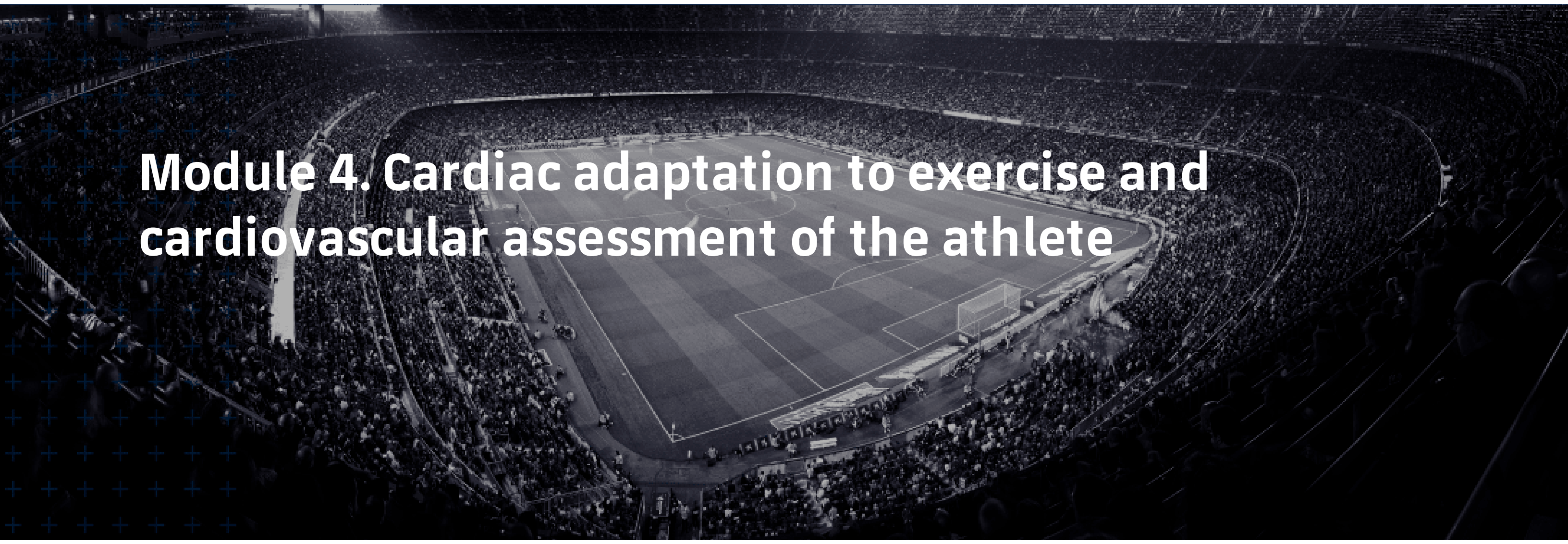

Module 4. Cardiac adaptation to exercise and cardiovascular assessment of the athlete

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Scientific evidence shows that:

> Physical exercise is effective in reducing mortality (Lee et al., 2014; Schnohr et al., 2013; Arem et al., 2015) and much of this beneficial nature is due to the associated prevention of cardiovascular disease, which is the most common cause of death in the [Western] world. (Grazioli, 2017, https://bit.ly/3KWBcpd)

Therefore, “public health agencies in different countries promote sports practice” (Cooper et al., 2015 cited in Grazioli, 2017, https://bit.ly/3KWBcpd). Accordingly, in recent decades there has been a significant increase in the number of people who engage in physical activity. To give but one example: the number of individuals who finish a 42 km marathon has increased fivefold in this period (Keefe et al., 2013 cited in Grazioli, 2017, https://bit.ly/3KWBcpd).

On the other hand, sudden death in sport, although rare, with a low incidence rate (estimated to be 1-2 per 100,000 athletes per year (Harmon et al., 2015 cited in Grazioli, 2017, https://bit.ly/3KWBcpd)), does have, nonetheless, high impact in the media, given that it involves unexpected deaths of young persons with ostensibly good previous states of health (Semsarian et al., 2015 cited in Grazioli, 2017, https://bit.ly/3KWBcpd).

> To maximize the benefits and minimize the risks that sport can produce during practice, pre-sports screening programs have been designed (Corrado et al., 2003). The objective of these is to detect diseases that could cause sudden death associated with sport and thus to establish specific treatment, or, when treatment is not possible, to indicate the definitive cessation of sports practice. (Grazioli, 2017, https://bit.ly/3KWBcpd)

Unit 4.1 Definitions

References

Unit 4.1 Definitions

In principle, and to establish a definition, it is useful to determine the relationship between an athlete and their sleep regimen; that is, if he or she loses resting hours in order to train, or, alternatively, rests to train better. The first is characteristic of amateur *recreational sport* and the second, of *competitive sport*.

As stated in the European Society of Cardiology guidelines, a recreational athlete engages in sports for pleasure and as a leisure time activity, while a competitive athlete is highly trained, focusing on performance and results (Pelliccia et al., 2021).

In a classification based on minimum exercise volume, we can establish a somewhat arbitrary division, since some recreational athletes, such as cyclists and long-distance runners, perform a greater volume of exercise than some professional athletes who participate in skill sports. However, this classification is useful in many cases to quickly assess whether an athlete may have structural changes that are justified by the sport. This concept was explained in Module 1 of this course.

4.1.1 Screening strategies in different countries

> Strategies for preventing sudden death vary according to the geographic location where they are carried out, since health policies and cost-benefit analyses are different in each region. In a simplified approach, we could divide prevention into two types, depending on the use of the ECG in the basic check-up: 1) the American model , which includes the family/personal history and the physical examination (Maron et al., 2015); 2) the European model, which adds the 12-lead electrocardiogram to the previous points (Corrado et al., 2005). (Grazioli, 2017, https://bit.ly/3KWBcpd)

To better understand this complex public health issue, a problem in many countries, we will describe both strategies from a historical perspective, using the available evidence.

American model

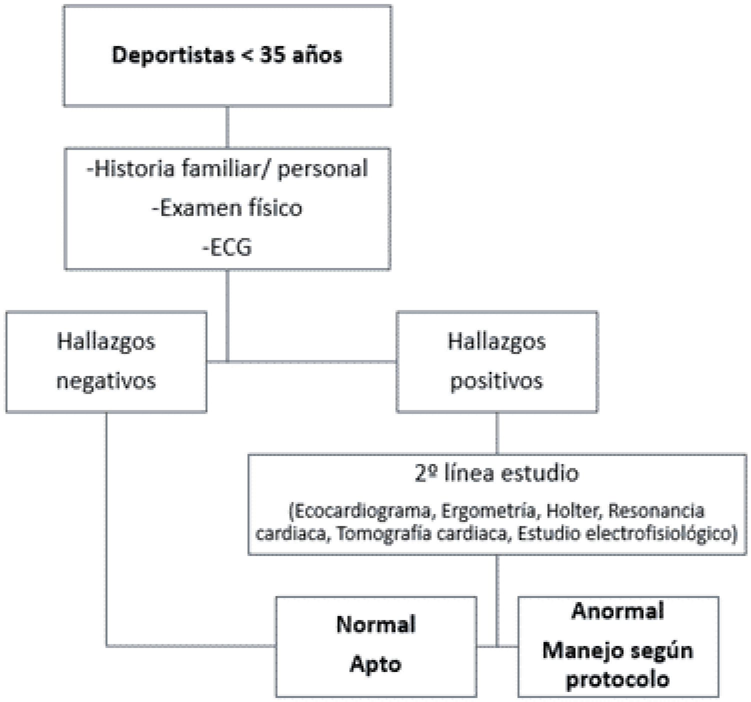
Already in 2005, the 36th Bethesda Conference, had suggested the use of the electrocardiography in pre-participation screening of competitive athletes, but it was not, however, included systematically, as was the family/personal history and physical examination (Maron and Zipes, 2005). Although it mentions the usefulness of the electrocardiogram and the echocardiogram, improving the sensitivity in the detection of pathologies that may cause sudden death, nowhere in the recommendation section is indicated the use of these two non-invasive diagnostic studies. The update of the Bethesda conference carried out in 2015 maintains the same recommendation, dismissing the routine use of the ECG in pre-participation screening (Maron et al., 2015). The reason against including the electrocardiogram is due to the excessive percentage of false positives (Brosnan et al., 2014). [...] The final decision not to include electrocardiography in the first line of screening would seem to be motivated by the cost-effectiveness analysis in the United States, where it is estimated that there are 60 million athletes: the health expenditure that screening would generate would not be justified, if the low incidence of sudden death in sport is compared with the high incidence of other causes of death in young people, such as accidents, homicides and suicides (Maron et al., 2014). However, the cost-effectiveness analysis does not mention that these last three causes of death are not preventable by any screening program, therefore, they are not comparable strategically. (Grazioli, 2017, https://bit.ly/3KWBcpd)

European model

In 2005:

The European Society of Cardiology published an expert consensus [level of evidence C] that is largely based on the experience of pre-participation screening that has been carried out in Italy since 1982 (Corrado et al., 2006). This expert consensus provides a practical approach toward performing pre-participation screening in young athletes. The first level of pre-participation screening includes the family and personal history, physical examination and electrocardiogram [Figure 1]. In cases where an alteration is found, a decision is made to request further, complementary studies that constitute a second line: imaging studies, such as Doppler echocardiography, cardiac magnetic resonance or coronary artery computed tomography; or, studies of myocardial electrical conduction, such as stress testing, 24-hour Holter-ECG or electrophysiological study (Grazioli, 2017, https://bit.ly/3KWBcpd).

4.1.2 Screening model recommended by the European Society of Cardiology



Source: Grazioli, 2017, https://bit.ly/3KWBcpd

Translation of Fig. 1:

Athletes<35 years of age

-Personal and Family History

-Physical Examination

-ECG

Negative Findings

Positive Findings

Second-line studies

(Echocardiography, Ergometry, Holter monitoring, cardiac resonance imaging, cardiac tomography, electrophysiological studies)

Normal: Eligible

Abnormal: Protocol Management

In all countries of the European Union, the recommendation to include the ECG in the pre-participation screening has been adopted (Corrado et al., 2011), although there are differences between countries and in the associations responsible: some limit screening to competitive athletes, while others include it for athletes who practice sports recreationally. In Catalonia, the consensus for the prevention of sudden death in sport was published (Sitges et al., 2013), which—based on the European model—suggests performing screening on all athletes in the three upper rings of Fig. 2, that is, a) family/personal history; b) directed physical examination, with both (a and b) as summarized in the

12-point model proposed by the American Heart Association (Maron et al., 2005); c) electrocardiogram. Then, the performance of additional tests—d) Doppler echocardiogram and, e) stress test—is reserved for subjects with abnormalities in the first basic tests, or, routinely, to competitive athletes with high physical demands (Mitchell III-C), or to those over 35 years of age. (Grazioli, 2017, https://bit.ly/3KWBcpd)

In Europe, although the European Society of Cardiology places the Doppler echocardiogram within the second line of studies, in practice, up to two thirds of doctors use it in the initial evaluation (D'Ascenzi et al., 2021), both in competitive and amateur sport. This is due to the usefulness that the ECG has demonstrated in detecting diseases that can cause sudden death in sport.

Figure 2: Schematic representation of the suggested pre-participation screening in Catalonia

Source: Grazioli, 2017, https://bit.ly/3KWBcpd

Translation of Figure 2:

History A

Physical Examination B

ECG C

Echocardiography D

Ergometry E

Screening by age group

Various research studies have included individuals of different age groups (under 35 years of age).

1. **Children**: "usually considered from the first year of life to 12 years" (Grazioli, 2017, https://bit.ly/3KWBcpd). A recently published study, which included 22,324 child athletes, found that the sensitivity of cardiovascular screening for the detection of cardiovascular pathology potentially causing sudden death was lower in this age group than in adolescents (Sarto et al., 2023). That is, in the case of cardiovascular screening in asymptomatic child athletes, the cost-effectiveness ratio is lower than in adolescents. This study recommends that screening in this age group be limited to the group of child athletes who present symptoms and/or have a family history of cardiomyopathy or sudden death (Sarto et al., 2023).

2. **Teenagers:**

   Individuals between 12 and 18 years of age. High school students are grouped in this age range. It is the group with the greatest scientific evidence, which includes high school adolescents to adults in their first years of university

(Mayer et al., 2012). (Grazioli, 2017, https://bit.ly/3KWBcpd)

In this age group, cardiovascular screening has been shown to have a high cost-benefit ratio for the detection of cardiovascular pathology potentially causing sudden death. Likewise, it has been confirmed that periodic repetition of cardiovascular screening is indicated in this age group, since it is in this period that several cardiomyopathies causing sudden death can show their first phenotypic expression; therefore, periodic repetition would be beneficial (Sarto et al., 2021).

3 **Young adults**: individuals between 19 and 35 years of age. The existing scientific evidence is less than in adolescents, but the available studies document a cost-effectiveness similar to that presented in adolescent athletes (Magalski et al., 2011).

The objective of pre-participation screening programs is to effectively and efficiently identify [i.e., with a high positive likelihood ratio] individuals at risk of sudden death in sport. We say "effectively" to refer to the success of a screening program when its sensitivity is close to 100%, and "efficient" to link

> that sensitivity to the least possible use of resources; thus, introducing the concept of cost-effectiveness. (Grazioli, 2017, https://bit.ly/3KWBcpd)

In people over 35 years of age, the most frequent cause of sudden death in athletes is no longer cardiomyopathy, but ischemic heart disease. The additional tests to the basic screening for evaluation in this age group, based on the recommendations of the European Society of Cardiology, are summarized below (Borjesson et al., 2019).

1. Asymptomatic individuals who exercise or are athletes with a low cardiovascular risk score. No additional testing is required.

2. In asymptomatic individuals who exercise, or athletes who have a high cardiovascular risk score—which would be a greater than 5% probability of having an ischemic event in 10 years—it is recommended that they complete the study with a maximal stress test. In the event that the stress test is doubtful, but not diagnostic, it is recommended that the study be completed with another noninvasive ischemia test, such as an echocardiogram, or stress MRI, or a coronary computed tomography angiography (also called coronary CT).

3. In symptomatic individuals who exercise, or in athletes, a coronary CT scan is proposed to stratify the risk, and, eventually, make a therapeutic decision.

4.1.2 First-line complementary tests in screening of athletes

Medical history and physical examination

The physical examination is oriented toward identifying signs of diseases related to sudden death in sports, based on the recommendations of the American Heart Association in the 14-point oriented questionnaire, which includes family/personal history and, in the last 4 points, the physical examination (Grizolia, 2017).

Personal history

1. Chest pain/discomfort/pressure related to exertion
2. Unexplained syncope/presyncope
3. Excessive and unexplained dyspnea/fatigue or palpitations associated with exercise
4. Preliminary examination for a heart murmur

5 High blood pressure

6 Prior restriction to participate in sports

7 Previous cardiac tests ordered by a doctor

Family history

8 Premature death (sudden and unexpected or otherwise) in a family member under 50 years of age, attributable to heart disease

9 Disability due to heart disease of a close relative under 50 years of age

10 Hypertrophic or dilated cardiomyopathy, long QT syndrome or other ion channel heart diseases, Marfan syndrome or clinically significant arrhythmias; specific knowledge of genetic cardiac conditions in family members

11 Preliminary examination for a heart murmur

Physical examination

11 Heart murmur

12 Femoral pulses to exclude coarctation of the aorta

13 Physical signs of Marfan syndrome

14 Blood pressure in the arm, when the athlete is sitting

Few studies have analyzed the diagnostic value of physical examination in isolation to detect diseases potentially linked to the risk of sudden death in sport (Fuller et al., 1997; Baggish et al., 2010; Magalski et al., 2011); in general, an incidence of close to 5% of abnormal findings in the physical examination is observed, but with limited specificity.

Therefore, we could summarize, as with the family and personal history, that due to its simplicity and low cost, the guided physical examination is a useful tool for preparticipation screening [using the 14-point checklist proposed by the American Heart Association] (Grazioli, 2017, https://bit.ly/3KWBcpd).

It is also very important to add some questions to this model questionnaire, related to the following points:

- **Type of sport**: the new classification proposed by the Italian group (Pelliccia et al., 2018) is used, which divides sports into those of skill, strength, mixed or endurance.

Table 1: Types of sport

Ability	Force	Mixed	Endurance
-Golf -Archery -Sailing -Table tennis -Equitation -Karate -Shooting sports -Sledding -Ski jumping	-Weightlifting -Judo -Boxing -Sprinting -Shotput/Discus -Javelin -Artistic gymnastics -Alpine skiing -Snowboarding	-Soccer -Basketball -Volleyball -Water polo -Tennis -Fencing -Handball -Rugby -Hockey	-Cycling -Rowing -Swimming -Distance Running -Canoe -Triathlon -Pentathlon -Ski mountaineering -Biathlon

Source: own elaboration

- **FIT-T or METs hour/week**: that is, the frequency, intensity and duration of activity that the athlete performs per week (Corrado et al., 2006). This allows the calculation of the METs hour/week that they perform; it is an accepted measure to be able to compare study populations (Jeong et al., 2019).

Table 2: FIT-T or METs hour/week

Frequency • Sessions/week
Intensity • Endurance: % average HR reserve or VO2 peak • Strength: % 1 RM or 5 RM (maximum repetition) • Mixed: % average CF reserve
Time • Days/week • Time/week (minutes or hours)
Type

- Strength, endurance or mixed
- Flexibility
- Coordination and balance

Source: own elaboration

- **Sports history**: refers to the number of years that the athlete has practiced one sport or another.

Electrocardiogram

In the 1980s:

> The electrocardiogram has been proposed as a useful diagnostic study in preparticipation screening (Corrado et al., 2006) and, since 2005, there has been a European consensus recommending its use; however, there remains some controversy about the usefulness of the electrocardiogram in the United States (Maron et al., 2015). [...] In 2013, the Seattle criteria were published (Drezner et al., 2013), which [...] decreased the percentage

of false positives to less than 5% (Brosnan et al., 2014). (Grazioli, 2017, https://bit.ly/3KWBcpd)

In 2014, refined criteria were published, using a color code similar to that of a traffic light, where 2 yellow points are considered to be a red; that is, a second line of study is required, improving specificity in those of African descent (Sheikh et al., 2014).

In 2017, a consensus of experts was published with international criteria (Sharma et al., 2018), and which adopted the format of the refined criteria while improving specificity. This is because the new consensus considers the following parameters to be normal: a) juvenile inverted T wave pattern V1-V2-V3 in less than 16 years; b) AV block up to 400 m/s; c) bradycardia > 30 bpm, and d) low atrial rhythm or junctional rhythm. This consensus considers Mobitz type II AV block as abnormal. This evolution to improve specificity without losing sensitivity was generated by various research groups worldwide (Baggish, 2015) —as shown in Figure 3—, and currently the international criteria are adopted (Sharma et al., 2018).

Figure 3: ECG history in athletes

Source: Own elaboration based on Sharma et al., 2018

Translation of Fig. 3:

ECG history in athletes

Regarding electrocardiogram alterations and the diagnostic capacity of each of them, there exist three that represent greater usefulness in decision-making: a) negative T waves, b) ventricular extrasystoles, and c) pre-excitation syndrome.

4.1.3 Second-line complementary tests in athlete screening

Doppler echocardiogram

The inclusion of echocardiogram in pre-participation screening has been proposed, because, sometimes, it provides a definitive diagnosis in response to a suspicion generated in the questionnaire, in the physical examination, or in the electrocardiogram; in addition, it provides added diagnostic value, fundamentally in three pathologies (Grazioli, 2014):

- **Hypertrophic cardiomyopathy with normal ECG:** In approximately 6% of adults (McLeod et al., 2009) and in up to 27% of asymptomatic adolescents (Savage et al., 1978), patients with hypertrophic cardiomyopathy present a normal ECG; therefore, in this group, echocardiography plays a major role in screening.
- **Anomalies in the origin of the coronary arteries**: the diagnosis of the origin anomaly can be carried out by echocardiogram, and due to the current advances in echocardiography imaging, better diagnostic sensitivity data have been described, now being close to 99% in adolescents (Labombarda et al., 2014).
- **Aortic diseases**: aortic root dilatation may be suspected upon physical examination, due to signs associated with Marfan syndrome, but it may also present lesser semiological expression in young people, or may not be associated with Marfan syndrome; therefore, it may go unnoticed on examination. In a large cohort of Olympic athletes, limits were established corresponding to the

> 99th percentile of the population, these being 40 mm for men and 34 mm for women (Pelliccia et al., 2010). However, current American recommendations propose the use of the Z-score and the 2 standard deviations (Braverman et al., 2015) with percentiles from another study carried out in a non-athlete population, based on age and body surface area (Devereux et al., 2012). [...] Another pathology to rule out is the coarctation of the aorta, with initial indications present in the femoral pulses (Bonow et al., 2005). Finally, a bicuspid aortic valve can be detected by a murmur during physical examination, and is one of the most frequent alterations that we can find in a pre-participation screening. (Grazioli, 2017, https://bit.ly/3KWBcpd)

The protocol commonly used in athletes "includes three classic views of the short parasternal axis, long parasternal axis, and 4 chambers, plus the aorta, and looks for the morphological heart diseases that most frequently cause sudden death" (Grazioli, 2017, https://bit.ly/3KWBcpd). These pathologies are detailed in the screening protocol, with 17 views in image or video (Weiner et al., 2012):

Parasternal long axis

1. 2D Image
2. Color Doppler of the mitral and aortic valves
3. Continuous RV inflow Doppler of tricuspid regurgitation

Parasternal short axis

4. 2D image of aortic valve with origins of coronary arteries
5. Aortic valve color Doppler
6. 2D image of pulmonary valve
7. Continuous pulmonary valve Doppler
8. 2D image at the level of the papillary muscle
9. 2D image at the vertex

Apical 4-chamber image

10 2D image of left and right ventricles

11 Pulsed Doppler of transmitral flow

12 Color Doppler of interatrial *septum*

13 PW DTI of the mitral *septum annulus*

14 TAPSE base of the RV

Apical five-chamber image

15 2D Image

16 Continuous aortic valve Doppler

Apical two-chamber image

17 2D Image

There is scientific evidence suggesting that, based on the identification of pathologies detectable by echocardiography, this technique would be useful for pre-participation screening, being applied at least once in the athlete's life (Stefani et al., 2008; Rizzo et al., 2012). However, more data are needed regarding the appropriate cost-effectiveness, depending on the geographical location being analyzed and the cost of living there (Wheeler et al., 2010; Leslie et al., 2012; Menafoglio et al., 2014). A recent publication by two working groups of the European Society of Cardiology (Mont et al., 2017) suggests that there are three limitations of adding Doppler echocardiography to the first line of work: a) the additional cost of the study, b) the limited experience in its use in screening programs and c) the lack of evidence on the added value of echocardiography to ECG in the detection of pathologies. (Grazioli, 2017, https://bit.ly/3KWBcpd)

Tissue Doppler provides added value when the E/A ratio of transmitral flow in athletes appears to have a restrictive value, due to the increase in flow during isovolumetric relaxation. In these cases, the presence of an e' greater than 10 cm/s in the mitral annulus is a normal sign in this condition. In this way, one more point is given in the differential diagnosis with hypertrophic cardiomyopathy, where the e' is usually decreased and less than 10 cm/s (Caselli et al., 2014).

Regarding the added value of speckle-tracking in the context of the athlete's heart, it is noted that it has greater use for differential diagnosis in early stages of hypertrophic or dilated cardiomyopathy and in the characterization of segmental motility disorders (Pelliccia et al., 2018).

Stress test

There is little scientific evidence regarding the usefulness of the stress test in pre-participation screening; its greatest benefit is focused on the detection of two alterations that may go unnoticed in the baseline 12-lead ECG:

- **Ventricular arrhythmia** that persists at maximum effort:

> The largest cohort study of stress tests shows a clear relationship between the detection of ventricular arrhythmia and the presence of heart disease that motivates a behavior in athletes. [...] Another study carried out on elite athletes shows that the presence of more than 10 ventricular extrasystoles during the stress test would be significantly related to the presence of heart disease (Verdile et al., 2015). Also, this test has an important role in the diagnosis of catecholaminergic polymorphic ventricular tachycardia, due to the appearance or increase of ventricular arrhythmia, as

> physical effort increases (Sarquella-Brugada et al., 2013). (Grazioli, 2017, https://bit.ly/3KWBcpd)

Also, to the extent that complex ventricular arrhythmia appears, that is, very frequent, multifocal extrasystoles, ventricular tachycardia or R on T phenomena (Refaat et al., 2021).

- **ST segment depression :**

> In athletes with an anomaly in the origin of the coronary arteries, this could be one of the indicators in one third of patients who may present ischemia during exercise (Frommelt et al., 2011). Regarding ST segment abnormalities as a marker of ischemia in early coronary disease [as previously mentioned, based on European recommendations], its use is indicated in asymptomatic athletes with high cardiovascular risk (Borjesson et al., 2011). (Grazioli, 2017, https://bit.ly/3KWBcpd)

However, this indication has been questioned, since—despite its usefulness in diagnosing silent coronary disease—there is no extensive scientific evidence to determine whether such diagnosis provides a prognosis. That is, it is not known whether such diagnosis reduces the incidence of sudden death at this stage of coronary disease (Kim et al., 2012 cited in Grazioli, 2017).

Exercise protocols in conventional stress testing

The Bruce protocol, which was described in the 1950s by Dr. Robert Bruce, is the most traditionally used protocol worldwide, and has taken root in cardiac risk assessment, especially for coronary artery disease (Husaini and Emery, 2023). The standard Bruce protocol uses a treadmill at 1.7 mph with a 10% incline, increasing by approximately 2%, and 1 mph every 3 min. Each successive stage increases the workload by approximately three metabolic equivalents. However, such large jumps in workload can make diagnostic accuracy difficult, and if catecholaminergic tachycardia is suspected, more rapid-ascending protocols that peak well before 10 min would seem to be helpful (Bhardwaj et al., 2022).

Athletes who generally achieve high workloads, with significant incline of the treadmill—which in Bruce's protocol can be greater than 20%—may have two problems:

1. Walking at a high speed and incline level. This does not replicate the type of exercise most athletes perform.
2. Limitation due to discomfort in the calf muscle. This discomfort is related to the inclination, rather than to cardiopulmonary exhaustion.

Therefore, it is useful that the exercise protocol is adapted to the initial physical condition of the individuals and allows the test to last between 8 to 12 minutes, which is why the protocol adapted to athletes is usually used, which begins with 6 km/hour, with a fixed slope of 1% and an increase of 1 km/hour for each minute (Fernández and Ruiz, 2013). With the added value, the test seems to be more suitable for the indirect estimation of VO2 maximum and the ventilatory threshold, or lactic threshold, at 93% of the maximum heart rate, at the peak of the effort.

Cardiopulmonary stress test

There are two common indications for this test in athletes: a) to improve performance, because gas exchange parameters can determine metabolic thresholds that help create various exercise zones and establish predetermined workouts; b) to help with the etiological diagnosis in the presence of an athlete with symptoms. In most cases, the athlete presents dyspnea disproportionate to the exercise performed (Husaini and Emery, 2023), giving parameters that help establish the differential diagnosis between the cardiological or respiratory components and aerobic detraining, with a special added value in microvascular ischemia of non-significant coronary disease of the epicardial arteries (Chaudhry et al., 2018).

Stress echocardiogram

Stress ultrasound is a technique for diagnosing ischemic heart disease and some valvular heart diseases. It consists of a stress test, to which are added baseline images and images at maximum effort. These are then compared, with the aim of diagnosing alterations in left ventricular motility secondary to ischemia, as referred to in the consensus of the European Society of Cardiology (Sicari et al., 2009). The increase in gradients with exercise can also be observed, in the case of valvular heart disease, with a sensitivity and specificity similar to myocardial perfusion SPECT (Peteiro and Bouzas-Mosquera, 2010), but at a lower cost. Usually, in the context of sport, the acquisition of baseline images and images immediately after exercise —that is, in the first minute of recovery—are taken when the athlete uses a treadmill or bicycle. However, if a person is unable to perform physical exertion, this test can also be performed with a pharmacological challenge; dobutamine, adenosine or dipyridamole are usually used.

Compared with conventional stress testing, images obtained at maximal effort improve diagnostic sensitivity by 16% (Bouzas-Mosquera et al., 2009), thereby reducing the number of false negatives. In summary, the main advantages of this study are: 1) lower cost; 2) no irradiation; and 3) greater comfort for the patient, since it is performed in less than 1 hour.

As a second line in screening, stress echocardiography has been shown to be useful for the differential diagnosis between athlete's heart and dilated cardiomyopathy; because, when it is the disease, the left ventricular ejection fraction does not increase, or does so slightly (<11%) (Millar et al., 2020). It is also used for the differentiation of arrhythmogenic cardiomyopathy, which presents a smaller change in fractional area, global strain rate and right ventricular wall strain, when compared to healthy athletes (Claeys et al., 2020).

24 hour ECG Holter

This study is an element of support for the early diagnosis of many diseases that athletes may present (Pelliccia et al., 2005). Today, there are several devices that use a band shirt with electrodes (Fabregat-Andres et al., 2014), which have facilitated use during training and, due to this, greater sensitivity in the search for arrhythmia.

In relation to ventricular arrhythmia in elite athletes, the finding of extrasystoles in an electrocardiogram or in an athlete's stress test constitutes the indication for a Holter, and there is a relationship with the existence of underlying heart disease when the number of ventricular extrasystoles is greater than 2000 in 24 hours (Biffi et al., 2002).

> Another indication is the diagnostic suspicion of arrhythmogenic right ventricular dysplasia, which constitutes a minor diagnostic criterion when there are more than 500 ventricular extrasystoles per day, or a major one, if there are more than 1000 (Marcus et al., 2010). Also, in the case of suspected hypertrophic cardiomyopathy, for the diagnosis of complex ventricular arrhythmia with a class I recommendation level (Gersh et al., 2011).
>
> Finally, symptoms of palpitations or syncope, or even suspicion of some type of supraventricular arrhythmia or atrioventricular block, are current indications for 24-hour ECG Holter monitoring (Zipes et al., 2015). (Grazioli, 2017, https://bit.ly/3KWBcpd)

In the last decade, thanks to the technological explosion, new devices have been developed for ECG monitoring, such as those that allow the recording of an ECG lead without associated cables. Thus, an ECG recording can be obtained during sports practice with a quality suitable for interpretation. These devices are increasingly used in the sports field, since they allow us to record the ECG in real training and/or competition conditions (Fabregat-Andres et al., 2014).

Magnetic resonance imaging

"Its usefulness has been described to improve diagnostic specificity and is part of the second line of studies" (Grazioli, 2017, https://bit.ly/3KWBcpd). Cardiac resonance allows for a more detailed assessment of the cardiac structure, with a more precise measurement of the volumes and parietal thicknesses of both ventricles. It also improves the diagnostic ability of echocardiography to assess the origin of the coronary arteries, in case there is suspicion of an anomaly (Villa et al., 2016).

The warning signs (red flags) that suggest the need to complete the study with a cardiac resonance are the following:

- **The presence of negative T waves in the ECG** is especially useful in these cases for the detection of localized or atypical forms of hypertrophic cardiomyopathy, improving the sensitivity of the echocardiogram, especially in segments that are difficult to visualize (Maron et al., 2009; Luijkx et al., 2013).
- **Frequent ventricular extrasystoles or unusual morphologies** in athletes, which indicate a high probability of underlying cardiac pathology (Zorzi et al., 2019).
- **Echocardiographic data of borderline ventricular hypertrophy or dilatation** as part of the differential diagnosis between adaptive

structural remodeling and incipient cardiomyopathy (Weiner et al., 2012).

In addition, cardiac resonance allows us to characterize myocardial tissue. The study of late enhancement with gadolinium allows us to identify areas of the myocardium with fibrosis. Therefore, it is especially useful for the diagnosis of chronic and acute myocarditis (Friedrich, 2008) and has an added diagnostic and prognostic value in various cardiomyopathies (Zorzi et al., 2016).

The utility of T1 mapping is mainly focused on improving sensitivity in the assessment of extracellular volume and diffuse fibrosis, without the need for gadolinium. In addition, it helps in the differential diagnosis or exclusion of diseases, such as myocarditis, amyloidosis or diffuse fibrosis, which increase the T1 value (normal value: 800-1000) (Moon et al., 2013).

Recently, stress assessment has been incorporated into the routine MRI study; this is achieved by incorporating a specially adapted supine bicycle. This assessment is currently scarcely available, but existing evidence has shown that it is a test with high sensitivity and specificity for the differential diagnosis between adaptive remodeling and incipient cardiomyopathy. Specifically, for the diagnostic differentiation between dilated cardiomyopathy and physiological ventricular dilation induced by exercise, an increase in left ventricular function of less than 11% would seem to have an important pathological significance (Claessen et al., 2018).

Computed tomography

"This noninvasive diagnostic technique is most useful in the detection of congenital or acquired coronary disease (Taylor et al., 2010) and has traditionally been used for the diagnosis of coronary anomalies (Villa et al., 2016)" (Grazioli, 2017, https://bit.ly/3KWBcpd).

In relation to early coronary disease, the use of the calcium score has been proposed as a screening in athletes over 35 years of age with moderate risk (La Gerche et al., 2013 cited in Grazioli, 2017). However, it does not seem to be useful in athletes who perform more than 5 hours of aerobic exercise per week (Defina et al., 2018) and although there may be a greater volume of atherosclerotic plaque, this is not related to the development of coronary events in the future.

Electrophysiological study

Electrophysiological study is an invasive test that is indicated in a small proportion of athletes, being the second-line study with the least indication, it is used to diagnose the following clinical scenarios (Zipes et al., 2015) a) AV block that appears with exercise, b) AV block that does not improve with exercise, c) AV block with coexisting bundle branch block, d) left bundle branch block and syncope, e) syncope on exercise of unexplained cause, f) paroxysmal supraventricular tachycardia in the exercise test, g) pre-excitation syndrome, h) complex ventricular arrhythmia. (Grazioli, 2017, https://bit.ly/3KWBcpd)

Genetic test

The indication for genetic testing basically occurs in three scenarios: a) family history of cardiomyopathy, b) family history of positive genotype, and c) athlete in the gray zone (between secondary adaptations to remodeling by sport and cardiomyopathy) (Castelletti et al., 2022). It is performed with the aim of ruling out six diseases: long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, Brugada syndrome, hypertrophic cardiomyopathy, arrhythmogenic cardiomyopathy, and dilated cardiomyopathy.

Importantly, in many genetic diagnostic laboratories, testing is performed using next-generation sequencing (NGS) panels, which include sequencing genes that are associated with the diagnosed or suspected disease. More comprehensive approaches include whole-exome sequencing (WES), which encompasses all coding regions of the genome, and whole-genome sequencing (WGS). It therefore involves sequencing all coding and non-coding regions of DNA.

Whole-genome sequencing provides a data set; interpreting it requires significant efforts in terms of volume and financial cost.

The problem arises because these diseases have a different incidence and likelihood ratio in the test. This conditions its usefulness and limits its use in screening. Therefore, apart from the test itself, it must be completed by a doctor who is a specialist in this field and who balances this data with the clinical context and the expression of the phenotype.

Legal aspects

In relation to the legal implications of pre-sports screening, it is interesting to note the current trend where the decision to participate in a competitive sport is made jointly by the athlete and the physician. This model of thinking is already expressed in the recommendations made by the experts in the United States, who make it clear that the recommendations are not intended to establish absolute mandates that must be followed in all cases, nor are they a medical standard of care; rather, they constitute a consensus reference document that is potentially useful in resolving predictably difficult clinical dilemmas (Mitten et al., 2015).

In short, the final decision rests with the informed athlete, who must synthesize this information in light of his or her own goals and aspirations. That is, shared decision-making is patient-centered (Kim & Dickert, 2022).

In Europe, recommendations highlight that current risk stratification algorithms for patients with cardiomyopathy are derived from a sedentary population, which may not be suitable for competitive athletes subject to increased physical and metabolic stresses during intense exercise. Thus, an individualized approach considering several factors, including symptomatic status, established risk factors, natural history of the disease, age of the athlete, duration of competition prior to diagnosis and characteristics of the sporting discipline, is suggested when advising on participation or disqualification in competitive sports (Pelliccia et al., 2019). Athlete involvement in the decision-making process is crucial, and athletes who fully understand and wish to participate in competitive sports, despite medical advice, should not jeopardize the physician providing the advice.

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