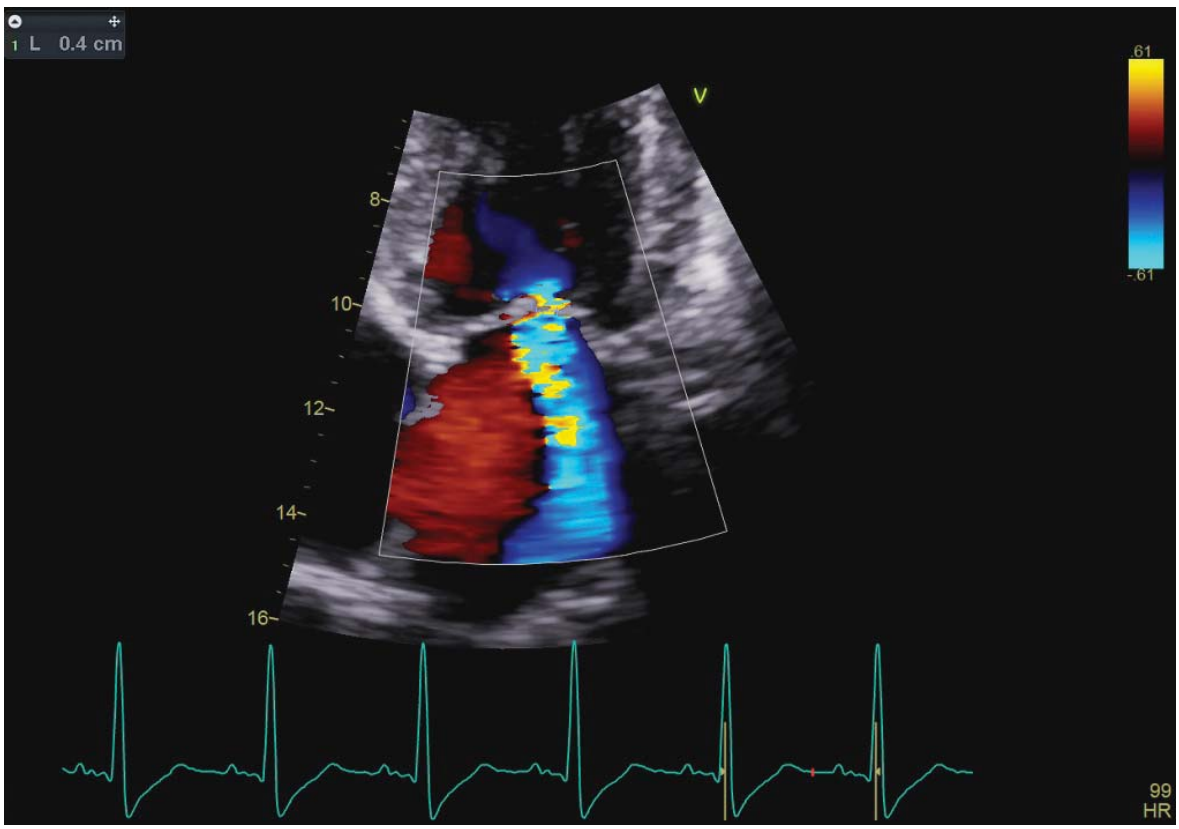

Figure 3. Transthoracic echocardiography, apical three chamber view, color Doppler: eccentric MR jet to left atrium posterior wall is seen.

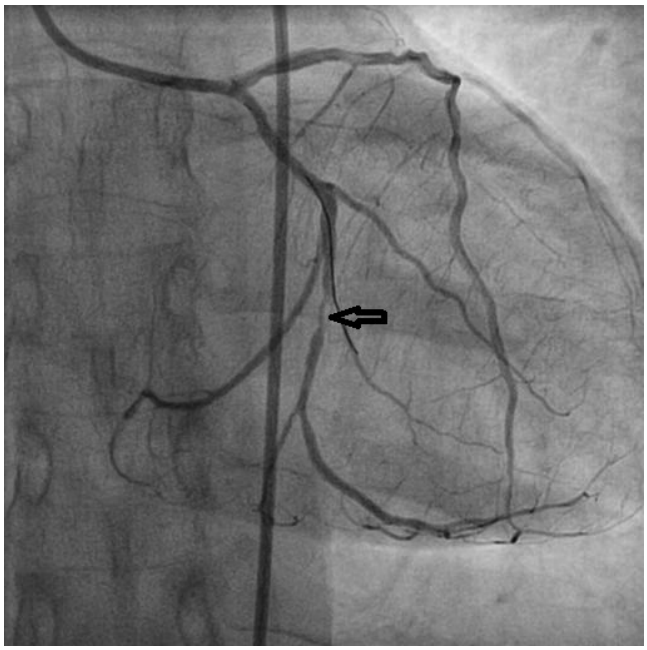

Figure 4. Coronary angiography reveals 40% stenosis of the proximal left anterior descending artery (LAD), 50-60% stenosis of the mid LAD, 80% stenosis of second obtuse marginal branch (arrow).

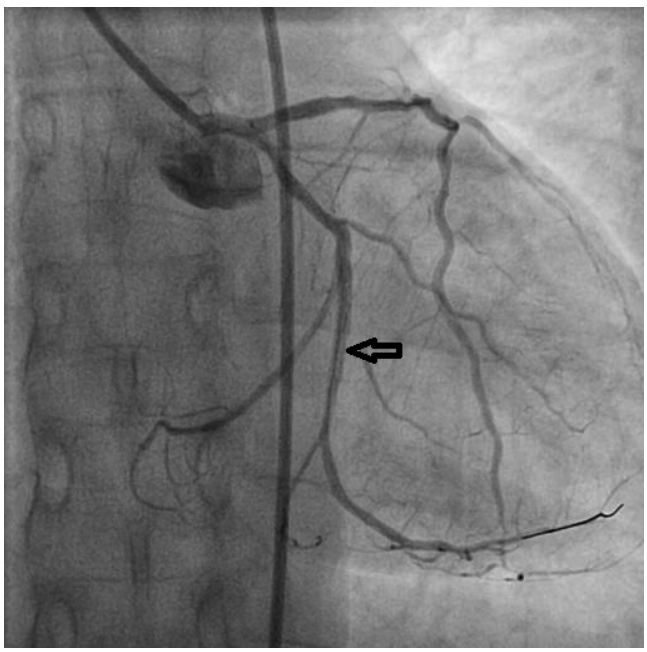

Figure 5. Percutaneous coronary intervention of the second obtuse marginal branch with a drug-eluting stent, with good final result (arrow).

(DES), with good final result (Figure 5). The medical treatment recommended included: beta blocker, angiotensin receptor blocker, diuretic, calcium channel blocker, statin and double antiplatelet therapy (clopidogrel and aspirin).

One month later, the patient described improvement of effort tolerance after angioplasty. A stress echocardiography test was performed, showing no signs of myocardial ischemia, but with the same aspect regarding MR as in the previous evaluation (moderate MR at rest, severe MR at exercise). Considering that the patient was asymptomatic, with normal LV dimensions, normal LV systolic function, improvement of LV kinetics, conservative treatment was decided, with follow up.

Three months later, the patient presented at the Emergency Department for retrosternal chest pain at moderate exertion in the last two weeks, the last episode in the day of admission. Coronary angiography was performed revealing patent OM2 DES, but significant progression of the proximal LAD lesions: 90% stenosis and serial significant stenoses of the mid LAD (Figure 6). Three DE stents were implanted in the proximal and mid-LAD, with optimal procedural result and without complications (Figure 7). Platelet response to aspirin and clopidogrel was tested, with optimal result. A month later, the patient was asymptomatic; transthoracic echocardiography revealed improvement of MR (mild to moderate at rest).

Four months after the last angioplasty, another stress echocardiogram was perfomed, showing new exercise-induced wall abnormalities of the anterior

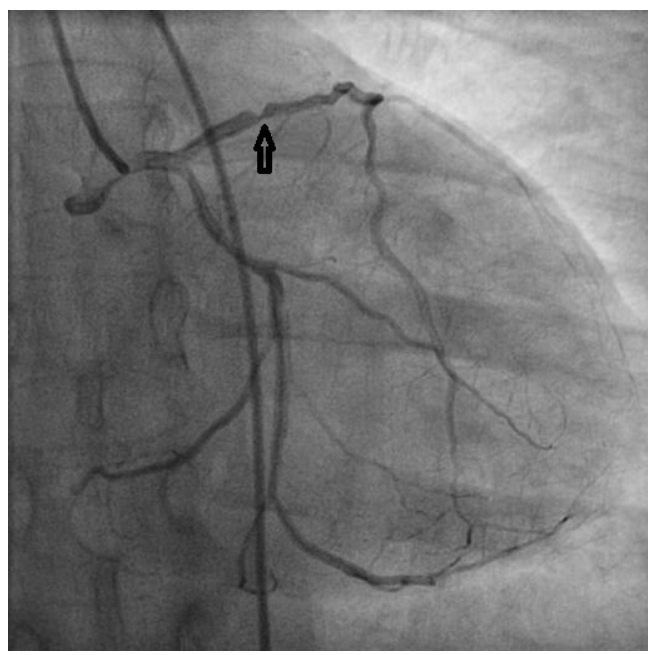

Figure 6. Repeated coronary angiography reveals permeable drug eluting stent on the second obtuse marginal branch, but significant progression of proximal LAD lession- 90% stenosis (arrow) and serial stenoses of the mid LAD.

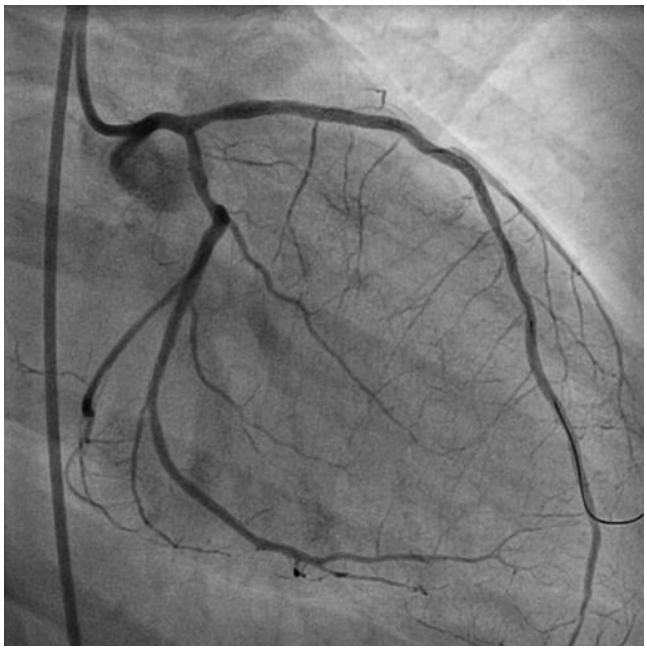

Figure 7. Percutaneous coronary intervention of the proximal and mid LAD with three drug-eluting stents, with good final result.

segments and worsening of MR during exercise (severe). In this context, a third coronary angiography evaluation was considered necessary. No new stenoses were revealed. Therefore, taking into consideration that the patient was asymptomatic, with normal LV dimensions and ejection fraction, normal left atrial volume, optimal medical therapy with aggressive risk factor modification were recommended and close follow-up of the patient.

DISCUSSION

Chronic secondary ischemic MR is the most common subtype of ischemic MR, being characterized by an imbalance between tethering forces and closing forces of the mitral valve, resulting in 95% of the cases from a type IIIb dysfunction (according to Carpentier's types of MR)- restricted systolic leaflet motion[3]. The mechanism of ischemic functional MR has been described in great detail by Levine and Schwammenthal.[4] The papillary muscles, normally parallel to the LV long axis and perpendicular to the leaflets, are displaced by the myocardial segments underlying them in an outward and/or apical direction in ischemic heart disease, restricting leaflet closure in systole. The posterior leaflet is more frequently affected and particularly the posteromedial scallop[4].

A special subgroup of functional MR is represented by those patients who have isolated infero-basal myocardial infarction with consecutive posterior leaflet tethering, but with preserved ejection fraction. In these cases heart failure symptoms can be explained by functional MR alone, and not by LV dysfunction[1].

Echocardiography remains the most important method of diagnosis and evaluation of secondary MR. A comprehensive approach is recommended, combining quantitative parameters, such as effective regurgitant orifice area (EROA) and regurgitant volume (RV) with qualitative parameters such as mitral filling pattern, pulmonary vein flow pattern, density of the MR signal on continuous wave Doppler, left atrial size, pulmonary artery pressure.[1,5] Compared to primary MR, lower thresholds have been established to define severe secondary MR (20 mm^2 for EROA and 30 ml for RV)[6].

Secondary MR is characteristically dynamic during exercise, therefore stress echocardiography can provide important prognostic information; it has been shown that an increase in the severity of MR defined as an increase of EROA more than 13 mm^2 and increased pulmonary artery pressure during exercise (≥60 mmHg) identifies a subgroup of patients at higher risk of cardiac events[2,7].

Regarding prognosis, several observational studies have shown that secondary MR is a poor prognostic element in patients with LV dysfunction compared to those who do not have secondary MR[1]. Trichon et al have studied 2057 patients with ischemic MR and chronic LV systolic dysfunction showing that MR is an independent predictor of mortality. The severity of MR plays an important role as there were significant differences in survival at one, three and five years in patients with moderate to severe versus those without MR or with mild MR[8] and it may lead to the development of MR. The frequency of MR and its relation to survival in patients with LV systolic dysfunction has not been completely characterized. We analyzed the histories, coronary anatomy, and degree of MR in patients with symptomatic heart failure and LV ejection fraction <40% who underwent cardiac catheterization between 1986 and 2000. Cox's proportional hazards modeling was used to assess the independent effect of MR on survival. Two thousand fifty-seven patients met study criteria; MR was common in this cohort (56.2%. Nevertheless, it is unclear if prognosis is independently affected by MR compared to LV dysfunction as there are no proofs of a survival benefit due to reduction of secondary MR[9].

The management of secondary ischemic MR requires integration of several parameters: clinical (e.g. symptoms of heart failure, comorbidities) and echo-

cardiographic (e.g. MR severity at rest and dynamic change during exercise, presence of mitral valve complex anomalies, the origin and direction of the regurgitant jet, the degree of LV remodelling, the coexistence of LV dyssynchrony, the presence and extent of viable myocardium)[3]. In contrast to primary MR, there is currently no clear evidence that the correction of secondary MR improves survival, therefore its management is challenging[9]. Guideline-directed medical treatment remains the first option, aiming to reduce symptoms, to prevent myocardial infarction and to revert or delay the LV remodelling process. Angiotensin converting enzyme inhibitors, beta-blockers, spironolactone, titrated diuretic therapy should be prescribed according to the current recommendations[3,9]. Furthermore, besides medical treatment, inappropriate tethering can be addressed by surgery involving the mitral valve or LV reshaping, whereas coronary revascularization or cardiac resynchronisation therapy can potentially reduce tethering as well as increase mitral valve closing forces[3].

Patients with secondary ischemic MR should undergo appropriate revascularization. Nevertheless, there are issues regarding MR relief by revascularization alone in chronic coronary artery disease. Aklog et al noted that moderate or severe MR persisted in 77% of revascularized patients[4,10]. Percutaneous or surgical revascularization is associated with improved survival compared to medical therapy alone in patients with MR[8], but the proper way of revascularization is still controversial. Surgery has potential benefits of achieving more complete revascularization and improving MR more effectively by a mitral valve procedure at the time of coronary artery bypass graft (CABG). However, surgical revascularization has a higher procedural risk compared with percutaneous coronary intervention (PCI), and it is unclear whether MR is merely a marker for more advanced left ventricular (LV) dysfunction or whether IMR itself should be a target for therapy[11]. Kang et al conducted a nonrandomized study of 185 patients who underwent myocardial revascularization by PCI or CABG. A propensity-matched analysis showed that cardiac events were fewer in the CABG subgroup[11]. However, about 90% of patients in this study had multivessel coronary artery disease, and CABG was the preferred treatment option for patients with 3-vessel disease.

Surgery in secondary MR has limited indications when concomitant revascularization is not an option, as it is hampered by a significant operative mortality, high rates of recurrent mitral regurgitation and no survival benefit[9,12]. It should be considered when patients are already scheduled for CABG or other cardiac surgery or when symptoms persist and are attributable to MR, despite optimal medical therapy[1,9].

The presented case illustrates the aspects discussed above. In a young man with ischemic coronary disease and secondary moderate MR, the management plan was established by a Heart Team including cardiologists, interventional cardiologists and cardiac surgeons. Optimal medical therapy and percutaneous myocardial revascularization were chosen, with relief of symptoms and mild improvement of MR. In conclusion, secondary MR needs to be closely and carefully assessed. Until new evidences emerge regarding the optimal treatment, every case requires a personalized management plan.

CONCLUSIONS

Secondary ischemic MR is a complex condition. The imaging diagnosis and assessment of secondary ischemic MR involves mainly echocardiography, with an important role played by stress echocardiography in terms of prognosis. The treatment should first be directed to the underlying LV dysfunction using guideline-directed medical therapy. Other methods could be added as needed (e.g. coronary revascularization and/or CRT). Mitral valve surgery should be indicated only when a clear benefit is foreseen.

Conflict of interest: none declared.

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