Module 1. Coronary heart disease

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The term “coronary artery disease” encompasses both anatomical anomalies and atherosclerosis. In this chapter, we will initially address the anatomical pathology and myocardial bridging, the possible variants, and their management in athletes. Then, we will develop the broad field of atherosclerosis.

Unit 1. Anatomical anomalies of the coronary arteries

References

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Coronary artery anomalies are an important pathology to consider in athletes, since, although they have a low prevalence (around 0.2%), they can be a cause of death in young patients (**Maron** *et al*., 2009).

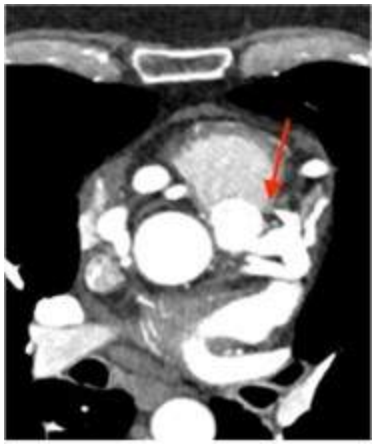
Currently, their classification is based on anatomical characteristics; therefore, there are three categories: **anomalies in the origin or course, anomalies intrinsic to the anatomy, and anomalies in the termination.** We will now describe the most important ones, leaving aside other possible anomalies considered of uncertain significance.

1.1.1 Anomalous origin from the trunk of the pulmonary artery

The left coronary artery originating from the pulmonary trunk (PT) — also known as ALCAPA, which stands for anomalous left coronary artery from pulmonary artery— together with a correct anatomy of the right coronary artery is called Bland-White-Garland syndrome. The presence of collateral circulation between both coronary arteries determines the degree of ischemia produced in the area irrigated by

this coronary artery of anomalous origin and, therefore, the presence or absence of symptoms (see Figure 1).

Figure 1. Anomalous origin of the left coronary artery from the pulmonary artery trunk (red arrow)



Source: own source.

This anomaly can also appear in the contralateral coronary artery, the right coronary artery being the one arising from the PT. In this case, it is called ARCAPA, *anomalous origin of the right coronary artery from the pulmonary artery* (**Radke** *et al.*, 1998; **Wesselhoeft** *et al*., 1968).

1.1.2 Coronary artery originating from an inappropriate coronary sinus

The origin of the right coronary artery from the left sinus of Valsalva, or the origin of the left coronary artery from the right sinus, is a rare

pathology that has been observed in up to 0.17% of autopsies and in up to 1.2% of patients in whom coronary angiography has been performed (Davis et al., 2001).

Generally, they have a benign course, except when they pass between both arterial trunks, as this is related to ischemia events due to different mechanisms, mainly coronary compression with dilatation of the PT and the aorta in situations of increased cardiac output, such as exercise. This ischemia exposes patients to a higher risk of sudden death, which is more frequent in those in whom the affected coronary artery is the left one. Also, by a similar mechanism, the interseptal course has been related to a higher incidence of sudden death.

In the case of coronary artery origin from another ostium, autopsy studies for sudden death have shown a greater presence of coronary alterations in athletes compared to the general population. This fact relates the events and clinical presentation of functional ischemia with exercise, with this alteration being the most related to sudden death in young athletes (Corrado et al., 2003).

1.2 Assessment of athletes

Published studies on athletes report that only 22% of patients with coronary anomalies have an electrocardiographic correspondence with exercise secondary to ischemic changes. Thus, if suspicion is high, guided mainly by the clinical presentation, a transthoracic or

transesophageal echocardiogram is recommended to assess the correct origin of the coronary arteries and their proximal course. In young patients, visualization of the *ostium* and the initial course of the left coronary artery is possible in up to 98% of cases, and of the right coronary artery in up to 80% of cases. In case of doubt, more advanced tests, such as cardiac MRI, will be used to avoid radiation from other tests such as computed tomography (CT) (**Cantinotti** *et al*., 2021).

Given the low prevalence, but the association with sudden death, especially in the case of anomalies such as ALCAPA and the origin of the left coronary artery from the right coronary sinus, the challenge is to make the diagnosis and determine the need and type of treatment in each case.

It is recommended to rule out the presence of ischemia with functional tests before engaging in sporting activities in all cases, since they can be related to narrowing of the vessel lumen or *ostium*, although those with a greater risk of ischemia are the cases with interarterial courses. In case surgical correction is performed, sporting activity should not be started before 3 months, always ruling out the presence of ischemia after treatment (**Pelliccia** *et al*., 2021).

The presence of ischemia disqualifies the athlete from participating in competitive sports (Table 1). In particular, the anomalous origin from the aorta with a large angulation and the course between the

pulmonary artery and the aorta are associated with a high risk of sudden death, so surgical correction is recommended in symptomatic cases. It is also recommended to avoid moderate- or high-intensity sports, due to the risk of ischemia and events associated with exercise.

Table 1. European Society of Cardiology and sport 2020 recommendations for the assessment of the athlete with coronary anatomical alterations for: Golf, (18 holes walking), table tennis (doubles and singles), shooting, curling, and bowling. PET: positron emission tomography. MRI: magnetic resonance imaging. SPECT: single photon emission computed tomography

Recommendation	Class	Level
Imaging tests (stress echocardiography, cardiac MRI with dobutamine or adenosine, PET/SPECT) are recommended to define high-risk patterns and stress tests (cycloergometer or treadmill) to assess the presence of ischemia.	II A	C
Competitive sporting activity can be considered in asymptomatic patients with coronary artery anomalies that do not course between the large vessels, do not have a slit-like orifice, or an intramural course, after informing the patient of the risk and demonstrating the absence of inducible ischemia.	II B	C
After surgical repair, sports participation should be considered at least 3 months after surgery. The absence of cardiological symptoms and the absence of inducible ischemia and/or complex exercise-induced arrhythmias should be confirmed.	II B	C
Participation in competitive sports is not recommended, with the exception of those of low-intensity demand in patients with an angulated origin or a course between the large vessels of the coronary artery.	III	C

Source: adapted from Pelliccia *et al.*, 2021.

1.3 Myocardial bridging

1.3.1 Definition and demographics

Myocardial bridging is the partial or total course under the myocardial fibers of a coronary artery. The entrapped portion of the artery is called the tunneled portion. It is considered superficial between 1-2 mm and deep beyond 2 mm.

Although it can be related to any of the coronary arteries, the most affected one is the anterior descending coronary artery, most frequently in its proximal and middle segment.

1.3.2 Pathophysiology

The main determining factors in the pathophysiology of the disease will be the length of the entrapped segment, its depth, its tortuosity, and the presence of atherosclerosis in the coronary artery that alters basal coronary flow.

In addition, a process of coronary steal is observed, which affects the small branches that arise from the entrapped portion of the coronary artery. The development of atherosclerosis has also been observed, typically in the area proximal to the tunneled segment, which is present even in pediatric patients. Although it was stipulated to be

related to shear forces or retrograde flow in this area during compression due to milking of the coronary, new targeted studies have not found a direct relationship.

Finally, continuous vessel compression has been related to the presence of vasospasm and coronary dissection due to endothelial damage (**Wu** *et al.*, 2016).

1.3.3 Clinical presentation

Myocardial bridging is usually a pathology that presents without symptoms. If there are symptoms, their peak occurs between the third and fourth decade of life. In the case of athletes, it should be noted that, in some studies, such as *RACE Paris*, which studied all major events occurring during 46 long-distance races in Paris between 2006 and 2016, a total of 18 acute coronary syndrome (ACS) events were described, with myocardial bridging present in one of them (Gerardin *et al.*, 2021). Although rare, there are also case reports of multiple myocardial bridging and syncope in a high-intensity runner, presumably related to ventricular arrhythmias secondary to myocardial ischemia (Alexandre et al., 2022).

1.3.4 Diagnosis

Advanced imaging tests are required to make the diagnosis, since, at baseline, it is rare to observe alterations in the electrocardiogram (ECG).

Diagnosis can be based on invasive and non-invasive methods. Among the former, catheterization allows for the objective identification of specific signs such as milking, which consists of

observing the decrease in diameter during ventricular systole of the lumen. This is considered significant when there is a >70% reduction in lumen during systole and a >35% reduction persists in mid and end diastole (Tarantini et al., 2018).

The use of non-invasive methods such as CT makes it possible to perform a higher percentage of diagnoses, since it allows for the diagnosis and observation of thinner or partial bridges that do not present a significant collapse of the lumen, which is decisive for the diagnosis in the case of catheterization.

Isotopic testing and stress echocardiography are particularly useful in the assessment of ischemia; moreover, the latter can define typical patterns such as septal involvement with preservation of apical territory; however, they do not allow for the observation of the bridge (Lin *et al.*, 2013).

1.3.5 Treatment

The scientific evidence for the treatment of myocardial bridging is based mainly on case series studies and expert opinion. In general, treatment is not recommended in asymptomatic patients.

In symptomatic cases, the first-line drugs are beta-blockers and calcium antagonists, which cause a lengthening of diastole by reducing the heart rate. As for percutaneous treatment, the available

studies are based on the use of first-generation metallic stents with a high rate of in-stent restenosis and with a radial resistance lower than that of current devices. Documented cases of fracture are rare, but stent perforation has been observed in up to 6% of these.

Surgical treatment is based on performing a coronary bypass or excising the muscular band. This depends on the length, tortuosity, and depth of the coronary artery. This approach seems to be more effective than percutaneous treatment in patients who do not respond to medical therapy (**Cerrato** *et al*., 2017).

For the management of the athlete, the anatomical characteristics should be assessed, as well as the presence of inducible ischemia. In the absence of ischemia, symptoms, and ventricular arrhythmias at peak exercise, participation in competitive sport is not contraindicated. In Table 2 of the 2020 ESC *Guidelines on sports cardiology and exercise in patients with cardiovascular disease* (Pelliccia et al., 2021), we find the recommendations, level of evidence C, of the European Society of Cardiology (ESC).

Table 2. Recommendations of the European Society of Cardiology and sport 2020 for sports practice in patients with myocardial bridging

Recommendation	Class	Level
The practice of competitive and/or recreational sports of any intensity can be pursued by patients with asymptomatic myocardial bridging in whom exercise at maximum intensity does not induce arrhythmias and/or ischemia.	IIa	C
Patients with myocardial bridging who present persistent ischemia and/or complex cardiac arrhythmias in a stress test at maximum intensity are advised against practicing competitive sports.	III	C

Source: adapted from Pelliccia *et al.*, 2021.

1.4 Atherosclerotic coronary artery disease

Acute and chronic ischemic pathology

Coronary artery disease (CAD) refers to the presence of atherosclerotic lesions in the epicardial coronary arteries. Although it is a chronic and progressive disease, its dynamic nature means that the clinical presentation can be in the form of either chronic or acute syndromes.

1.5 Chronic ischemic heart disease

1.5.1 Definition

Chronic ischemic heart disease is a disease that affects the coronary arteries and whose clinical characteristics remain stable over time.

In general, it can be classified into two types, **symptomatic chronic ischemic heart disease**, in the form of stable angina, and **asymptomatic chronic ischemic heart disease**, with or without underlying ischemia.

Stable angina is defined as a clinical syndrome characterized by chest discomfort, usually in the form of tightness, which may radiate to the jaw, shoulders, back, or arms. Typically, it is triggered by exercise and relieved by rest or nitroglycerin, to which it responds quickly, and it is attributable to myocardial ischemia. This may be due to the onset of atherosclerosis or to the persistence of ischemia after treatment of an acute condition (Hjemdahl et al., 2006).

As for asymptomatic ischemic heart disease, this group includes patients who have first presented with an acute coronary syndrome (ACS) or stable angina, but who have already been treated and are found to be asymptomatic and without ischemia data in provocation tests.

1.5.2 Evaluation

A thorough medical history remains the cornerstone of the diagnosis. The characteristics of pain allow us to classify it in 3 categories: typical, atypical, and non-anginal (see Table 3).

Table 3. Classification of precordial pain according to its clinical characteristics

Types of precordial pain.	
Typical	Oppressive precordial pain
	Triggered by exercise or stress
	Rapidly subsides with rest or nitroglycerin
Atypical	2 characteristics
Non-anginal	≤1 characteristic

Source: own source.

For the study of these patients, the following tests are recommended:

- Blood tests with troponin levels as an indicator of chronic or acute myocardial damage, depending on the context and its kinetics, HbA1c levels, cholesterol, thyroid hormones, and renal function.
- Baseline ECG to detect alterations, mainly of the ST segment and repolarization (flattening or inversion of T waves), as well as arrhythmias.
- Chest X-ray, which will help in the diagnosis of heart failure and to assess other causes of precordial pain

(mainly respiratory and skeletal pathology).

- Echocardiogram, indicated for all symptomatic patients (IB ESC indication) (**Neumann** *et al*., 2020), helps assess ventricular dysfunction or segmental hypokinesia suggestive of CAD, but also of valvular pathology or data of ventricular overload.

1. Estimation of the probability of CAD

The ESC proposes the use of clinical presentation, together with age and sex, as factors to determine the probability of coronary artery disease (see Table 4). High risk is defined as those patients with a pre-test probability higher than 15% and, in this case, further study is required. In cases where the probability is less than 5%, its presence is considered unlikely and, unless specific details of anamnesis indicate a high risk, further diagnostic testing is not considered. In patients with a probability of between 5 and 15%, it is recommended to assess other factors that act as modulators, modifying this probability.

Table 4. Pre-test probability of coronary obstructive disease based on symptoms, age, and type of anginal pain. Green: Low probability. Yellow: Intermediate probability. Orange: High probability

	Typical		Atypical		Non-anginal	
Age	Male	Female	Male	Female	Male	Female
30 - 39	3%	5%	4%	3%	1%	1%
40 - 49	22%	10%	10%	6%	3%	2%
50 - 59	32%	13%	17%	6%	11%	3%
60 - 69	44%	16%	26%	11%	22%	6%
70+	52%	27%	34%	19%	24%	10%

Source: own source based on Neumann *et al.*, 2020.

2. Diagnostic test based on the probability of CAD

When deciding on the study to be performed, the patient's wishes must always be considered, as well as the benefit that he can obtain from the treatment, whether invasive or not. In selected patients, it is possible to initiate treatment based on clinical diagnosis or to perform noninvasive ischemia tests to guide treatment. In patients with high probability of CAD, when therapeutic management through a medical approach is difficult or when there is a high risk of events, cardiac catheterization is a helpful option.

In the rest of the patients, functional tests to determine ischemia or coronary angiography by CT are recommended. Among the functional tests, the most commonly used are SPECT (single photon emission computed tomography) and PET (positron emission tomography) of myocardial perfusion, stress echocardiogram, or MRI with

adenosine/dipyridamole. Whenever possible, exercise as a stressor will be chosen, and only in patients who, for medical reasons or physical incapacity, are unable to do conventional exercise, tests with pharmacological stress will be chosen.

1.6 Individual event risk assessment

After diagnosis, an individual risk assessment of events should be performed. Here we must emphasize the difference between the individual risk in the patient assessed for stable angina and the patient in whom the overall individual risk is assessed. The SCORE charts help evaluate the 10-year risk of death of cardiovascular origin, considering patients as high risk if they have a risk over 5%. Nonetheless, it should be emphasized that these charts are useful in asymptomatic patients.

1.6.1 Treatment

Treatment has two objectives: the treatment of angina and baseline ischemia, as well as the prevention of cardiovascular events.

Antianginal treatment

Among the antianginal treatments, beta-blockers and calcium channel blockers stand out as first-line drugs. Second-line drugs include long-acting nitrates and negative chronotropes, such as

ivabradine, which is especially useful in patients with non-limiting angina.

A specific case is the control of acute angina with exercise. In such situation, the use of oral nitrates is recommended, preferably in spray form, due to their faster action. Avoid administration while standing upright due to the risk of hypotension and syncope.

Antiplatelet therapy

The aim of antiplatelet therapy is to reduce thrombotic events. This reduction in thrombotic risk is always accompanied by an increased risk of bleeding. The main drugs used include acetylsalicylic acid and clopidogrel.

The use of other inhibitors of this receptor, such as prasugrel (irreversible) or ticagrelor (reversible), is only recommended in the case of temporary percutaneous revascularization or in cases of acute coronary syndrome, and not routinely in chronic coronary syndrome.

Myocardial revascularization

In the absence of symptom control, revascularization of hemodynamically significant lesions is an option that may reduce unfavorable outcomes in this population.

1.7 Acute ischemic heart disease

1.7.1 Definition

ACS is defined as the presence of symptoms of ischemia that appear at rest or are triggered by lesser exertion than usual.

The main classification includes acute ST-elevation myocardial infarction (STEMI), acute non-ST-elevation myocardial infarction (NSTEMI), and unstable angina.

The electrocardiogram (ECG) allows for the differentiation of the first two entities. The former will show a persistent ST-segment elevation (>20 min) (see Figure 2), while the latter is characterized by ST-segment depression or repolarization disturbance with flattening or inversion of the T waves, although it can also be observed with a normal ECG.

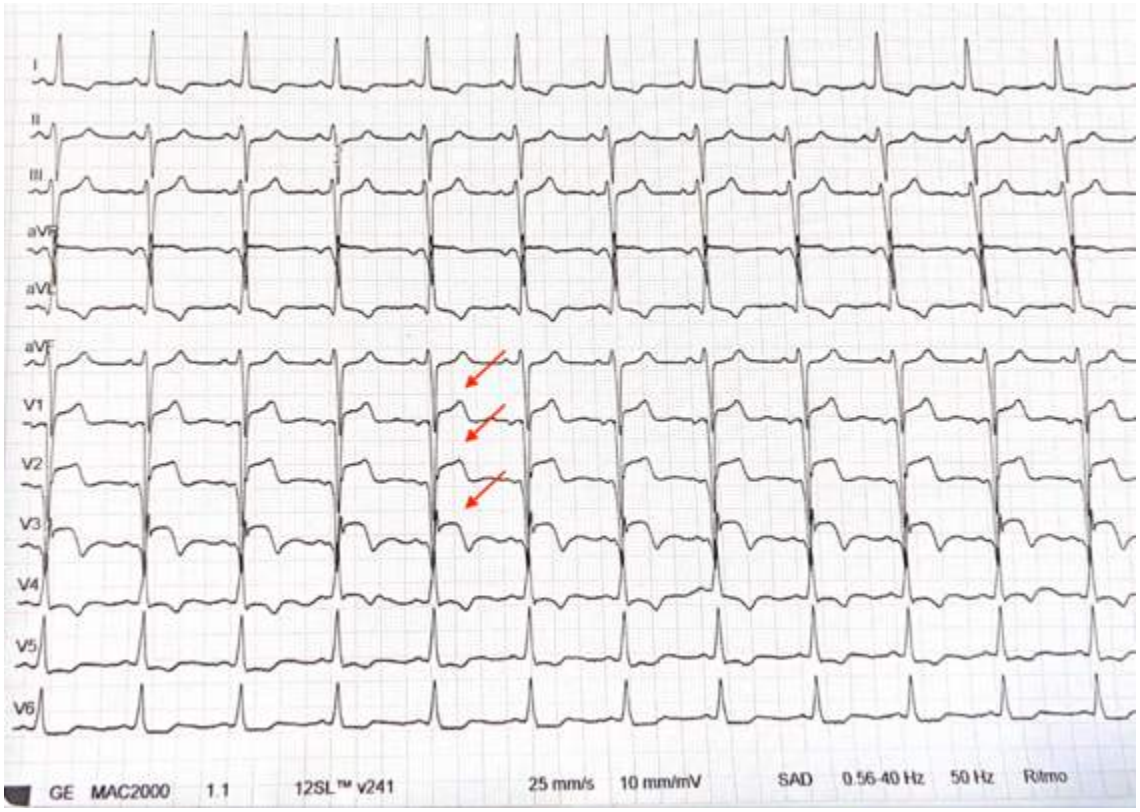
Secondly, what defines unstable angina and differentiates it from acute myocardial infarction (AMI) is the associated myocardial injury, which is determined by the positivity of myocardial necrosis markers in infarction, but not in unstable angina.

1.7.2 Diagnosis

It is worth remembering that ACS is a clinical diagnosis. The tests should not support its diagnosis, but rather their subclassification. Other pathologies with precordial pain that are not ACS, such as aortic dissection, aortic stenosis, acute pericarditis, esophageal spasm, or gastric ulcer, should always be considered.

The ECG is the first test to be performed and its use is recommended within the first 10 minutes of the patient's arrival (see Figure 2). In case the condition is not considered a STEMI, determining the positivity or not of the myocardial necrosis markers, always having ruled out other causes of acute chest pain, is what will determine the diagnosis of STEMI vs. unstable angina.

Figure 2. Electrocardiogram showing ST-segment elevation in the anterior precordial leads (red arrows)



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1.7.3 Treatment

Although the advanced in-hospital treatment of these entities is beyond the scope of this topic, it should be noted that, in cases classified as STEMI, emergent coronary angiography is indicated if it is available within 120 minutes of diagnosis. In those patients in whom this is not possible, fibrinolysis with subsequent coronary angiography is recommended urgently or early depending on the evolution.

In the case of NSTEMI, coronary angiography is not an emergent criterion and can be deferred and performed during admission.

Concerning the treatment of these entities, regardless of the approach, whether with medical or percutaneous treatment, double antiplatelet therapy is indicated for ACS secondary to atherosclerotic lesions for 12 months. Aspirin should always be combined with clopidogrel, ticagrelor, or prasugrel, depending on the patient's clinical characteristics, as well as their thrombotic and hemorrhagic risk. We recommend the reader to see both the European and American guidelines for the management of this syndrome (**Collet** *et al*., 2021; **Gulati** *et al*., 2021).

In addition to hospital treatment, cardiac rehabilitation programs are a key element in the patient's recovery. Although they have not shown a reduction in mortality, they have shown an improvement in the patient's quality of life and a reduction in hospitalizations, when there is heart failure.

In cases of acute coronary syndrome, the start of cardiac rehabilitation should be early and, at least, for 8 to 12 weeks after the cardiac event (Anderson et al., 2016), although, in this case, it may be up to 3 to 6 months to reach the appropriate level to participate in sporting events. In competitive athletes, a cardiopulmonary exercise test (CPET) is recommended to stratify risk. It is important to remember that each week that the start of exercise is delayed means an additional month of exercise to obtain the same results (**Haykowsky** *et al*., 2011).

1.8 Management of athletes with coronary artery disease or at risk of developing it

Coronary artery disease is the most frequent cause of sudden cardiac death in senior athletes (>35 years). Nevertheless, physical activity is one of the most effective therapies to prevent the development of atherosclerosis and, therefore, of coronary disease.

At least 30 minutes of moderate-intensity physical activity 5 days a week is recommended, as it is associated with an improvement in the cardiovascular risk profile, reducing lipid levels, blood pressure, obesity, insulin resistance and contributing to an improved endothelial function (**Piepoli** *et al.*, 2016).

However, intense physical activity appears to be associated with sudden death events at follow-up. This risk is minimal in young athletes under 35 years old without cardiovascular comorbidities, but is of greater importance in senior athletes, in whom there may be concomitant cardiovascular disease (**Albert** *et al.*, 2000).

It has been estimated, based on records of marathon athletes, that the risk of sudden death in the population between 35 and 45 years old is 1/50000 (**Kim** *et al.*, 2012), and they generally have a better prognosis, given the associated characteristics of the event (witnessed, baseline condition of the athlete, early defibrillation). Consequently, it is essential to use tools to estimate individual risk in

senior athletes practicing high-intensity exercise or in those with cardiovascular disease, primarily established coronary artery disease.

1.8.1 Risk determination

The first assessment is to determine the individual risk factors of each patient. Among the main factors are sex and age, as well as a family history of heart disease or sudden death. Modifiable risk factors should also be considered, such as arterial hypertension, dyslipidemia, diabetes *mellitus*, and smoking.

The use of the European SCORE risk scales, which estimate the 10-year risk of death of cardiovascular origin, is recommended. It is worth mentioning that these scales are mainly used in asymptomatic patients.

Besides, we want to emphasize that, although the ultimate goal of the study in high-risk senior athletes is to determine the presence or not of coronary artery disease, recent studies have shown that, in this population, there is a higher burden of stable plaques, even though the long-term impact of this finding is unknown (**Aengevaeren** *et al*., 2017).

1.8.2 Patient assessment

Individuals with risk factors for CAD are generally recognized in screenings performed prior to sporting events or actively through the assessment of senior athletes, as recommended, in 2011, by the European Society of Cardiology and the European Association for Cardiovascular Prevention and Rehabilitation (Borjesson et al., 2019a). Any assessment should consider the individual cardiovascular risk of each patient and the volume of exercise (intensity, duration, and frequency) to which the patient is exposed.

Individuals at risk for CAD or asymptomatic individuals in whom coronary artery disease has been detected during screenings

The initial assessment is similar to that indicated in section 3.1.2 on ischemic heart disease. Patients with a goal of starting a sporting activity of at least moderate intensity and who have a high risk according to the SCORE scale, alterations in the physical examination, baseline ECG, or symptoms suggestive of ischemia, should undergo an assessment by means of a stress test.

In addition to the aforementioned SCORE risk stratification charts, the use of new imaging techniques makes it possible to detect a larger number of patients at risk. In this case, we highlight the detection of coronary calcium through CT in those patients at moderate initial risk, allowing them to be reclassified as low or high risk (**Greenland** *et al*., 2004). Despite the usefulness of coronary calcium assessment, this is

an anatomical test that does not allow the assessment of functional repercussions.

- If the stress test result is normal, the presence of CAD is unlikely.
- If the test result is borderline or not interpretable, another test, such as a cardiac magnetic resonance imaging (CMR) or SPECT, is recommended.
- If the test result is positive, cardiac catheterization is recommended to confirm the presence and severity of CAD.

In situations of borderline alterations, a functional test is recommended to rule out ischemia. Among them, isotopic stress tests or a CMR with adenosine/dipyridamole are recommended. A stress echocardiogram is the echocardiogram of choice, given the absence of radiation and the use of contrasts. In pathological cases, and depending on the level of risk, a coronary angiogram through CT or catheterization are the indicated tests.

For patients at risk for CAD and those asymptomatic in whom CAD is detected during screening, aggressive management of atherosclerosis risk factors is necessary.

Given the benefits of sport in this disease, individuals with risk factors should be restricted from competitive sports only if high risk is demonstrated by functional testing or if there is disease progression during serial assessments (**Borjesson** *et al*., 2019b).

During follow-up, individuals at high risk for atherosclerotic CAD and asymptomatic individuals in whom CAD is detected during screening and who participate in intense exercise should be evaluated with a maximal stress test or functional imaging test annually (**Pelliccia** *et al.*, 2021).

Patient with known coronary artery disease

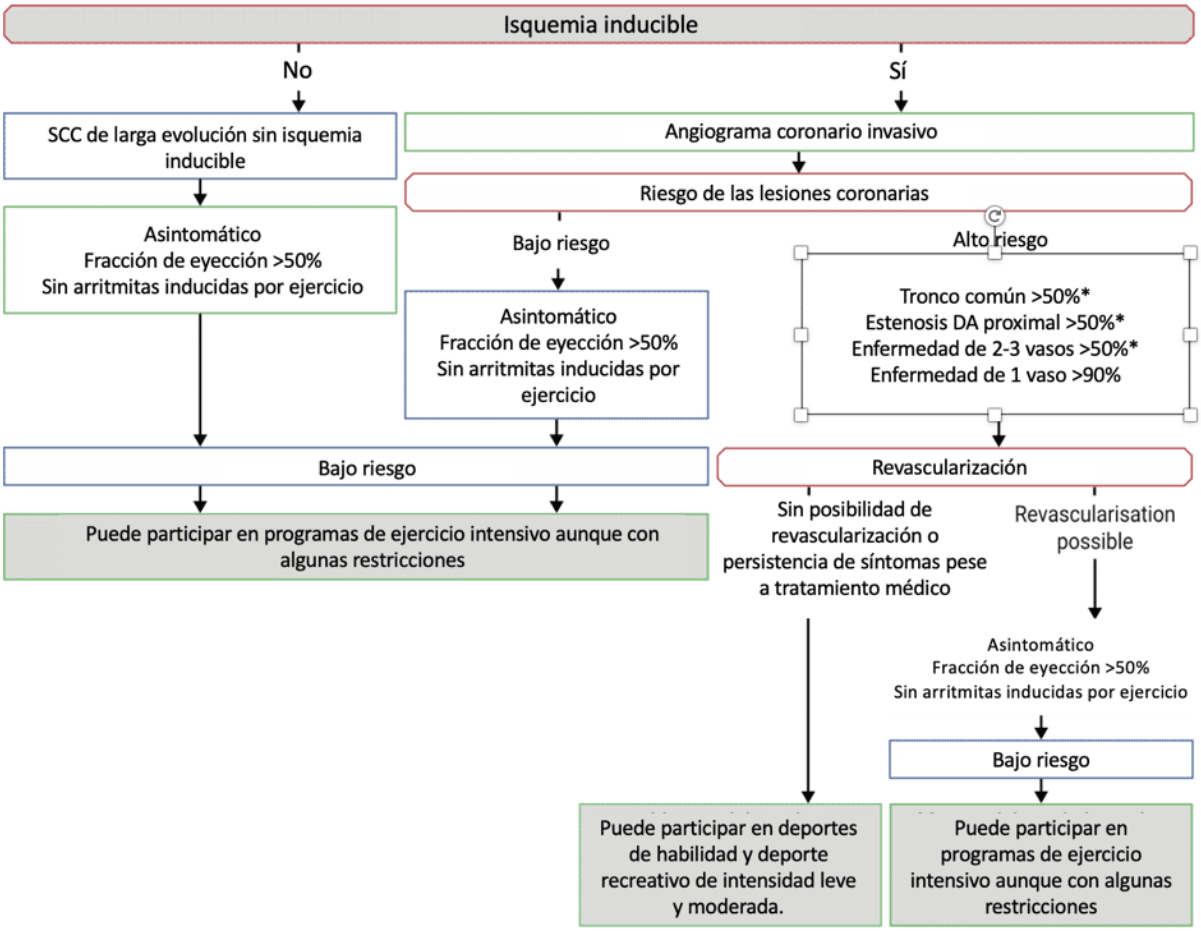
Individuals with chronic coronary syndrome without alterations in the stress test, where there is no inducibility of ischemia or who have intact ventricular function, can be considered low risk and practice sports at a competitive level.

It should be noted that in some sports, such as marathons or sports with varied intensity that involve frequent start-stop movements (for example, soccer or basketball), athletes are more exposed to myocardial ischemia, so that more stringency should be applied when determining eligibility. In patients over 60 years old with chronic coronary syndrome, a restriction in the practice of high-intensity, varied-intensity or endurance sports is proposed. The reason is that age is an additional strong predictor of adverse events during exercise.

Individuals with high-risk coronary features, after revascularization, can resume sports practice at 3-6 months, provided that a maximal physical stress test or a normal functional imaging test is obtained.

In cases in which the presence of ischemia is observed, despite pharmacological treatment or revascularization, the athlete is considered unfit to participate in competitive sports, with the possible exception of low-intensity skill sports. Such individuals can participate in regular low- and moderate-intensity recreational exercise, 2 to 3 times per week, with a target below 10 beats of the ischemic threshold and arrhythmia level, provided that risk factors and symptoms are adequately treated and there is regular clinical monitoring (see Figure 3 and Table 5).

Figure 3. Clinical evaluation and recommendations for sports participation in people with established coronary artery disease



Source: **Pelliccia** *et al.*, 2021, https://goo.su/rZfyQj.

Table 5. Recommendations for sports practice in patients with chronic coronary syndrome. CCS: chronic coronary syndrome

Recommendations	Class	Level
Risk stratification for cardiac events is recommended in individuals with established, long-standing CCS prior to the initiation of sporting activity.	I	C
Regular follow-up and risk stratification of patients with CCS is recommended.	I	B
Management according to current SCC guidelines is recommended in all patients at high risk of coronary events.	I	C
Sport, both competitive and recreational (with some exceptions such as older athletes and sports with extreme cardiovascular demand) can be considered in individuals at low risk of exercise-induced adverse events.	IIA	C
Recreational sport may be considered in patients at high risk of cardiac events, including those patients with persistent ischemia, as long as it is performed below the ischemic threshold.	IIB	C
Competitive sporting activity is not recommended in individuals at high risk of exercise-induced adverse events or those with residual ischemia, with the exception of skill sports under an individual recommendation.	III	C

Source: adapted from Pelliccia *et al.*, 2021.

Image references

CV: cardiovascular; DA: Spanish acronym for left anterior descending coronary artery (LAD); SCC: Spanish acronym for chronic coronary syndrome (CCS); TC: Spanish acronym for left main coronary artery (LM); *: with documented ischemia or a hemodynamically relevant lesion defined by fractional flow reserve (FFR) <0.8 or instantaneous wave-free ratio (iFR) <0.9.

We should specifically consider patients undergoing treatment with antiplatelet or anticoagulant drugs. People taking dual antiplatelet agents, especially when combined with oral anticoagulants, should avoid contact sports, due to the risk of bleeding.

In the case of ischemia with non-obstructive coronary artery disease (INOCA), it is recommended to follow the same exercise recommendations as for long-standing chronic coronary syndrome.

Exercise prescription

Physical exercise after cardiac events has been proven to positively reduce cardiovascular mortality and improve patients' functional capacity (**Mitchell** *et al*., 2019). Physical activity, even of low intensity, is associated with a reduction in mortality of up to 50% in post-infarction patients (**Ekblom** *et al*., 2018). Exercise, as a continuous variable, has demonstrated a J-curve in terms of its results. For example, Williams and Thompson (2014) observed a threshold in jogging at around 7 km per day; up to this figure a benefit was identified in patients after a cardiac event; however, above this limit the risk increased.

Cardiac rehabilitation has been shown to improve patients' quality of life and reduce hospitalizations in the presence of heart failure. In cases of acute coronary syndrome, initiation of cardiac rehabilitation should be early and for at least 8 to 12 weeks after the cardiac event (**Anderson** *et al*., 2016), although up to 3 to 6 months may be required to reach the appropriate level to participate in sporting events in patients with CAD.

In individuals with non-ST-segment elevation infarction or CCS classification who have had complete revascularization and have no residual ischemia, exercise training can be increased at a faster rate, until the recommended exercise level is reached. It is important to remember that each week that the start of exercise is delayed means an additional month of training to obtain the same results (**Haykowsky** *et al*., 2011).

In low-risk cases, a progressive adaptation of at least 3 months is recommended before participating in competitive activities. In addition, periodic follow-up is recommended for the management of cardiovascular risk factors, stratification according to changes in cardiovascular risk factors (CVRF) and the patient's age, reassessment for myocardial ischemia, and reassessment for any new symptoms related to cardiac pathology.

As for competitive athletes, careful individual assessment is required before starting high-intensity competitive sports. In competitive athletes, an echocardiogram, a maximal stress test with 12-lead ECG recording, or PET are recommended for risk stratification before resuming sporting activity. Ergospirometry adds specific information on aerobic and anaerobic thresholds, guiding the prescription and progression of exercise intensity (**Pelliccia** *et al.*, 2021).

For sports in a recreational context, similar principles of risk stratification apply. Before starting to practice them, a

symptom/maximum limit stress test should be performed. High-risk patients with a CCS classification are not eligible for competitive sports, although low-intensity skill sports or those below the angina threshold, such as golf, may be considered.

1.9 Exercise prescription based on conventional ergometry and ergospirometry data

Exercise prescription must always be individualized according to the baseline characteristics and specific goals of each patient.

Determining the physical fitness of each patient, i.e., his or her current exercise capacity, is essential in order to determine the baseline exercise prescription. The two most commonly used tests for this purpose are the conventional stress test and the ergospirometry or cardiopulmonary stress test.

1.9.1 Determination of exercise capacity

Conventional stress test

The conventional stress test consists of doing supervised exercise, either on an infinite treadmill or on a cycloergometer, with electrocardiographic and blood pressure monitoring. In the case of

using a cycloergometer, it is important to remember that a slight underestimation of the exercise will be made, since consumption in the upper extremities is lost. This test helps evaluate:

- Electrocardiographic alterations suggestive of ischemia or presence of arrhythmias
- Tension and chronotropic response to exercise
- Presence of symptoms and exercise threshold that trigger them
- Determination of functional capacity based on exercise intensity, age, and sex

Ergospirometry

Ergospirometry or CPET is the most accurate test for measuring oxygen consumption and exercise capacity. It is the current gold standard and is recommended by the main European and American cardiology associations.

Its use is indicated both in the prescription of exercise and to assess the response to it, being able to adjust the prescribed regimen according to the patient's evolution.

1.9.2 Prescription of exercise based on functional capacity

Exercise prescription is based on four main characteristics grouped under the acronym “FITT”.

- Frequency: How many times per week to train?
- Intensity: What exercise load is to be used?
- Type: What type of exercise should the patient do?
- Time: How long should the exercise be performed?

In addition, it is recommended that the exercise contain several stages, with a warm-up and a cool-down phase.

Warm-up phase

The warm-up is an introductory exercise that serves as a bridge between the patient's baseline activity and the workload imposed for the session. A warm-up of at least 10 minutes is recommended, prior

to exercise, since the presence of ST-segment alterations, suggestive of myocardial ischemia, as well as ventricular extrasystoles, has been observed in up to 70% of healthy patients who start exercise abruptly (Barnard et al., 1973). This should reach at least a range of 20 bpm of the minimum target exercise heart rate.

Cool-down phase

This phase consists of a progressive reduction of exercise to the basal level of activity. It allows for a faster reduction of accumulated lactic acid, reduces the catecholaminergic peak observed after exercise and avoids the sudden reduction of preload due to the reduction of venous return produced by muscle compression. It is in this phase that symptoms occur most frequently (**Hoffman** *et al*., 1978).

1.9.3 Exercise intensity

Intensity is considered one of the most crucial variables in exercise prescription. It must be sufficiently important to cause a beneficial adaptation at the cardiovascular level, but without exceeding the limit that causes symptoms, electrocardiographic changes, or blood pressure alterations.

Minimum exercise

The goal is to reach at least 50-60% of the maximum frequency, which corresponds to that of the highest metabolic rate (MET) (Swain and Franklin, 2002) or oxygen consumption. If cardiological symptoms occurred, the frequency at which they appeared will be considered the maximum frequency.

The goal during the first weeks is to increase the patient's functional capacity above 5 METs. This threshold is important, since a capacity below this figure has been related to a worse prognosis and is where the greatest benefit occurs in relation to the exercise performed (**Myers** *et al*., 2004).

The increase over time of the load should be progressive and always adapted to the patient, but, in general, an increase of 2 minutes' duration is recommended (Glowacki et al., 2004) or around 2.5% of intensity each week (Warburton et al., 2006) until reaching 70-85% of the maximum heart rate. The primary motivation for the progression in intensity is that a decrease of up to 16% in mortality has been observed for each METs increase in maximal activity (**Kodama** *et al*., 2009).

In the particular case of cardiac rehabilitation following a cardiac event, initial prescription can be challenging, as the population presents a highly variable exercise capacity.

In deconditioned or severely limited patients, whose maximum exercise is 2 to 3 METs, starting the activity with a minimum of 50 to 70 % of the peak may be at the baseline resting activity. In these situations, intermittent exercise strategies with 1 to 3 min. pauses are recommended, which allow the patient to recover and do not discourage him to stop exercising.

The ultimate goal is to obtain a good functional capacity for the age range and sex of each patient (Franklin et al., 2022). The benefit obtained at the cardiovascular level with greater increases in functional capacity is proportionally much smaller in relation to the exercise to be performed and, therefore, is not the main goal.

If we use ergospirometry as a source of measurement, we can observe that aerobic capacity improves when training above the first aerobic threshold and, in the case of cardiovascular prevention, both primary and secondary, an exercise load that is lower than, but close to, the second ventilatory threshold is recommended (**Lavie** *et al*., 2009).

Thus, initial exercise sessions should target the first ventilatory threshold. Progressively, the goal should be to move towards the second threshold. Once exercise close to, but below, the second threshold has been achieved for at least 30 minutes, a new CPET should be performed to assess exercise capacity and set new goals.

The use of goals, such as exercise zones based on the anaerobic thresholds proposed by the American council, have proven to be useful in motivating the patient, allowing a higher exercise intensity to be achieved.

1.9.4 Duration and frequency

The duration and frequency will be determined by the intensity of the exercise, i.e., the higher the intensity of the exercise, the shorter the duration, and vice versa.

Although the usual recommendation is to at least train for 10-15 minutes to improve cardiorespiratory fitness, it should be noted that some studies point to the cumulative benefit of repeated shorter sessions (Franklin et al., 2022). Generally, the benefit obtained beyond 30 minutes or more than 5 weekly sessions is proportionally lower; moreover, in these cases, a higher rate of injury has been observed (**Pollock** *et al*., 1977).

Based on this, the essential recommendation is to perform moderate-intensity physical activity (40-59% VO2 max) for at least 30 minutes, 5 days per week, or intense activity (>60% VO2 max) for at least 20 minutes, 3 days per week (**Haskell** *et al*., 2007).

Exercise should be adapted, and the patient should start with light loads and progressive increases, as previously described. In patients

unaccustomed to exercise, the use of excessive loads without prior adaptation is associated with an increased risk of acute cardiac events (Harris et al., 2017) and maladaptive response, such as arterial calcification and the development of atrial fibrillation (**Franklin** *et al*., 2020).

In summary, exercise prescription must be individualized to the patient and his goals. In the case of coronary pathology, early initiation reduces the time required to achieve the established goals. Activity should be initiated with a goal of 50% of maximum or symptom-triggering heart rate, and the load should be increased progressively, aiming to achieve a fitness level classified as “good” for the age and sex and, with it, all the associated health benefits. In athletes, the goal may be greater, i.e., to achieve his or her pre-event fitness levels. This goal can be attained in many cases, but the path towards it must be progressive and always guided by the patient's pathology and clinical evolution.

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