CONSENSUS

ARGENTINE SOCIETY OF CARDIOLOGY

Consensus Statement on Cardiac Diseases in Elderly Patients / Abbridged Version

VALVULAR HEART DISEASES

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Abbreviations

AS	Aortic stenosis	LVEF	Left ventricular ejection fraction
AVA	Aortic valve area	MG	Mean gradient
AVAI	Aortic valve area index	SV	Stroke volume
EF	Ejection fraction	SVI	Stroke volume index
HTN	Hypertension	Zva	Valvuloarterial impedance
LV	Left ventricle		

1. INTRODUCTION

According to the 2014 World Health Statistics published by the World Health Organization, (1) life expectation has been prolonged, so that for a girl born in 2012 life expectancy is around 73 years, while for a boy it is 68 years, representing a 6-year increase with respect to the 1990 average. However, there are differences among countries; thus, in high-income countries, the probability of life expectancy for a boy is 76 years, 16 more than for those living in low-income countries, and in the case of girls the difference is even higher, reaching 19 years (82 vs. 63 years). In Argentina, survival has also extended to 77 for women and 73 for men. This marked increase in life expectancy has led to the growth of the elderly population, and it is expected that the population over 80 years will be four times higher in the forthcoming years.

Degenerative valvular heart disease increases in frequency and severity with the passage of time, and an eighth of the population over 75 years has significant valvular heart disease. We therefore face a disease with growing prevalence, which poses the debate on the management of these elderly patients, mainly when confronting intervention decision-making. The presence of comorbidities is very frequent and their evaluation is a key aspect in this population management. Extracardiac vascular disease (carotid, abdominal or peripheral aorta), renal and hepatic dysfunction, stroke and chronic obstructive pulmonary disease must be carefully considered. Currently, it is possible to assess cognitive and functional capacities and frailty to reach the best therapeutic decision.

Treatment has improved in the last years, especially progress in surgical techniques, which enables the inclusion of patients who years before would not have been considered for surgery, with reasonable perioperative morbidity and mortality and with postoperative ventricular and valvular function level and quality of life comparable to that of a similar age population. (3, 4) This progress should be added to the development of percutaneous valve implantation techniques which, as better results are obtained, force a reformulation in the management of this population. (5, 6)

Currently, the initial age limit to consider an elderly population is between 65 to 70 years, but survival is increasingly extending. Thus, it should be borne in mind that the indications postulated in this Consensus statement are going to change, depending on whether they should be applied to a 65 to 70-year old patient without comorbidities or to an octogenarian or nonagenarian patient with comorbidities. Sound clinical judgment should prevail in medical decisions, also taking into account the patient and his family's preference.

FRAILTY

Treatment decisions in elderly patients should be based on analysis of the balance between risk and benefit for each individual patient. The risk of procedures should be compared against natural evolution mortality or with short or mid-term medical treatment. This risk evaluation should include comorbidities and frailty.

The latter appears at advanced age as a decline in the general condition and increase in vulnerability, expressed as weakness and reduction of the physiological reserve, generating inability of adapting to stressful situations as for example, interventions. It is the most difficult expression to manage in old age, as vulnerability generates difficulties in homeostasis after any stressful situation, and sometimes minor situations originate disproportionate abnormalities from which it is difficult to recover. (7) Frailty may develop as a progressive decline, but also as the inability to recover in patients who previously seemed robust.

Frailty may be defined as a state of vulnerability in stressful situations, due to decline in neuromuscular, metabolic and immune physiological reserve. (8) This should be added to mobility, force, nutrition and physical capacity disorders, and cognitive and social conduct abnormalities. (9-11)

Age, comorbidities and motor impairment are associated to frailty, but this may exist independently of these factors. Neither are cognitive abnormalities an integral part of the concept defined as frailty, although this is associated with mild cognitive decline that may become progressive. (12-14)

Different indexes can measure frailty. Most take into account physical functions, walking speed and cognitive functions. The Katz index measures six basic activities of daily life as feeding, grooming, dressing, using the bathroom, mobility (getting in and out of bed without help) and continence. (15) The inability to perform one of these activities indicates the presence of mild frailty and two or more, moderate to severe frailty.

The Cardiovascular Health Study Index (16) is also well used and has been the origin of many other indexes. It assesses weight loss (>5% in the last year), weakness (decrease in grip force), decrease in walking speed (>6 seconds to walk 5 meters), exhaustion (level of effort required to perform daily chores) and decrease in the level of physical activity. Presence of at least three criteria indicates frailty and is independently associated with longer hospital stay, complications and mortality after surgery. (17)

Other indexes have tried to simplify the application of these criteria maintaining their ability to predict mortality, as the Survey of Health, Ageing and Retirement in Europe (SHARE), (18) the Study of Osteoporotic Fractures (SOF), (19) The Rockwood Frailty Index (20) and the Edmonton scales. (21)

AORTIC STENOSIS

Prevalence of aortic sclerosis increases with age and is present in approximately 25% of the population over 65 years and in more than 48% of people above 75 years. Between 2% and 6% of people over 75 years of age have severe aortic stenosis (AS) and the risk is higher in men. (22) Prevalence of severe AS with aortic valve area ≤0.8 cm2 and outflow tract velocity ratio≤0.25 also increases with age from 1-2% at 75 years to 6% at 85 years. (23).

Etiology

Degenerative AS is the main etiology in the elderly patient. There is growing evidence about the possible association of several clinical factors with the development of calcific aortic valve stenosis, as age, male gender, smoking, hypertension (HTN), LDL cholesterol level, Lp(a) and diabetes. (24) These findings support the notion that atherosclerosis plays an important role in the progression of AS, although more recent studies could not show and independent association between aortic sclerosis and vascular disease. (25)

Some histopathological studies support the concept that calcific aortic valve stenosis represents an active process and is not simply the inevitable consequence of age. It is probable that endothelial injury caused by mechanical stress on the aortic side of the valves initiates an active inflammatory process, similar, but not identical, to that of atherosclerosis. (25)

The second cause is calcific bicuspid valve. After 70 years of age, 60% of patients have a calcific tricuspid valve and the rest a calcific bicuspid valve, whereas at a younger age the proportion is reverse. (26)

Symptoms

Once symptoms develop, patient mortality with AS is high without valve replacement, with survival below 50% at 2 years. It is important to point out that despite the marked difference in prognosis between symptomatic and asymptomatic patients, there is ample superposition in aortic jet velocities, mean gradients (MG) and valve areas between both groups. This implies that severe AS is better defined as the point in which the patient's metabolic demands cannot be satisfied for a certain degree of valvular narrowness, and probably this is also associated with body size and the level of activity. (22)

Average age for symptom onset in patients with degenerative calcification of aortic tricuspid valve is 70 to 80 years. In contrast, patients with secondary calcification of congenital bicuspid aortic valve present with this condition at 50 to 60 years, and those with rheumatic AS at a wider age range, spanning from 20 to 50 years.

The identification of aortic disease in elderly patients is hindered by the superposition of symptoms with those not suffering the disease and due to an unspecific physical exam. Symptoms such as chest pain, fatigue, intolerance to exertion, dizziness and vertigo are very common in this population and may obey to other causes, so that often aortic disease is not considered in the differential diagnosis. (27)

While the classical symptoms of aortic stenosis are angina, dyspnea and syncope, the most common symptom at disease onset in elderly persons is exercise tolerance worsening.

Low flow, low gradient aortic stenosisand preserved systolic function

Low flow, low gradient AS with normal ejection fraction (EF) is characterized by aortic valve area (AVA) <1 cm2and/or aortic valve area index (AVAI) <0.48 cm2/m2, stroke volume index (SVI) <35 ml/m2, MG <40 mmHg and preserved EF (≥ 50%). (28, 29)

The most frequent etiology of this form of AS is the degenerative presentation, observed in elderly patients (generally women) with significant hypertrophy and associated with two or more risk factors that may elicit increased arterial stiffness (vascular load) and/or coronary artery disease. Valvuloarterial impedance (Zva) is a useful parameter in the evaluation of these patients, which estimates overall left ventricular (LV) afterload taking into account valvular and vascular load. Valvuloarterial impedance is calculated as:

$$Zva=(SAP+MG)/SVI$$

where SAP is brachial arterial pressure measured with sphygmomanometer and MG is mean aortic gradient, which may be corrected or not for pressure recovery. It is advisable to perform this correction when the aortic root is small (sinotubular junction <30 mm). A Zva value >5 mmHg/ml/m2 indicates increased global afterload.

Aortic valve visualization by transesophageal echocardiography (degree of calcification, AVA by planimetry), assessment of the calcification score by computed tomography and the dimensionless coefficient (LV outflow tract integral/aortic flow integral) are also useful. In this particular group of patients, decision making is difficult when the patient presents symptoms and/or decompensated heart failure. In order to establish the correct diagnosis, cardiac catheterization is frequently performed, in which the transvalvular aortic gradient recorded is lower than that obtained by Doppler ultrasound, further hampering the diagnosis of AS severity. (30) In the face of the apparent discrepancy between low gradients and AVA <1cm2 in the presence of normal EF, potential errors that might underestimate AVA by Doppler ultrasound (error in the outflow tract diameter measurement) are generally assumed, and the conduct in these patients is oriented to the follow-up of a "non-significant" AS, ruling out aortic valve replacement or percutaneous implant as therapeutic option. (31, 32) It has been recently reported that the long-term prognosis of patients with low flow, low gradient AS and normal EF is very similar to that of patients with preserved gradients and that this presentation form approximately occurs in 10-25% of patients with severe AS. (29)

Patients with low ejection fraction, low flow and low gradient

Low flow, low gradient and low EF AS is considered when MG is ≤40 mmHg and EF is <40%. However, the greatest doubt is generated when MG is below 30 mmHg. In general, this is accompanied by ventricular dilatation with eccentric hypertrophy and calcific aortic valve with significant reduction of AVA. In some circumstances there is doubt on whether the patient carries a true AS or a mild to moderate AS with severe ventricular dysfunction, generally secondary to associated ischemic heart disease, a clinical condition termed as pseudostenosis. (33) In this case it is useful to induce an increase in transvalvular flow with the administration of low dose dobutamine. (34, 35) The increase of stroke volume (SV), effective AVA ≥0.3 cm2 or a final area >1cm2 (36, 37) are considered criteria supporting pseudostenosis. If the valve area is not modified (<1 cm2) and the gradients increase same as SV, the patient is considered to present true aortic stenosis. A third possibility is that dobutamine infusion does not increase SV and therefore does not modify either AVA or the gradients, which is observed in patients with severe LV function impairment, generally secondary to myocardial necrosis sequel. The 20% increase in SV with dobutamine can establish that the patient has contractile reserve, which is associated with better postoperative prognosis. (38) Nevertheless, it should not be used to determine whether the patient must be subjected or not to an intervention. It is also useful to visualize the aortic valve with transesophageal echocardiography (degree of calcification, AVA by planimetry), the assessment of the calcium score by computed tomography (>1,650A), the projected AVA for a theoretical transvalvular flow of 250 ml/s and the dimensionless coefficient (outflow tract integral/aortic flow integral) which is independent of flow and can establish the degree of blood acceleration in its passage through the aortic valve. A value ≤0.25 indicates that blood has accelerated 4 times in its passage through the aortic valve, which is compatible with severe AS.

Physical exam

While a loud grade 4/6 murmur can denote severe stenosis, most elderly patients with severe AS have only grade 2 or 3/6 and in some cases even weaker murmur. The clinical diagnosis can be complicated due to the high frequency of systolic murmurs heard on auscultation in the elderly. Around one third of all elderly patients admitted to hospital present basal systolic murmurs, but most of them do not suffer from AS. Therefore, sensitivity and specificity of systolic murmurs are low to detect AS in the elderly. In these cases, the intensity of the aortic component of the second noise may be very useful. When this is of low intensity or inaudible, significant AS may be suspected. The late acme of the murmur can also be useful to determine the severity of the stenosis, but this sign may be absent if there is coexisting significant aortic regurgitation. (39)

The slow increase and low amplitude of the carotid pulse have high specificity and low sensitivity for severe AS in the elderly.

Complementary studies

Electrocardiogram and chest X ray findings do not differ from those obtained in younger adults. (22)

Ergometry and radioisotope studies

Ergometry is used in the asymptomatic patient with severe AS and ambiguous symptoms to define the relationship between hemodynamic severity and clinical symptoms. When required, it must be performed with care, with close supervision and fast test termination upon blood pressure drop, excessive ST-segment depression or arrhythmia generation. The same recommendations as for the young adult are valid, with the limitation that many elderly patients cannot perform the ergometric test due to concomitant osteoarticular diseases and that dyspnea may be difficult to interpret in this population.

Indication for ergometry in aortic stenosis

Class I

- Asymptomatic severe aortic stenosis. (Level of evidence C)

Class II

- Asymptomatic moderate aortic stenosis. (Level of evidence B)

Class III

- Symptomatic severe aortic stenosis. (Level of evidence C)

Cardiac Doppler ultrasound

Normal ageing of the aortic valve produces characteristic changes that may be observed with echocardiography, as enhanced valve architecture with increased prominence of coaptation edges and fibrous thickening with or without calcification of the leaflets' body. These changes intensify with age and, thus, valve stenosis increases in frequency from 2% at 75 years of age to 6% for the 85-year group. (40)

Therefore, Doppler ultrasound is an essential element to define what can be a reasonable valvular impairment due to age from a genuine stenosis. Moreover, the time interval between the observation of valvular sclerosis and the clinical and Doppler echocardiographic evidence of significant stenosis can be only of 5 to 10 years.

Left ventricular hypertrophy develops and progresses together with stenosis severity. But in some cases a disproportionate hypertrophy can be detected, especially in elderly patients due to greater prevalence of coexisting diseases as HTN, senile septal hypertrophy or myocardial infiltration by amyloid tissue.

In elderly patients, the coexistence of coronary heart disease is high, so a depressed left ventricular function may be the consequence of ischemia or myocardial necrosis. In these cases, if the gradient is only moderately increased, it may be difficult to define whether it is a severe stenosis with left ventricular systolic function impairment or coronary heart disease or cardiomyopathy associated with mild or moderate stenosis. Dobutamine stress testing, evaluating changes in ventricular function, gradients and area can aid the differential diagnosis in these situations. (41, 42)

Conversely, in the follow-up of the asymptomatic patient with severe senile AS, moderate to severe calcification may be considered a high risk element, as the expected progression in these patients is faster and should be monitored more often. The same criterion applies in the event of aortic jet velocity >4 m/s and/or fast progression of aortic jet velocity (>0.3 m/s/year). Both variables (moderate to severe aortic valve calcification and velocity >4m/s and/or rate of velocity change) were independent prognostic predictors of the need for valve replacement. (43, 44)

Indications of Doppler ultrasound for the diagnosis of aortic valve stenosis

Class I

- Systolic murmur suggestive of aortic stenosis in a patient with or without symptoms. (Level of evidence B).
- To establish differential diagnosis between valvular, subvalvular and supravalvular aortic stenosis. (Level of evidence B).

Class II

- Patients with aortic coarctation due to its frequent association with bicuspid aortic valve. (Level of evidence B).

Class III

- Patients with aortic ejective murmur characterized as functional or associated with a hyperdynamic circulatory state. (Level of evidence B).

Role of cardiac Doppler ultrasound for the assessment of aortic valve stenosis severity

Although M and 2D mode echocardiographic assessment data guide on the degree of aortic valve stenosis (see cardiac Doppler ultrasound), these studies have limitations in a vast number of patients. This technique is necessary to accurately and reliably quantify transvalvular gradient and AVA by means of color Doppler ultrasound. (45-47) The information obtained is essential in specific cases in which the correct assessment of the degree of stenosis helps to decide a therapeutic conduct as important as heart valve surgery. In cases in which transthoracic evaluation is limited, it is possible to reliably estimate AVA by planimetry from a transesophageal view. (48) Moreover, in cases of aortic valve stenosis with not so high pressure gradient and significant ventricular systolic function impairment, dobutamine stress echocardiography helps to differentiate patients with severe stenosis in whom the gradient is reduced due to low cardiac output from those with less significant stenosis and myocardial impairment secondary to another disease. (54)

Current classification of aortic stenosis severity

Peak aortic transvalvular velocity, MG, and effective AVA and AVAI obtained by Doppler ultrasound are used to assess AS severity. Mean transvalvular gradient depends on transvalvular flow and must be recorded from the view where peak velocity is maximum, including the right parasternal view using transducer with and/or without image (Peedof). Aortic valve area calculation is operator dependent, especially the outflow tract diameter measurement and must be normalized by body surface area (AVAI) to avoid overestimating the degree of stenosis in patients with small surface area. Due to the discordance between AVA and MG reported by previously published guidelines, (49-51) according to Gorlin's equation, AVA of 1 cm2corresponds to MG of 26 mmHg; therefore, severe AS is defined for AVA<0.8cm2, corresponding to MG of 41 mmHg. (31, 53, 54) Aortic valve area should not be used as the only information to classify the degree of stenosis, but considered together with the gradient, transvalvular flow, ventricular function, degree of hypertrophy and type of ventricular geometry, degree of valve calcification and blood pressure. The dimensionless ratio (outflow tract integral/aortic flow integral) allows evaluating the presence of severe AS in patients in whom left ventricular outflow tract (LVOT) diameter cannot be measured due to inadequate ultrasound window (Table 1)

The cut-off points specified in Table 1 should be considered in patients with normal EF and normal SVI (>35 ml/m2). The term "critical" AS is preserved for AVA <0.6 cm2.and/or AVAI of 0.36 cm2/m2. Some patients

Table 1. Aortic stenosis severity: measurements

	Mild	Moderate	Moderately severe	Severe
AVA (cm2)	>1.5	1.5-1	1-0.8	<0.8
AVAI (cm2/m2)*	>0.9	0.9-0.6	0.6-0.48	<0.48
MG (mmHg)	<13	13-25	26-39	≥40
Peak velocity (m/s)	2–3	3-3.5	3.6-3.9	≥4
Dimensionless ratio				≤0.25

*for body surface are of 1.67 m2
AVA: Aortic valve area. AVAI: Aortic valve area index. GM: Mean gradient.

with severe stenosis (AVA<0.8 cm2) may present low gradient (MG <40 mmHg) and reduced EF (<40%) and should be identified separately from patients with "pseudostenosis". (49) In these cases a dobutamine stress test should be performed to confirm stenosis severity if AVA increases <0.2 cm2 or persists at 0.8 cm2. (36, 37) Also, LV reserve flow can be determined if SV increases >20%. (35) More recently, in patients with severe AS, MG <40 mmHg, normal EF (>50%) and decreased SVI (<35 ml/m2), AS has been described as "paradoxical". (29, 55) (See Low flow, low gradient severe aortic stenosis and preserved systolic function).

In patients with HTN, the study must be performed once blood pressure has been normalized. (56) It should be considered that in patients with small aortic root (sinotubular junction <30 mm) the phenomenon of pressure recovery may overestimate the degree of stenosis. (57) Hence, pressure recovery should be substracted from peak and mean gradients obtained by Doppler ultrasound, with pressure recovery calculated according to the following equation:

$$\text{Pressure recovery} = 4(\text{VAo2}– \text{VLVOT2}).\ 2\ (\text{AVAc/Ao})\ .\ 1 - (\text{AVAc/Ao})$$

where AVAc (vena contracta area) is the valve area obtained by the continuity equation and Ao is the area at the sinotubular junction level. The velocities at the aortic and LVOT levels should be maximum or mean according to the intended gradient correction (peak or mean).

The transvalvular aortic gradient is a reliable indicator of the degree of aortic valve stenosis, but it is important to rule out secondary causes of increase (circulatory hyperdynamic states, associated aortic valve regurgitation, etc) or decrease (low cardiac output, etc); in these situations, the gradient becomes more dependent on the transvalvular flow regime than on the degree ofstenosis. It should be recalled that the maximum gradient obtained by Doppler ultrasound may be slightly higher than that registered during catheterization, since, different from the former that reports instantaneous maximum gradient, the latter evaluates "peak to peak" gradient, resulting from comparing left ventricular and aortic systolic pressures.

Some alternative parameters suggestive of severe aortic valve stenosis are:

- Maximum aortic valve resistance >500 dynes/s/cm-5
- Mean aortic valve resistance >300 dynes/s/cm-5
- Maximum left ventricular outflow tract velocity/maximum transvalvular aortic velocity ratio <0.25
- Shortening fraction/maximum transvalvular aortic gradient ratio <0.7
- Time to flow acme/left ventricular ejection period ratio >0.5.

It is important to point out that in published studies on aortic valve resistance there is significant dispersion of confidence intervals, turning difficult the identification of a cut-off point between severe, moderate or mild forms.

Serial echocardiogram is also important in asymptomatic patients developing systolic dysfunction (LVEF<50%); although infrequent, this finding is indication of aortic valve replacement. (58)

Dobutamine stress echocardiography

In patients with left ventricular dysfunction and difficult stenosis degree assessment, the dobutamine stress test at progressive doses not exceeding 20 mcg/kg/min is useful to assess myocardial contractile reserve and consequently to detect an increase in aortic transvalvular gradient, reduced as a result of low cardiac output. Dobutamine stress echocardiography is especially useful in the AS patient with decreased MG (≤30 mmHg), low cardiac output and low EF. (59) Firstly, it rules out the possibility of aortic pseudostenosis (a situation in which the limitation in aortic valve opening is mainly the result of ventricular dysfunction and not of critical aortic valve disease) in which an increase in AVA >0.2 cm2 with slight increased gradient due to a rise in ventricular SV is observed during dobutamine infusion. In addition, dobutamine stress echocardiography provides information relative to the presence or not of myocardial contractile reserve (increase in SV > or < 20%), a relevant factor when predicting outcome.

In general, the following answers can be observed after this test:

- cardiac output ↑↑↑ - valve area ↑↑↑ - gradient↑non-severe stenosis (pseudostenosis if the area increases above 0.2 cm2, with final area >1 cm2)
- cardiac output ↑↑↑ - valve area ↔ / ↑ - gradient ↑↑↑severe stenosis (with contractile reserve, increase in stroke volume >20%)
- cardiac output↔ / ↑ - valve area ↔ - gradient - ↔ not conclusive (indicates scarce or absent myocardial reserve and has poor prognosis).

Multislice computed tomography

A computed tomography scan is useful to evaluate the ascending aorta, calcium distribution on the leaflets and aortic walls and the number of leaflets. It is also useful to measure the aorta and the aortic annulus before percutaneous implantation, and it may be used to rule out coronary artery disease in the subgroup at low risk.

Its ability to detect the presence of valvular calcification offers information on the amount and severity of this calcification which correlate with valve stenosis severity and prognosis even in the low flow, low gradient subgroup. (60-64) A calcium index ≥1100 AU provides sensitivity of 93% and specificity of 82% to diagnose stenosis with valve area <1 cm2. Calcium load is associated with stenosis severity, but it is also an independent predictor of events with a relative risk increase of 1.06 per 100 AU increase. A value > 500 AU is a predictor of symptom development, fast stenosis progression and death.

Cardiac catheterization

An elderly patient with severe AS who will undergo valve surgery requires a preoperative coronary angiography to evaluate the presence of coronary heart disease and consequently the need of simultaneous coronary bypass surgery. Frequently, elderly patients with moderate AS require an early coronary angiography during the course of the disease, as the angina symptoms may obey to a coexistent coronary artery disease.

If clinical and echocardiographic data are typical and concurrent of severe AS, coronary angiography may be the only necessary evaluation during catheterization.

A complete hemodynamic assessment with right chamber catheterization to establish stenosis severity may be required when there are discrepant findings between clinical and echocardiographic data, evidence of associated valve disease or pulmonary hypertension.

Patients with severe AS and low cardiac output often present small transvalvular gradient and it is sometime difficult to differentiate this type of patients from those with mild or moderate AS and low cardiac output. In both cases, presence of depressed cardiac output contributes to the severity criteria obtained through area assessment, as the Gorlin equation tends to underestimate the real valve area in these conditions. (65)

Indications for hemodynamic study in elderly patients with aortic stenosis

Class I

- Symptomatic patient with non-invasive, non- conclusive studies regarding the degree of severity (Level of evidence B). *
- Patients in planned valve replacement (Level of evidence C).
- Patient with asymptomatic moderate or severe aortic stenosis and left ventricular dysfunction (EF <50%), in order to rule out coronary heart disease (Level of evidence C).
- To evaluate coronary and aortic root anatomy in patients who will undergo ascending aorta surgeries (ruling out anomalous origin allows defining surgical strategy) (Level of evidence C).

*Except in this case, in the remaining situations the study indication is exclusively for coronary angiography.

Medical treatment

Medical treatment does not differ with respect to younger patients. (22) Symptomatic patients must undergo surgical valve replacement with biological prosthesis or eventually percutaneous replacement if they meet the criteria. In asymptomatic patients, the mainstay of medical treatment is patient and family information, close periodical follow-up to evaluate symptom occurrence or ventricular function decline, management of preload and afterload conditions in non-cardiac surgical procedures and strict control of HTN.

Hypertension is a key factor. Due to the superposition of age groups in which both diseases reach their highest prevalence, hypertension is frequent in patients with AS. From the physiopathological point of view, HTN may be a risk factor for AS also adding greater pressure overload to the LV by increasing systemic vascular resistance to an already enhanced afterload due to valve stenosis, thus generating a double overload. When HTN is associated with asymptomatic AS, it confers 56% increase in vascular events and doubles mortality. (66)

Treatment of HTN in the context of AS must follow normal basic guidelines, starting at the early stages of valve disease, since although there is risk of a drop in SV, this can only occur at advanced stages of the disease, when valvular calcification is so marked that it acts as a fixed obstruction. It is therefore suggested to start with low doses, slowly increasing them until an adequate control is attained. Even when there are no studies that allow recommending a specific antihypertensive agent, care should be adopted with the use of diuretics, especially in the AS group with small ventricles, where the fall in preload is more probable. Angiotensin-converting enzyme inhibitors could add their effect on ventricular fibrosis to the benefit on blood pressure reduction, (67, 68) while beta-blockers are drugs of choice when there is associated coronary artery disease (Class I recommendation, Level of evidence B). (69)

In the last years, it was postulated that treatment with statins would afford benefits by preventing the progression of valvular calcification; however, up to the present, three large controlled, randomized studies have not shown any benefit of statins in limiting the hemodynamic severity and its clinical consequences when administered to patients with mild or moderate stenosis (Class III recommendation, Level of evidence A). (70-72)

In some patients with severe AS and decompensated heart failure, in functional class IV, vasodilator treatment under invasive hemodynamic monitoring has been shown to be beneficial to achieve greater stabilization, prior to urgent valve replacement. As there is risk of reduced cardiac output during treatment with sodium nitroprusside, hemodynamic monitoring is essential to verify that cardiac output increases when systemic vascular resistance is reduced, allowing the patient to reach the intervention in better hemodynamic conditions (Class IIb recommendation, Level of evidence C). (73)

Indication for surgical treatment

Age itself is no longer a limitation for aortic valve replacement because this surgery may be performed at any age. Currently, it represents 60 to 70% of valve surgery in the elderly.

Elderly patients have specific characteristics, since they generally have worse overall condition and more comorbidities prolonging hospitalization and increasing perioperative mortality (1%-14%). (6, 75-78) Comorbidities will increase mortality above these percentages at any age. (76, 77)

Although the risk-benefit ratio may be very acceptable in the elderly population, it is desirable that both the treating physician and the patient and his family are informed about the higher rate of complications at this age, such as cardiac arrhythmias, requirement for long-term ventilatory support, heart failure, perioperative infarction in 3 to 8% of cases, and cerebrovascular events in up to 11% of cases. (76, 77)

Risk factors that increase operative mortality are: functional class, absence of sinus rhythm, need for emergency surgery, occurrence of associated coronary artery disease, female gender, outflow tract and aortic annulus narrowing, extensive calcifications of the aortic root, need for concomitant mitral valve surgery, HTN and the presence of LV systolic dysfunction. Another factor related to major complications is extensive valvular calcification, which, with friable tissues, makes valve surgery in the elderly particularly difficult.

It should be noted that coronary artery bypass surgery with simultaneous valve replacement increases mortality, which in the elderly may reach 4.5-12% depending on the series. (76-79)

Perioperative variables associated with increased mortality in valve surgery of the elderly include: time of aortic cross-clamping and extracorporeal circulation, use of inotropic drugs, complicated extracorporeal circulation weaning and the need for immediate reintervention. (76)

Indications for surgical treatment in aortic stenosis.

Indication	Class	Level of evidence
Symptomatic patients with moderately severe or severe aortic stenosis.	I	B
Asymptomatic patients with moderately severe or severe aortic stenosis, with positive exercise test (due to symptom development or drop in blood pressure).	I	B
Patients with moderately severe or severe aortic stenosis who must undergo cardiac surgery for other causes.	I	B
Patients with moderately severe or severe aortic stenosis and LV dysfunction (LVEF <50%).	I	C
Symptomatic patients with moderately severe to severe aortic stenosis with low-flow, low-gradient and impaired ejection fraction, in whom presence of contractile reserve is established.	I	C
Symptomatic patients with moderately severe or severe aortic stenosis with low-flow, low-gradient (<40 mmHg) and normal ejection fraction.	IIa	C
Symptomatic patients with moderately severe or severe aortic stenosis with low-flow, low-gradient and impaired ejection fraction, in whom the amount of necrotic tissue due to coronary heart disease has been discarded as the cause of ventricular dysfunction and without contractile reserve.*	IIa	C

* Only centers with surgical experience and the possibility of circulatory assistance.
LV: Left ventricular. LVEF: Left ventricular ejection fraction

An important factor is related to the choice of prosthesis, since mechanical valves require anticoagulation, with the added risk of prosthetic thromboembolism and hemorrhage, while biological valves have lower durability. This debate occurs in young patients, but as the longevity of the bioprostheses is directly proportional to age, they are the best choice for elderly patients. The frequency of structural deterioration of a bioprosthesis at 15-year follow-up is 63% for patients aged 40 to 49 years, but only 10% for those over 70 years. (80) Octogenarian patients have lower life expectancy than that of the structural deterioration of bioprosthetic heart valves; therefore, they should be the choice for these patients. (81)

A situation that may occur especially in elderly patients, mainly in women, is the presence of small aortic annulus. This implies the need to use small prostheses, number 21 or 19, which have a higher gradient and worse hemodynamics, with higher probability of postoperative prosthesis-patient mismatch, less functional improvement, lower reversal of hypertrophy, increased late in-hospital mortality and sudden death. (82-85) Probable options involve the use of mechanical prostheses that have lower gradient than bioprostheses with the same valvular diameter, but with the disadvantage of anticoagulation. If bioprosthesis placement is decided, an enlargement of the aortic annulus should be performed, which complicates surgery, (86) or else use of prosthesis without stent, which requires adequate experience. (87)

Balloon valvuloplasty

It involves dilatation of the aortic valve with a balloon. It was initially used only in young patients with congenital non-calcific stenosis, (89) but later Dr. Cribier et al. employed it in adult patients as a palliative therapy. There are several mechanisms by which balloon valvuloplasty increases valve area and it is related to the etiology of valve stenosis. In patients with degenerative calcific valve stenosis, the main mechanism is the fracture of calcium deposits in the leaflets. In cases due to rheumatic fever, the predominant mechanism is commissural separation. Balloon valvuloplasty also causes a stretching of the valve apparatus in unfused commisures.

Valvuloplasty series show that although the area improves, the frequency of complications reaches 12%, and the actuarial survival at 1, 3 and 5 years was 55%±3%, 25%±3% and 22%±3%, and the actuarial survival free of events was 33%±2%, 13%±2% and 2%±1%, respectively. Poor short-term results are due to a rate of almost unacceptable restenosis, in addition to a high rate of overall and vascular access complications, which, after an initial enthusiasm, led to practically discontinuing the procedure. However, in recent years it has resurfaced, not as a final treatment, but as a temporary solution, a bridge to more definitive treatment, either endovascular or surgical, especially in patients in poor clinical or hemodynamic condition in whom stability is desired before proceeding to another intervention, or in those symptomatic patients who require urgent major noncardiac surgery.

Percutaneous aortic valve replacement.

Percutaneous transcatheter implantation of aortic valve prosthesis (90) is a less invasive procedure than surgery, which makes it particularly interesting for the group of patients at high risk or with no surgical possibility. (91) Although surgical replacement remains the treatment of choice, it has been observed that 30% of patients who have surgical indication do not receive it for reasons related to old age, functional capacity deterioration or presence of comorbidities that excessively increase surgical risk. (92)

Three randomized, controlled studies have evaluated the efficacy and safety of the procedure. The PARTNER B study showed 20% absolute reduction in all-cause mortality in the first year after the procedure, with improved quality of life, in a group of patients considered inoperable when compared with optimal medical therapy, which included percutaneous valvuloplasty. (5) The PARTNER A study, involving high surgical risk patients who were randomized to percutaneous or surgical aortic valve replacement, demonstrated that percutaneous replacement was not inferior in terms of mortality at 2-year follow-up. The percutaneous replacement group had higher prevalence of neurological events and major vascular complications, while the surgical group had more bleeding complications. (93) The STACCATO study included low risk patients over 75 years, randomized to transapical percutaneous implant versus surgery and was discontinued due to a significant increase in complications in the first group. (94)

The independent, multicenter, prospective European SENTINEL Registry, (95) which included 4,571 patients from 137 centers in 10 countries between 2011 and 2012, is a reflection of the current daily practice of this procedure. Mean age was 81.4±7.1 years, with equal representation of both genders. The logistic EuroSCORE was 20.2±13.3 and femoral access was 74.2%. The reported incidence of complications was: in-hospital mortality 7.4%, stroke 1.8% and myocardial infarction 0.9%. Rates of vascular complications (3.1%) were similar with both prostheses, SAPIEN XT and CoreValve (p=0.15). Mortality was lower in the transfemoral access (5.9%) than in the transapical (12.8%) and other access (9.7%, $p < 0.01$) pathways. In the multivariate analysis, predictors of mortality were: old age, high logistic EuroSCORE, presence of pre-procedural mitral regurgitation ≥ grade 2 and implant failure.

An important aspect to consider is that although there is clear evidence of procedural effectiveness and short and mid-term durability, there is still scarce evidence on long-term results. In two clinical serial echocardiographic and tomographic follow-up studies at 3.5 and 5 years, reoperation rate was low. Color Doppler ultrasound showed a slight reduction of prosthetic valve area (0.06 cm2/year) without worsening of aortic regurgitation. The computed tomography showed no leaflet thickening, fusion, calcification or fracture of the support mesh. (96, 97)

The most frequent complications of the procedure include death, stroke (2-7%), (98) vascular complications, conduction disorders (3-35%) and prosthesis dysfunction due to bad apposition, migration and paravalvular regurgitation (5%), a complication which also has prognostic value. Aortic dissection or rupture, periaortic hematoma, cardiac tamponade, mitral regurgitation and obstruction of the coronary ostium may occur less frequently.

There are anatomical contraindications to the procedure as inadequate left aortic annulus size (<18 mm or >29 mm), active endocarditis, left intraventricular thrombus, plaques with mobile thrombi in the ascending aorta and aortic arch, short distance between the annulus and coronary ostia that may cause their obstruction, and inadequate vascular access by insufficient diameter, calcification or excessive tortuosity of access vessels. Among relative contraindications are: hemodynamic instability, severe ventricular dysfunction (EF<20%), extensive coronary artery disease, bicuspid or not calcific aortic valve and, in the case of transapical access, severe lung disease or inaccessible ventricular apex.

There are two key procedural aspects: one aspect is the joint decision-making of a medical team consisting of clinical cardiologists, interventional cardiologists, cardiovascular surgeons and specialists in cardiovascular imaging diagnosis; the other aspect is to carry out the procedure in a center with cardiac surgery. (99)

The medical team is essential to provide the best clinical judgment for the selection of patients, both for inoperable patients as, specially, for those at high risk who remain candidates for surgery and in whom percutaneous treatment is decided after evaluating the advantages and disadvantages of both techniques. These patients may be defined by risk scores, either the EuroSCORE ≥20% or the STS ≥10%; although, the former may overestimate operative mortality, the latter could then be more real (99). The ArgenSCORE is presented as a good alternative in our country, where it also demonstrated prospectively good performance, power of discrimination and adequate calibration for aortic valve replacement. (100)

Patients considered inoperable are those with severe respiratory failure (FEV1 <1000 ml), DLCO <30%, severe liver disease (MELD >25-CHILD B), (101) irradiated chest, porcelain aorta and coronary bridges that hinder thoracotomy.

Other aspects to be included in decision making are the concepts of frailty and futility. Frailty refers to the patient's clinical aspects associated with excess comorbidities and poor general condition. These patients should not be candidates for this type of procedures, as they would not change their condition (e.g. bedridden patients or patients with advanced dementia). Several scores assess frailty. (15-21) The concept of procedural ineffectiveness refers to the existence of a patient classification at low and intermediate risk, where surgical treatment is still the usual procedure; patients at high risk, where surgery and percutaneous implant are similar; inoperable patients, where percutaneous treatment is better and should be considered the first option; and extreme risk patients, in whom, due to comorbidities or life expectancy <1 year, the prognosis will not change.

Indications for percutaneous aortic valve replacement

Indication	Class	Level of evidence
Percutaneous valve implant is indicated in patients with symptomatic severe aortic stenosis who are not considered candidates for surgical treatment by the cardiac team, and who have a chance to improve their life quality and expectancy for more than one year despite the presence comorbidities.	I	B
Percutaneous valve implant may be considered in symptomatic patients with severe aortic stenosis, high surgical risk staged by the American Society of Thoracic Surgery score, the EuroSCORE or the ArgenSCORE, who are deemed candidates liable for surgery, but in whom the cardiac team considers indicating this treatment based on the risk-benefit ratio.	IIa	B
Symptomatic patients with severe aortic stenosis, moderate and low surgical risk and without criteria for inoperability.	III	B
Symptomatic patients with severe aortic stenosis, with comorbidities that generate life expectancy <1 year.	III	C

AORTIC VALVE REGURGITATION

The prevalence of aortic valve regurgitation increases with age, reaching 30% of elderly patients. It is usually of mild to moderate degree.(23) Valvular dysfunction may occur as a result of degenerative alterations that characterize the process of aging, of aortic root disorders (primary or secondary to hypertension) and less frequently of infectious endocarditis or a bicuspid valve. In recent years, another cause of aortic regurgitation is percutaneous valve implantation, which may lead to periprosthetic failure, generally poorly tolerated, as it occurs acutely on a hypertrophic ventricle. Thus, even mild degrees are associated with increased mortality. (93, 102) According to its presentation it may be acute or chronic.

Treatment

Chronic aortic regurgitation

Medical treatment

Vasodilator therapy: Hemodynamic benefit has been reported in patients with chronic aortic regurgitation treated with vasodilators. (103, 104)

Reduction of ventricular diameters and regurgitant fraction is observed, both with nifedipine as hydralazine and angiotensin-converting enzyme inhibitors. There is also evidence of reduction and/or delay for the need of valve surgery in asymptomatic patients with good left ventricular function treated with nifedipine. A study also showed that asymptomatic patients with ventricular dysfunction treated with nifedipine normalize postoperative ventricular function and have longer survival at 10 years. (105)

Based on these concepts, vasodilators would have indication in chronic severe aortic regurgitation in symptomatic patients who cannot undergo surgery, in patients with ventricular dysfunction and in severe heart failure to improve clinical conditions before surgery. In asymptomatic patients with severe aortic regurgitation and preserved ventricular function the evidence is still contradictory regarding the benefit in terms of delay in symptom onset or ventricular dysfunction. (106, 107)

Surgical Treatment

It represents 3 to 5% of cardiac surgeries in the elderly. (108) In asymptomatic patients it is indicated when there are signs of ventricular function deterioration by reduced EF or marked LV dilatation. Symptoms are the most common reason for surgery indication in elderly patients.

Indications for surgical treatment of chronic aortic regurgitation

Indication	Class	Level of evidence
Symptomatic patients with chronic severe aortic regurgitation (dyspnea or angina) attributable to valvular dysfunction independently of ventricular function.	I	B
Asymptomatic patients with chronic severe aortic regurgitation and LV dysfunction evidenced by the approach to one of the following parameters: systolic diameter of 55 mm, shortening fraction <25% or ejection fraction at rest <50%.	I	B
Patients with severe chronic aortic regurgitation who will undergo coronary artery bypass surgery, of the ascending aorta or other valves.	I	C
Asymptomatic patients with chronic severe aortic regurgitation, with LVEF >50%, but with extreme LV dilatation (diastolic diameter >75mm).	II	B
Patients with moderate chronic aortic regurgitation who will undergo coronary artery bypass surgery, of the ascending aorta or other valves.	II	C
Patients with chronic severe aortic regurgitation and normal systolic LV function at rest (EF >50%), when the degree of LV dilatation exceeds diastolic diameter of 70 mm or systolic diameter of 50 mm, when there is evidence of progressive LV dilatation, decreased exercise tolerance or abnormal hemodynamic responses to stress.	II	C
Asymptomatic patients with normal systolic function and adequate exercise tolerance.	III	C

LV: Left ventricular. LVEF: Left ventricular ejection fraction. EF: Ejection fraction.

Indications for surgical treatment of chronic aortic regurgitation: special situations

Indication	Class	Level of evidence
In patients with absence of bicuspid valve or genetic/familial cause of aortic dilatation, the recommended threshold for elective surgery is an aortic diameter of 55 mm; (degenerative thoracic aneurysms, chronic aortic dissections, intramural hematomas, penetrating atherosclerotic ulcers, mycotic aneurysms, or pseudoaneurysms) with or without severe aortic regurgitation (109).	I	B
Patients with Marfan syndrome and dilatation of the ascending aorta ≥50 mm.	I	C
Ascending aorta dilatation ≥45mm in patients with Marfan syndrome and risk factors (family history of aortic dissection, growth >5 mm/year), with or without aortic regurgitation.	II	C
Ascending aorta dilatation ≥50 mm and bicuspid aortic valve with risk factors (aortic coarctation, hypertension, family history of dissection, growth >5 mm/year).	II	C
Symptomatic severe coronary artery disease untreatable with angioplasty with moderate or severe aortic regurgitation.	II	C

MITRAL REGURGITATION

Mitral regurgitation is a valve disease that tends to increase in frequency and severity with age, especially with increasing mitral annulus calcification. (110, 111) In patients over 75 years, operative mortality is higher, mainly if mitral valve replacement is necessary and if myocardial revascularization is also required. (76, 77) Taking into account these factors and the life expectancy of an elderly patient, the goal of surgery should focus on improving the quality of life in symptomatic patients, rather than a possible life extension. Therefore, contrary to younger patients, symptoms rather than data on ventricular size and function are the main guide to perform surgery. The remaining patients may be adequately managed with medical treatment. Valve repair technique should be the initial technique of choice whenever possible, since it offers good results in this population and does not require long-term anticoagulation. (112)

Etiology

Mitral regurgitation at this age may be due to organ damage such as prolapse, rupture of chordae tendineae, annular calcification or functional causes. The latter may be due to ischemia or myocardial infarction involving papillary muscle function or to ventricular dilatation with loss of ventricular geometry, which pulls the papillary muscles and chordae tendineae downwards and backwards, with or without dilatation of the valve annulus. In patients over 70 years requiring surgical treatment, degenerative mitral regurgitation is the most common cause. (113)

Treatment

Even when surgery is indicated in asymptomatic patients with ventricular dysfunction criteria, in elderly patients symptoms should frame a surgical conduct. This is based on the lower life expectancy predicted in patients older than 75 years, in the higher surgical difficulty of extensive annular calcification, the greater surgical mortality of ischemic-necrotic functional mitral regurgitation and the increased presence of comorbidities. Consequently, medical treatment is recommended for all elderly patients in asymptomatic stage.

Indications for surgical treatment

Symptomatic severe organic mitral regurgitation has surgical indication and is the main reason for surgery. In elderly patients, the indication for surgery in asymptomatic patients should be carefully evaluated, as the limited natural life expectancy and/or the presence of comorbidities in octogenarians or even older patients, turn the criteria of incipient ventricular dysfunction insufficient to justify perioperative morbidity and mortality. In the asymptomatic patient the decision-making is then controversial, since there are no controlled studies to support this conduct, except in special selected cases from patients with potential for valve repair.

In asymptomatic patients with signs of LV dysfunction [EF <60%, end-systolic diameter >40 mm (>22 mm/m2)], valve repair may be advocated if the individualized risk-benefit ratio and patient's age justify it.

When LV function is preserved (EF >60%, end systolic diameter <40 mm), the presence of atrial fibrillation or systolic pulmonary hypertension at rest (>50 mmHg) direct the conduct towards the intervention independently of mitral valve repair feasibility.

Once the cut-off points established in the guidelines are met, patients should be operated on as early as possible (within 3 months) as the delay may lead to deterioration of contractile function and to greater impact on the right chambers with increased pulmonary systolic pressure.

If the patient is not suitable for valve repair, the benefit of early surgery is less than the risks, and therefore, close and regular monitoring is imperative.

Symptomatic patients with severe impaired LV function (EF <30%), in whom mitral valve repair is feasible, may benefit from this procedure. An intervention of this nature should be addressed only in centers with experience and ventricular assist device availability.

However, patients with severe ventricular function impairment (EF <20%), severe pulmonary hypertension and/or right ventricular dysfunction may be considered for heart transplantation given the high risk of valve surgery and the poor long-term results.

Indications for surgical treatment in chronic mitral regurgitation

Indication	Class	Level of evidence
Patients with severe mitral regurgitation with symptoms attributable to valve disease, EF>30% and end-systolic diameter<55 mm.	I	B
Asymptomatic patients with severe mitral regurgitation and ventricular dysfunction parameters (EF ≤60% and/or end-systolic diameter ≥45 mm).	I	B
Patients with severe mitral regurgitation with indication of myocardial revascularization surgery.	I	C
Mitral valve repair should be the technique of choice in relation with valve replacement in patients with severe chronic mitral regurgitation, with surgical indication and high durability expectancy.	I	C
Asymptomatic patients with severe mitral regurgitation, with preserved ventricular function, and pulmonary hypertension >50 mmHg at rest or pulmonary hypertension >60 mmHg with exercise.	IIa	C
Asymptomatic patients with severe mitral regurgitation, with preserved ventricular function, presenting with recent atrial fibrillation.	IIa	C
Asymptomatic patients with severe mitral regurgitation due to flail valve, with intermediate ventricular function parameters, low surgical risk, high repair feasibility (>90%) and high durability expectation.	IIa	C
Valve surgery should be considered in asymptomatic patients with severe mitral regurgitation, with intermediate ventricular function parameters (end-systolic diameter 40-44 mm), low surgical risk and high repair feasibility (>90%) presenting left atrial volume index >60 ml/m2 and/or progression of neurohormonal activation (progressive increase of natriuretic peptides).	IIa	C
Symptomatic patients with severe mitral regurgitation, with severe impaired left ventricular function (EF between 20% and 30%), refractory to medical treatment (including resynchronization therapy), with low co-morbidities and in whom valve repair is highly feasible.	IIa	C
Asymptomatic patients with severe mitral regurgitation, with preserved ventricular function, adequate stress tolerance, low surgical risk, high repair feasibility (>90%) and high durability expectation.	IIb	C
Symptomatic patients with severe mitral regurgitation, with severe left ventricular function impairment (EF between 20% and 30%), refractory to medical treatment (including resynchronization therapy), with low co-morbidities and in whom valve repair is unlikely.	IIb	C
Asymptomatic patients with severe mitral regurgitation, preserved left ventricular systolic function, adequate exercise tolerance and low probability of undergoing valve repair.	III	C

EF: Ejection fraction.

Indications for surgical treatment in functional mitral regurgitation

Indication	Class	Level of evidence
Patients with severe mitral regurgitation and indication for revascularization and EF>30%.	I	C
Moderate mitral regurgitation with indication of myocardial revascularization (annuloplasty).	IIa	C
Symptomatic patients with severe mitral regurgitation, EF<30%, who will undergo revascularization and have evidence of high feasibility (annuloplasty).	IIa	C
Surgery may be considered in patients with severe mitral regurgitation, EF >30%, symptomatic despite optimal medical treatment (including resynchronization if necessary), if they have few comorbidities and have no indication for revascularization.	IIb	C

EF: Ejection fraction

Conflicts of interest

None declared. (See author´s conflicts of interest forms in the web / Supplementary Material).

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