

Asymptomatic aortic regurgitation: recommendations and dilemmas

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Abstract

Aortic regurgitation (AR) is the third most common valvular disease, which more often affects younger people, mostly men. Untreated severe AR leads to advanced left ventricular (LV) remodeling, which results in LV systolic dysfunction, which consequently leads to the heart failure. There is no clear consensus for the management of asymptomatic patients with hemodynamically significant AR who do not meet guideline-defined echocardiographic criteria. In these patients, there is a debate about the optimal therapeutic approach, that is, whether to replace the aortic valve in an early, asymptomatic phase, or wait for the symptom onset and/or systolic dysfunction and LV enlargement in order to intervene. Through this case, we present the approach to the patient from his first visit to the doctor, as well as the diagnostic process that led to the diagnosis of severe AR and pericarditis, which turned out to be the case of the patient's symptoms, as well as the dilemma in the further treatment of the patient.

Key words

asymptomatic aortic regurgitation, echocardiography, cardiac MRI, cardiopulmonary exercise testing, pericarditis

Introduction

Aortic regurgitation (AR) is the third most common valvular disease, occurring more frequently in younger patients, predominantly men¹. The most common cause of AR is a degenerative process affecting the valve leaflets, following with a bicuspid aortic valve^{1,2}. Infective or rheumatic endocarditis and aortic dissection are less frequent causes of AR. Hemodynamically significant AR leads to volume overload of the left ventricle (LV). Untreated severe AR results in advanced remodeling of the LV, characterized by dilation and eccentric hypertrophy, leading to LV systolic dysfunction and consequently to the development of heart failure³. The main indication for interventional treatment are symptoms caused by AR most commonly dyspnea and fatigue². On the other hand, there is no clear consensus on intervention for asymptomatic patients with hemodynamically significant AR who do not meet echocardiographic criteria defined by guidelines. Among these patients, there is a debate about the optimal therapeutic approach, whether to proceed with aortic valve replacement in the early asymptomatic stage or wait for the onset of symptoms and/or systolic failure and LV enlargement and then intervening. We present the case accentuating the dilemmas faced by cardiologists/cardiac surgeons dealing with this issue.

Case presentation

A 41-year-old male presented to the Emergency Centre of the University Clinical Center due to sudden severe chest pain, sharp and tearing in nature, propagating to the neck, and towards the shoulders. The patient reports history of hypertension, which is treated with an ACE inhibitor. Physical examination revealed a rough diastolic murmur over the entire precordium, with the punctum maximum over the aortic orifice. An electrocardiogram showed sinus rhythm with a heart rate of 97 beats per minute, without ischemic ST and T wave changes. Blood samples were taken for laboratory tests, and due to suspicion of acute aortic syndrome, the patient underwent multi-slice computerized tomography (MSCT), which showed no signs of acute aortic syndrome. Previously taken laboratory analyses (including troponin and D-dimer) were within reference ranges. After ruling out acute aortic syndrome, acute coronary syndrome, and pulmonary embolism, and as the symptoms had meanwhile alleviated, the patient was discharged home with advice to follow up with a cardiologist for echocardiography or stress testing if necessary. The patient returned for the scheduled outpatient visit stating that the pain still occasionally occurs but with slightly less intensity, and resolves with analgetics (Ibuprofen). Echocardiography revealed mild aortic dilation in the thoracic segment, bicuspid aortic valve, and significant aortic regurgitation of 4+ (Figure 1), with an enlarged left ventricle (end-diastolic diameter 7.0,

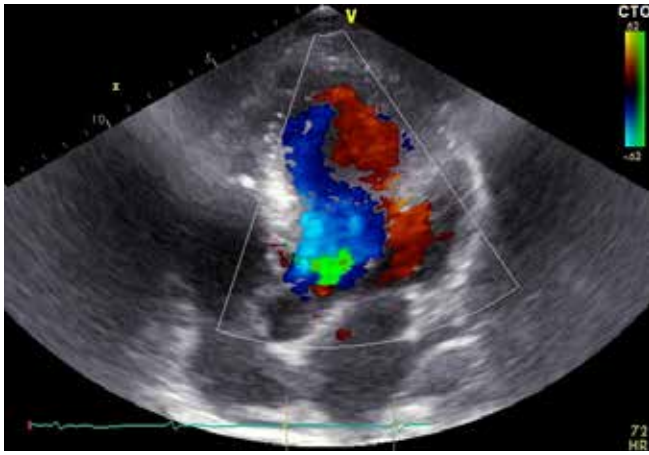


Figure 1. Echocardiographic image showing aortic regurgitation

end-systolic diameter 4.8) and preserved overall systolic function (left ventricular ejection fraction 65%), without clear abnormalities in kinetics. Subsequently, the patient underwent cardiometabolic evaluation in the form of cardiopulmonary exercise testing (CPET) on a semi-supine ergobicycle to assess functional capacity and symptomatic status. A maximal CPET was performed as the test was terminated at fifth stage V at 150 W load, reaching anaerobic threshold (peak O_2 consumption achieved 24 mL/(kg·min), which is 52% of predicted), during which the patient remained asymptomatic. Other parameters of the cardiopulmonary exercise testing are listed in Table 1. Finally, in order to determine the severity of AR and the degree of LV burden more precisely, cardiac MRI was performed in three standard planes without contrast enhancement and after contrast enhancement. The MRI findings showed an enlarged left ventricle, no signs of myocardial fibrosis, and confirmed a degenerative bicuspid aortic valve with severe aortic regurgitation up to 4+ (regurgitant volume 31 ml, regurgitant fraction 39%). Additionally, circumferential pericarditis (Figure 2) was observed during this examination, which most likely was the cause of the patient's chest pain.

Table 1. Cardiopulmonary exercise testing parameters

	Load (W)	HR (/min)	BP (mmHg)	Sp O_2 (%)
	/	76	147/80	97
	15	92	159/91	97
	45	93	158/86	96
	90	112	184/87	99
	135	140	205/97	96
Max	150	141	210/94	99
5 th rest minute	/	97	147/82	89

Legend: HR – heart rate, BP – blood pressure, Sp O_2 - oxygen saturation

After reviewing all the performed tests and the patient's clinical condition, as well as having a detailed discussion with the patient, ibuprofen was advised at therapeutic doses for treating pericarditis. As there is no consensus on when to intervene in asymptomatic patients with

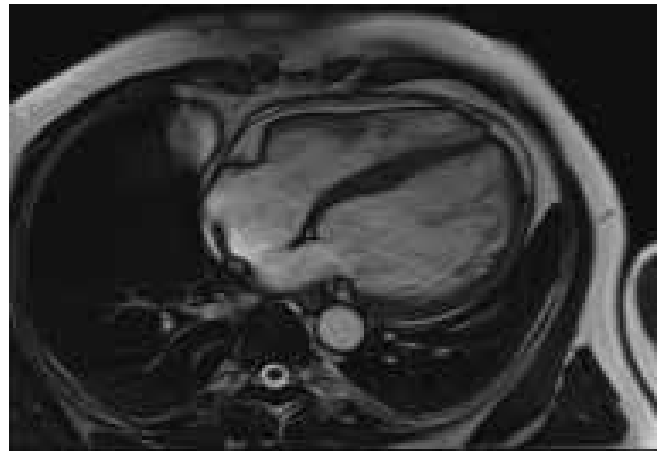


Figure 2. MRI image showing pericarditis

severe AR who do not fulfill echocardiographic criteria for intervention, the patient was advised with conservative treatment and frequent monitoring to detect promptly any symptom onset or deterioration in echocardiographic parameters, which are clear indication for surgical aortic valve replacement.

Discussion

Considering that patient was entirely asymptomatic, as confirmed by exercise testing, and diagnostic methods (CPET, echocardiography, MRI) showed borderline preserved cardiopulmonary capacity, as well as borderline dimensions and LV ejection fraction, the decision whether to refer the patient for surgical treatment or further diagnostic monitoring is extremely challenging, given that current guidelines, due to insufficient evidence, are unclear for asymptomatic patients with chronic severe AR and without significant dilatation of the ascending aorta. Watchful waiting and regular echocardiographic follow-up until meeting any of the aforementioned criteria is recommended by guidelines.

The optimal timing for surgical treatment of patients with severe chronic asymptomatic AR has not been precisely established, and the current approach is based on a combination of symptom onset time, echocardiographic assessment of AR severity, and LV remodeling (LV ejection fraction $\leq 50\%$ or left ventricular end-systolic diameter > 50 mm or indexed left ventricular end-systolic diameter > 25 mm/m² in patients with small body surface area)². Since percutaneous aortic valve replacement in patients with AR is not yet recommended (studies evaluating this method are ongoing), surgical aortic valve replacement is currently the only interventional method used.

Relying solely on echocardiographic criteria for setting indications for surgical treatment, a number of patients undergoing aortic valve surgery already have irreversible myocardial fibrotic changes at the time of intervention⁴. On the other hand, cardiac MRI has high precision in determining the severity of AR and selecting patients for surgical treatment. There is data indicating that to determine the optimal timing for surgical treatment, before irreversible myocardial damage occurs, it is

crucial to determine parameters indicating AR severity (echocardiographically determined vena contracta, left ventricular end-diastolic volume index - EDVI, as well as AR volume and regurgitation fraction determined by MRI), then parameters indicating remodeling and sub-clinical left ventricular failure (MRI-determined EDVI or left ventricular global longitudinal strain determined by echocardiography), serum levels of natriuretic peptides, as well as the patient's age^{5,6}. These parameters are independent predictors of early disease progression, and their combination has a higher predictive value than individual parameters in determining the risk of decompensation in the early stages of the disease and selecting patients for early surgical treatment while still in the asymptomatic phase^{5,6}. Timely surgical treatment has been shown to be associated with significant reverse remodeling and normalization of LV structure and function, while perioperative mortality is significantly reduced using new surgical techniques⁷⁻⁹.

Although previous guidelines favored a conservative approach in patients with severe asymptomatic AR and preserved left ventricular ejection fraction, there is increasing evidence supporting early surgical treatment of this specific valvular disease. For this reason, the multicenter randomized ELEANOR trial (Early aortic valve surgery versus watchful waiting strategy in severe asymptomatic aortic regurgitation; NCT 05438862) has been initiated, aiming to compare outcomes in two groups of asymptomatic patients with severe asymptomatic AR and preserved left ventricular systolic function, one in which patients undergo early surgical treatment of the AR and one in which patients are conservatively treated and intensively monitored to detect symptoms and signs of heart failure or a decrease in LV ejection fraction, when they are promptly referred for surgical treatment

according to class I of the current recommendations for valvular disease treatment². The results of this trial are expected in 2026.

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Sažetak

Asimptomatska aortna regurgitacija: preporuke i dileme

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Aortna regurgitacija (AR) je treća po učestalosti valvularna bolest, koja se češće javlja kod mlađih osoba, pretežno muškaraca. Nelečena teška AR dovodi do uznapredovalog remodelovanja leve komore (LK), što za posledicu ima sistolnu disfunkciju LK i nastanak srčane insuficijencije. Ne postoji jasan konsenzus za lečenje asimptomatskih pacijenata sa hemodinamski značajnom AR koji ne ispunjavaju vodičem definisane ehokardiografske kriterijume. Kod ovih pacijenata vodi se debata o optimalnom terapijskom pristupu, to jest da li pristupiti zameni aortnog zalistka u ranoj, asimptomatskoj fazi, ili čekati na pojavu tegoba i/ili sistolnog popuštanja i uvećanja LK kako bi se intervenisalo. Kroz ovaj slučaj prikazan je pristup pacijentu od njegovog prvog javljanja lekaru, kao i dijagnostički proces koji je doveo do postavljanja dijagnoza teške aortne regurgitacije i perikarditisa, za koji se ispostavilo da je uzrok tegoba, kao i dileme u daljem tretmanu pacijenta.

Ključne reči: asimptomatska aortna regurgitacija, ehokardiografija, magnet srca, ergospirometrija, perikarditis