Module 3. Valvulopathies and aortopathies

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References

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We all know that exercise is associated with multiple benefits, which is why all people with cardiovascular disease should be encouraged to engage in some type of physical activity in order to maintain a healthy lifestyle. But in certain cases, such as severe valvulopathies, the prescription of adequate exercise can be complicated.

In the western world, valvular heart disease is predominantly a pathology secondary to a degenerative process and generally develops from the sixth decade of life onwards. However, there is a percentage around 1-2% of young individuals with valvulopathy, the vast majority being a congenital disease (**Gati** *et al.*, 2019).

The information available on the impact of intense physical activity on the progression of valvular heart disease is limited, and for this reason, current recommendations are based on consensus opinion. In fact, we do not know whether regular physical exercise can delay the development of severe valvulopathies. Nevertheless, the implementation of cardiac rehabilitation programs in these individuals has demonstrated an improvement in functional capacity, muscle strength, flexibility, and quality of life.

The treatment of individuals with valvular heart disease who exercise requires a structured approach that includes several key factors, such as symptomatic status, functional capacity, the type and nature of the valvular lesion, the impact on ventricular structure and function, and the effect on pulmonary pressures. As a general advice, the assessment of valvulopathies begins with a general clinical evaluation, followed by relevant imaging studies and recommendations based on severity and symptomatology.

In this chapter we will cover the most common valve pathologies (aortic and mitral), emphasizing the recommendations related to physical exercise, as well as aortic diseases, both of genetic and acquired etiology.

Aortic valve pathology

Aortic stenosis

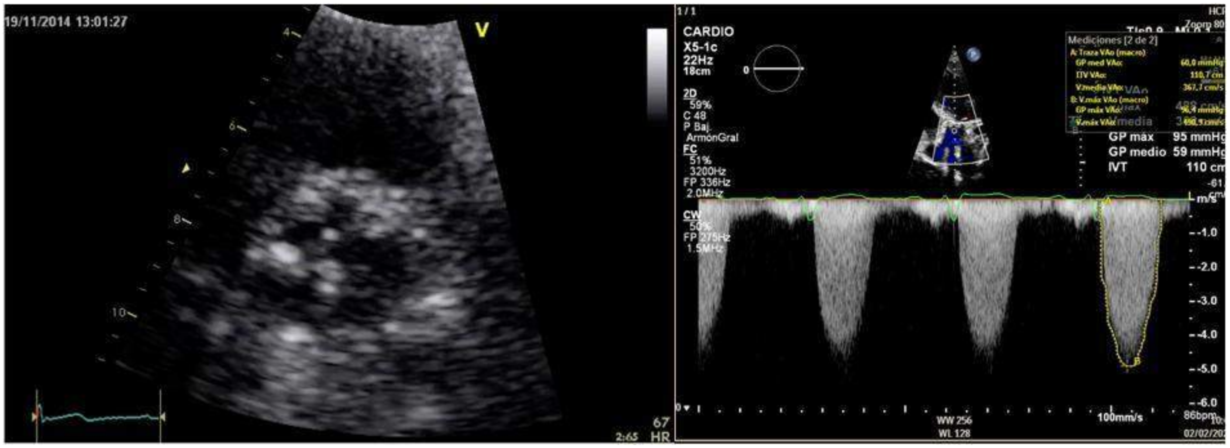
Aortic stenosis (AS) is a well-known cause of exertion-related sudden cardiac death, but accounts for less than 4% of events in young athletes (Maron, 2003). A history of decreased exercise tolerance, exertional dyspnea, or exercise-induced angina in an athlete with a systolic murmur should raise suspicion of valvulopathy.

Its most frequent etiology in the elderly population is degenerative, but in young individuals the presence of an underlying congenital pathology, such as bicuspid aortic valve (BAV), must be ruled out (**Baumgartner** *et al*., 2017).

Evaluation

Doppler echocardiography is the standard method for its evaluation, allowing us to make a severity grading. Its severity is classified according to specific clinical guidelines (Baumgartner et al., 2017) based on the pressure gradient across the aortic valve (maximum and mean gradients) and the estimated degree of valvular opening (area). It is recommended to be performed at least once a year (Figure 1).

Figure 1. 66-year-old male with exertional dyspnea. Echocardiographic image of a heavily calcified tricuspid aortic valve with significant stenosis and gradients confirmed by continuous Doppler signal, indicating severe valvulopathy



Source: own source.

In certain cases, a stress echocardiogram may be useful to assess dynamics, as well as to unmask possible subclinical ventricular dysfunction. This test is of utmost importance in patients with at least moderate AS or in those with systolic dysfunction, in whom it will allow us to differentiate true severe AS from pseudosevere AS, in addition to providing information on possible contractile reserve.

In addition, performing a stress test in athletes will allow us to assess the functional class and rule out the presence of arrhythmias. Hemodynamic parameters, such as a drop in blood pressure during the test or failure to increase blood pressure by 20 mm Hg, are indicators of high risk.

Recommendations

Recommendations for asymptomatic athletes (Table 1):

- Patients with mild AS and normal left ventricular (LV) size and function can participate in all sports.
- Patients with moderate AS and normal LV systolic function can participate in all competitive sports if they show good functional capacity, normal hemodynamic response, and absence of complex arrhythmias during maximal exercise.

Recommendations in case of symptomatology:

- Patients with moderate or severe AS or with LV dysfunction at rest or demonstrated on stress ultrasound and complex ventricular arrhythmias should refrain from competitive sports and/or high-intensity physical training. The usual physical activity recommendations can be made to maintain cardiovascular health (Van Buuren et al., 2021).
- Patients with severe stenosis should be referred for surgical treatment, after which the recommendations established for athletes with valve prostheses should be followed.

Table 1. Recommendations for exercise and sports practice in asymptomatic athletes with aortic stenosis

Recreational exercise		
	Recommendation	**Class/Level**
Slight	Any type of recreational sport and high-intensity strength and/or aerobic exercise can be practiced.	IC
Moderate	Individuals with good functional class, normal stress test, and normal ejection fraction may perform low-to-moderate intensity exercise.	IIaC
Severe	Individuals with good functional class, normal stress test, and normal ejection fraction may perform low-intensity exercise.	IIbC
	Participation in high-intensity recreational sports is not recommended.	IIIC
Competitive exercise		
Slight	There are no contraindications for competitive sports.	IC
Moderate	Individuals with good functional class, normal stress test, and normal ejection fraction may perform low-to-moderate intensity competitive exercise.	IIbC
Severe	Participation in low-intensity skill sports could be considered.	IIbC
	Participation in moderate- or high-intensity competitive sports is not recommended.	IIIC

Source: own source based on Pelliccia *et al.*, 2012.

Aortic insufficiency

Aortic insufficiency (AI) is a valvulopathy which has an etiopathogenesis that includes congenital heart disease such as BAV, rheumatic fever, endocarditis, Marfan syndrome, or aortic dissection (Otto et al., 2021).

Athletes with chronic AI may remain asymptomatic for many years. Once ventricular function deteriorates, symptoms may appear, including exertional dyspnea, arrhythmias, and in advanced cases, angina.

Evaluation

Athletes with AI must undergo an annual physical examination with echocardiography. The severity of the AI is established according to clinical guidelines (**Baumgartner** *et al*., 2017) by evaluating the regurgitation jet through a color Doppler echocardiogram (Figure 2) and continuous Doppler, sometimes using other indirect parameters, such as flow reversal in the descending thoracic or abdominal aorta. It is important to rule out the presence of underlying BAV as a cause of the valvulopathy.

Figure 2. 23-year-old amateur male athlete. Transthoracic echocardiography images with color Doppler signal (4- and 3-

chamber views) suggestive of severe aortic insufficiency. LV: Left ventricle; LA: Left atrium; RV: Right ventricle

Source: own source.

In doubtful cases or cases with suboptimal echocardiographic imaging, a cardiac magnetic resonance imaging (CMR) is recommended as a complementary tool for the accurate assessment of severity and valvular morphology.

We must bear in mind that this is a pathology that causes an overload of both LV volume and pressure, resulting in an increase in cavity size in both systole and diastole. It is often difficult to differentiate LV dilation produced by physical training in athletes from pathological dilation produced by a valvulopathy itself. We will consider LV end-diastolic diameter (LVEDD) >60 mm and LV endsystolic diameter (LVESD) >49 mm for men and 38 mm for women as above-normal limits (**Zoghbi** *et al.*, 2017).

A stress test (or a stress test with oxygen consumption) may be useful in assessing functional capacity, hemodynamic response, and possible inducibility of arrhythmias with exercise.

Recommendations

As for asymptomatic athletes, they may participate in competitive sports in the following cases (Table 2):

- Mild or moderate AI, with normal LV ejection fraction and up to mild-moderate LV dilation (LVESD <50 mm in men, <39 mm in women or <25 mm/m^2 in either sex).
- Athletes with severe AI, ejection fraction <50% with non-dilated ventricles, if there is no evidence of progression of valvulopathy (stable assessment in recent years).

Table 2. Recommendations for asymptomatic athletes with aortic insufficiency

Recreational exercise		
	Recommendation	**Class/Level**
Slight	Any type of recreational sport and high-intensity strength and/or aerobic exercise can be practiced.	IC
Moderate	Individuals with good functional class, normal stress test, and normal ejection fraction, as well as with non-dilated left ventricle, can perform recreational aerobic and/or static exercise of any intensity.	IIaC
Severe	Individuals with good functional class, normal stress test, mild or moderate left ventricular dilation, and normal ejection fraction will be able to perform low-to-moderate intensity exercise.	IIbC
	Participation in moderate-to-high intensity sports is not recommended if there is ventricular dysfunction or exertion-induced arrhythmias.	IIIC
Competitive exercise		
Slight	There are no contraindications for competitive sports.	IC
Moderate	Individuals with good functional class, normal stress test, and normal ejection fraction will be able to perform competitive exercise.	IIaC
Severe	Participation in low-to-moderate intensity sports could be considered in individuals with normal ejection fraction, mild-moderate left ventricular dilation, and normal stress test.	IIbC
	Participation in moderate- or high-intensity competitive sports is not recommended in case of ventricular dysfunction or exertion-induced arrhythmias.	IIIC

Source: own source based on Pelliccia *et al.*, 2012.

Athletes with symptoms, ejection fraction <50%, LVESD >50 mm or >25 mm/m^2, or LVEDD (>70 mm or >35.3 mm/m^2 [men], >65 mm or >40.8 mm/m^2 [women]) should not participate in competitive sports (**Van Buuren** *et al*., 2021).

Athletes with severe valvulopathy should be referred for surgical treatment, after which the recommendations established for individuals with valve prostheses should be followed.

Bicuspid aortic valve

Bicuspid aortic valve (BAV) is the most common congenital heart condition in both the general population (0.5-2%) and athletes (2.5%), showing higher prevalence in males (Siu and Silversides, 2010). This is an aortic valve that has only two leaflets, instead of three, and one of them is usually larger. There are different types of valve morphology or morphotypes depending on the fusion pattern of the leaflets. The presence of a raphe or fibrous thickening between the two fused leaflets is common in BAV and may be calcified. Rarely, the BAV has two symmetrical leaflets and no raphe (pure BAV). The most frequent form is that which appears by fusion of the right and left coronary leaflets (**Siu and Silversides**, 2010) (Figure 3).

Figure 3. A: Pure bicuspid aortic valve by fusion of right and left coronary leaflet without raphe; B: Bicuspid aortic valve by fusion of right and left coronary leaflet with raphe (arrow); C: Bicuspid aortic valve by fusion of right and non-coronary leaflet with calcified raphe (arrow)

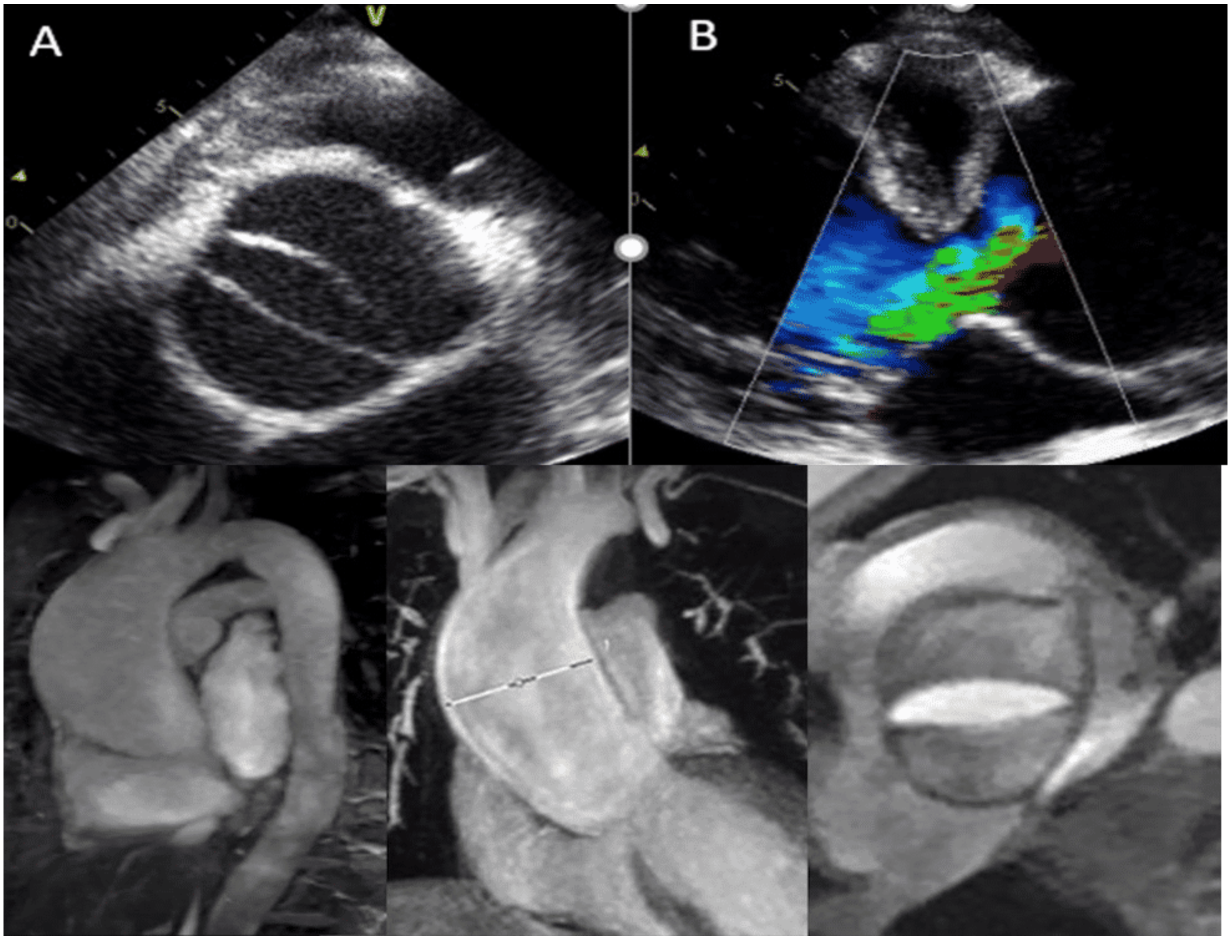
Source: Masip et al., 2022, https://goo.su/SYCjbw.

Athletes with BAV may have with both insufficiency and stenosis, the management of which is similar to that of individuals with tricuspid aortic valve.

According to the articles published to date, the hemodynamic effects of intensive exercise do not seem to have a negative impact on its progression. Boratia et al. (2019), in a 3-year follow-up study comparing elite athletes with BAV to athletes with tricuspid aortic valve and non-athletic BAV patients, observed that high-intensity training and sports competition did not aggravate the valvulopathy in affected individuals. In another study, with a 13-year follow-up, it was also observed that progression of valvular disease occurred independently of sporting activity and that most athletes with BAV showed a benign clinical course (**Spataro** *et al*., 2008).

This pathology is actually known as a valvulo-aortopathy (Figure 4), since valve dysfunction is associated, in almost half of the cases, with aortic dilation, and is considered a risk factor for aortic dissection. Although initial reports of aortic dissection in the BAV population estimated incidences of up to 8.6%, lower rates are now described with excellent long-term survival, being even similar to that of the general population (**Michelena** *et al*., 2015).

Figure 4. A: Transthoracic echocardiography image of bicuspid aortic valve due to fusion of right and left coronary leaflets; B: Color Doppler image of bicuspid aortic valve with significant insufficiency; C: MRI with ascending aorta aneurysm in patient with bicuspid aortic valve



Source: Masip *et al.*, 2022, https://goo.su/SYCjbw.

It is likely that several factors, such as genetic predisposition, cellular matrix remodeling processes, or hemodynamic and biomechanical disturbances, may explain the natural history of the valvulopathy. Current eligibility guidelines for competitive athletes suggest that the increase in blood pressure that occurs during intense physical exertion may elevate aortic wall tension, placing subjects with bicuspid aortopathy at increased risk for dilation and rupture.

Evaluation

Given the high interindividual variability observed, a comprehensive echocardiographic evaluation is crucial for the management of this condition. This study should include evaluation of the aorta, valve function, left ventricular size and function, and aortic size, from the aortic root to the aortic arch. In rare cases, BAV is associated with an anomalous origin of the coronary arteries, so the examination should include identification of both coronary ostia.

Currently, it is recommended to include in the echocardiographic report not only absolute values of diameters, but also z-scores incorporating height, weight, age, and sex, with aortic dilation being defined as a z-score →2.0, which corresponds approximately to the 98th percentile of the general population (**Braverman**, 2011). Notably, although increased body surface area (BSA) is associated with larger aortic diameters, there is a nonlinear relationship, with a plateau between aortic root dimensions and height (>189 cm; >175 cm in women) and BSA (>2.3 m^2) in very tall individuals (**Gati** *et al.*, 2019). This condition makes it difficult to assess aortic size in tall individuals and tall athletes, and it is important to avoid attributing aortic enlargement in tall (or large) athletes solely to height, BSA, or a physiologic response to exercise.

If the transthoracic echocardiographic evaluation does not allow for an accurate visualization of the aorta or in case of moderate to severe aortic dilation, a cardiac CT or cardiac MRI should be performed. It is important to pay special attention with close monitoring and through imaging techniques when a rapid change in aortic size occurs, i.e., →0.5 cm/year or when the diameters around the surgical indication are reached (in this case, diameters >55 mm) (**Evangelista** *et al*., 2018).

In addition, for complete risk stratification, a stress test is recommended.

Recommendations

Eligibility for participation in competitive sports is determined by several factors including symptomatic status, functional capacity, type and severity of valvular disease, alterations in myocardial structure and function, pulmonary artery pressure, and risk of arrhythmias.

In general, the guidelines are that, in the absence of aortopathy, exercise recommendations are identical to those for individuals with tricuspid aortic valve. On the other hand, with regard to aortic dilation, individuals with an aortic root above the normal range (>40 mm) or →43 mm in tall men and →39 mm in women with a body surface area greater than 2.2, should not participate in sports associated with a greater load, such as weight lifting and isometric exercise, and competing only in sports of low-to-moderate cardiovascular demand is recommended, similar to other aortopathies of non-genetic etiology (**Van Buuren** *et al.*, 2021). These limits are defined by the absence of aortic remodeling from these events, regardless of the body surface of the individual (as opposed to other cavities, such as the left and right ventricle, which grow in accordance with the body surface) (**Pelliccia** *et al.*, 2012).

Moreover, antibiotic prophylaxis for endocarditis has to be recommended for all individuals with BAV (Van Buuren et al., 2021).

Mitral valve pathology

Mitral insufficiency

Mitral insufficiency (MI) can be secondary to a variety of possible causes, the most common in the athletic population being mitral valve prolapse (MVP) which will be discussed specifically below. Other common causes are rheumatic heart disease, infective endocarditis, and connective tissue diseases (such as Marfan syndrome), as well as other secondary forms caused by lack of leaflet coaptation, as occurs in dilated cardiomyopathy and the presence of coronary artery disease (**Iung** *et al.*, 2019).

The severity of MI is related to the magnitude of regurgitant volume, resulting in LV dilation and increased left atrium pressure and volume to accommodate regurgitant volume and maintain systolic volume within normal limits. As with AI, the distinction between LV dilation caused by athletic training versus that caused by severe MI is difficult to differentiate when LVEDD is <60 mm (or <40 mm/m^2). However, LVEDD measurements >60 mm suggest the presence of severe MI and, perhaps, the need for valvular surgical repair (**Baumgartner** *et al.,* 2017).

In general, exercise does not produce significant changes or, in the regurgitant fraction, it even produces a slight decrease due to the reduction of systemic vascular resistances. Nonetheless, when an increase in blood pressure or heart rate during exertion or occurs, this can lead to marked increases in regurgitant volume and pulmonary capillary pressures, resulting in symptoms.

Evaluation

Athletes with MI should undergo a follow-up transthoracic echocardiography at least annually. Additionally, a stress echocardiogram can be performed during an activity that closely matches the exercise demands of the sport the individual practices, in order to assess changes in severity and increases in pulmonary artery pressures. In cases of poor transthoracic window, it may be necessary to resort to a transesophageal echocardiography or an MRI. The latter will help us quantify ventricular volumes and the presence of fibrosis.

Recommendations

- Athletes with mild-to-moderate MI in sinus rhythm with normal LV size and function and normal pulmonary artery pressures can participate in all competitive sports (Table 3).

- If patients have moderate MI in sinus rhythm, with normal LV systolic function or mild LV dilation, they may still participate in all competitive sports.

- Athletes with severe MI in sinus rhythm, with preserved systolic function, and mild LV dilation can participate in low-intensity and some moderate-intensity sports.

- Athletes with MI of any severity, severe left ventricular dilation, pulmonary hypertension, or any degree of left ventricular systolic dysfunction at rest should not participate in competitive sports, with the possible exception of low-intensity sports.

- Athletes with a history of atrial fibrillation who are on long-term anticoagulation therapy should not participate in sports that involve any risk of physical contact.

- In patients with MI secondary to previous endocarditis infections or chordae rupture, valve tissues could theoretically suffer more damage or tearing; therefore, recommendations should be more restrictive (**Van Buuren** *et al*., 2021).

- Athletes with severe valvulopathy should be referred for surgical treatment, after which the recommendations established for individuals with valve prostheses should be followed.

Table 3. Recommendations for asymptomatic athletes with mitral insufficiency

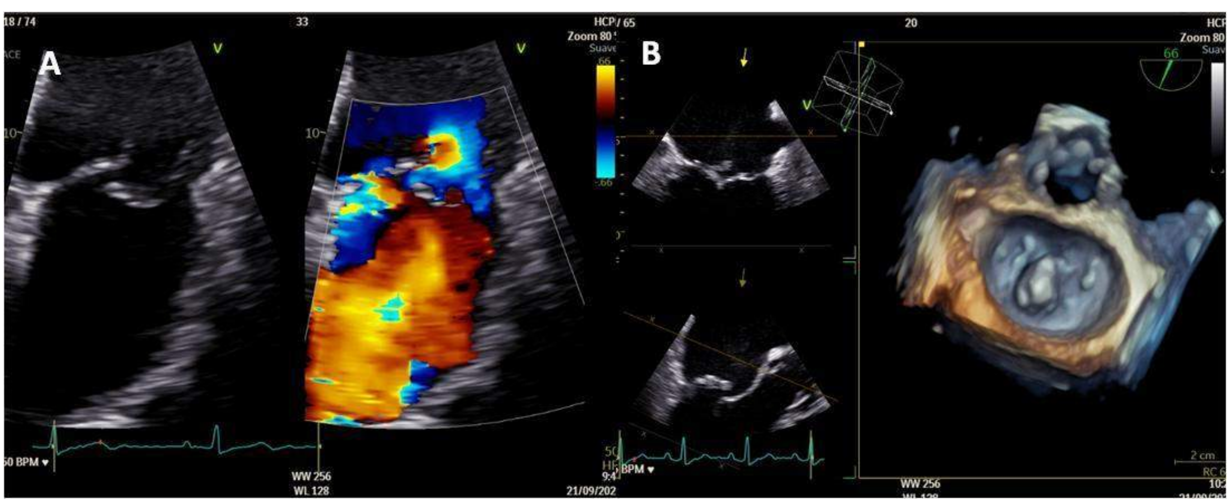
Recreational exercise		
	Recommendation	Class/Level
Slight	Any type of recreational sport and high-intensity strength and/or aerobic exercise can be practiced.	IC
Moderate	Individuals who meet the following criteria may engage in recreational exercise: • LVEDD <60 mm or <35.3 mm/m² in men or <40 mm/m² in women • Ejection fraction ≥60% • Pulmonary artery systolic pressure (PASP) at rest <50 mm Hg • Normal stress test	IIaC
Severe	Individuals who meet the following criteria may engage in low-to-moderate intensity recreational exercise: • LVEDD <60 mm or <35.3 mm/m² in men or <40 mm/m² in women • Ejection fraction ≥60% • PASP at rest <50 mm Hg • Normal stress test	IIbC
Competitive exercise		
Slight	There are no contraindications for competitive sports.	IC
Moderate	Individuals who meet the following criteria may engage in competitive exercise: • LVEDD <60 mm or <35.3 mm/m² in men or <40 mm/m² in women • Ejection fraction ≥60% • PASP at rest <50 mm Hg • Normal stress test	IIaC
Severe	Individuals who meet the following criteria may engage in low-intensity competitive aerobic and skill-based exercise: • LVEDD <60 mm or <35.3 mm/m² in men or <40 mm/m² in women • Ejection fraction ≥60% • PASP at rest <50 mm Hg • Normal stress test	IIbC
	Participation in competitive sports is not recommended for athletes who do not meet the above criteria.	IIIC

Source: own source based on Pelliccia *et al.*, 2012.

Mitral valve prolapse

Mitral valve prolapse (MVP) is a common condition that has a clear genetic predisposition, resulting in myxomatous changes of the mitral valve leaflets. The estimated incidence of MVP is between 0.2% and 0.4% per year in the general population (Van Buuren et al., 2021). Excessive elongation and thickening of the leaflets and chordae of the mitral valve cause prolapse of the leaflets into the left atrium in systole (at least 2 mm beyond the annular plane) with potential progressive MI due to loss of coaptation. It may affect one or both leaflets (Figure 5).

Figure 5. A: Transthoracic echocardiography image of a 28-year-old female patient with posterior leaflet prolapse (arrow) and severe insufficiency; B: Transesophageal echocardiography image of the same individual, with a 3D reconstruction image confirming the prolapse



Source: own source.

The natural history is generally benign, with a 10-year mortality risk of 5%; however, MVP has been considered the leading cause of severe MI requiring surgical intervention in developed countries (**Sabbag** *et al*., 2022).

This pathology has been classically related to a greater predisposition to arrhythmogenic sudden cardiac death (SCD), which is its most feared complication. In an Italian registry that included 650 patients under 40 years old who had suffered SCD, it was shown that 7% of these occurred in the context of MVP, with the 60% of the cases being women.

Investigations with patients with MVP, where ECG studies were available, mostly revealed inverted T waves in the lower limb leads, as well as ventricular extrasystoles with right bundle branch block ventricular morphology. These abnormalities suggest that the mechanical effects of MVP may create an arrhythmogenic environment that can lead to potentially fatal sustained arrhythmias in some patients. These electrical changes have also been related to structural changes, with increased scarring in the inferobasal wall and papillary muscles having been observed in patients with MVP, a finding described, according to the series, in almost 90% of those who died in the context of MVP. A more recent study examined 36 living patients with arrhythmic MVP and confirmed the presence of inferobasal and papillary muscle fibrosis in cardiovascular disease. It was detected by MRI in 93% of the cases, compared to those without arrhythmia, where late scarring was observed in only 14% of cases. The authors also described mitral annulus disjunction more frequently in those with MVP and ventricular arrhythmias compared to those without arrhythmias (**Essayagh** *et al*., 2021).

Other studies suggested the possibility of other risk markers, such as ventricular arrhythmias shown on the Holter monitoring, severe mitral insufficiency, LV systolic dysfunction or the presence of a family history of SCD (**Sabbag** *et al*., 2022).

It is possible that MVP-related mortality in younger individuals occurs mainly in genetically susceptible individuals, whereas, in older patients, MVP-related mortality could be multifactorial.

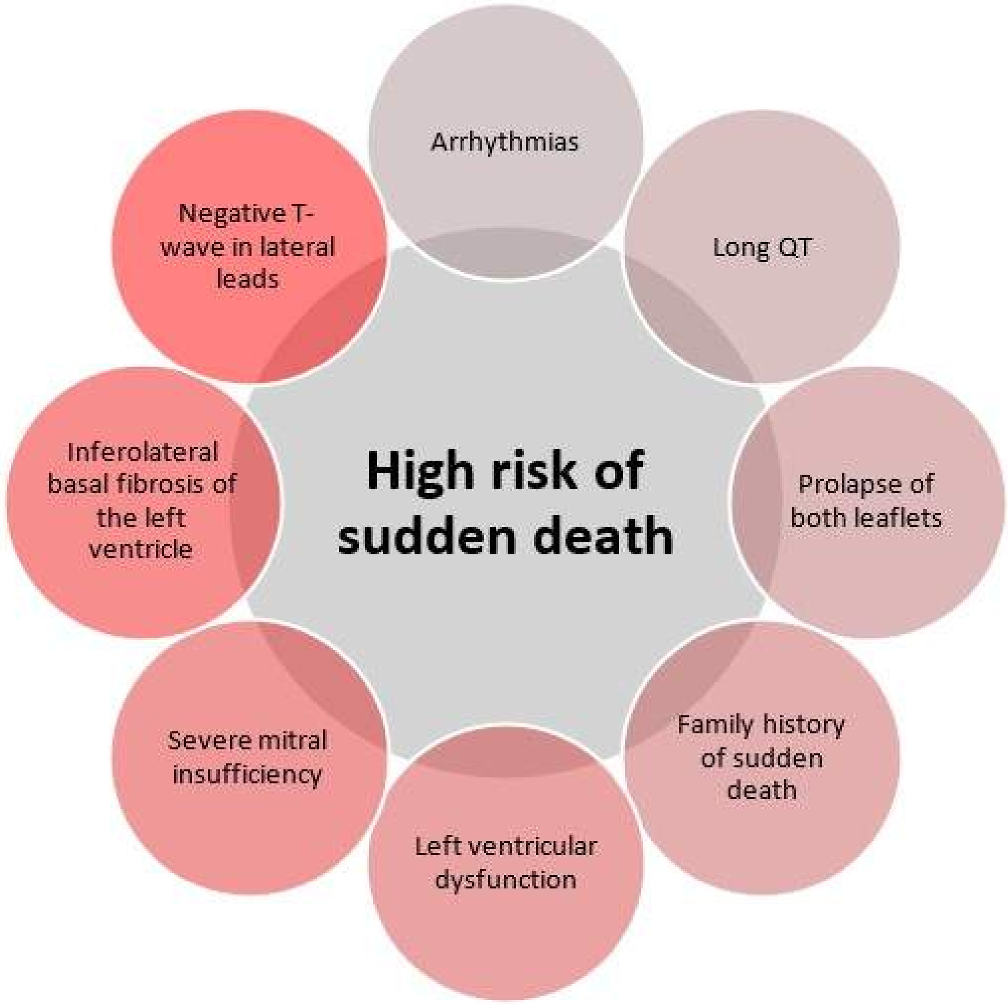
What is unclear is whether MVP exacerbates the risk of SCD in athletes. The article by Essayagh et al. (2021) provides important information on the natural history of this pathology. Investigators described that up to 26% of individuals had T-wave inversion or ST-segment depression. The presence of repolarization abnormalities was the most important independent predictor of severe ventricular arrhythmias in this cohort.

Based on these data, we believe that the follow-up of these patients should include, in addition to an echocardiography/a stress echocardiography, as in the rest of MI, a Holter monitor to rule out arrhythmic component.

Recommendations

In general, most physically active people with MVP who have mild-to-moderate regurgitation can participate in all sports competitions. If the aforementioned risk markers are present (Figure 6), exercise should be restricted to low-intensity competitive sports.

Figure 6. Risk markers for sudden death in mitral valve prolapse



Source: own source.

In the case of MVP associated with severe regurgitation, the recommendations will be the same as for the presence of such isolated valvulopathy (**Van Buuren** *et al*., 2021).

Mitral stenosis

The etiopathogenesis of mitral stenosis (MS) is almost always rheumatic (**Iung** *et al*., 2019). During exercise, the increase in heart rate and left atrial filling is associated with an increase in gradients across the mitral valve, which may lead to acute pulmonary edema, even suddenly. Moreover, chronic elevation of pulmonary venous pressure will be associated with pulmonary hypertension and right ventricular hypertrophy.

The long-term effects of regular intensive exercise on MS progression, pulmonary vasculature, and ventricle are unknown, although exercise may exacerbate atrial growth and may contribute to the development of atrial fibrillation, increasing thromboembolic risk.

Evaluation

The etiopathogenesis of mitral stenosis (MS) is almost always rheumatic (**Iung** *et al.*, 2019). During exercise, the increase in heart rate and left atrial filling is associated with an increase in gradients across the mitral valve, which may lead to acute pulmonary edema, even suddenly. Moreover, chronic elevation of pulmoFor its evaluation, a Doppler echocardiogram is required. The severity of MS is defined by the mitral valve area and transvalvular gradients, as specified in the guidelines (Iung et al., 2019).

In these patients, a stress echocardiography provides additional objective information by allowing the assessment of changes in transmitral gradient and pulmonary artery pressure. It is also important to remember that the pressure gradient across the valve depends, to a large extent, on transvalvular flow and the diastolic filling period, factors that will vary greatly with the increase in heart rate during exercise. A mean gradient >15 mm Hg or pulmonary artery pressure >25 mm Hg during exercise is indicative of significant MS. Besides, if this increase exceeds 40 mm Hg during exercise, it is a clear indicator of poor prognosis in these patients.

Thus, in patients with MS and minimal or no symptoms, who want to participate in competitive sports, a stress test should be performed, at least up to the level of activity that approximates the demands of the sport to be practiced.

This clinical and imaging evaluation should be performed at least annually.

Recommendations

- Athletes with mild MS (mitral valve area >2.0 cm^2, mean gradient <10 mm Hg at rest) in sinus rhythm can participate in all competitive sports if their pulmonary artery pressure at rest is <40 mm Hg (Table 4).

- Athletes with severe MS (mitral valve area <1.5 cm^2), both in sinus rhythm and atrial fibrillation, should not participate in competitive sports, with the possible exception of low-intensity sports.

- Athletes with MS of any severity with pulmonary artery pressure >40 mm Hg should avoid all competitive sports.

- Athletes with MS of any severity in atrial fibrillation receiving anticoagulant therapy should not participate in competitive sports involving risk of bodily contact or collision.

- Atheletes with severe valvulopathy should be referred for surgical or percutaneous treatment, after which the recommendations established for individuals with valve prostheses should be followed.

- In those individuals who have undergone valvuloplasty as a treatment, recommendations are based on the residual transmitral gradient value.

- After mitral valve replacement, patients may participate in mixed and skill sports, provided that valve function is satisfactory and there is no evidence of hemodynamic disturbance (**Van Buuren** *et al*., 2021).

Table 4. Recommendations for asymptomatic athletes with mitral stenosis

Recreational exercise		
	Recommendation	**Class/Level**
Slight	Recreational sports of any intensity are recommended for individuals with a PSAP <40 mm Hg at rest and a normal stress test.	IC
Moderate	Light-to-moderate intensity recreational sports are recommended for individuals with PSAP <40 mm Hg at rest and a normal stress test.	IIbC
Severe	Participation in moderate-to-high intensity sports is not recommended.	IIIC
Competitive exercise		
Slight	Competitive sports are allowed for individuals with PSAP <40 mm Hg at rest and a normal stress test.	IC
Moderate	Light-intensity competitive sports are allowed for individuals with PSAP <40 mm Hg at rest and a normal stress test.	IIaC
Severe	Participation in competitive sports is not recommended.	IIIC

Source: own source based on Pelliccia *et al.*, 2012.

Valve prosthesis and valve repair

Following valve replacement or repair surgery, recovering individuals should rehabilitate with an exercise program that ideally lasts 12 weeks and gradually increases in duration, and they may begin to exercise more vigorously after this period of time, when the sternal injury has fully healed.

The patient undergoing cardiac surgery has certain characteristics to be taken into account, namely: Possible presence of anemia, sympathetic hyperactivity, and tachycardia disproportionate to the effort made. It is considered that a sternotomy usually heals around 6-8 weeks post-surgery. At that point, inclusion in a complete cardiac rehabilitation program should be considered. Until then, various breathing exercises are usually recommended, as well as a walking program that gradually increases in distance and intensity. Participation in such programs has been associated with fewer events at follow-up.

There are currently no data on the natural history of a replacement or repair in individuals who exercise intensively, so current consensus recommendations are relatively conservative in terms of follow-up of operated individuals. In fact, as with native valves, athletes should undergo an annual re-evaluation with an echocardiography and a stress test after the surgery, which should be performed at an intensity compatible with the sport the athlete wants to practice.

Additionally, it is important consider that the hemodynamic changes associated with the prosthetic valve are suboptimal, and there may be some flow limitation through the prosthetic valve. For this reason, in general, it is recommended that these patients have the same exercise limitations as asymptomatic athletes with moderate native valvulopathy, as long as ventricular function is preserved and pulmonary artery pressure is within normal limits (**Van Buuren** *et al*., 2021).

Anticoagulation is often mandatory for mechanical prostheses and for those patients with atrial fibrillation (AF), which further limits the choice of competitive sports. Contact sports or sports associated with trauma (such as competitive cycling, hiking, windsurfing, etc.) should be specifically avoided (**Van Buuren** *et al*., 2021).

Aortopathies

Aortic pathology of genetic etiology

Hereditary thoracic aortic disease (HTAD) comprises a broad spectrum of diseases defined by the occurrence of aortic disease, mainly in the form of aneurysm or dissection. These entities can be classified as non-syndromic, when the disorder is limited to aortic disease, and syndromic, when extra-aortic manifestations are included. In patients with non-syndromic aortic disorder, about one third have a family history of aortic disease, indicating a genetic component, although the pathogenic variant is detected in only 20% of patients (**Elefteriades and Farkas**, 2010).

However, a strong gene-disease association can be observed in syndromic aortic diseases, such as Marfan syndrome (MS). This is the most frequent syndromic aortopathy, so we will focus on this one.

MS is a rare disease with autosomal dominant inheritance. Up to 95% of patients have a causative variant in the FBN1 gene, leading to a pathogenic alteration in the extracellular matrix protein fibrillin 1 (**Franken** *et al*., 2017). Fibrillin microfibrils are extensible polymers with an important role in extracellular tissue, providing elasticity to connective tissues. In addition, this molecule is widely distributed in connective tissue, both elastic and non-elastic. A prevalence of MS in the general population of 1-5:10000 has been described (**Franken** *et al*., 2017). Nevertheless, this prevalence could be higher in athletes who participate in certain sports, such as volleyball, basketball, or high jump.

The principal manifestations involve the cardiovascular system (including mitral insufficiency, caused by valve prolapse and aortic root dilation), as well as skeletal and ocular abnormalities. Diagnosis can be made on the basis of clinical manifestations, family history, and/or genetic analysis, according to Ghent's criteria.

Aortopathy, responsible for progressive aortic dilation, can lead to aortic dissection in severe cases, being the main cause of morbidity and mortality in this cohort.

Few studies in the scientific literature evaluate the effect of exercise on MS. There are three relevant studies, only one of which was carried out in humans, with different training protocols, in order to evaluate the effect of physical activity on aortic function and structure. Studies in mice models with MS demonstrated that moderate-to-intense dynamic exercise training induced an improvement in aortic wall elasticity or no significant reduction in aortic diameter compared to sedentary control animals.

As for the study carried out in humans, a 3-week rehabilitation protocol was applied to 18 patients with MS who had undergone cardiovascular surgery. The authors reported several benefits in terms of physical fitness, quality of life, and psychological well-being. This study also demonstrated the feasibility of training in these patients in the absence of adverse events during their 1-year follow-up. Nevertheless, we should point out that the exercise intensity proposed in this work was low, thus not being representative of what we do in regular practice (**Cheng and Owens**, 2016).

Despite the fact that in patients with MS the most serious risk is progression to aortic dissection, several studies have highlighted abnormalities in size, function, and deformation in these individuals.

It should be noted that these patients have a characteristic morphotype of low muscle mass with associated decreased maximal quadriceps strength. In addition, patients with MS have frequent musculoskeletal pain, which can have a deleterious effect on endurance work.

Recommendations

In patients with MS, intense competitive physical activity is generally not recommended, regardless of aortic dimensions. Thus, they should be limited to low-intensity skill sports (e.g., golf, bowling) to avoid an excessive increase in systemic blood pressure associated with isometric exercise, which could trigger an acute aortic syndrome. The data, although nonspecific, suggest that it may be sensible to avoid activities that may acutely elevate systolic blood pressure (SBP) above 200-220 mm Hg or require the Valsalva maneuver, particularly if the aorta is already aneurysmal (**Cheng and Owens**, 2016).

Patients should also avoid contact sports, such as boxing or soccer, due to their skeletal and cardiovascular susceptibilities (**Cheng and Owens**, 2016).

Regarding recreational sport, recommendations are established depending on the type of sport for individuals without (or with mild) aortic dilation (**Cheng and Owens**, 2016).

Table 5. Recommendations according to the type of sport for individuals without (or with mild) aortic dilation

ALLOWED	INDIVIDUALIZED ASSESSMENT	CONTRAINDICATED
Bowling Golf Walking Tennis (doubles) Stationary bike Treadmill Weightlifting (low intensity)	Basketball Handball Tennis (singles) Skiing Athletics Soccer Swimming Cycling Horseback riding	Ice hockey Climbing Windsurfing Weightlifting (high intensity) Surf Diving

Source: own source.

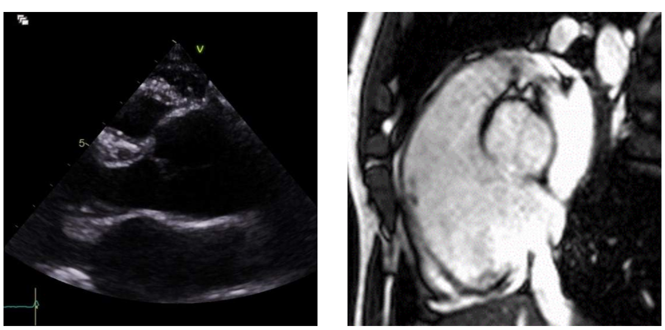
However, it is noteworthy that in recent years it has been suggested that regular physical activity could play a vital role in cardiovascular prevention in patients with MS, from the point of view of its positive effect on arterial hypertension. Recreational exercise could, therefore, be included in routine clinical management based, until now, on the prescription of treatment with beta-blockers and/or angiotensin II receptor antagonists (ARBs). Consequently, designing a tailored and personalized exercise program could be beneficial in these individuals.

These recommendations extend to all patients with aortic disease of genetic origin or collagenopathy.

Aortic pathology of acquired etiology

Dilatation of the thoracic aorta is a progressive condition resulting from aging, and is secondary to the pathological conditions of possible genetic etiology already described. Changes in the elastic properties of the vascular wall occur with age, leading to loss of elasticity and distensibility, as shown in Figure 7 (Monda et al., 2022).

Figure 7. A: Echocardiographic image of an aortic root aneurysm in a senior athlete; B: Magnetic resonance imaging of a patient with an aortic root aneurysm



Source: own source.

Moreover, mild enlargement of the aortic root has been observed in athletes. Few studies have been performed in athletes with tricuspid aortic valve, so the question of whether aortic enlargement occurs as a physiological adaptation to chronic exercise is largely unresolved.

Pelliccia et al. (2012) noted that in 2,317 athletes (8-year follow-up), only a small subset, around 1%, had an aortic root greater than the estimated 99th percentile in the same population, which is →40 mm for men and →34 mm for women. Thus, the vast majority of male and female athletes in this large cohort showed aortic dimensions that, regardless of body size and type of sport, were below these values considered thresholds. The authors concluded that an aortic root dimension →40 mm in trained male athletes (and →34 mm in female athletes) is unlikely to represent the physiological consequence of heart adaptation to training. Male athletes with an enlarged aortic root at the initial assessment experienced additional dimensional increase during follow-up (2.5 times greater than athletes with a normal aortic root), with the largest increases occurring after they finished their sports careers (**Pelliccia** *et al.*, 2012).

The underlying mechanism is not fully understood. According to the data in the current scientific literature, the most important determinant of aortic dilation is considered to be the systemic blood pressure response to exercise. Nonetheless, the combination of several other factors, such as type of sport, intensity, duration, and genetic factors, plays an important role in determining aortic enlargement.

Other studies indicated that sex, age, body surface area, ethnicity, systemic blood pressure, left atrial diameter, ventricular mass, and years of training may also be predictors of aortic dilation (**Monda** *et al*., 2022). In terms of body surface area, we must consider that the aortic diameter increases until reaching a plateau, as indicated by studies in basketball players. In fact, in a cohort from the National Basketball Association (NBA), the maximum diameter found was 42 mm, and only 4.6% of athletes had diameters greater than 40 mm (**Engel** *et al*., 2016). For this reason, aortas with diameters above these limits should lead us to suspect an underlying pathology.

Concerning the type of sport, it has been suggested that endurance sports have a greater impact on aortic root dimension. In particular, the impact of sport on aortic dimensions has been addressed by several authors, suggesting that aortic dimensions were larger in athletes who practice sports with a high dynamic component. Similar data were reported in other studies, indicating that male endurance athletes showed a larger aortic root diameter compared to male power athletes, whereas no significant differences were found for females (**Pelliccia** *et al*., 2012). This observed effect of resistance exercise may be due to the fact that the arterial pressure peaks in isometric activities are, although more significant, of short duration; whereas in the case of dynamic exercise, these pressure increases are prolonged (although smaller), causing constant tension in the aorta.

Recommendations

According to current guidelines, athletes can be classified into low, low-intermediate, intermediate, or high risk for acute aortic syndromes according to valve morphology (i.e., tricuspid versus bicuspid aortic valve), aortic diameter, and diagnosis of MS or other inherited diseases of the thoracic aorta (Table 6). Therefore, we will differentiate the following cases:

- Athletes with tricuspid aortic valve and aortic diameter <40 mm are considered low risk and might participate in all types of sports, although endurance is preferred over power sports.
- Patients at intermediate-low risk are those with mild aortic dilation (40-45 mm), in whom very high-intensity exercise should be avoided.
- Finally, in athletes with an aortic diameter of 45-50 mm (intermediate risk) or >50 mm (high risk), sport should be avoided (**Monda** *et al.*, 2022).

Table 6. Recommendations for athletes with aortic pathology

	Low risk	Low-intermediate risk	Intermediate risk	High risk
Diagnosis	*<40 mm aorta in bicuspid or tricuspid valve *Turner syndrome without aortic dilation	*Marfan without aortic dilation *40-45 mm aorta in bicuspid or tricuspid valve *After successful surgery in patients with a bicuspid aortic valve	*Moderate aortic dilation (40-45 mm in Marfan; 45-50 mm in bicuspid or tricuspid valve) *After successful surgery in patients with Marfan or hereditary aortopathies	*Severe aortic dilation (>45 in Marfan, >50 in bicuspid or tricuspid valve) *After surgery with sequelae
Recommendations	*All sports are allowed, with preferenc e given to endurance sports.	*It is recommended to avoid high-intensity or contact sports. *Preference for endurance sports is recommended.	*Only skill, mixed-type, or low-intensity endurance sports are allowed.	*Sports should be avoided.

Source: own source based on Pelliccia *et al.*, 2012.

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