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Long-term observation of the patient after CABG with asymptomatic high-grade aortic regurgitation – a clinical case study

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Abstract

Introduction: The aortic valve regurgitation (AR) is a heart defect consisting of the retrograde flow of blood from the aorta to the left ventricle due to the improper closure of the aortic valve leaflets. It occurs approximately in 13% of men and 8.5% of women, and the incidence increases with age. A crucial issue in regards to a patient with asymptomatic AR, especially of a high degree, is determination of the time of qualification for invasive treatment.

Aim: To draw attention to the necessity of holistic approach to a patient with asymptomatic high-grade aortic regurgitation. Moreover, the complications of delayed implementation of invasive treatment were discussed.

Case report: A clinical case of a 62-year-old patient with a history of coronary artery bypass grafting and with AR – stage II, accidentally detected two years later in a control echocardiogram, was presented. Despite gradual progress of regurgitation, none of the disturbing symptoms were noted, whereas cardiac parameters were systematically monitored using ECG, ECHO and CT imaging. Beta blockers, ACE inhibitors, loop diuretics and aspirin were used as conservative treatment. After 10-year transthoracic echocardiographic follow-up due to progression of AR and development of heart failure, the patient was qualified to surgical replacement of the aortic valve. This procedure significantly improved the patient's quality of life.

Summary: The key element in the treatment of chronic asymptomatic AR is the individualization of the therapy. An essential role is played by appropriate pharmacotherapy, precise monitoring using transthoracic echocardiography, which is recommended as the first-line imaging strategy. Delaying in the implementation of surgical treatment may result in failure of the therapy and the onset of serious complications.

Key words: aortic regurgitation, asymptomatic, aortic valve replacement

Introduction

Chronic aortic valve regurgitation (AR, *aortic regurgitation*) is a heart defect occurring in about 13% of men and 8.5% of women. Its incidence increases significantly with age, with the peak falling between the 4th and 6th decades of life [1, 2]. The degenerative changes developing with age, as a result of progressive fibrosis and calcification of the valve leaflets are the main risk factors of AR and they are observed in about 50% of diagnosed cases. Other factors that predispose to the development of this defect include: a bicuspid aortic valve (15%), rheumatic fever (15%), infective endocarditis (10%), aortic inflammation (5%), as well as connective tissue systemic diseases (ankylosing spondylitis, rheumatoid arthritis), severe chronic hypertension, Marfan syndrome, atherosclerosis, and aortic injuries and radiotherapy [3]. The pathogenesis of this disorder is based on the retrograde blood flow from the aorta to the left ventricle during closing of the aortic valve. The gradually increasing diastolic heart overload leads to compensatory changes of the left ventricle, including eccentric hypertrophy of the walls, increased susceptibility and enlargement of its cavity.

The defect is usually characterized by asymptomatic course lasting several months or even many years. Patients are then in a chronic, compensated phase of the disease. However, with the passage of time, hemodynamic disorders intensify with subsequent decompensation. The consequence of this is an irreversible failure of the left ventricle, as well as an increased risk of sudden cardiac death [4, 5].

Aim of the work

The aim of this work, based on the presented clinical case, was to analyze the difficulties in determining the appropriate time of qualification for surgical treatment of patients with long-term asymptomatic AR and to show the consequences that would result from the delay in making such a decision.

Case report

A 62-year old man, in 2003 underwent coronarography examination, which revealed critical stenosis of the right coronary artery (RCA) on the border of the central and proximal section, in the discharge place of the marginal branch. In addition, a stenosis of a distal section of the trunk of the left main coronary artery (LMCA) was made visible in 50-60%, and small mural changes of the left anterior descending artery (LAD), diagonal artery (DA), ramus intermedius artery (RI) and circumflex artery (Cx) were also proved. At the same time, the radionuclide ventriculography (RVG) scan showed insignificant dilatation of the left heart ventricle without disorder of contractility with left ventricular end-diastolic diameter (LVEDD) – 18 mmHg, the aortic valve insufficiency was not determined back then. The patient was qualified for surgical treatment, and in June 2003 he underwent the LIMA-LAD *(left anterior mammary artery – left anterior descending)* surgery, Ao-OM1 *(aorta – first obtuse marginal)* and Ao-RCA *(aorta – right coronary artery)* surgeries. Echocardiography check-up performed 2 years later, showed symmetric overgrowth and dilatation of the left heart ventricle with LVEDD – 6.3 cm and with the IVsd – 1.5 cm *(interventricular septal thickness at diastole)*. Additionally, first degree mitral insufficiency with second degree tricuspid insufficiency and second degree aortic valve insufficiency were diagnosed. Based on the double computer tomography and during regular echocardiographic examinations performed in the subsequent years, progressive dilatation of the heart was observed in the area of left ventricle with left ventricle ejection fraction (LVEF) – 50% as well as disorders in its contractility in the form of sectional septum hypokinesis, frontal and lateral walls. Chronic heart insufficiency was diagnosed in the NYHA I class. Also, an aneurysm bulge (13x10x5mm) occurred on the frontal wall of the part of ascending aorta. In turn, insufficiency of the tricuspid aorta valve progressed (III degree). The ECHO examination revealed a significant insufficiency of the valve, that is improper shape and movement of the non-coronary cusp, and to a smaller extent, of the right one, both in the closing and opening phase of the valve. Moreover, first degree hypertension developed in the patient. During the physical examination at the left edge of the sternum, a holodiastolic murmur of the decrescendo type (so called „*seagull's cry murmur*") was heard, at about 4/6 in the Levine scale. What is interesting, during the physical examination, despite progression of the aortic insufficiency, no alarming symptoms, i.e. deterioration of physical exertion tolerance, shortness of breath, pain in the chest or palpitations, were recorded. In 2011 on the basis of

the coronarography and aortography examinations, the closure of the LIMA-LAD graft as well as the progression of aortic insufficiency (III/IV degree) were diagnosed. Chronic heart insufficiency evolved into the NYHA II degree, with LVEF – 45%. Nonetheless, due to the lack of significant clinical symptoms, the surgery of the defect was deferred and it was decided to wait for the next 2 years. In the preventive treatment, beta blockers, aspirin, loop diuretics and ACE inhibitors were used. Due to such pharmacological treatment, in the following years a progressive drop of diastolic pressure was recorded – down to the value of 45 mmHg – as well as a significant increase in the LVEDD value to 7.2 cm [Fig.1, Fig. 2, Fig. 3., Table 1]. Increase of the dimensions of the left heart ventricle and dilatation of the upper lobal veins were also made visible in the performed chest X-ray [Fig 4]. The electrocardiogram (ECG) presented the features of the overload of the left heart ventricle. As a result of the above-mentioned changes, the patient was qualified for re-operation. On 23.08.2013 the coronary artery bypass graft (CABG) Ao-LAD was conducted with simultaneous implantation of the biological prosthesis of the aortic valve Hancock II no. 25. After implantation, the valve undertook proper function with PG max *(maximum pressure gradient)* – 32 mmHg, PG mean – 18 mmHg, Vmax – 2.8 m/s, and LVEF increased to 50%. In the postoperative period, there were several heart rhythm disorders, in the form of atrial fibrillation. The return to the sinus rhythm was obtained by means of pharmacological treatment. The patient in a general good condition was discharged home with recommendations such as warfarin, amiodaron, furosemide, bisoprolol, spironolactone, ramipryl, acetylsalicylic acid.

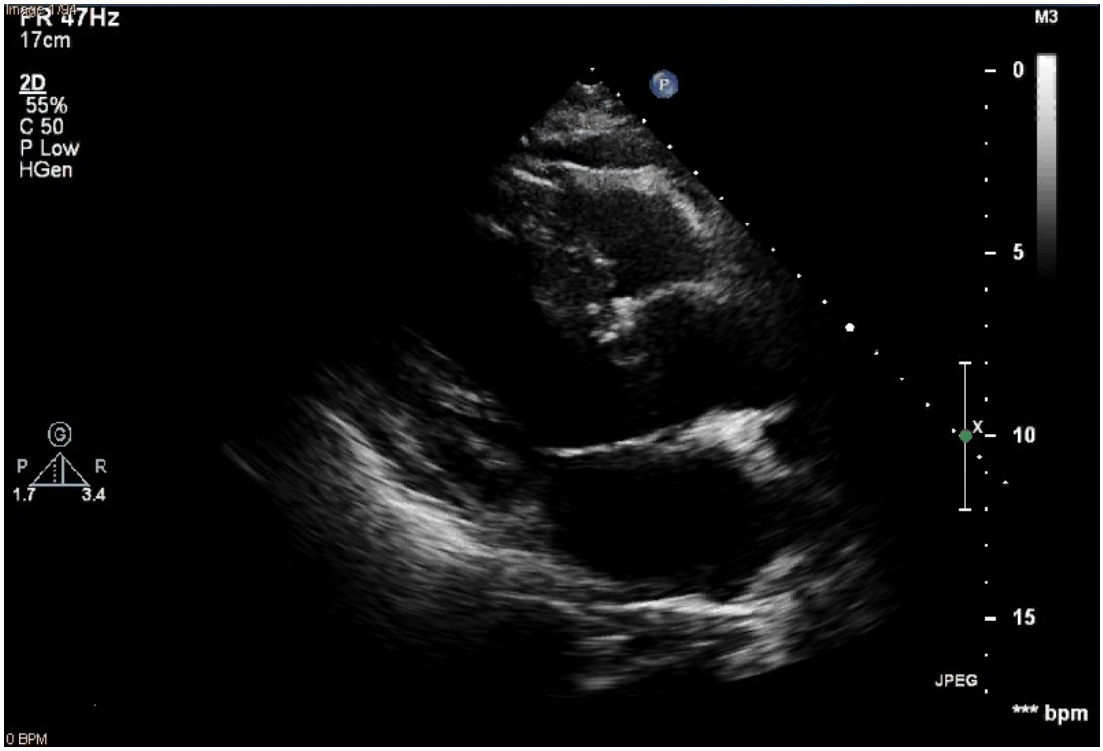

Figure 1. Transthoracic echocardiogram. Parasternal projection in the long axis. A small volume of fluid is visible in the pericardial sac. Widening of the aortic bulb. Thickened aortic valve leaflets.

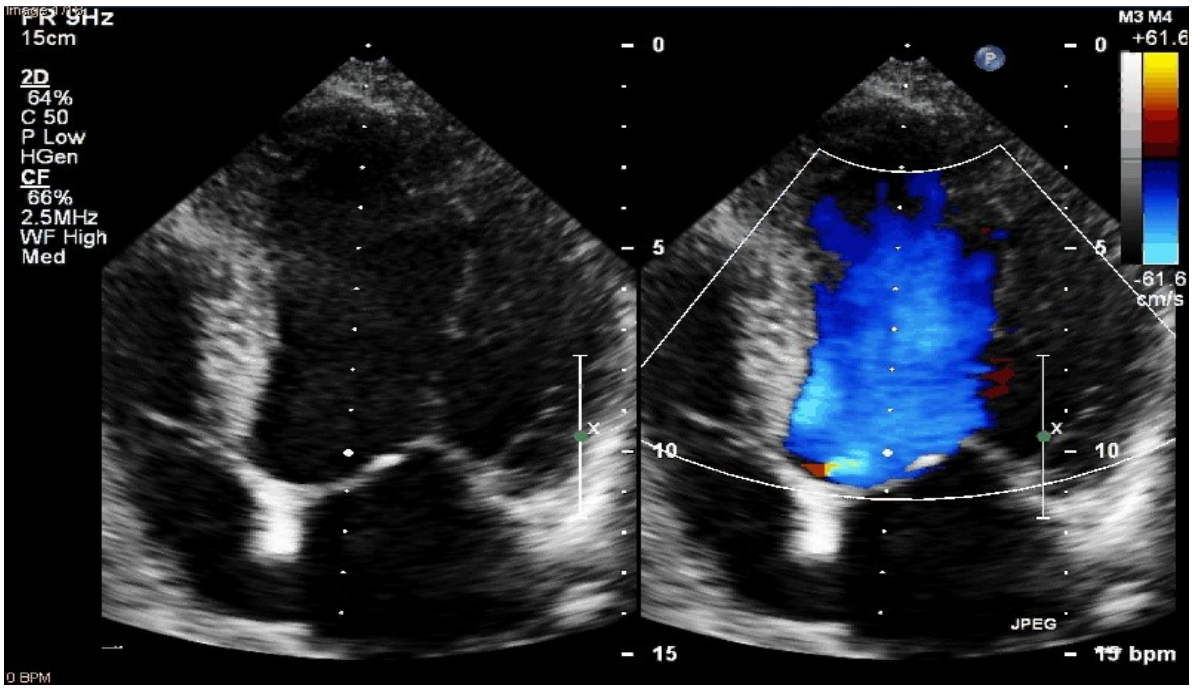

Figure 2. Transthoracic echocardiogram. 4-chamber apical projection. Color Doppler examination technique. Left ventricular enlargement and return wave of large aortic regurgitation are visible.

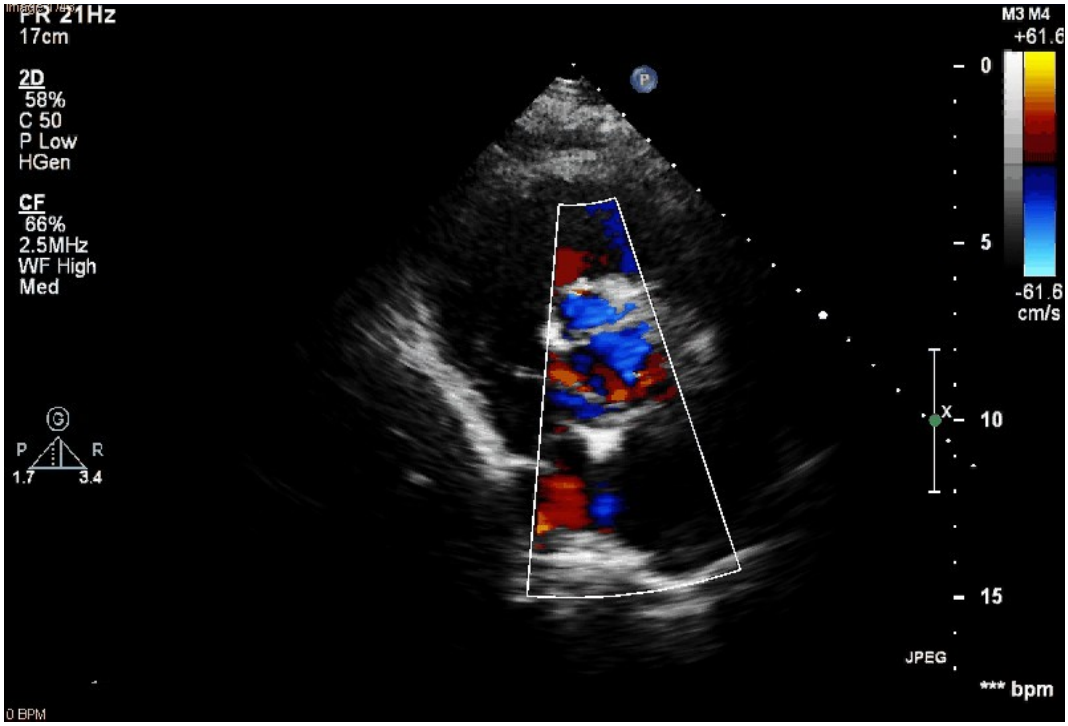

Figure 3. Transthoracic echocardiogram. Short sternal projection. Reverse blood flow is visible. Qualitative (on a scale from 1 + to 4+) assessment of the range of the return wave of aortic regurgitation.

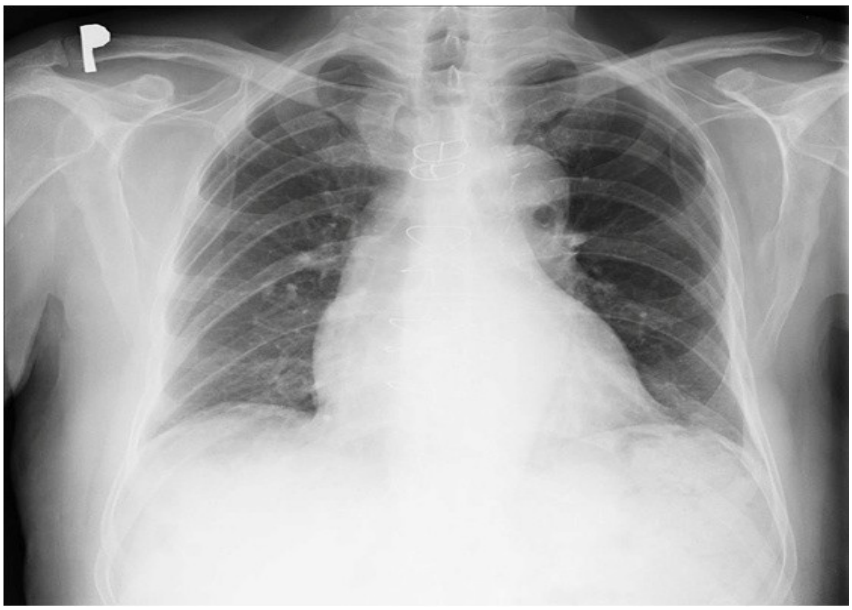

Figure 4. X-ray image of the patient's chest. Enlargement of the transverse dimension of the left ventricle, prominent aortic arch, widening of the high lobe veins and upper mediastinum (thyroid?) are visible.

YEAR	EF (%)	LVEDD (mm)	EDV (ml)	AORTIC BULB (mm)	AR STAGE	BLOOD PRESSURE (mmHg)
2005	51	60	151	37	II/III	180/50
2006	55	64	202	37	III	140/70
2007	58	63	222	38	III	170/70
2008	58	63	237	38	III	150/50
2009	50	65	240	40	III	130/55
2010	50	66	245	42	III	140/60
2011	45	67	247	42	III/IV	130/60
2012	50	63	242	40	III/IV	140/70
2013	50	72	261	42	III/IV	120/45

Table 1. Data summary based on echocardiographic control protocols since the first discovery of AR in 2005.

Discussion

Chronic AR in most cases is characterized by a long-term asymptomatic course. Nevertheless, despite the lack of noticeable clinical symptoms of this defect, a gradual increase in the volume of the return blood flow and the left ventricular end-diastolic volume (LVEDV) is observed. The consequence of the described hemodynamic changes is the progressive myocardial remodeling in the form of myocyte hypertrophy and reorganization of the extracellular matrix [6]. According to scientific reports, such altered heart can weigh up to 1000 g at autopsy [2]. Initially activated compensatory mechanisms have become exhausted over time, leading to an irreversible left ventricular dysfunction. As a result, clinical symptoms appear in 25% of cases in the period of one year after decompression of left ventricular function [3]. The most common first manifestation of chronic AR is exertional dyspnoea, fatigue, and a decrease in exercise tolerance. During the physical examination, attention is drawn to the significant amplitude of blood pressure with increased systolic pressure and often indeterminate diastolic pressure, with coexisting Corrigan's pulse. Therefore, auscultation of the heart is particularly important in the initial diagnosis of valvular heart diseases. It is not uncommon that confirmation of the diagnosis of severe AR is a loud, holodiastolic decrescendo murmur, so-called seagull's cry murmur, also known as

Gallavardin's phenomenon, best heard at the left side of the sternum. It was first described by French physician Louis Gallavardin and Ravoult in 1925, while studying angina pectoris. This murmur, imitating the cooing sound of a seagull, is usually characterized by a musical timbre and a high frequency, appearing when the regurgitant flow presents high velocities [7, 8]. The above case is therefore an accurate reflection of the characteristic course of this defect, because the patient did not report any complaints neither at rest or during physical exercises during the 10 years of the disease.

In assessing the severity of AR, monitoring of the follow-up, and choosing the therapeutic methods, the crucial factors are: semi-quantitative echocardiographic parameters, such as end-systolic left ventricular diameter (LVESD), LVEDD, and LVEF assessed in the transthoracic echocardiographic examination (TTE). Besides, colour Doppler is recommended as a noninvasive, highly sensitive and specific technique for detecting AR and providing visualization of the regurgitant jet. At the same time, continuous and pulsed wave Doppler as a quantitative method, provides additional haemodynamic information. Nowadays, beyond commonly used two-dimensional (2D) imaging echo, three-dimensional (3D) echocardiography, tissue Doppler and strain rate imaging have increasing importance in obtaining accurate measurements and assessment of valve morphology, especially in patients with borderline left ventricular ejection fraction. While it is recommended that patients with mild to moderate AR can be reviewed once a year, and echocardiography performed every 2 years, all asymptomatic patients with severe AR and normal left ventricular function should be seen for a follow-up at least every year or even at 3-6 months intervals in case of newly diagnosed patients. This includes also patients with rapid progression of AR, or who come close to thresholds for surgery. ECG, which may be normal in mild AR and may show LV hypertrophy in moderate to severe AR, plays a significant role among other diagnostic tools. Besides, chest X-ray also has important meaning, as it may reveal LV enlargement, as well as aneurismal dilatation of the ascending aorta, usually occurring in patients with AR coexisting with primary disease of the aortic wall. The above-mentioned diagnostic methods have proven to be extremely useful in assessing the described patient's case, and highlighted typical changes for AR. RVG, which was performed on our patient, is rarely used to serial assessment of LVEF at rest and during exercise. Either the cardiac magnetic resonance (CMRI), or the subsequent invasive diagnostic methods such as aortic root angiography, should be considered only when the diagnosis cannot be determined by noninvasive imaging

and when patients have suspected or known coronary artery disease (CAD), especially those with previous CABG [4, 9-11].

Pharmacological treatment and surgical intervention – an ideal moment for optimal surgical decision

The standard procedure in heart valve disease in everyday clinical practice of not only cardiologists, but also cardiac surgeons, is based on the guidelines issued by the American College of Cardiology, American Heart Association, and ESC/EACTS as well. Nowadays, pharmacological treatment and surgical intervention are mentioned among approved methods for the treatment of AR.

Vasodilatative drugs are taken into account in the pharmacological management. They mainly reduce LVEDV, strain of blood vessel wall and afterload, while at the same time improve the function of the left ventricle and reduce its mass. Nevertheless, their effectiveness has not been clinically confirmed so far. Previous observations have displayed that the therapy with angiotensin-converting-enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB) or dihydropyridine calcium channel blockers (CCBs) is justified only in the case of coexistence of AR and hypertension, because of their hypotensive effect, like in the discussed patient [6, 12-13].

Initially suggested advantageous influence of vasodilators in prolonging the asymptomatic period and postponing the surgical intervention in the sick with normal blood pressure has not been shown unambiguously. Furthermore, it is worth to emphasise that during beta-adrenolytic treatment in high-grade AR, special caution should be exercised due to their influence on prolonging diastolic time with simultaneous increasing the volume of regurgitation [14]. It is also recommended to treat patients with hydralazine [12]. Patients with normal LVEDD do not need pharmacological management, while the ones with increased LVEDD are recommended to take nifedypine or ACEI, as long as there are no contraindications to prescribe them. In case of the described patient, the use of mentioned drugs (ramipryl, bisoprolol), resulted in a good therapeutic effect. According to most recent guidelines issued by ESC/EACTS 2017 it is also suggested to continue the treatment with ACEI, ARB or beta-adrenolytics in patients who have had heart failure symptoms or hypertension in spite of surgery replacement of the aortic valve.

The appropriate moment to qualify the patient with asymptomatic AR, especially high-grade, to reparative surgery, is extraordinarily essential from the viewpoints of distant consequences, the prognosis, as well as the quality of life. It is thought that not until

symptoms develop, or significant extension and dysfunction of the left ventricle occur, the decision to surgical replacement of the valve generally may be postponed without higher risk in this group of patients. According to the newest guidelines issued by ESC/EACTS 2017, as well as defined criteria during qualification of discussed patient with high-grade AR to the operation (2013), absolute recommendations are: impairment of LV function (LVEF) ≤50%, LV enlargement with LVEDD >70mm or LVESD >50 mm [9-10]. In the described case, symptomless 62-year-old patient with LVEF = 50%, LVEDD = 72 mm and previous CABG surgery is in the I class of the recommendation, in which evidence for effectiveness and clinical utility of a surgical intervention is unambiguous, and there are strong circumstances as to its validity. Recommendations for surgical treatment in analysed case in the light of current best-evidence guidelines were summarized in table 2 [Table 2].

Clinical observations show that the outcomes of early surgical management on patients with at most moderate left ventricle systolic dysfunction in the NYHA I or II class are generally good, and the perioperative mortality rate does not exceed 1-3%, whereas the distant survival is similar to the general population [15]. According to the available literature data, in patients with asymptomatic AR with initially preserved left ventricle systolic function (LVEF ≥50%), its symptomless dysfunction develops in <1.3% patients annually, and the rate of sudden, unexpected death in this group is lower than 0.2% annually [15].

Age, as an unmodifiable risk factor, worsens the prognosis of the surgery. Moreover, the individuals who underwent CABG, aortic or other heart valve surgery are in the special risk factor group. Multidisciplinary team decision-making to perform the operation should also take into account aetiology of AR, the life expectancy and operative risk in every patient.

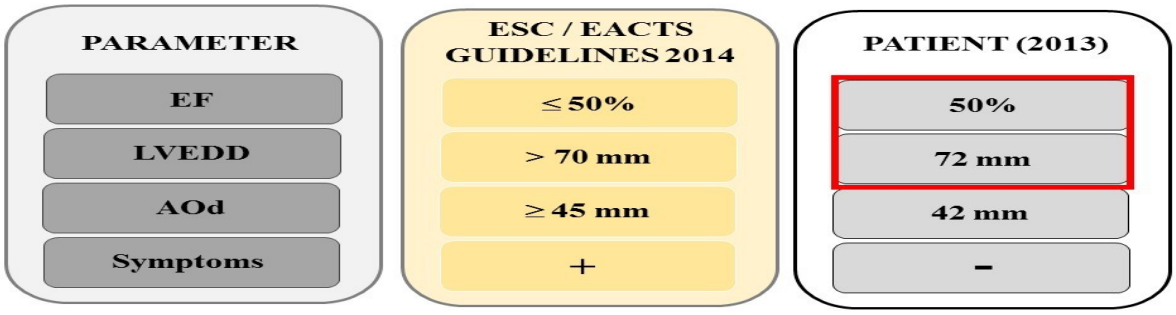

Table 2. Recommendations for the surgical intervention in patients with asymptomatic AR. **LVEF/EF** – ejection fraction, **LVEDD** – left ventricle end-diastolic diameter, **AOd** – aortic root diameter

Documented cases and observational studies in the literature

Scientific reports confirm that evaluation of hemodynamic changes in the course of asymptomatic AR, as well as that clinical status of patients are integral parts of the treatment. In the literature, we can find numerous examples confirming the importance of assessing not only the size and systolic function of the left ventricle, but also quantitative parameters (left ventricular end-diastolic pressure – LVEDP, aortic regurgitant volume – RV, aortic regurgitant fraction – RF) and the effect of the extra-valvular factor – anatomy of ascending aortic root (AO). In the study of 126 patients (33 women and 93 men, mean age 35 ± 11 years) with asymptomatic AR undergoing long-term follow-up (mean time 7 ± 3 years), it was found that clinical and echocardiographic status of 107 patients was stable, which constituted 84.92% of examined ones [16]. It was observed that only AOd has increased, but merely in patients with increased LVEDD and both tricuspid and bicuspid valve. It has also been proven, that all investigated parameters: age, LVEDD, LVEF, LVEDP, RF, RV and aortic root diameter (AOd), have significant prognostic values in the evaluation of AR progression. Aortic valve replacement (AVR) procedure was performed in 19 patients, but the frequency of the indication to AVR due to hemodynamic progression (n=7) and gradual significant AOd (n=7) was similar. An important conclusion from the study is the fact that an increase in LVEDP by 1 mmHg above the norm enhances the risk of AVR by as much as 83%. It has also been demonstrated that the probability of a 10-year survival by patients with chronic AR without the necessity for surgery AVR is 85%. In the analyzed case of our patient, AVR was also performed after 10 years of observation.

On the other hand, the case of a 23-year-old patient with asymptomatic AR and hypertension demonstrates the importance of systematic monitoring by means of subsequent echocardiographic examinations and determining the adequate time to qualify for surgery before irreversible changes, that prevent recovery of normal left ventricular function after surgical correction of the defect, develop [15]. It should be remembered that although the irreversible deterioration of left ventricular function is usually accompanied by congestive heart failure symptoms, they may sometimes occur imperceptibly, without clinical symptoms. In the aforementioned case, it was decided to carry out the surgical treatment of the defect due to enlargement of the LVEDD from 63 to 73 mm during 2 years of observation, with identified echocardiographic features of elevated diastolic pressure in the left ventricle as well as no improvement after pharmacological treatment.

Summary

Chronic AR is often characterized by many years of asymptomatic course. While it is not difficult to identify hemodynamically significant AR and to assess its stage, it is an enormous problem for both cardiologists and cardiac surgeons to determine the indications for surgical treatment at the most adequate time, especially in an asymptomatic patient. Moreover, performing the surgery at the appropriate time prevents any irreversible damage to the left ventricular muscle that could occur if surgery was delayed. Then, the correction of the defect would not lead to a reduction in the diameter of the left ventricle and improvement of its function. Parameters such as: age, LVEDD, LVEF, LVEDP, RF, RV, AOd have significant value in predicting progression of the defect and qualification for surgical treatment. Therefore, systematic and regular monitoring by means of subsequent echocardiographic assessment of left ventricular dimensions and its functional parameters, as well as close evaluation of the patient's clinical condition, is of fundamental importance. Pharmacological treatment with beta-blockers, ACE inhibitors and dihydropyridine calcium antagonists should be considered in regards to patients with normal left ventricular function. There is no universal single treatment protocol for patients with asymptomatic AR. Although there are general guidelines for the management of AR, in each case therapy should be individualized and adapted to the patient's clinical condition as well as comorbidities.

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