

Module 2. Managing Medical Pathologies 2

2.1 Heart and Sports

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Sudden cardiac death and Sports: Magnitude of the problem, causes and strategies to prevent it

The prevalence of sudden cardiac death (SCD) in sports can be considered relatively low since 1-2 out of 100,000 athletes suffer it annually. (Sharma, Estes, Vetter and Corrado, 2013). However, it causes a great social impact as it occurs in young people unexpectedly, and, at the same time, it contradicts the idea that exercising is a healthy life attitude.

The SCD rule of 5 in sports has been described from a practical approach:

It represents a 5% of the total incidence of SCD in the general population (Marijon, Uy-Evanado, Reinier, Teodorescu, Narayanan et al., 2015).

5% of them occur in female athletes (Bohm, Scharhag y Meyer, 2016).

5% of them occur in competitive athletes. However, they represent a relative risk 5-fold higher than in those who practice recreational sports (Marijon, Tafflet, Celermajer, Dumas, Perier et al., 2011).

How the prevalence is estimated varies according to the different groups analysed in Europe (Corrado, Basso, Rizzoli, Schiavon, and Thiene, 2003; Manonelles Marqueta et al., 2007; Marijon et al., 2011; Finocchiaro, Papadakis, Robertus, Dhutia, Klavdios Steriotis et al., 2016) or in North America (Maron, Doerer, Haas, Tierney, and Mueller, 2009). This variation is explained in three main points:

- A) the epidemiological characteristics of each region;
- B) the average age of people;
- C) the different registers or methodologies used to get the data since this is the main cause of such incidence variation.

The following results as regards the causes of SCD in sport practice have been obtained from a meta-analysis of the above-mentioned studies:

Table 1: Causes of Sudden Death in Sports

SD Causes in Sports	%
Hypertrophic Cardiomyopathy	30%
Anomalies of coronary arteries origin	15%
Left ventricular hypertrophy	11%
Arrhythmogenic right ventricular dysplasia	6%
Myocarditis	5%
Anomalies of the aorta	5%
Early heart disease	5%
Other causes	23%

Source: prepared by the authors.

Sports with acyclical exercise; those which provoke a rapid rise of heart rate are the ones in which a higher number of sudden deaths were registered. However, it also depends on the country where it was analysed. American football can be taken as an example since it is the first cause of SCD in North America (Maron et al., 2009).

The pre-participation screening recommended by the European Society of Cardiology (Corrado, Pelliccia, Bjørnstad, Vanhees, Biffi et al., 2005) is considered to be the main and most used method worldwide to prevent sudden deaths in sports.

Figure 1. Pre-participation screening recommended by the European Society of Cardiology

Pre-participation Screening recommended by the European Society of Cardiology

- Family and personal history of the patient.
- Physical Examination.
- 12-lead electrocardiogram (ECG).
- A second line of screening is performed if the basic screening is altered: further studies such as an electrocardiogram, an exercise stress test, an ECG-Holter for 24 hours, a cardiac MRI or an electrophysiological study are performed.



Source: adapted from the European Society of Cardiology.

The aim is to be able to identify in people a disease which can be considered a potential cause of SCD in sports. The model suggested in the United States does not include the ECG and it is only based on a questionnaire which takes into account the medical record and the physical examination. However, there is a lack of scientific evidence that supports its use due to its limited sensitivity.

Two main elements exist as secondary prevention for SCD in sports: a medical plan and an external automatic defibrillator, as suggested by FIFA (Fédération Internationale de Football Association, for its name in French) (Dvorak, Kramer, Schmied, Drezner, Zideman et al., 2013). For this prevention to be successful, it is vital to carry out a previous and annual training of the responsible ones and an automatic communication between the defibrillator and the local emergency system which performs the advanced life support.

The following table summarizes the most relevant aspects of SCD and its prevention in athletes.

Table 2: Sudden Cardiac Death

Incidence	Main causes	Primary prevention	Secondary prevention
1-2 out of 100,000 athletes/year	<ul style="list-style-type: none"> - Hypertrophic Cardiomyopathy - Coronary heart disease - Anomalies of coronary arteries origin 	<ul style="list-style-type: none"> - Cardiac screening before participation in sports - Family and Personal Report - Physical Examination - ECG 	<ul style="list-style-type: none"> - Medical plan - External automatic defibrillator

Source: prepared by the authors.

Usefulness and Methodology of the pre-participation screening

The prevention strategy for sudden death in sports (by means of the pre-participation screening in order to identify the possible diseases that can cause it) is different depending on where it is carried out. There are two models that differ one from the other because they do or don't include the electrocardiogram:

- 1) the American model which includes the family and personal history and the physical examination (Maron et al., 2015).
- 2) the European model which adds the 12-lead ECG to the above-mentioned points (Corrado et al., 2005).



The debate about the usefulness of an electrocardiogram is generated by the false positives and the influence they have on the cost-benefit analysis (Sharma, Drezner, Baggish, Papadakis, Wilson et al., 2017).

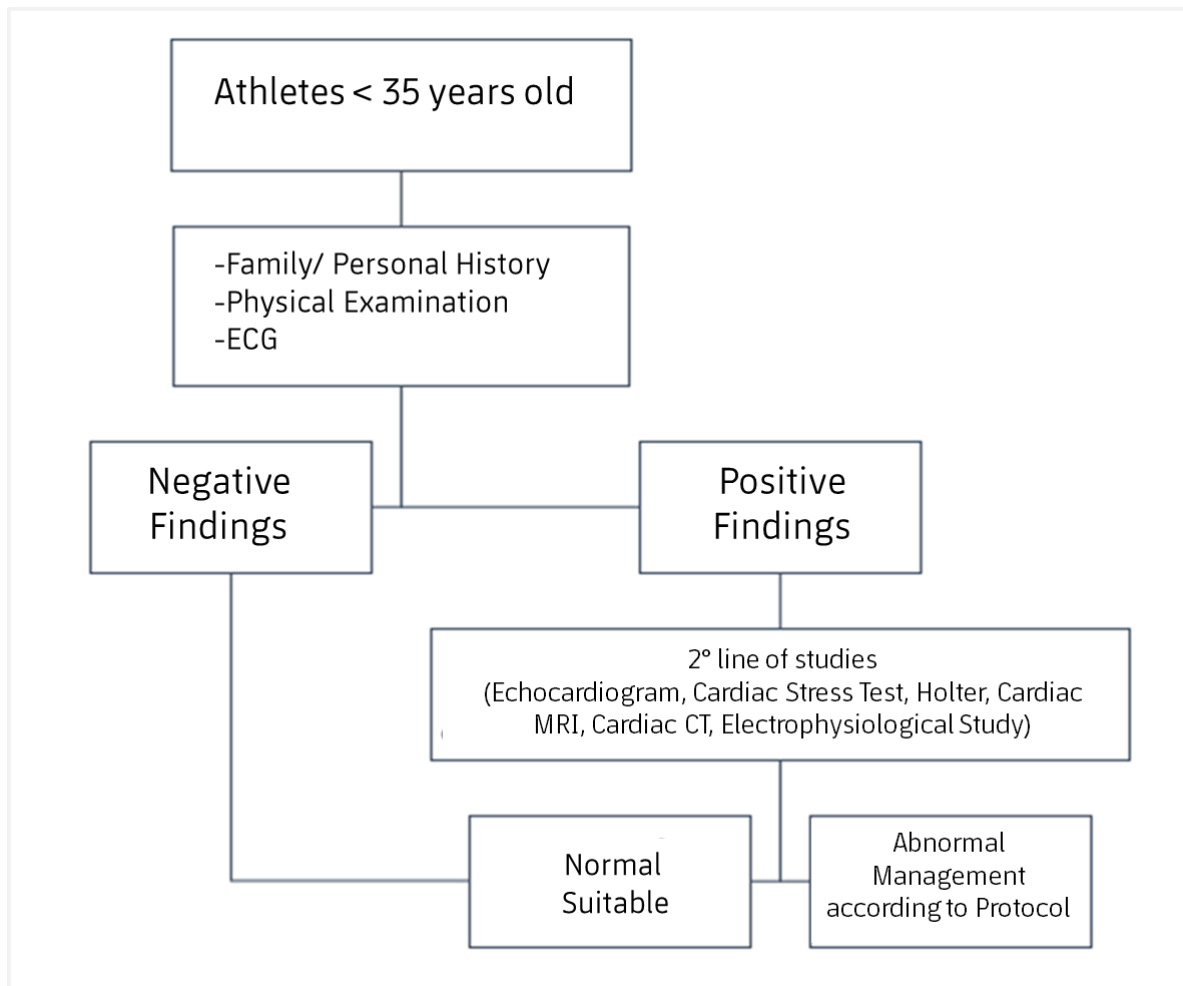
There is an accepted limit in international literature at the age of 35 since the atherosclerotic heart disease becomes, as of that age, the main cause of sudden death with a difference of, at least, four times higher than the rest of the aetiologies (La Gerche, Baggish, Knuuti, Prior, Sharma et al., 2013). The causes on people younger than 35 are mainly congenital cardiopathies that generate complex arrhythmias. These are direct causes of death in the context of physical effort. On older people, the cause is a ischemic cardiopathy.

The European Society of Cardiology published a consensus of experts in the year 2005 that is mainly based on the experience of the Italian pre-participation screening (Corrado, Basso and Andrea, 2006, as cited in Grazioli, 2017). At the first level of the pre-participation screening, the family and personal history, the physical examination, and the 12-lead ECG are included (Figure 1). In the case of any alteration, other type of studies which constitute a second line of screening with additional image studies are required such as the Doppler echocardiogram, the cardiac MRI or the CT in coronary arteries, as well as those which study the electrical conduction such as the stress test, the ECG-Holter for 24 hours or the electrophysiological study (Grazioli, 2017). Currently, the European Union recommendation to include the ECG in the pre-participation screening is adopted. However, there are differences in the enforceability of the second line of studies (Corrado et al., 2011, as cited in Grazioli, 2017).

To athletes over 35 years old, apart from the first line, the level of physical activity calculated in MET (metabolic rate unit of measurement) per hour and per week, a questionnaire about symptoms, and the European score of cardiovascular risk are added. The latter takes into account the classic risk factors such as: age, gender, total cholesterol, blood pressure, and tobacco consumption in order to evaluate the need to perform a stress test (Borjesson, Urhausen, Kouidi, Dugmore, Sharma et al., 2011).



Figure 2: Pre-participation screening recommended by European Society of Cardiology



Source: Corrado et al., 2005, in Grazioli, 2017, p. 19.

In Catalunya the European model is taken as a base and athletes are suggested to carry out the three top bands (Sitges et al., 2013; Figure 2). This is: a) the family and personal history; b) a directed physical examination (both summarised in the 12-point-model proposed by the American Heart Association (Maron, Douglas, Graham, Nishimura, and Thompson, 2005); c) electrocardiogram. Additional tests such as the Doppler echocardiogram and the rutinary stress test are saved for competitive or high physical demand athletes (Mitchell III-C), or for athletes over 35 years old (Grazioli, 2017).

The objective of adding these additional tests is to increase the sensitivity in people with hypertrophic cardiomyopathy and normal ECG with anomalies of coronary arteries origin or with aortic root dilation. The final aim is to improve the sensitivity in coronary heart disease and cardiac arrhythmias that are noticed while exercising. This screening model has demonstrated to have an effective cost when a group of competitive teenager athletes was analysed (Grazioli, 2017).

Figure 3: Schematic representation of the pre-participation screening suggested in Cataluña



Source: Grazioli, 2017, p. 20.

Historia	History
Ecocardio doppel	Doppler echocardiogram
Examen físico	Physical Examination
Prueba esfuerzo	Exercise Stress Test
ECG	ECG

The athlete's electrocardiogram

The regular sport activity produces a series of morphological and functional adaptations in the heart of the human being that can be observed in the electrocardiogram (ECG) with varied changes. How it is expressed depends on the age, the gender, the race and the type, duration, and intensity of training, as well as the sporting history of the person (Boraita Pérez, Serratosa Fernández and National Centre for Sport Medicine. High Council for Sports. Madrid, May 1998).

The guides of the European Society of Cardiology (ESC) recommend to carry it out (Mont, Pelliccia, Sharma, Biffi, Borjesson et al., 2017) together with the medical record and the physical examination as part of the cardiovascular screening of the athlete. This is because of its capacity to detect cardiomyopathies and channelopathies and its cost-effectiveness relationship. Thus, the correct interpretation by the doctors involved in the sports screening is essential (Serratosa Fernández, Pascual Figal, Masiá Mondéjar, Sanz de la Garza, Madaria Marijuan et al., 2017).

The new criteria for the interpretation of the athlete's ECG have been recently released (Drezner, Sharma, Baggish, Papadakis, Wilson et al., 2017). The ECG findings are classified into normal, borderline, and abnormal (see Table 1).

- The normal findings are the sinus bradycardia, the prolongation of the PR interval, the Mobitz type I 2° AV block, the ectopic or migratory atrial rhythm, and the junctional escape rhythm.
 - The presence of these results is considered to be a physiological finding and it is recommended to check that they are solved by exercising.
 - The incomplete right bundle branch block is considered to be a sign of adaptation to training.
 - No further evaluation is required when any pattern of early repolarization and the presence of T wave inversion V1-V4 with preceding J point elevation and convex ST elevation in black athletes appear in isolation without any other clinical or electrocardiographic data of the disease (Serratosa Fernández et al., 2017).
- The findings classified as borderline are left or right axis deviation, right or left atrial enlargement, and the complete right bundle branch block (Kim, Noseworthy, McCarty, Yared et al., 2011).
 - When each of them is observed in isolation, it is not considered a pathology, but when two or more appear combined, further evaluation is required. (Serratosa Fernández et al., 2017).
- The following alterations in the ECG could be indicative of an underlying heart disease:
 - The T wave inversion is one of the findings with the highest clinical relevance in the athlete's ECG (Schnell, Riding, O'Hanlon, Axel Lentz, Donal et al., 2015). Its pathological significance is determined by its location, the gender, the age, and the athlete's race.
 - The 0.05 mm ST segment depression in two or more contiguous leads, the presence of Q waves, the complete left bundle branch block (Kim y Baggish, 2015), the QRS higher than 140 ms duration, and the presence of the epsilon wave force us to discard a structural heart disease.
 - There are other findings that could suggest a heart disease such as: a prolonged corrected QT interval (QTc of 470 ms in men and of 480 ms in women), and Brugada Type I pattern.
 - Other findings which required further evaluation are the rhythm alterations such as: profound sinus bradycardia (lower than 30 bpm), a PR interval of



400ms, Mobitz Type II 2° AV block, 3° AV block, the ventricular pre-excitation (PR lower than 120ms and the presence of delta wave), the presence of two ventricular extrasystoles in ECG, the atrial tachyarrhythmias (supraventricular tachycardia, fibrillation or atrial flutter) and, last but not least important, ventricular tachycardias (Serratosa Fernández et al., 2017).

Table 3: Summary of the normal, abnormal and borderline findings when interpreting the athlete's ECG according to the international consensus 2017

Normal Findings in the ECG
No further evaluation required
QRS voltage criteria for right and left ventricular hypertrophy
Incomplete right bundle branch block
Early repolarization
ST elevation followed by T wave inversion V1-V4 in black athletes
T wave inversion V1-V3 in minors younger than 16 years old
Sinus bradycardia or arrhythmia
Ectopic atrial or junctional rhythm
1° AV block or Mobitz Type I 2° AV block
Borderline Findings in the ECG
The presence of two or more of these findings requires further evaluation
Right ventricular axis deviation
Right atrial enlargement
Left ventricular axis deviation
Left atrial enlargement
Complete right bundle branch block
Abnormal Findings in the ECG
Further evaluation required
T wave inversion
ST segment depression
Pathologic Q waves
Complete left bundle branch block
QRS duration higher than 140 ms
Epsilon wave presence
Ventricular pre-excitation
Prolonged QT interval
Brugada Type I pattern
Profound sinus bradycardia (lower than 30 bpm)
PR interval → 400 ms
Mobitz Type II 2° AV block

3° AV block
→2 premature ventricular contractions
Atrial tachyarrhythmias
Ventricular tachyarrhythmias

Source: adapted from Serratosa Fernández et al., 2017.

Other cardiology tests for the athlete's diagnostic study

The presence of signs or symptoms suggestive of heart disease in the initial cardiovascular screening forces the doctor involved to further evaluate to discard or confirm the presence of an underlying cardiac disease. Below there is a summary of the most used cardiovascular diagnostic tests for a precise evaluation and useful consideration according to the age of the person, the symptoms described by the athlete, the clinical signs and clinical suspicion.

A) Exercise stress test or Cardiac stress test:

The stress test is used to evaluate the body response to a metabolic overload situation. In athletes, the stress test is a key tool used to assess the body from two perspectives: evaluating their right medical condition by means of prevention and early diagnosis of cardiovascular disease, and, on the other hand, supporting the training process.

There are specific indications about cardiac aspects in athletes' stress tests (Rabadán, y Boraita, 2005; Manonelles Marqueta, Franco Bonforte, and Naranjo Orellana, 2016). These are:

- Evaluation and behaviour during the test of the typical ECG changes observed in the athlete while resting. This is useful to check the resolution with the exercise of the Mobitz Type I 1° and 2° AV block, the ectopic or migratory atrial rhythm, and the junctional escape rhythm.
- Evaluation of professional athletes, of those who practice extreme or maximum demand sports, and athletes over 35 years old due to their higher prevalence of coronary artery disease (Borjesson et al., 2011).
- Evaluation of athletes with suspected heart disease: T wave inversion and ST segment depression, prolonged QT interval, presence of ventricular pre-excitation (useful to evaluate the risk of the accessory pathway), history of effort syncope, study of ventricular extrasystoles (if they disappear while exercising is a sign of being benign), 1° AV block higher than 400 ms, suspected exercise-induced tachyarrhythmias and the case of profound sinus bradycardia.
- Study and follow-up of athletes with diagnosed heart disease that, initially, do not affect the physical exercise (of Teresa Galván, April-June 2017), to indicate their aptitude to practice sports.



- Asymptomatic athletes under 35 years old with inexplicable sudden cardiac death family history related to sports in first-degree relatives (of Teresa Galván, April-June 2017).

B) 24-Hour Holter Monitoring (ECG Holter):

The ECG Holter monitor records your heart frequency and rhythm continuously over 24 hours for subsequent analysis. It is recommended to monitor athletes during a training session, especially if there are symptoms while exercising. This will increase the diagnostic yield.

Instructions for use in athletes:

- Repeated syncope or syncope during the effort mainly when a cardiogenic origin is suspected.
- Study of frequent palpitations: suspicion of supraventricular tachyarrhythmia (paroxysmal supraventricular tachycardia, fibrillation, and atrial flutter) and ventricular tachyarrhythmias.
- Study of rhythm disturbances in basal ECG: presence of 1° AV block higher than 400 ms, presence of Mobitz Type I and II 2° AV block, 3° AV block, two or more ventricular extrasystoles in basal ECG or presence of ventricular extrasystoles during the exercise stress test, prolonged QTc interval, ventricular pre-excitation, Type I Brugada syndrome, and marked sinus bradycardia (30 bpm).
- Evaluate the presence of arrhythmias in case a cardiomyopathy or a myocarditis is suspected (Delise, Biffi, Giada, Gulizia and Inama, 2017).

C) Transthoracic echocardiogram (TTE):

The TTE is part of the advanced cardiovascular evaluation. It is used when clinical manifestations or exploratory findings suggesting cardiovascular pathologies are detected during the initial screening. Using M-mode, two-dimension, Doppler and with colour imaging enables the obtention of relevant information about the structure and function of the myocardium, the valves, the great vessels, the coronary arteries origin, and the pericardium. Thus, as part of a medical examination programme, the TTE can be considered the best diagnostic test for the detection of the main causes of sudden cardiac death in young athletes.



Figure 4: TTE instructions for use in athletes



Source: prepared by the authors.

It is important to mention how useful the stress echocardiography is for the evaluation of changes in the ST and T wave in the resting ECG in case there is suspicion of coronary anomalies or coronary artery disease based on the athlete's age (Franklin, Fletcher, Gordon, Noakes, Ades et al., 1997).

D) Cardiac magnetic resonance (Cardiac MRI):

The Cardiac MRI is a high-precision reproducible technique that provides a more accurate measurement of the cardiac morphology since it outdoes certain limitations of the echocardiography. Besides, the Cardiac MRI is considered to be the preferred technique for the morphologic and functional evaluation of the right ventricle. It is also used for the myocardial fibrosis detection (Martínez, 2015; Prakken, Velthuis, Cramer and Mosterd, 2009).

Cardiac MRI Instructions for use in athletes:

- Suspicion of hypertrophic cardiomyopathy due to the fact that the Cardiac MRI enables the detection of hypertrophy in the lateral and apical segments as well as a more accurate measurement of the parietal thickness.
- Suspicion of arrhythmogenic cardiomyopathy. The cardiac MRI is the preferred technique for this diagnosis.



- Suspicion of dilated cardiomyopathy. The cardiac MRI provides a better evaluation of the cavity volumes and the presence of intramyocardial fibrosis.
- When myocarditis is diagnosed. The cardiac MRI is used to evaluate the extent of the myocardial affection at the acute moment and the appearance of fibrosis during the monitoring.
- Suspicion of coronary artery disease. In this case it would be useful to perform a Stress Cardiac MRI.

E) Computed Tomography Scan (CT) in athletes:

The CT of coronary arteries is especially useful when there is suspicion of coronary artery disease since it enables their angiographic evaluation in a non-invasive way. Besides it enables the accurate study of the coronary anatomy and its epicardial functioning. This is of great interest in case there is suspicion of coronary arteries anomalies or intramyocardial bridging (Sperandi, Guerra, Tranchita, Minganti, Lanzillo et al, 2017).

The TC of aorta enables a more accurate study of the aortic diameters since it is a very useful technique for cases of aorta dilation.

F) Other diagnostic techniques in the cardiac evaluation of the athlete:

The use of nuclear cardiac imaging is not recommended as a first line study for professional athletes. For example, the MIBI-SPECT detects perfusion abnormalities in areas with left ventricular hypertrophy in athletes' healthy hearts. Thus, this is considered a false positive (Bortram, Toft and Hanel, 1998). The positron emission tomography scan has been only used in the research field.

Cardiac Adaptation to Exercise Training: Physiological Cardiac Remodelling and prospective Pathological remodelling

Sports training provokes a series of structural and electrical adaptations in the heart which have been typically called *Athlete's heart* (Stout, 2008).

This functional and structural cardiac remodelling is directly related to the type, duration, and intensity of the training.

In this way, the endurance sports which demand a higher oxygen consumption during long periods of time are those in which the heart experiences more marked electrical and structural adaptations (Pelliccia, Culasso, Di Paolo and Maron, 1999). On the other hand, the clinical expression of such cardiac adaptation to exercise must include the influence that individual factors such as race, gender, and the genetic component have on it.

The exercise-induced left ventricle remodelling is characterised by an increased chamber size and a slight enlargement of the ventricular wall thickness (Pelliccia et al., 1999; Utomi, Oxborough, Ashley, Lord, Fletcher et al., 2014). This myocardium thickening can be more marked in athletes with high strength training load and in black athletes when exceeding



the physiological limit of 13 mm and when simulating a hypertrophic cardiomyopathy. In athletes, the enlargement of the myocardium thickness occurs together with an increase of the ventricular chamber size. Thus, a left-ventricular end-diastolic diameter (LVEDD) bigger than 54 mm or a relationship between that volume and the increased mass of such ventricle would lead to a physiological remodelling. On the other hand, the hypertrophic cardiomyopathy induces a reduction of the left ventricle diastolic function (it slows the relaxation) while in the athlete, this is normal or even supranormal (Caselli, Maron, Urbano Moral, Pandian, Maron, et al., 2014). See Table 1 for further reference.

As mentioned before, the left ventricle dilation is common in the athlete's heart but such dilation rarely exceeds the normal limits (Pellicia et al., 2002). However, an extreme left ventricle remodelling characterized by a marked ventricular dilation (higher than 60 mm) and a systolic function (of contraction) on the lower limit of normal in a 45-50 % has been described in groups of athletes with high resistance training loads (Abergel, Chatellier, Hagege, Oblak, Linhart et al., 2004). These signs lead to the performance of the differential diagnosis with a dilated cardiomyopathy. Additionally, as part of this process of the heart adaptation to exercise, an increase in the stringiness degree of both ventricles that, in some cases, can simulate a non-compaction cardiomyopathy has been described (Gatti, Chandra, Bennett, Reed, Kervio et al., 2013). The final objective of all the structural and functional changes of the heart in response to training is to improve the cardiac output while exercising. So, in the differential diagnosis between the left ventricle physiological remodelling and the cardiomyopathies mentioned above, it is vital to evaluate that ventricle functional response to training which is expected to be preserved or increased in the first case (Gatti et al., 2013).

Traditionally, the athlete's heart study was focused on the left ventricle. During the last decade, the advances in the heart imaging techniques have helped to delve into the knowledge of the right ventricle (RV) and the atria adaptation to exercise. These heart chambers, when at rest, work under low intracavitary pressure which drastically increases while exercising. Thus, these chambers become more vulnerable to the increase of the myocardial wall stress experienced during the exercise (La Gerche, Heidbüchel, Burns, Mooney, Taylor et al., 2011). In fact, the high resistance training loads in a small percentage of athletes have been related to an extreme RV remodelling characterised by a marked dilation of such ventricle, a slight reduction of its contractile function, and a higher incidence of ventricular arrhythmias (Heidbüchel, Hoogsteen, Fagard, Vanhees, Ector et al., 2003). All these signs force the performance of a differential diagnosis with a real arrhythmogenic right ventricular cardiomyopathy (ARVC), but also with an exercise-induced potential adverse RV remodelling.

The echocardiographic parameters that would lead to a physiological remodelling are:

- the increase in the contractile function of the RV in response to exercise;



- the harmonious dilation of all the heart chambers with a LV/RV ratio superior to 1 (Bauce, Frigo, Benini, Michieli, Basso et al., 2010).

On the other hand, a selective dilation of RV outflow tract and the presence of segmental alterations of such ventricle contractility would make us think of a ARVC (Bauce et al., 2010). Take Table 1 as a summary.

In this way, doing endurance exercise has been related to an increased incidence of developing atrial fibrillation (Calvo, Ramos, Montserrat, Guasch, Coll-Vinent et al., 2016). The underlying pathophysiological mechanisms have not been well-defined yet but a pathological remodelling of both atria seems to play an important role.

The echocardiographic parameters that would lead to a potential pathological atrial remodelling are:

- severe dilation of the atrial cavity;
- failure to increase its contractile and reservoir function during the exercise (Sanz de la Garza et al., 2016; Gabrielli, Bijmens, Brambila, Duchateau, Marin et al., 2016).

Table 4: Echocardiographic parameters for the differential diagnosis between the athlete’s heart and the most prevalent cardiomyopathies

	Hypertrophic Cardiomyopathy	Athlete’s Heart
LV End-diastolic Diameter	← 45mm	> 54mm
LV volume/mass Ratio	Reduced	Normal
LV Diastolic Function	Reduced	Normal or supranormal
	Dilated Cardiomyopathy	Athlete’s Heart
Resting LV Contractile Function	Reduced	Normal or slightly reduced
Increase in LV contractile function when exercising	Diminished	Normal or supranormal
	Non-compaction Cardiomyopathy	Athlete’s Heart
Stringiness Location	Apical	Medium
	Diminished	Normal or supranormal



Increase in LV contractile function when exercising		
	arrhythmogenic right ventricular cardiomyopathy	Athlete's Heart
Right Ventricle Dilation	Predominant Outflow Tract	Global
Segmental Alterations in Motility	Yes	No
RV/LV Volume Ratio	→1	< 1
Increase in RV contractile function when exercising	Diminished	Normal or supranormal

Source: Sanz de la Garza et al., 2016; Gabrielli et al., 2016

Cardiac Pathology and Sport

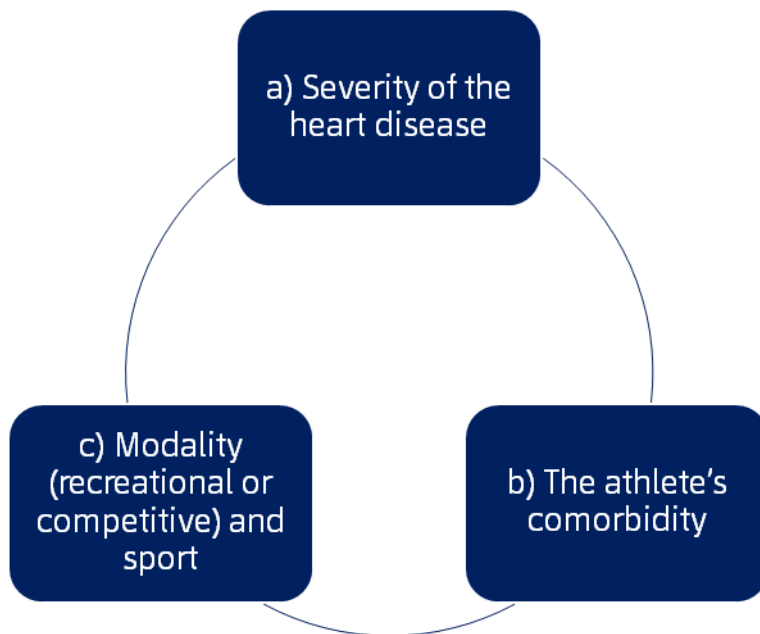
The main heart diseases that might be found in a pre-participation screening are divided into three groups:

- cardiomyopathies (Table 5);
- valve diseases and aortic pathologies (Table 6);
- arrhythmias and channelopathies (Table 7).

The specific congenital cardiopathies will not be mentioned in this lesson because the advice for physical activity is generally given by specialised units in hospitals in charge of controlling them. A piece of advice in relation to the intensity of recommended exercise is given in red and yellow colours for each of the alterations found depending on the type of sport, either recreational or competitive. However, the decision must always be individualised and personalised according to three elements:



Figure 5: Factors to consider when deciding to do a sport



Source: prepared by the authors.

References in Tables 5, 6, and 7:

Yellow (A): competitive sport Mitchell IA; recreational sport: low to moderate static component and intensity < 75 % maximum heart rate or < 6 of BORG-scale.

Red (R): competitive sport is contraindicated; recreational sport: low static component and intensity < 60 % maximum heart rate or < 5 of BORG-scale. (Grazioli et al., 2016, p. 3).

Abbreviations: LV, left ventricle; EF, ejection fraction; DD, diastolic diameter; RV, right ventricle; PASP, pulmonary artery systolic pressure.

Table 5: Recommendation in cardiomyopathies

Cardiomyopathies	Yellow (Y)	Red (R)
LV Hypertrophy	IVS or PPD 13-15 mm	IVS or PPD > 15 mm or diagnosis of hypertrophic cardiomyopathy
RV Function	LVEF 30-50 %	LVEF < 30 %
Coronary heart disease	If there is risk criterion*	

ARVC	Asymptomatic [^]	Symptoms
Myocarditis-pericarditis		Contraindicated in acute phase [°]

Source: adapted from Grazioli et al., 2016, p. 3.

Recommendations in cardiomyopathies.

*Heart disease risk criteria: 1) LVEF < 50 %, 2) symptoms, 3) ischemia or arrhythmia in the stress test; 4) significant coronary artery stenosis; 5) incomplete percutaneous or surgical coronary revascularization.

[°] Physical activity can be performed after normalisation: laboratory markers, ECG, Echo (LVEF > 55 % and absence of pericardial effusion), Holter (without arrhythmia).

[^] Symptoms: pre-syncope, syncope, resurrected sudden cardiac death, malignant ventricular arrhythmia in 24-hour Holter monitoring or stress test. (Grazioli et al., 2016, p. 3).

Table 6: Recommendations in valve diseases and aortic pathologies

Valve diseases and aorta	Yellow (Y)	Red (R)
Aortic or pulmonary stenosis	Low to moderate: maximum flow rate 2.6-4.0 m/s	Moderate to severe: maximum flow rate > 4.0 m/s. Evaluate surgery.
Mitral stenosis	Mitral area 1.0-1.5 cm ² and PASP maximum stress > 50 mmHg	Mitral area < 1.0 cm ² or PASP maximum stress > 50 mmHg. Evaluate surgery.
Aortic or mitral insufficiency	Moderate/Severe insufficiency, DDVE < 63 mm and LVEF > 55 %	Moderate/Severe insufficiency, DDVE > 63 mm and LVEF < 55 %. Evaluate surgery.
Bicuspid aortic valve. Normal functioning: all sports	Regurgitation or low to moderate stenosis	Regurgitation or moderate to severe stenosis. Evaluate surgery.



Mitral valve prolapse	In case there is any risk criterion #.	
Dilated aortic root	40-45 mm	> 45 mm
Coarctation of the aorta	Z-score > 3, or arm-leg gradient > 20 mmHg, or stress hypertension	

Source: own adaptation from Grazioli et al., 2016, p. 4.

Recommendations in valve diseases and aorta. # "Mitral valve prolapse risk criteria: syncope, ventricular arrhythmia, family history of sudden cardiac death, severe mitral insufficiency" (Grazioli et al., 2016, p. 4).

Table 7: Recommendations in arrhythmias and channelopathies

Arrhythmias and channelopathies	Yellow (Y)	Red (R)
Atrial fibrillation, atrial flutter. Anticoagulation yes, Collision sports no	Controlled HR in stress and no structural pathology	Uncontrolled HR in stress or structural heart disease
Ventricular arrhythmia	Ventricular Extrasystoles > 2000/24 hours and they don't increase with stress	Non-sustained VT or Ventricular extrasystoles that increase in stress
Sinus bradycardia, Mobitz Type I 2° AV block (Wenckebach)		HR < 30 bpm or pauses > 3 seconds, or blocks that are not normalised with stress
Mobitz Type II 2° AV block or 3° AV block	Asymptomatic ^, without heart diseases which normalises the block with stress	Symptoms ^ or with congenital heart disease



Pre-excitation syndrome or paroxysmal supraventricular tachycardia	Recreation: radiofrequency ablation: suggested	Competitive: radiofrequency ablation: indicated
ICD (automated implantable cardioverter defibrillator)	Only in sports with no collision risk	
Brugada syndrome	Asymptomatic ^	Symptoms ^
Long or short QT syndrome	Asymptomatic ^	Symptoms
Catecholaminergic ventricular tachycardia	Asymptomatic ^	Symptoms ^

Source: adapted from Grazioli et al., 2016, p. 4.

Recommendations in arrhythmias and channelopathies. ^ "Symptoms: pre-syncope, syncope, resuscitated sudden cardiac death, malignant ventricular arrhythmia in 24-hour Holter monitoring or stress test" (Grazioli et al., 2016, p. 4).



2.2 Life-threatening respiratory disease and sudden cardiac death in sports

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Introduction

Drobnic, Sala, Labrador, Unnithan, and Cardona (2014) state that

The recreational or high-level sports practice presupposes a good condition and a physical excellence, a health condition far away from diseases or even [without them]. That is why the continuous and planned exercise together with the proper precautions taken by the athlete make them have a good health condition and help them prevent injuries, recover better, avoid complications of certain [pathologies] that can coexist with high level technical exercise, or even improve their prognosis. However, being an athlete does not mean not having congenital or inherited disorders or those which are difficult to diagnose or prevent if we do not have previous data that help us discover them. It does not mean not having diseases that can worsen even when having a good sporting performance due to reasons caused by the disease as such, the environment or the physical exercise performed under certain conditions...

The positive effect of physical exercise and an active life has been widely documented in chronic and respiratory diseases, in particular, in asthma. The unfortunate fact that an athlete, an apparently healthy person, dies suddenly while doing sport seems to question the bases of prevention and makes us reconsider how the disease is being controlled. This kind of event mobilises the specialists in preventive diagnosis of those pathologies that can lead to death in sports.

Concept of Sudden Cardiac Death in Sports

The term sudden cardiac death (SCD) has been used in different ways by epidemiologists, clinicians, pathologists or specialists in legal medicine. From a clinical point of view, it is common to consider that sudden deaths occur due to natural reasons. This leaves out accidents, poisonings, suicides, etc during the first hour after symptoms start...

The body system responsible for the failure can be diverse. However, the sudden cardiac death represents more than 90% of all the cases of sudden deaths. That is why, the sudden death is considered to be only cardiogenic popularly and even in scientific forums. The ischemic cardiopathology is present in more than 80% of people who suffer a sudden death. Especially, in people over 35-40 years old. Before that age, it is relatively frequent to think of a hypertrophic cardiomyopathy, especially among young athletes, (p.36) and, in general, of a subclinical myocarditis. Other diseases associated with this age but which occur in a few numbers of cases are the Type Wolff-Parkinson-White pre-excitation (Torner, Brugada, Smeets, Bayés de Luna et al., 1991), the arrhythmogenic right ventricular dysplasia (Thiene, Nava, Corrado, Rossi and Pennelli, 1988), the mitral prolapse and other valve diseases, and the congenital coronary anomalies. The real incidence of sudden death varies from one country to another depending on the prevalence of the ischemic cardiopathology which is much more reported in countries from the north of Europe and in the United States than in the Mediterranean basin. According to the World Health Organisation (WHO), the incidence of sudden cardiac death in industrialised areas varies between 20 to 160 per a hundred thousand inhabitants per year among people aged between 35 to 64 (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014).

The sudden death (SD) in athletes extends the interval when death takes place. Normally during the first 24 hours after the sporting event. The objective of this extension in time is to expand the reception time frame of all those processes that lead to that result from a sport-related perspective. Thus, by knowing the relationship between the exercise and the pathology leading to death, different preventive, diagnostic or therapeutic models can be established to prevent the process. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, p. 36).

The prevalence of sudden cardiac death in sports has been estimated in 1 per 200,000 inhabitants per year in people under 35 years old, and in 1 per 18,000 in people over that age (MacAuley, 1998). Similar to “what happens with non-athletic people, [most of the times, the SD] has a cardiovascular origin, [and] in people under 35, it is associated with unsuspected structural heart diseases”, apart from the ones mentioned before (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014, p. 36).



It is important to mention that if identifying the cause of a sudden death is complicated, it is even much more difficult to do it with cases of sudden death in athletes. In most of the cases, it is based on the data which appear in the press and is presented by professionals involved in the process. This makes us think that even though this is all we have, it is not all that exists. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, pp. 36-37).

The concept of sudden death is a binding element of the most drastic outcome in sports. If called differently, its incidence would be lower and, consequently, its prevalence since it is only related to the cause of the death. In this way, the magnitude of a problem which lies, among other things, in a proper study and monitoring of the athlete would falsely be diluted (Drobnic, July 2008). As it was established by the statistics mentioned, the sudden death in sports has always been related to the heart and this is the way it is evaluated in the athlete's diagnosis criteria (Maron, 2007; Crawford, 2007). However, the causes of death while doing physical activity can be many.

Table 8: Systems of adaptation to stress while exercising

Systems of adaptation to stress while exercising
Cardiovascular
Metabolic
Nervous
Endocrine
Respiratory

Source: prepared by the authors.

Table 9: Diseases associated with exercise that can appear in an apparently healthy person

Diseases associated with exercise that can appear in an apparently healthy person
Thermal shock
Cerebral haemorrhage
Haemoptysis
Anaphylactic shock

Source: prepared by the authors.

Currently, the concept of unknown undiagnosed disease and excellent previous health condition in relation to sudden death has become obsolete due to the advancement in preventive diagnosis. It is clear that what matters is that the identification process is in progress. This means that the



diagnosis is done, can be done or is expected to be done as a necessary basic step.

Consequently, as the term sudden death is related to these characteristics, from a preventive point of view, it is more useful to start using the term life-threatening disease or pathology. This is, a disease that, under certain conditions, could lead to a fatal outcome. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, p. 37).

From the point of view of the Medicine in physical education and sport, it is considered that the exercise can be a trigger, a contributor or the main cause. If we consider it a life-threatening pathology, we could define and work on the prevention of this sudden death (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014).

Patient with respiratory distress and the risk of death while exercising

When a specialist physician is asked about a patient with respiratory distress who practices or wants to start any sport or entertaining activity that requires physical effort and stress of the adaptation systems to it, that doctor is responsible for knowing the patient’s idiosyncrasy, the diseases he/she suffers and their interaction with medication, the stress level or intensity, and the environment where he/she will evolve and will be exposed to. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, p. 37).

Table 10: Main antecedents to consider when the patient suffers from respiratory distress

Main antecedents to consider when the patient suffers from respiratory distress
Spontaneous pneumothorax
Congenital Lung Abnormalities
Chronic airflow limitation
Prior sensitisation to certain food and insects’ bites
Asthma

Source: prepared by the authors.

When making reference to Pneumology, most of the observed pathologies lead to a shortness of breath with exercise. While exercising, the patient’s life will never be at risk due to the fact that the intensity of the exercise will be limited by such respiratory disease. It is also true that certain diseases



with certain characteristics must be taken into account, especially if the body undergoes not only a physical but also an environmental stress... It is not necessary to make reference to unique and special cases which do really not justify an excess of zeal most of the times... (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014, p. 37).

But of course, these cases should be useful to alert the athlete and the patient and recommend them to follow the advice and prescriptions given (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014). Moreover, when these pathologies can occasionally put their lives at risk.

Normally, the patient with respiratory distress that can do high- intensity and structured exercise, considered to be a sport, even at a high level, is the one who suffers from asthma. Thanks to the easiness of travelling and new technology, some patients with other diseases can perform certain activities and access places where they can test their cardiopulmonary system. Some of the activities carried out at recreational centres are trekking, hiking, climbing, diving or balloon rides. (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014).

Near 300 million people suffer from asthma and almost 250,000 die annually because of underdiagnosis, inadequate treatment or delay in medical assistance during the final crisis. In Spain, this rate is calculated as follows: 0.4/100,000 male inhabitants and 0.1/100,000 female inhabitants aged from 5 to 34 years old. This rate is similar to the one in other countries with the same socio-economic level and same age range. However, life-threatening asthma has decreased in general. The percentage of hospital admission of people with acute asthma with a risk of life intensified by exercise are 0.2 % in Spain, between 300 and 350 cases, and a 0.5 % in Latin America, between 600 and 700 with respect to all the causes. The age range is wide and athletes are not the only ones included in this group. All types of effort are considered. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, p. 38).

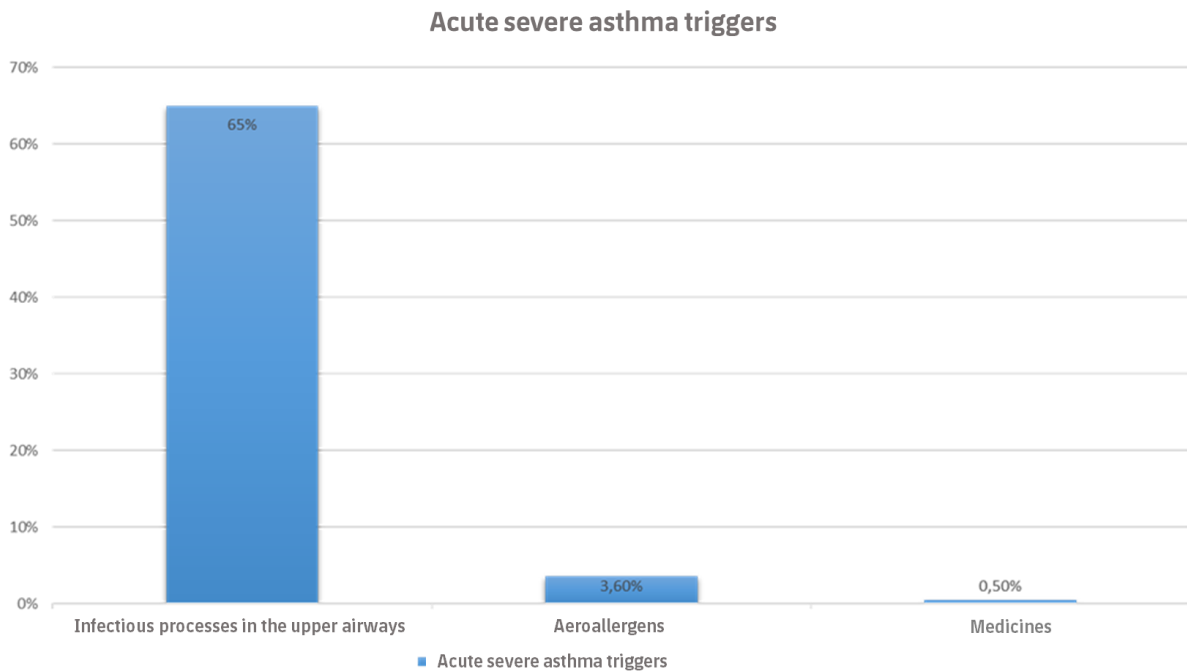
It is important to know that exercise is the main cause of the exacerbation that leads to hospital admission.

There is no register, in any case, of deaths which have taken place during sport practice. It seems to be non-relevant data because of the lack of



literature about it, but the fact is that it is extremely difficult to get information about those deaths. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, p. 38).

Figure 6: Acute severe asthma triggers



Source: prepared by the authors.

When exercise is involved in triggering acute severe respiratory distress, it is not always easy to consider it a contributing factor or final trigger. Instead, it is possible to take it as one of the main incentives. Anyway, sudden deaths caused by asthma or anaphylactic crisis are not considered cases of sudden cardiac deaths even though they occur relatively fast and unexpectedly. They are considered deaths caused by an asthma attack while exercising, by doing exercise and eating certain food the person is especially sensitive to, by a previous severe health condition or by other triggering reasons such as infections, aeroallergens, Hymenoptera stings, medicine, etcetera (Drobnic, 2007). In any case, the base disease is known by the patient, the physician, and, sometimes, by people close to them.

A first step for a patient with asthma is to know the causes that can aggravate the asthma. The most common causes are prior hospital stay, undertreatment for different reasons, and obesity (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014). The analysis of the relationship between the asthma severity markers and the risk of death makes their recognition determining: the amount and the severity of hospital admissions the previous year, the prescription of three or more drugs, or the introduction of oral corticotherapy, and any possible psychosocial problems of the patient help to better identify the group of



severe asthmatics, those with a higher risk of death. Undoubtedly, these factors should be considered of great importance when prescribing exercise to these people (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014).

In fact, the common denominator of deaths caused by asthma in sports is based on the severity of the base disease, persistent, moderate or severe asthma, on the little treatment adherence from part of the patient, and, in general, on an underestimation of the disease (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014). This underestimation is not necessarily related to an alexithymia, this is a lack of recognition of the seriousness of the crisis. Instead, it is related to the lack of concern about their asthma which is based on disorders of a psychosocial nature. In some people, they depend on the patient's age and development phase and maturity such as pre-adolescence and adolescence, and on their relationship with the disease. Aspects that are accessible with a good education and monitoring.

Comorbidity and the weather

By means of the education and evaluation of the patient, we must identify the causes that can lead to a crisis in an asthmatic patient, the comorbidity of acute asthma in patients who also suffer from rhinitis, for instance, [and moreover] their relationship with the weather conditions, typical of outdoor sport activities, some of them recreational ones and practiced by a great amount of people. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, p. 39).

From an epidemiological point of view, the severe asthma crisis does not only depend on socioeconomic or intellectual circumstances or on the treatment adherence. Instead, it depends significantly on the adequacy of the weather conditions for many reasons. The storms, the presence or absence of rains, the wind speed and direction, the atmospheric pressure, or the temperature can have a drastic influence on the worsening of the basal asthma. Hospital admissions for asthma cases increase when there is high humidity and low atmospheric pressure as well as when the temperature is low and its range is wider (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014).

During storms, the osmotic pressure increases and pollen grains break into breathable particles. Thus, there is a higher chance that a patient with rhinitis suffers from an acute crisis. The cold and dry air is a key and important factor in stress-induced asthma attacks. Similarly, other climate aspects lead to basal asthma destabilisation. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, p. 39).



These contexts can definitely lead to a fatal outcome.

Table 10 includes all these aspects to help us understand which characteristics of asthma, the patient and the context should be taken into account for the prevention of the risk of life-threatening acute asthma crisis. It can definitely be taken as a summary of this chapter.

The appearance of sudden cardiac death cases during childhood and adolescence is unusual (Byard, James and Gilbert, 2002). However, we must take it into consideration in children and adolescents with asthma since half of the cases happen between the age of 10 and 20. Besides, there is no difference between the recreational and competitive sport practice. This is important since not all children take part in sport competitions but all of them play (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014).

We should not be scared of the complex relationship between asthma and exercise, but we must always respect it. The message to the patient must be clear. Even though active sport participation must be advised, physicians must reinforce the concept that asthma is a life-threatening disease with serious potential health effects, but which can be controlled with appropriate measures.

Considering respiratory-induced deaths while exercising cases of sudden cardiac death or not should be important to us since they do occur, they can be identified, measured and evaluated. The aim should be preventing them, or at least, decreasing the number of cases as it already occurs with those of cardiovascular origin. (Drobnic, Sala, Labrador, Unnithan, and Cardona, 2014, p. 40).

We are not wrong to think that sudden deaths in sports related to the respiratory system and allergies do exist. They are of diverse origin and could be avoided if we knew a little bit more about them and we acted accordingly (Drobnic, Sala, Labrador, Unnithan and Cardona, 2014).

Table 11: Circumstances related to the worsening of asthma episodes and life-threatening asthma attacks

Area	Worsening of asthma	Life-threatening asthma
Sport	Intrinsic severity of asthma.	Admissions in the last year.



In general	Level of treatment adherence. Comorbidity of asthma and rhinitis. Neutrophilic asthma. Low sociocultural level. Weather-related aspects. Women: days of menstrual period. Obesity and low level of physical fitness.	Psychosocial problems of the patient. Prescription of three or more drugs. Start of oral corticotherapy. Admissions in the last year. Psychosocial problems of the patient. Prescription of three or more drugs. Start of oral corticotherapy.
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Source: adapted from Drobnic, Sala, Labrador, Unnithan and Cardona, 2014.

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