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TESI DI LAUREA

CARDIOPULMONARY FUNCTIONAL EVALUATION AND COMPETITIVE SPORTS ELIGIBILITY IN SUBJECTS WITH CONGENITAL HEART DISEASES

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1. Abstract

Introduction. Congenital heart disease (CHD) includes various cardiac malformations and affects approximately 0.5-1% of the global population. With the improvement of medical and surgical interventions, nearly 90% of CHD patients now survive into adulthood, particularly in developed nations. This has led to a growing interest in both recreational and competitive sports participation in this population. Over the last 15 years, recommendations regarding sports involvement changed significantly from pathology-focused guidelines to the more recent personalized clinical and functional approach outlined by the European Societies of Cardiology (ESC 2020). In Italy, the presence of specific guidelines (COCIS 2017 and COCIS 2023) represents a valuable tool for better assessing competitive sports eligibility in patients with CHD.

Aim of the study. The primary aim of this study is to classify the eligibility for competitive sports in a large population of patients with congenital heart disease (CHD) using the evaluative algorithm from the 2020 European Society of Cardiology guidelines. Additionally, the study assesses the change in competitive sports eligibility according to current Italian protocols (COCIS) from the 2017 to the 2023 edition.

Materials & methods. A retrospective analysis was conducted on 493 patients who underwent surgical correction for congenital heart disease (CHD) and were subsequently monitored at the University-Hospital of Padua. Resting morphological and hemodynamic parameters were evaluated based on echocardiographic and/or cardiac MRI reports provided by the patients. Cardiovascular and functional parameters during exercise were assessed through maximal cardiopulmonary exercise testing.

Results. Median (IQR) age was 17 (13; 22.5) years; 321 patients (65,1%) were males. 31% were in class D, 14,2% in class B, 26,1% in class C and 28,1% in class A. 216 subjects (46,0%) performed structured physical training in the whole population, corresponding to the 59,4% of subjects in class A, 44,1% of those in

class B, 39,4% of those in class C and 40,7% of those in class D. CRF and the main functional parameters were similar between class A and B, but significantly different between class A vs. classes C and D (VO2/Kg) and VO2% of predicted A vs. C and vs D $p<.0001$). Also functional impairment resulted significantly higher in patients in the lower class of sport eligibility (C and D) than in the higher ones with a prevalence of impaired CRF of 22.5% in class A, 42.5% in class B, 55.1% in class C and 57.0% in class D ($p <.0001$). Paired comparison showed significant differences in CRF (VO2/Kg) between trained and untrained subjects both within and across ESC 2020 classes, while no difference was significant among paired group of different classes, but with the same physical activity level. A multivariable stepwise regression model showed that structured exercise training is a significant independent determinant of functional capacity in people with surgically corrected CHD.Sports eligibility comparison showed that from COCIS 2017 to COCIS 2023 about the 17,7% more of patients eligible only for skill disciplines could be evaluate for all competitive sports.

Conclusion. The application of the ESC 2020 guidelines to a large population of individuals with congenital heart disease (CHD) reveals that only about one-third of subjects should avoid all types of competitive sports. However, even those unable to participate in competitive sports can benefit from individualized exercise prescriptions aimed at preserving and improving functional capacity. The comparison with the COCIS 2023 guidelines, which include an additional level of recommendation, enhances the medical-sports evaluation for granting eligibility. It shows that patients deemed eligible exclusively for skill-based sports can, in the presence of specific criteria, actually participate in all competitive sports. Cardiorespiratory fitness (CRF) is higher in classes of subjects permitted to perform competitive sports, with a significant decrease observed from class A to class D. Observations revealed that within class D, individuals engaging in physical exercise demonstrate a superior functional capacity compared to untrained class A subjects. This finding highlights the essential role of physical exercise in reducing mortality and morbidity, decreasing cardiovascular risk, enhancing overall and disease-free survival, and serving as a preventive measure for non-communicable diseases in patients with CHD. Subjects who regularly engage in structured exercise exhibit higher CRF both within and across different ESC 2020 classes. Structured exercise is an independent determinant of CRF, regardless of age, sex, and morpho-functional characteristics in this large CHD population. These findings, derived from a real-life and cross-sectional observational study, suggest that individualized and structured exercise prescriptions can significantly enhance CRF levels in individuals living with CHD.

2. Riassunto

Introduzione. Le cardiopatie congenite (CHD) includono varie malformazioni cardiache e colpiscono circa lo 0,5-1% della popolazione mondiale. Grazie ai progressi negli interventi medici e chirurgici, quasi il 90% dei pazienti con CHD ora sopravvive fino all'età adulta, soprattutto nei paesi sviluppati. Questo ha portato a un crescente interesse per la partecipazione sportiva, sia ricreativa che competitiva. Negli ultimi 15 anni, le raccomandazioni riguardanti l'attività sportiva sono evolute da linee guida focalizzate sulla patologia a un approccio clinico e funzionale personalizzato, come delineato dalle Società Europee di Cardiologia (ESC 2020). In Italia, la presenza di linee guida specifiche (COCIS 2017 e COCIS 2023) rappresenta uno strumento complementare per valutare al meglio il rilascio di idoneità sportiva agonistica nei pazienti con CHD.

Scopo dello studio. L'obiettivo principale di questo studio è classificare l'idoneità per gli sport agonistici in una vasta popolazione di pazienti con cardiopatia congenita (CHD) utilizzando l'algoritmo valutativo delle raccomandazioni del 2020 delle Società Europee di Cardiologia. Inoltre, lo studio valuta la possibilità di concedere l'idoneità agli sport agonistici secondo le normative italiane vigenti e confronta le discipline consentite dai protocolli italiani (COCIS 2017 e COCIS 2023) con quelle permesse dalle raccomandazioni europee (linee guida ESC 2020).

Materiali e metodi. Un'analisi retrospettiva è stata condotta su 493 pazienti sottoposti a correzione chirurgica per cardiopatie congenite (CHD) e successivamente monitorati presso l'Azienda Ospedale-Università di Padova. I parametri morfologici ed emodinamici a riposo sono stati valutati sulla base dei referti ecocardiografici e/o di risonanza magnetica cardiaca forniti dai pazienti. I parametri cardiovascolari e funzionali durante l'esercizio sono stati valutati tramite test cardiopolmonare.

Risultati. L'età mediana (IQR) era di 17 (13; 22.5) anni; 321 pazienti (65,1%) erano maschi. Il 31% era in classe D, il 14,2% in classe B, il 26,1% in classe C e il 28,1% in classe A. 216 soggetti (46,0%) hanno svolto esercizio fisico strutturato nell'intera popolazione, corrispondenti al 59,4% dei soggetti in classe A, al 44,1% di quelli in classe B, al 39,4% di quelli in classe C e al 40,7% di quelli in classe D. La CRF e i

principali parametri funzionali erano simili tra le classi A e B, ma significativamente diversi tra la classe A rispetto alle classi C e D (VO2/Kg) e VO2% del predetto A rispetto a C e D (p <.0001). Anche la compromissione funzionale è risultata significativamente più elevata nei pazienti nelle classi di idoneità più basse (C e D) rispetto a quelle più alte, con una prevalenza di CRF compromessa del 22,5% in classe A, del 42,5% in classe B, del 55,1% in classe C e del 57,0% in classe D (p <.0001). Il confronto tra soggetti allenati e non allenati ha mostrato differenze significative nella CRF (VO2/Kg) sia all'interno che tra le classi ESC 2020, mentre nessuna differenza è risultata significativa tra i gruppi di classi diverse, ma con lo stesso livello di attività fisica. Un modello di regressione multivariata ha mostrato che l'allenamento fisico strutturato è un determinante significativo indipendente della capacità funzionale nelle persone con CHD corretta chirurgicamente. Il confronto dell'idoneità sportiva ha mostrato che dal COCIS 2017 al COCIS 2023 circa il 17,7% in più di pazienti idonei solo per le discipline di destrezza potrebbe essere valutato per ottenere l'idoneità per tutti gli sport competitivi.

Conclusione. L'applicazione delle linee guida ESC 2020 a una vasta popolazione di individui con cardiopatia congenita (CHD) rivela che solo circa un terzo dei soggetti dovrebbe evitare ogni tipo di sport agonistico. Tuttavia, anche coloro che non possono partecipare agli sport agonistici possono beneficiare di prescrizioni di esercizi personalizzati mirati a preservare e migliorare la capacità funzionale. Il confronto con le linee guida COCIS 2023, con l'aggiunta di un ulteriore livello di raccomandazione, arricchisce la valutazione medico-sportiva per il rilascio dell'idoneità, mostrando che pazienti idonei esclusivamente per sport di destrezza possono in realtà, in presenza di specifici criteri, praticare tutti gli sport agonistici. La fitness cardiorespiratoria (CRF) è più alta nelle classi di soggetti idonei a svolgere sport agonistici, con una diminuzione significativa osservata dalla classe A alla classe D. Le osservazioni hanno rivelato che all'interno della classe D, gli individui che praticano esercizio fisico dimostrano una capacità funzionale superiore rispetto ai soggetti non allenati della classe A. Questo risultato sottolinea il ruolo essenziale dell'esercizio fisico nella riduzione della mortalità e morbilità, nella diminuzione del rischio cardiovascolare, nel miglioramento della sopravvivenza globale e libera da malattia, e come misura preventiva per le malattie non comunicabili nei pazienti con CHD. I soggetti che praticano regolarmente esercizio strutturato presentano una fitness cardiorespiratoria superiore sia all'interno delle stesse classi ESC 2020 sia tra diverse classi. L'esercizio strutturato è un determinante indipendente della fitness cardiorespiratoria, indipendentemente da età, sesso e caratteristiche morfo-funzionali in questa vasta popolazione con CHD. Questi risultati, derivati da uno studio osservazionale trasversale, suggeriscono che le prescrizioni di esercizi strutturati e personalizzati possono migliorare significativamente i livelli di fitness negli individui con CHD.

3. Introduction

Epidemiology and classification

Congenital heart disease (CHD) consists of a wide variety of anomalies and malformations involving the heart and great vessels that develop *in utero* during the growth of the cardiovascular system and are present at birth even if they are discovered much later, and thus, are popularly known as birth defects[1]. CHD is also the most common cause of major congenital heart diseases[2] with a reported birth prevalence that varies widely among studies worldwide. Nevertheless, it is generally stated that the incidence of CHD is 8 per 1000 live births[3]. 90% of cases exhibit a multifactorial etiopathogenesis, while the remaining 10% fall into syndromes linked to chromosomal mutations or single-gene mutations.

CHDs can be classified into three major categories:

- Right-to-left shunts, also known as "cyanotic CHDs", occur when blood flows abnormally from the right side to the left side of the heart, allowing poorly oxygenated blood to enter the systemic circulation, resulting in cyanosis. It includes Tetralogy of Fallot (ToF), Transposition of the great arteries (TGA), tricuspid atresia (TA), truncus arteriosus (PTA), total anomalous pulmonary venous connection (TAPVC), double outlet right ventricle (DORV) and Ebstein's anomaly.
- Left-to-right shunts or "acyanotic CHDs", which lead to heart failure due to volume overload and progressive pulmonary hypertension. Due to increased pulmonary flow, if these anomalies are not corrected, they can lead to cyanosis (Eisenmenger syndrome). These are the most common forms of

CHDs including patent foramen ovale (PFO), patent ductus arteriosus (PDA), ventricular septal defects (VSDs) and atrioventricular septal defects (AVSDs), partial anomalous pulmonary venous connections (PAPVC).

- Obstructions, such as pulmonary stenosis (PS), coarctation of the aorta (CoA), aortic stenosis (AS)[1]

Diagnosis

First, the assessment and diagnosis of congenital heart disease in pediatric or adult patients starts from the diagnostic suspicion. The age at diagnosis may depend on the severity of the condition[4]. The characteristic signs are dyspnea, cyanosis, loss of appetite, and growth delay. Some specific signs may be related to syndromic patterns.

Then, a clinical evaluation is necessary: the peripheral pulses are palpated, which should normally be bilaterally palpable and normosphygmic. In the presence of a congenital heart defect such as aortic coarctation, strong radial pulses and hyposphygmic or even absent femoral pulses may be palpated, or asymmetries between the two sides of the body may be observed. Following this, auscultation of cardiac foci is performed, carefully analyzing the tones and the presence or absence of murmurs. In presence of a turbulence associated with abnormal blood flow through a valve or chamber, a murmur can be auscultated during cardiac cycles, facilitating the identification of underlying cardiac abnormalities[4].

Notable pathological findings among the tones and murmurs include:

- Systolic murmurs: may be indicative of regurgitation due to atrioventricular valve regurgitation (mitral valve and tricuspid valve), stenosis of semilunar valves (aortic valve and pulmonary valve), or secondary to a ventricular septal defect (VSD), especially in the presence of a hemodynamically significant left-to-right shunt. Atrial septal defect (ASD) is also characterized by a systolic murmur over the pulmonary area due to increased flow velocities through this valve.
- Diastolic murmur or “rumble:” typical of conditions leading to blood flow obstruction through the atrioventricular valves, or due to semilunar valve insufficiency.

- Fixed splitting of the second heart sound: found in conditions characterized by pulmonary overcirculation;
- Gallop rhythm: presents with additional tones in diastole (third and fourth heart sounds), which are characteristic of patients with heart failure.

All these finds just raise suspicion about the presence of a congenital heart condition in the patient, necessitating further instrumental investigations to conclude to a definitive diagnosis of a CHD[4]:

- Chest X-ray is no longer considered essential for diagnosis, despite it remains a primary examination. It enables assessment of the heart-to-chest ratio, which, if altered, indicates cardiomegaly. The shape of the heart and vessels can also provide suspicion of specific conditions[5]. Over time, this imaging has been gradually supplanted with the advent of echocardiography.
- Transthoracic echocardiography is the gold standard for diagnosing congenital heart conditions. It is based on ultrasounds to observe the organ ventricular and valvular functionality and dynamic, in addition to its anatomical aspects. The technique offers precise information without risks to the patient, allowing it to be performed frequently, both before and after any corrective surgical intervention, as well as for long-term follow-up. Fetal echocardiography is also useful during pregnancy to assess the cardiac development and well-being of the fetus, but it is only performed in the presence of risk factors for congenital heart defects: a positive family history of congenital heart disease, pathologies of the mother during pregnancy or exposure to teratogenic factors during embryonic development in the first trimester, such as gestational diabetes, infections, alcohol abuse.
- Transesophageal echocardiography is an invasive method performed under sedation. It consists in introducing an ultrasound probe into the oral cavity to reach the esophagus. Leveraging the strategic position of the esophagus, which lies posterior to the heart, this technique yields high-quality images, especially for structures not easily accessible via conventional transthoracic echocardiography (e.g. pulmonary veins and atrial septum[5]). It is also used for the anatomical study of heart valves, especially in the context of repair or replacement surgeries.

- Cardiac magnetic resonance imaging and cardiac computed tomography (MRI and CT) are non-invasive investigations used in association with angiography and cardiac catheterization. Cardiac MRI with gadolinium is useful for detecting myocardial scars (potential arrhythmic triggers), observing prosthetic structures, assessing the extent of valve regurgitation or shunts, and highlighting other factors that may impact ventricular function in athletes. It also measures wall thicknesses, chamber volumes, and evaluates the presence of edema and/or adipose replacement. CT represents the best method for evaluating small anatomical structures, such as coronary arteries, and for obtaining accurate three-dimensional anatomical reconstructions, but it exposes to radiation compared to MRI.
- Cardiac catheterization is performed under general anesthesia using X-ray equipment and contrast medium injection and is primarily indicated nowadays for measuring intra-cardiac pressures. It is used for diagnosis in cases where pulmonary hypertension is suspected from first-line imaging that needs confirmation; and as therapy without resorting to traditional cardiac-thoracic surgery. Other indications include assessment of PVR, ventricular diastolic function (including constrictive and restrictive physiology), shunt quantification, coronary angiography, and evaluation of extracardiac vessels such as aortic pulmonary collateral arteries when non-invasive evaluation leaves uncertainty[6]
- Angiography consists in a catheter introduced into the radial or femoral artery and, through retrograde movement, it is guided to the heart where the contrast medium is injected. Its primary purpose is to obtain images that facilitate the diagnosis of congenital heart and coronary circulation defects, as well as to understand information regarding flows and pressures within the chambers and vessels.

Management and treatment

To understand the rationale behind the prescription of medical or surgical therapy and the reasons for the denial of eligibility for competitive sports, we must focus on the complications of CHD that can, in the long term, lead to the patient's death. Some of the main complications that occur are heart failure, infectious endocarditis, and malignant arrhythmias[6] . In addition to these major complications, patients may also develop cyanosis, pulmonary hypertension, and growth delay. The complications determine the prognosis and the possibility of granting competitive sports eligibility, moreover they influence the treatment.

The key treatment for heart failure in adult CHD patients remains its prevention by optimizing haemodynamics and heart rhythm. This requires systematic follow-up to facilitate timely intervention. In a biventricular circulation, standard heart failure treatment can be extrapolated to CHD patients with a systemic left ventricle and may be applied in patients with a systemic right ventricle, although it remains uncertain whether the known benefits of treating a failing left ventricle can be expected. Pathophysiology of patients with an atrial switch, and especially Fontan palliation, differs from a 'regular circulation' and standard heart failure therapy must be applied cautiously.

Concerning arrhythmias, in all patients, evaluation for a reversible cause of an arrhythmia and for new or residual haemodynamic abnormalities should be performed. Maintenance of sinus rhythm is the aim in most CHD patients. Patients with documented arrhythmias or at high risk for postprocedural arrhythmias considered for percutaneous or surgical (re)interventions should be discussed in a multidisciplinary team with expertise in interventions and invasive treatment of arrhythmias.

Pulmonary arterial hypertension (PAH) in CHD is a progressive disease with poor prognosis. High suspicion of PAH, and regular assessment for the presence of PAH in patients with shunt lesions, after defect closure is recommended. Proactive treatment is required in all PAH patients, including those with Eisenmenger syndrome. Women with CHD and confirmed pre-capillary PH should be counselled against pregnancy.

Finally, cyanotic patients present with a multisystem disorder and are at risk for both bleeding and thrombotic complications, causing a therapeutic dilemma. Routine phlebotomies must be avoided as they put patients at risk for iron-deficient anemia and cerebrovascular complications. Therapeutic phlebotomy is only indicated in the presence of moderate/severe hyperviscosity symptoms. Cyanotic patients have a very balanced, but fragile, pathophysiology and any intervention puts the patient at high risk. Prophylactic measures are the mainstay of care to prevent and avoid complications.[7]

Medical therapy is therefore essential in the long-term management of arrhythmias, arterial hypertension, heart failure, prothrombotic risk and for the control of individual cardiovascular risk factors. The most common treatments are diuretics, antihypertensives (ACE-inhibitors, sartans, calcium channel blockers), beta-blockers and sodium-glucose cotransporter type 2 inhibitors (liraglutide). In addition, antiarrhythmics (flecainide, amiodarone), antiaggregants and anticoagulants are prescribed.[7]

Approximately 75% of CHDs are non-critical, as they do not require surgical intervention within the first year of life, while only 25% necessitate immediate post-natal correction, representing a significant cause of neonatal cardiac urgency[6]. Over the years there has been an evolution of surgical strategies, but today there is an increasing diffusion of endovascular corrective techniques (such as the closure of atrial defects using patches), while surgery methods are considered for complex cases and may require longer surgical times. The interventions that are carried out are classified into:

- Corrective, in which the heart defect is corrected in a single intervention, often through percutaneous patch implantation. They are used to close ASD and VSD.
- Palliative, that are reserved for patients for who it is not possible to obtain an adequate anatomical correction. These are interventions with a non-negligible surgical risk and in which the final hemodynamic compensation may still be unstable and susceptible of complications.[8]

The whole management of CHD should take place in specialized CHD centers with multidisciplinary expertise. Sometimes it is necessary to perform corrections or palliations in multiple stages (e.g., Fontan procedure).

In addition to medical and surgical therapy, patients with congenital heart diseases can and should benefit from all the positive effects of physical exercise, both in terms of reducing cardiovascular risk and improving exercise capacity and quality of life. Regular practice of moderate-intensity physical activity is sufficient, preferably aerobic activities such as walking, cycling, or swimming. These activities do not pose a risk of trauma or excessive overload on the cardiovascular system and significantly improve the exercise capacity of patients and their quality of life by enhancing physical perception, well-being satisfaction, and overall health status.[8]

Benefits and risks of exercise training in CHD patients

Exercise can be used in a dose-dependent manner to positively impact health outcomes for individuals with a chronic condition. Historically, the impact of aerobic rather than other types of exercise on cardiovascular health in the general population has been studied the most. Recently, however, there has been more focus on resistance training and its impact on muscle mass.

- Aerobic exercise: a recent systematic review in 621 children with CHD participating in regular aerobic exercise training programs reported an average of 8% increase in VO2max, a validated measure of exercise capacity. None of the patients in these studies experienced adverse exercise-related events.
- Resistance training: low-to-moderate intensity strength training of individual muscle groups is safe in the majority of CHD patients (i.e., a high number of repetitions 10–15, with lower resistance). High-intensity strength training may increase the risk of injury and could increase blood pressure, decrease cardiac output, and cause bradycardia in some patients with CHD. High-intensity strength training should be avoided in this group until further research is available.
- Flexibility and mobility training: dynamic stretching exercises have been included as a component of numerous exercise intervention studies (such as warm-up prior to aerobic or resistance training). This type of low-intensity movement prepares the body for exercise; therefore, children with CHD can likely safely participate in flexibility training.[9]

The overarching objectives of exercise training in patients with CHD are to improve health, exercise tolerance, and quality of life. Several studies in diverse populations of patients with surgically repaired CHD have reported improvements in exercise tolerance after various exercise training programs, including VO2 max, peak oxygen consumption, peak oxygen pulse, total treadmill walking time, heart rate recovery, walking distance, power output, and oxygenation of respiratory muscles[10]. Adults with CHD who participate in frequent physical activities (e.g., more than twice per week) maintain a higher VO2 max than their sedentary counterparts.[11] A systematic review of 31 studies on the effect of exercise training in 621 children and adults with CHD found that 23 of these studies reported improvements in VO2 max and muscle strength, with no adverse effects identified.[12]

On the other hand, feared complications associated with exercise in patients with CHD include malignant arrhythmias, exercise-induced hypertension, aortic dissection, myocardial ischemia, heart failure exacerbation, worsening cyanosis, syncope, and sudden cardiac death. All elements of the clinical profile should be considered in determining risks. For example, high-impact sports might be associated with additional risks in patients receiving anticoagulation therapy or with implantable cardioverter-defibrillators. Although most studies on short-term exercise training programs in diverse populations of patients with CHD have related no adverse events, common sense and sound clinical judgement should prevail. Naturally, patients with major unaddressed lesions (e.g., critical aortic stenosis, severe aortic root dilation, anomalous coronary artery with symptoms) were excluded from such studies.[10]

Cardiopulmonary Exercise Testing (CPET)

Physical activity could play a crucial role in the treatment for individuals afflicted with CHD. However, a significant portion of these patients experiences limited endurance during physical exertion, necessitating a thorough evaluation of their functional capabilities before initiating any structured exercise plan.[13]

Children with congenital or acquired heart disease often have impairment of their functional capacity. This occurs in the preoperative, postoperative, as well as in the long-term setting and may be the result of the primary cardiac problem, treatment of that problem or hypoactivity leading to detraining. Lunt et al. found that adolescents with congenital heart disease (CHD) were less likely to reach minimum exercise requirements and perform vigorous exercises than were healthy adolescents. Cardiopulmonary exercise testing (CPET) provides objective information about the functional status of heart, lungs and peripheral muscle. This information can be of value in making clinical decisions resulting in a reduced use of hospital facilities, and improved quality of life and functional capacity.[14]

CPET in children with CHD has several indications.

The first is to assess the physical capacity or aerobic capacity of a child with a CHD. This can be used to provide recommendations for physical activity in sports, occupation, or rehabilitation. Recommendations for sports participation are available elsewhere.[15] Moreover, a CPET can determine whether a patient's complaints of fatigue have a physical etiology.

The second indication for exercise testing in CHD is to provide indications for surgery (e.g. pacemaker implantation, valve replacement), therapy (medication or rehabilitation) or additional more invasive/demanding tests (e.g. cardiac CT/MRI, nuclear imaging, or heart catheterization).

Moreover, the stress of the CPET can be used to evaluate the success of interventions such as pacemaker implantation, closure of shunt (normalizing in exercise SaO2 %), or ablation of arrhythmogenic substrates. In addition, CPET can be used to diagnose inherited arrhythmia syndromes (e.g. LQTS and CPVT) or chronotropic incompetence.

The third indication for CPET is to evaluate the adequacy of medication, for instance β-blockers, angiotensin-converting enzyme inhibitors and digoxin in heart failure.

The fourth indication is to assess the risk for future disease complications, for instance the arrhythmic burden; and the fifth indication for CPET is to instill confidence in children and parents. Parents of children with a CHD are often overprotective of their child, even though the underlying disorder is only small and might not be restrictive for performing physical activities including competitive sports (e.g. children with a small ventricular septum defect or atrial septum defects). It usually provides confidence in their child's ability to perform physical exercise when parents see their child running on a treadmill or cycling on an ergometer with high heart rates till exhaustion without any complications. In adult cardiac patients after myocardial infarction (MI), it has been shown that the confidence of the patient and their spouse can be significantly improved when a CPET is performed three weeks after the MI.[16]

Lastly, CPET can be used to show improvement of physical rehabilitation in children with CHD. Furthermore, a fitness assessment including CPET can be helpful in motivating children with CHD to maintain a healthy body weight or to combat overweight/ obesity.[14]

This multifaceted evaluation, combined with comprehensive quality of life assessments, routine medical examinations, and other diagnostic procedures, is useful to provide a holistic understanding of the health status of patients undergoing treatment for congenital heart conditions[17]. Such an integrative approach, incorporating electrocardiographic, hemodynamic, and respiratory parameters during exercise, has proven to be highly effective in evaluating the cardiorespiratory efficiency of patients, elucidating the underlying physiological responses to exercise, and establishing predictive prognostic models based on test outcomes.

In recent years, the utilization of cardiopulmonary exercise tests (CPET) has surged within clinical practice, enabling the confirmation of various pathological conditions affecting the cardiovascular, pulmonary, and musculoskeletal systems[18]. CPET serves as a precise tool for assessing arrhythmias or ischemic modifications through continuous electrocardiographic monitoring, analysis of blood pressure trends, assessment of aerobic and work capacities, evaluation of heart rate response, and determination of ventilation/perfusion ratios. These tests can be administered either on a cycle ergometer or treadmill, utilizing sophisticated instrumentation including a 12-lead electrocardiograph and a pneumotachograph paired with an analyzer for gases exchanged by the patient (oxygen and carbon dioxide). Data acquired from these tests are processed using software algorithms, generating multiple graphs (Wassermann 9 panel plot [19]) indicative of the individual's adaptation to exercise in terms of ventilation and metabolic responses[20].

Modern ergospirometric systems facilitate real-time assessment of gas exchange dynamics at rest, during exercise, and throughout recovery phases, providing detailed insights into oxygen consumption, carbon dioxide production, and ventilatory patterns[21]. Key parameters such as peak oxygen consumption (VO2 peak) and the ventilation to carbon dioxide production ratio slope (VE/VCO2 slope) hold particular significance[22], with VO2 peak emerging as a robust predictor of survival in cohorts with advanced heart failure or heightened cardiovascular risks[23]. Furthermore, the assessment of ventilatory thresholds, including the anaerobic threshold (AT or first ventilatory threshold) and respiratory compensation point

(RCP or second ventilatory threshold), offers valuable guidance in tailoring individualized aerobic exercise programs[21]. These thresholds serve as crucial benchmarks for determining optimal exercise intensities and heart rate targets, thereby enhancing overall aerobic capacity and work performance[24].

Recommendations for participation in competitive sport in adolescent and adult athletes with congenital heart disease (ESC 2020)

The participation of people with CHD in sports activities has increased in recent years. During years, better medical care for children with CHD has greatly improved their chances of reaching adulthood[6]. Consequently, in developed countries, there are now more adults than children living with CHD. While efforts to decrease long-term health issues should target the specific congenital heart defect[25], it is also important to focus on reducing cardiovascular risk factors, such as a sedentary lifestyle[26]. The positive impacts of exercise on individuals with CHD are well-documented, as is its role in preventing the development of acquired cardiovascular risk factors and non-communicable diseases[27]. Exercise-related complications (adverse effects on heart function, disease progression, and sudden cardiac death) have often discouraged physical activity among these patients[28]. In recent years, there has been a paradigm shift in exercise prescription protocols. Traditionally, assessments focused only on anatomical defects[15]. Instead, a modern approach evaluates also the physio-pathological dynamics and functional capacity of patients with congenital heart conditions. This has led to the formulation of the 2020 ESC Guidelines for recommendations regarding physical activity for patients with CHD.[29]

Current guidelines for physical activity in adolescents and adults with congenital heart conditions are based on the evaluation of five parameters:

1. Ventricular function.
2. Pulmonary artery pressure.
3. Aortic dimensions.
4. Occurrence of arrhythmias.

5. Arterial oxygen saturation at rest and during exercise.

Furthermore, there has been a refinement in the classification of sports compared to the taxonomy proposed by Mitchell et al.[30] which previously delineated sports into static and dynamic categories based on the mechanical actions of engaged musculature. This updated classification is related to hemodynamic alterations induced by exercise and their prolonged impact on cardiac morphology. Consequently, sports are now grouped into four distinct categories[31] (Figure 1):

- Skill-based sports.
- Power-based sports.
- Mixed sports.
- Endurance sports.

This categorization enables the individualized prescription of physical activity type and intensity for each patient, considering the specific hemodynamic demands imposed by different sports.

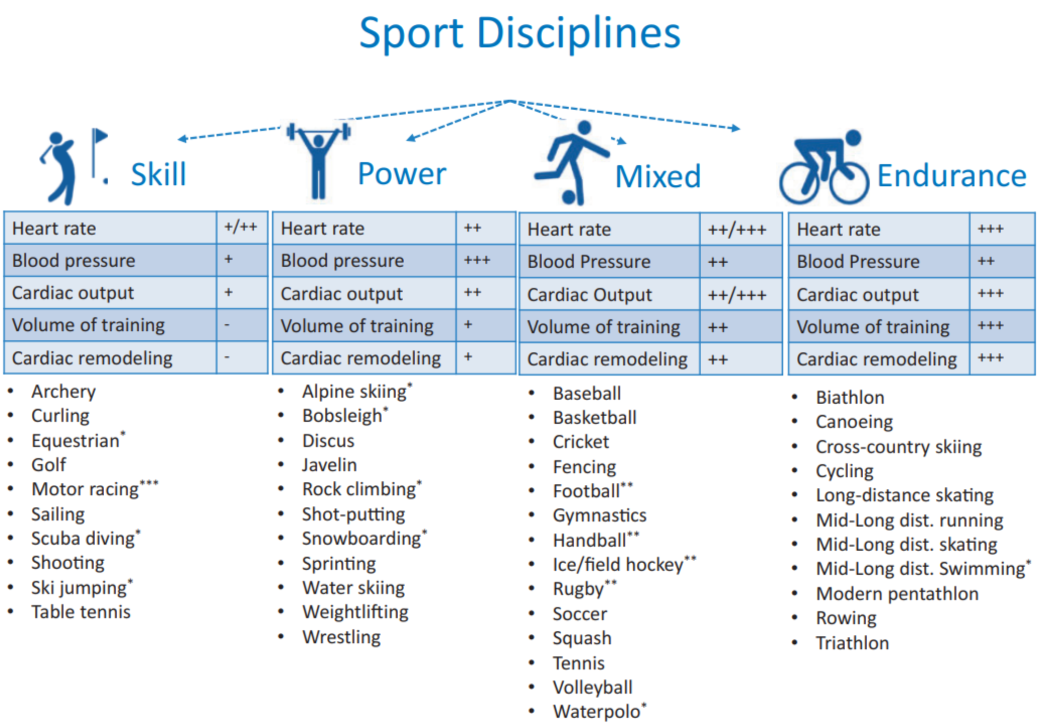

Figure 1. *Schematic representation of the four different types of sport disciplines, modified after Pelliccia et al. The common hemodynamic changes and cardiac remodeling occurring because of long-term training are indicated for each type of*

*sport. Symbols: **indicates sport with increased risk of bodily collision. *Indicates sport with intrinsic risk of serious harm or death for athlete and/or spectators in the event of syncope.*

During the evaluation of the parameters mentioned in the previous paragraph, it is necessary to assign individual athletes to a category of recommended sports disciplines (see Table I). Specifically:

A. CLASS A (green column): eligibility to practice all sports. This occurs when all parameters are within the normal range or there is evidence of mild hypertrophy and a slight increase in pressure or volume.
B. CLASS B (orange column): the patient is eligible to practice dexterity sports, power sports, or mixed sports, with restrictions for endurance disciplines. The patient falls into this category if at least one of the parameters is outside the normal range.
C. CLASS C (brown column): the patient can only participate in dexterity sports. This category applies if at least one of the parameters is outside the normal range and falls within the cases reported in the corresponding column in Table II.
D. CLASS D (red column): patients are limited to performing sports only at an amateur level, thus being excluded from the possibility of engaging in competitive sports activities. This occurs when the patient has severe structural defects, hemodynamic or electrophysiological alterations. For these patients, it would be advisable to follow the recommendations for amateur activities published in the 2013 work by Budts and colleagues[32]

Some clarifications must also be made for patients with more than mild aortic dilation. These patients should avoid engaging in sports disciplines with a high static component (i.e., most power sports and some dexterity sports such as motor sports). Patients with significant dilations should pay attention to high-impact disciplines that could pose a considerable risk of injuries (aortic dissections or aneurysm ruptures).

1. Ventricles	No systolic dysfunction No/mild hypertrophy No/mild pressure load No volume load	Mild systolic dysfunction Volume load without remodelling	Moderate systolic dysfunction Moderate hypertrophy Moderate pressure load Volume load with mild remodelling Single ventricle physiology Systemic right ventricle	Severe systolic dysfunction Severe hypertrophy Severe pressure load Volume load with severe remodelling
2. Pulmonary artery pressure	Low probability of pulmonary hypertension	PH without RV dilatation or dysfunction		PH with RV dilatation or dysfunction
3. Aorta	No/mild dilatation	Moderate dilatation	Severe dilatation	Dilatation approaching indication for repair
4. Arrhythmia at rest/during exercise	No arrhythmia	Mild arrhythmic burden Non-malignant arrhythmia		Significant arrhythmic burden Malignant arrhythmia
5. Saturation at rest/during exercise	No central cyanosis		Mild central cyanosis	Severe central cyanosis
	A	B	C	D
	When all applicable	When ≧1 parameters applicable AND no parameter falls within columns C or D	When ≧1 parameters applicable AND no parameter falls within column D	When ≧1 parameters applicable
Choice of competitive sport	All sports	Skill, Power, or Mixed sports	Skill sports only	NO COMPETITIVE SPORT

Table I. *Algorithm used for the classification of athletes into the four classes*[32]*, based on the previously described parameters.*

COCIS (Italian cardiological guidelines for competitive sports eligibility)

The Italian classification is based on the physiological responses of the heart and blood vessels to exercise, as well as what happens following regular exercise practice. This classification therefore includes the long-term adaptations of the heart and blood vessels in different sports disciplines. The acute responses to physical exercise can be synthesized based on the responses of heart rate, blood pressure and peripheral resistances, but also based on the type of "stimulus", for example continuous, short, or long duration. COCIS distinguishes four groups of sports:

- GROUP A - It includes sports where excellence is linked to technical or skillful abilities of the athlete involving a response of the neuro-adrenergic system, with a moderate increase in HR and possibly BP, for periods of work interspersed with more or less long pauses (as in equestrian sports, sailing, shooting sports, etc.). In such disciplines, the hemodynamic overload is modest or absent, so the heart does not undergo substantial morphological adaptations. However, in some sports of this group, the cardiovascular effort is considered at least moderate (sailing, horse riding, figure skating, etc.).

- GROUP B - It includes power sports that are characterized by anaerobic energy expenditure in which there is an increase in myocardial mass due to predominantly systolic overload (afterload).
- GROUP C - It includes sports that present combined elements (aerobic/anaerobic metabolism), which involve an intermittent increase in preload (and/or afterload), with periods of intense work alternating with recovery phases. A typical functional model of team sports with a ball (e.g., football, rugby, basketball, etc.). In such situations, the adaptive stimulus on the heart produces an increase in endocavitary dimensions, accompanied by a parallel increase in wall thickness of the left ventricle.
- GROUP D - It includes sports with isotonic-dynamic muscle activity, with largely predominant aerobic energy expenditure (long-distance running, cycling, cross-country skiing, etc.). In these endurance athletes, there is an increase in cardiac output, predominantly characterized by an increase in preload resulting in eccentric cardiac remodeling.

It is important to underline, before reading our work, that the classification Groups A, B, C, and D of the aforementioned sports do not correspond to the ESC eligibility Classes assigned to patients (Class A, B, C, and D). Concerning the COCIS guidelines, we have considered ESC Classes A and B as a single category ("eligible for all sports").

4. Introduction to the research study

Exercise plays a pivotal role in enhancing overall health and fitness. This is particularly significant for individuals with congenital heart disease (CHD), a condition characterized by structural abnormalities of the heart present from birth[33,34]. These anomalies can range from simple defects with no symptoms to complex malformations with severe, life-threatening symptoms[33]. CHD affects approximately 1% of live births globally and poses unique challenges for maintaining physical fitness and engaging in competitive sports.
In individuals with CHD, regular exercise has been shown to improve cardiorespiratory fitness, motor skills, and muscular oxygenation, including that of

the respiratory muscles[33,35]. This enhancement in physical capacity can lead to better ventilation efficiency and reduced respiratory muscle fatigue, particularly at higher exercise intensities[35]. Consequently, a reduction in ventilatory limitations and an improvement in exercise tolerance are observed.
In Italy, the cardiovascular screening for competitive sports in individuals with CHD is guided by protocols established by a joint cardiological committee of several scientific societies that define the cardiovascular screening and the eligibility criteria to competitive sport, known as the COCIS (2023). These protocols, which align with European and American recommendations, offer pathology-specific guidelines focusing on key aspects such as ventricular function, valvular insufficiency, pressure gradients, arrhythmias, and signs of exercise-induced myocardial ischemia[36]. The role of Cardiopulmonary Exercise Testing (CPET) is particularly emphasized in evaluating these individuals, especially for those with complex CHD[37].
Despite the established benefits of exercise, the eligibility criteria for competitive sports for individuals with CHD can vary significantly among different guidelines. Italian protocols (COCIS) and European guidelines (ESC) offer different perspectives on the classification of sports and the criteria for eligibility. The ESC guidelines are generally more permissive, allowing for competitive sports participation even in moderate-to-severe cases of CHD based on morpho-functional characteristics more than the disease itself, while the COCIS protocols are more conservative and disease-based.
This research aims to compare the eligibility for competitive sports according to the COCIS protocols with the ideal eligibility derived from the ESC recommendations. It seeks to analyze the implications of these differences and the potential impact on individuals with CHD[33,35].

Understanding these aspects is crucial for developing comprehensive guidelines that ensure their safety in engaging in competitive sports. This study will contribute to the ongoing dialogue on optimizing exercise recommendations and eligibility criteria for individuals with congenital heart disease, ultimately aiming to improve their quality of life and longevity.

5. Aims of the study

A first aim is to describe eligibility for competitive sports in a large population of patients with congenital heart disease according to the evaluative algorithm proposed by the recommendations of the European Societies of Cardiology in 2020.

The second aim is to evaluate the impact of exercise training, both recreational and competitive, in determining functional capacity in this specific population.

Finally, to assess the clearance for competitive sports applying new Italian protocols (COCIS 2023).

6. Material and methods

The is an observational study conducted between January 2020 and May 2024. During this time frame, patients attended the Sports and Exercise Medicine Division of the University Hospital of Padua for routine follow-ups.

Population

The study was conducted on a population of 493 patients with different congenital heart diseases who underwent surgical interventions in childhood and were subsequently managed and followed up with periodic check-ups by the Sports and Exercise Medicine Division and the Pediatric Cardiology Unit of the University Hospital -of Padua.

All these patients were followed up with an institutional diagnostic–therapeutic multidisciplinary pathway of clinical assistance that provides periodic check-up by the Pediatric Cardiology Unit of the Department of Women's and Children's Health, University of Padova (Italy) and includes a functional evaluation with maximal CPET performed in our Centre. Clinical information concerning diagnostic and imaging examinations was collected from medical records or provided directly by the patients at the visit and after consent had been obtained. The level of physical activity was evaluated with standardized questions and patients were defined trained if they performed structured exercise both recreational or competitive, and untrained in all other cases. Patients with the most commonly represented congenital heart disease groups were included in the study. In particular seven main groups with were identified: transposition of the great arteries (TGA), aortic coarctation (CoA), aortic bicuspid valve, left outflow tract stenosis (LVOT), univentricular heart undergoing Fontan intervention, tetralogy of Fallot (ToF) and congenital pulmonary valve stenosis. Also complex congenital heart diseases were included. Exclusion criteria were the lack of all necessary information, coronary anomalies, cardiomyopathies, Marfan and Ehler-Danlos because the management and evaluation of these subjects go beyond ESC 2020.

Cardiac imaging

The patients presented to the Sports Medicine Physician reports from imaging investigations (echo color doppler, cardiac MRI, and/or angioCT/angioMRI) carried out at the University Hospital of Padua, Department of Women's and Children's Health, Pediatric Cardiology Unit or at other Centers.

The main echocardiographic parameters considered in this study include the ejection fraction (EF) of the left ventricle (LV), the thickness of the interventricular septum (IVS) and the posterior wall (PW) of the LV, the LV mass indexed for body mass, the qualitative and quantitative description of the right ventricle (RV), RV function through fractional shortening (FAC) and/or TAPSE, and the dilation of the ventricles, expressed as LV end-diastolic volume (EDV) or RV end-diastolic area (EDA) indexed for body mass were evaluated[38]. For patients under 16 years of age, z-scores were considered[39].

The presence of pulmonary hypertension was indirectly assessed using echocardiographic technique by measuring the tricuspid regurgitation velocity (TRV) and estimating pulmonary artery pressure (PAP). The dimensions of the aortic bulb and ascending aorta were also included in the echocardiographic reports or in angioMR/angioCT aimed at studying the aorta. Z-scores were used for patients under 16 years of age.

Reference values and their categorization are present in Table II.

Table I Definition of variables

Variables	Definitions
Ventricles[a]:	
Ventricular dysfunction	*Left and right ventricles:*
• No dysfunction	EF ≥ 55%
• Mild dysfunction	45% ≤ EF < 55% (or normal systemic RV function)
• Moderate dysfunction	30 ≤ EF < 45%
• Severe dysfunction	EF < 30% (or impaired systemic RV function)
Ventricular hypertrophy	*Left ventricle:*
• No hypertrophy	Wall thickness (cm): ♂ <1.1 ♀ <1.0 or LV mass (g/m^2): ♂ 50–102, ♀ 44–88
• Mild hypertrophy	Wall thickness (cm): ♂ 1.1–1.3 ♀ 1.0–1.2 or LV mass (g/m^2): ♂ 103–116 ♀ 89–100
• Moderate hypertrophy	Wall thickness (cm): ♂ 1.4–1.6 ♀ 1.3–1.5 or LV mass (g/m^2): ♂ 117–130, ♀101–112
• Severe hypertrophy	Wall thickness (cm): ♂ ≥1.7 ♀ ≥1.6 or LV mass (g/m^2): ♂ ≥131 ♀ ≥113
	Right ventricle:
	Qualitative and quantitative echocardiographic evaluation
Ventricular pressure overload	*Left and right ventricles:*
• No pressure overload	No significant LVOT or RVOT gradient (PSV < 2.6 m/s), no obstruction in great arteries
• Mild pressure overload	2.6 m/s ≤ PSV <3 m/s for LVOT and RVOT obstructions and PPS; for CA, peak arm-leg gradient <20 mmHg
• Moderate pressure overload	3 m/s ≤ PSV ≤4 m/s for LVOT and RVOT obstructions and PPS
• Severe pressure overload	PSV >4 m/s for LVOT and RVOT obstructions and PPS; for CA, peak arm-leg gradient ≥20 mmHg
Ventricular volume overload[b]	*Left and right ventricles:*
• No volume load	Absent or mild to moderate valve regurgitation or shunt
• Volume load without remodelling	Severe valve regurgitation or shunt with non-dilated RV and LV [RV EDA (cm^2/m^2) ♂≤12.6, ♀≤11.5; LV EDV (mL/m^2) ♂≤74, ♀≤61] and preserved systolic function
• Volume load with mild remodelling	Severe valve regurgitation or shunt with RV or LV dilatation with preserved systolic ventricular function
• Volume load with severe remodelling	Severe valve regurgitation or shunt with RV or LV dilatation with impaired systolic ventricular function
• Ventricle physiology	Single- or bi-ventricular circulation
	Systemic LV or systemic RV
Pulmonary artery pressure	
• No evidence of PH	TVRV[c] ≤2.8 m/s and no additional echocardiographic findings suggestive of PH or mPAP<25 mmHg on right heart catheterization
• PH with no RV dilatation or dysfunction	mPAP≥25 mmHg on right heart catheterization without RV dilatation or dysfunction
• PH with RV dilatation or dysfunction	mPAP≥25 mmHg on right heart catheterization with RV dilatation or dysfunction
Aorta	
• No/mild dilatation	Normal (≤35 mm) or borderline sizes (≥35 to <40 mm) of the aorta, z-score ≥2 to <3[d]
• Moderate dilatation	Aorta size ≥40 to <45 mm, z-score ≥3 to <4
• Severe dilatation	Aorta size ≥45 to <50 mm, z-score ≥4
• Size reaching indication for repair	Aorta size ≥50 mm
Arrhythmia	
• No arrhythmia	Absence of or infrequent arrhythmias (<500/24 h) PVC on a Holter monitor, which do not worsen with exercise
• Mild arrhythmia burden/non-malignant arrhythmia	Frequent or coupled PVC or controlled atrial fibrillation/atrial flutter, which do not worsen with exercise
• Significant arrhythmia burden/potentially malignant arrhythmia	Atrial fibrillation/atrial flutter, which worsen with exercise
	Non-sustained or sustained ventricular tachycardia or PVC burden that increases during exercise
Arterial oxygen saturation at rest/during exercise	
• No central cyanosis	No clinical signs; transcutaneous saturations in the range of 96–100%, at rest and during exercise
• Mild cyanosis	Transcutaneous oxygen saturations between 90% and 95%, at rest or during exercise
• Severe cyanosis	Transcutaneous oxygen saturations <90%, at rest or during exercise

Table II. *CA, coarctation; EDA, end-diastolic area; EDD, end-diastolic diameter; EDV, end-diastolic volume; EF, ejection fraction; LV, left ventricle; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVOT, left ventricular outflow tract stenosis; PAP, pulmonary artery pressure; PPS, peripheral pulmonary stenosis; PSV, peak systolic velocity; PVC, premature ventricular complex; RV, right ventricle; RVEDD, right ventricular end-diastolic* *diameter; RVOT, right ventricular outflow tract; TVRV, tricuspid valve regurgitation velocity. Reference values from Lang et al.*[40]*. a Interpretation of chamber wall thickness, size, and function should take into consideration the athlete's demographics and sporting discipline. b Serial imaging is necessary, particularly when uncertainty exists relating to the severity and hemodynamic impact of specific lesions and exercise regimes. c In individuals with a systemic right ventricle the values refer to mitral valve regurgitation velocity. d To follow common practice, z-score values should be used over absolute values if they fall into different categories in an individual patient–athlete*

Assessing algorithm

Each patient was evaluated following the diagnostic flow-chart proposed by the ESC 2020 recommendations [32] (Figure 2). The first step involved a careful medical history with particular attention to the underlying pathology, surgical interventions and any cardiac catheterization performed. Comorbidities, drug therapy, type of physical activity performed, and the presence of cardiovascular symptoms were also recorded. Secondly, the imaging examinations (cardiac echocolorDoppler, cardiac MRI/TC) carried out at the Centre for Advanced Interventional Cardiology and Hybrid Correction of Congenital Pathologies and acquired in childhood of the Padua University Hospital or at other specializes centers shown by the patient, were examined. 24-hour electrocardiographic Holter monitoring was performed with a 12-lead recorder (Edan-Holter System, SE-2012 series, Edan Instrument Inc, Shenzen-China) and analyzed by experienced physicians using dedicated software (Edan-Holter ECG – V1.36, Edan Instrument Inc, Shenzen-China).

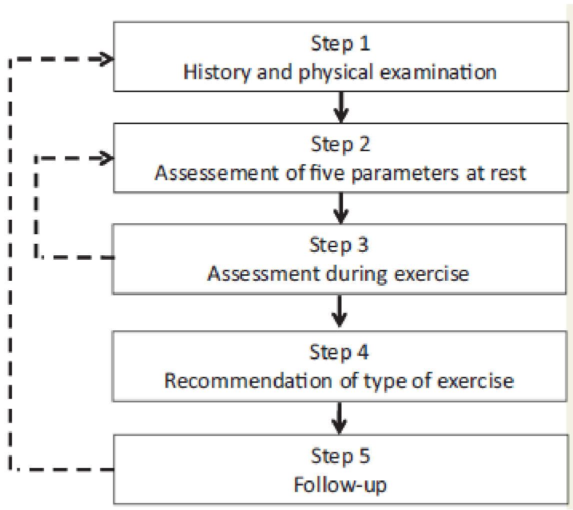

Figure 2. *Flowchart to follow in order to evaluate a high-level athlete with CHD.*[32]

CPET

All patients involved in the study performed a maximal cardiopulmonary exercise test (CPET) on a treadmill, following the Bruce's incremental protocol, or on a cycle ergometer, with incremental protocols (10 or 15 Watt/minute). The test was carried out until patient's exhaustion with continuous electrocardiographic monitoring (Cardiosoft) and a breath by breath sampling of ventilatory parameters (Jaeger-Masterscreen-CPX system-Carefusion). The test was considered maximal if it met at least one criterion among a respiratory exchange ratio (RER) $\geq$ 1.10, Borg rating of perceived exertion 18/20, and a reached heart rate $\geq$ 85% of the predicted value by age [41]. Maximum work capacity was measured as the estimated Metabolic Equivalent of Task (METs). Systolic blood pressure (PAS) and diastolic blood pressure (PAD) were assessed by auscultatory method at rest, at submaximal and maximal workload and every two minutes during the exercise and recovery phase. The possible arrhythmic burden, the presence of alterations in the ventricular repolarization phase and the chronotropic behavior expressed with reserve HR were assessed. Peripheral oxygen saturation (SpO_2) was monitored continuously at rest and during the entire test.

Patients' classification

Patients' eligibility to competitive sports were performed following the ESC 2020 guidelines diagnostic flow chart [32] i.e. ventricular morphology and function, pulmonary artery pressure, aorta size, presence of arrhythmias and peripheral oxygen saturation. The precise description of all parameters included in the evaluation algorithm is available in the ESC 2020 guidelines [32]

Based on the above-mentioned parameters, patients were categorized according to the four categories of competitive sport eligibility identified by the ESC 2020 recommendations [32]

If all parameters were within normal limits or there was evidence of mild hypertrophy or mild pressure/volume overload, no restrictions were placed on any type of sport (Class A). When even just one of the parameters was altered and depending on the hemodynamic commitment required by the sporting discipline, restrictions were applied, excluding endurance sports (Class B) or allowing only skills sports (Class C) [32]. Athletes with severe structural alterations, symptoms or major hemodynamic or electrophysiological alterations were excluded from competitive sport (Class D).

Statistical analyses

All data were collected in an EXCEL spreadsheet and analyzed the Statistical Package for Social Science (SPSS Inc., Chicago, IL, USA). All continuous variables were tested for normality with the Shapiro-Wilk test and, based on their distribution were described by mean±SD or median values with interquartile range. Dichotomous variables were expressed in percentages. intergroup comparisons were performed by Kruskal-Wallis test followed by the Dunn's multiple comparison post hoc test. Pearson's χ^2 test was used to compare dichotomous variables. A stepwise multivariable linear regression analysis was performed in order to evaluate independent determinants of functional capacity. [41,4242].

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7. Results

Clinical characteristics – whole population

493 patients (321 males, 65.1%) with a median age of 17 years (IQR 13; 22.5) were recruited (Table III). 216 subjects (46,0%) performed structured physical training in the whole population, corresponding to the 59,4% of subjects in class A, 44,1% of those in class B, 39,4% of those in class C and 40,7% of those in class D. The mean BMI for adult subjects was 20.9 ± 3.9 kg/m^2, while for individuals aged < 16 years the mean BMI percentile was 49. The most frequently represented congenital heart diseases were CoA (17.8%), ToF (15.4%), TGA (11.3%), univentricular hearts undergoing Fontan surgery (8.9%), bicuspid aortic valve (5.4%), LVOT obstructions (3.2%) and congenital pulmonary valve stenosis (2.8%).

Table III shows also the morpho-functional characteristics for the whole study population obtained from the echocardiographic and/or cardiac magnetic resonance (cMR) reports that patients brought in at the visit time. The availability of imaging data (ultrasounds and/or cMR) was variable due to the clinical setting and individual follow-up and potentially differed from patient to patient, but in all enrolled subjects the available data allowed categorization into the ESC 2020 classes, the COCIS 2017 and the COCIS 2023 classes. The median left ventricle ejection fraction (EF) was 61.8 % with 11.6% of the patients that had ventricular dysfunction. The Tricuspid Annular Plane Systolic Excursion (TAPSE) was 18.3 (15; 22) mm, with 24.3% of patients having right ventricle dysfunction. 17.9% of the subjects showed left ventricular hypertrophy, the diastolic filling pattern was preserved in 82.1% of the population. 33.4% of the population had pressure overload, with predominant mild pattern (74.3%). Volume overload was present in 28.6% of the population. In 52.6% it was associated with dilatation of the ventricle with preserved ventricular function while in 3.7% dilatation was also associated with ventricular dysfunction. Indirect ultrasound signs of pulmonary hypertension were found in 16.2% of patients. 91.3% had no or mild dilatation of the aorta, while moderate or severe dilatation was found in 6.3% and 2.5% of the subjects, respectively.

	Mean±SD or Median (IQR)	N (%)
Age, years	17.0 (13.0-22.5)	
Male sex		321 (65.1)
BMI (adults), kg/m²	20.9±3.9	
BMI (children & adolescents), percentiles	49.0 (21.8-76.0)	
EF, %	61.8±13.8	
Left ventricle disfunction		55 (11.6)
Mild		46 (83.6)
Moderate		7 (12.7)
Severe		2 (3.6)
TAPSE, mm	18.3 (15-22)	
Right ventricle disfunction		112 (24.3)
Right ventricle hypertrophy		53 (12.1)
IVS, mm	8.2±1.7	
PP, mm	8.4±2.4	
LVM, g/m²	82.3±26.8	
Left ventricle hypertrophy		80 (17.9)
Left ventricle end diastole volume, mL	63.5 (48.0-79.0)	
Diastolic disfunction		89 (27.2)
E/A ratio	1.89 (1.5-2.25)	
E/E' ratio	6.62 (5.25-8.18)	
Pressure oveload		148 (33.4)
Mild		110 (74.3)
Moderate		22 (14.8)
Severe		16 (10.8)
Volume overload		133 (28.6)
LV: Normal dimension and function		12 (9.7)
LV: Dilated with normal function		70 (52.6)
LV: dilated and impaired function		5 (3.7)
Univentricular heart		46 (34.5)
Pulmonary hypertension		76 (16.2)
Ascending aorta diameter (Valsalva's sinus), mm	29.6±5.8	
Ascending aorta diameter (tubular tract), mm	30.0 (25-35)	
Ascending aorta diameter (Valsalva's sinus), Zscore	0,17 (-0.81-1.68)	
Ascending aorta diameter (tubular tract), Zscore	1,65 (0.0-3.55)	
Aortic dilation		
No/mild		438 (91.3)
Moderate		30 (6.3)
Severe		12 (2.5)

***Table III**. Clinical and morpho-functional characteristics of whole population (493 patients).*

Clinical characteristics of subjects in different ESC 2020 classes

Class D (no competitive activity) represented approximately one third of the whole population (31%), followed by classes A (all types of sports, 28.1%), C (only skill sports, 26.1%), and B (mixed, skill and power sports, 14.2%). Figure 3 shows the distribution of the four ESC 2020 sports fitness classes within the main CHD groups. Patients with TGA, CoA and Interatrial/Interventricular abnormalities showed more than 50% of subjects in class A-B. On the other hand, patients with ToF, bicuspid aortic valve belonged predominantly to classes C/D. The only two groups in which there was no subject in class A-B were those of patients with Fontan's correction for univentricular heart, but it must be noted however that slightly less than 50% of these subjects could participate in skill sports.

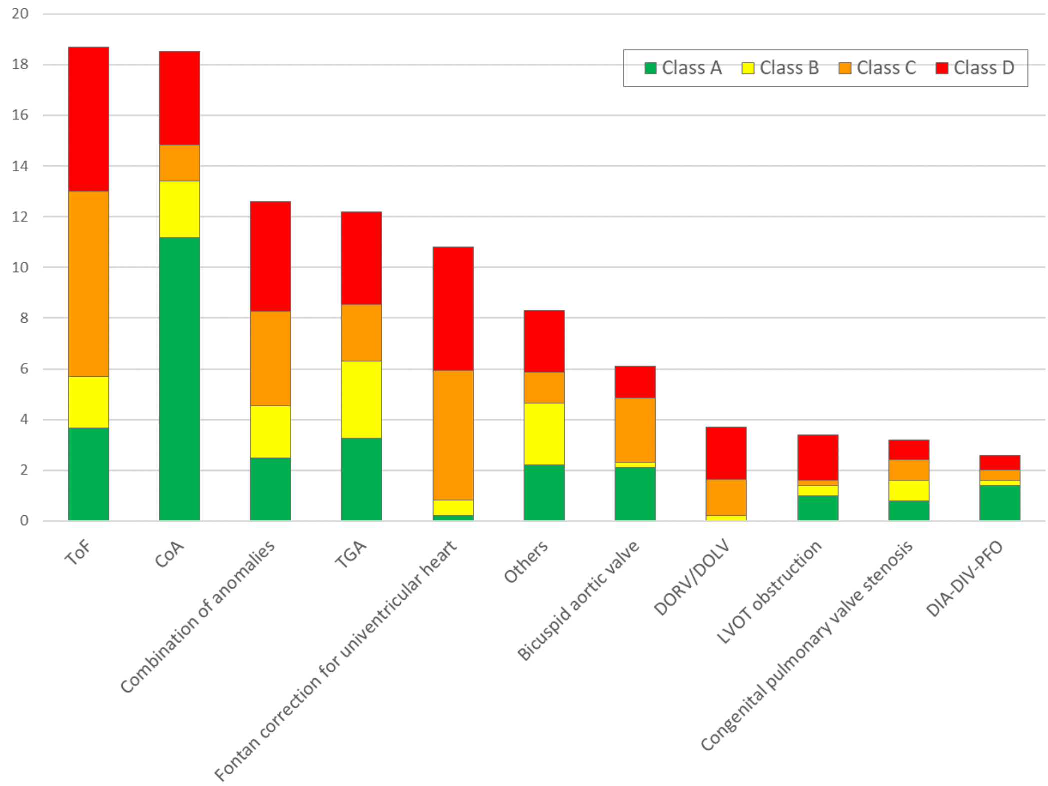

Figure 3. *Distribution of the four ESC 2020 sports fitness classes within the main CHD groups. ToF: Tetralogy of Fallot; CoA: Aortic Coarctation; TGA: Transposition of the Great Arteries; DORV/DOLV: Double Outlet Right Ventricle/Double Outlet Left Ventricle; LVOT: Left ventricle outflow tract stenosis; DIA-DIV-PFO: Atrial septal defect-Ventricular septal defect-Patent Foramen Ovale.*

The causes of downgrading agree with the algorithm indicated by the ESC2020 guidelines (figure 4). The main reasons for down grading from Class A to Class B were the presence of mild LV dysfunction (21 patients), the presence of pulmonary hypertension without RV dilatation/ dysfunction (18 patients) and the presence of non-complex arrhythmias (12 patients). Downgrading in Class C with dilated right ventricle was primarily due to volume overload but with normal function (37 patients), to mild desaturation at rest or during exercise (12 patients) or to moderate pressure overload (6 patients). The causes of classification in Class D were the presence of complex arrhythmias (35 patients), the presence of pulmonary hypertension with right ventricle dilatation and/or dysfunction (20 patients), severe desaturation at rest or on exertion (23 patients), severe ventricular hypertrophy (11 patients) and severe pressure overload (10 patients). The combinations of more than one factor were also detectable in these 3 classes of eligibility and equal to the 16.6% in class B, 44.8% in class C and 38.4% in class D, respectively.

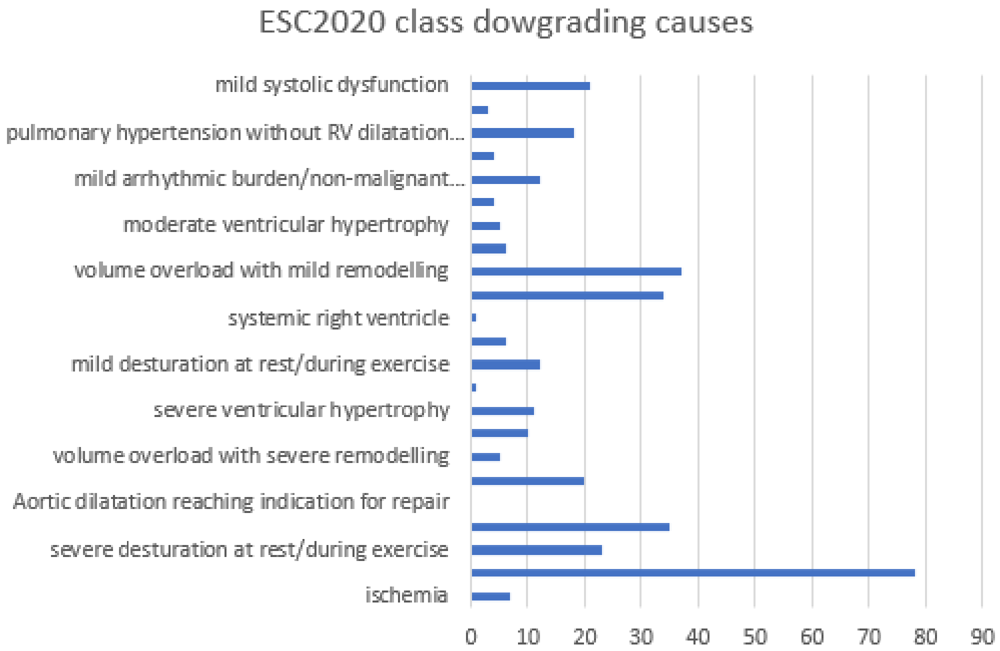

Figure 4. *Causes of downgrading according to the algorithm indicated by the ESC2020 guidelines. On the x-axis, the absolute frequencies are represented.*

Cardiopulmonary parameters

Most of patients performed the exercise test on treadmill and all patients gained at least one criterion of maximal effort. Cardiopulmonary parameters assessed and their comparison among ESC2020 classes are shown in Table IV.

	A	B	C	D
n	139	70	129	153
Age, years	15,0 (12,0-19,0) °*§	17.5 (12,0-23,0)	18,0 (14,0-24,0)	18,0 (14,0-25)
BMI, Kg/m²	20,7±3,7	21.0±3,7	20,7±3.8	21,3±4,3
HR%predicted	92.0 (88.0-96.8) °*§	88.0 (84.0-94.0) §	88.0 (81.6-93.0)	88.0 (79-92.0)
RERpeak	1.18 (1.12-1.25)	1.18 (1.09-1.26)	1.19 (1.11-1.26)	1.20 (1.13-1.28)
PASrest, mmHg	120 (110-125)*	117.5 (105-122.8)	115 (105-120.8)	118 (105-125)
PADrest, mmHg	68 (60-73)	65.5 (61-70)	70 (60-75)	68 (60-75)
PAS peak, mmHg	150 (140-175)*	150 (140-163)	150 (130-160)	150 (130-160)
VO_2 peak, l/min	2,0 (1,68-2,56) °*§	1.9 (1,45-2,46)	1.70 (1,37-2,45)	1,77 (1,32-2,48)
VO_2 peak mL/kg/min	39,1 (33,4-44,3) °*§	36.0 (28.2-41.9) §	32.0 (27.4-40.3)	32.0 (27.0-38.3)
VO_2 peak %predicted	94,4±16.5 °*§	84.2±18.0	82.4±20,2	80.1±20,0
VO_2 peak<85%predicted	24.1%°†	52.2%	56.2% †	59.2% †
METs peak	15.9 (13.4-17.0) °*§	14.6 (13.1-16.8)	14.7 (12.7-16.8)	14.4 (12.3-16.2)
VE/VCO_2slope	28.2 (26.1-30.5) * §	29.3 (26.8-32.6)	29.6 (27.1-33.7)	30.0 (26.6-34.1)
OUESs	1903.0 (1624.7-2338.7) °*§	1745.9 (1402.3-2093.2)	1680.1 (1389.1-2281.8)	1678.0 (1311.0-2313.5)
O_2pulse%predicted	99.3±19.1§	95.5±19.0	95.2±21.2	94.2±24.1
O_2pulse early plateau	20 (14.5%) †	20 (28.6%)	36 (29.5%) †	37 (25.2%)
O_2pulse deflection	4 (2.9%)†	6 (9.1%)	13 (10.7%)	22 (15%)†

Kruskal-Wallis or ANOVA and Bonferroni post-hoc analyses of functional parametes among ESC2020 classes. °<0.05 vs.B *<0.05 vs. C; § <0.05 vs. D; † Chi-square p value < 0.05

Table IV. *Clinical and functional parameters among sport eligibility classes ESC 2020.*

A slight statistically but not clinically significant difference is visible for age and BMI. Oxygen consumption at exercise peak (VO_2 peak) is significantly higher in class A than C and D classes either when expressed in absolute value [2,0 (1,68-2,56) vs. 1,7 (1,37-2,45) and 1,77 (1,32-2,48) mL/min], relative to body weight [39,1 (33,4-44,3) vs. 32 (27,4-40,3) and 32 (27-38,3) mL/Kg/min] and as percentage of the predicted for age and sex (94,4±16,5 vs. 82,4±20,2 and 80,1±20,0 %). These results were confirmed also dividing subjects in trained and untrained (Supplementary table IV).

	A		B		C		D		P
	Trained	Untrained	Trained	Untrained	Trained	Untrained	Trained	Untrained	
	79	53	30	37	49	76	57	83	
Age, years	14.0 (12.0-18.0)	16.0 (12.0-20.0)	12.5 (11.0-17.8)	20.0 (15.0-23.0)	17.0 (11.0-22.0)	19.0 (16.0-26.0)	18.0 (14.0-23.0)	19.0 (14.0-26.0)	<0.001
VO_2/Kg, mL/min/Kg	41.5 (37.1-47.6)	33.7 (29.4-40.5)**	39.7 (30.1-44.2)	31.5 (26.6-39.0)*	35.5 (30.6-43.5)	29.9 (24.8-37.6)**	35.4 (30.6-43.4)	29.7 (24.4-37.4)**	<0.001
VO_2 % predicted	98.0 (87.0-108.0)	92.0 (73.5-100.0)*	92.5 (73.2-103.0)	79.0 (69.5-89.5)*	88.0 (77.0-98.0)	78.0 (64.0-91.0)**	86.0 (68-101.0)	76.0 (64-91.0)**	<0.001

Supplementary table IV. *Kruskal-Wallis post-hoc analyses of functional parametes between trained and untrained subjects in the same ESC2020 class. *<0.05; **<0.001.*

Categorizing the subjects based on their functional capacity, we note a progressive increase in the percentage of subjects with reduced functional capacity defined by a VO_2 peak < 85% of the predicted for gender and age from class A (24,1%) to class

D (59.2%). The mean exercise intensity at peak of exercise (expressed ad METs) is also significantly higher for subjects in class A than those in the other classes. The mean VE/VCO_2 slope was quite similar despite significantly different between class A and C-D, nevertheless this difference does not match to a high clinical significance due to the correspondence to the same ventilatory class. In addition, it is noticeable that abnormalities of the oxygen pulse pattern are significantly more frequent in classes C and D.

The comparison of functional capacity between sedentary subjects and those performing structured physical activity, independently from type and intensity of exercise training show a significant difference between trained and untrained subject.

In each ESC2020 class the difference between trained and untrained subjects in VO_2peak, both relative to body weight and expressed as percentage of the predicted for age and sex, is statistically significant ($p <0.001$), demonstrating a higher cardiorespiratory fitness of trained than untrained subjects (Supplementary Table IV), despite a slight age difference between groups. Among trained subjects VO_2peak/Kg was significantly different only between extreme classes: i.e. class A [(41.5 (37.5-47.6) ml/min/Kg] and classes C and D [35.5 mL/min/Kg, and 35.4 mL/min/Kg, p 0.001, respectively]. Similar results were reported for the VO_2 expressed as percentage of predicted for age and sex [A 98.0 (87.0-108.0) % vs. C 88 %, and vs. D 86.0 %]. Otherwise, among untrained subjects the VO_2peak/kg of subjects in both classes A and B was significantly higher than that of subjects in both classes C and D as reported in Supplementary Table V (A vs. C $p < 0,001$; A vs. D $p < 0,001$; B vs. C p 0,006; B vs. D p 0,002). Nevertheless, the percentage of the predicted for age and sex was significantly different only between subjects in the extreme classes [class A vs. C (p <0.001) and vs. D (p <0.001)].

VO2/Kg	< 0.001 (overall)
post-Hoc intraclass comparison	
A trained vs. untrained	< 0.001
B trained vs. untrained	0.018
C trained vs. untrained	< 0.001
D trained vs. untrained	< 0.001
post-Hoc interclass comparison	
A trained vs. B untrained	< 0.001
A trained vs. C untrained	< 0.001
A trained vs. D untrained	< 0.001
B trained vs. C untrained	< 0.001
B trained vs. D untrained	< 0.001
B trained vs. A untrained	0.157
C trained vs. D untrained	< 0.001
C trained vs. A untrained	0.257
C trained vs. B untrained	0.027
D trained vs. A untrained	0.351
D trained vs. B untrained	0.040
D trained vs. C untrained	< 0.001
VO2%pred	< 0.001 (overall)
post-Hoc intraclass comparison	
A trained vs. untrained	0.007
B trained vs. untrained	0.040
C trained vs. untrained	0.005
D trained vs. untrained	0.007
post-Hoc interclass comparison	
A trained vs. B untrained	< 0.001
A trained vs. C untrained	< 0.001
A trained vs. D untrained	< 0.001
B trained vs. C untrained	0.006
B trained vs. D untrained	0.002
B trained vs. A untrained	0.905
C trained vs. D untrained	0.002
C trained vs. A untrained	0.797
C trained vs. B untrained	0.050
D trained vs. A untrained	0.424
D trained vs. B untrained	0.125
D trained vs. C untrained	0.019

Supplementary table V. *Comparisons among only trained and untrained subject.*

As reported in figure 5 there were noticeable differences among trained and untrained subjects belonging to different ESC2020 classes. In particular, it is relevant that trained subjects class A have showed the best cardiorespiratory fitness [VO_2peak/Kg 41.5 (37.1-47.6) mL/min/Kg; VO_2peak %of predicted 98.0 (87.0-108.0)] compared to all other subjects and in particular compared to all the untrained subjects. More relevant, it can be seen that trained subjects in class D have a significantly higher cardiorespiratory fitness [VO_2peak/Kg 35.4 (30.6-43.4); VO_2peak %of predicted 86.0 (68-101.0)] than untrained subjects in class C [VO_2peak/Kg 29.9 (24.8-37.6); VO_2peak %of predicted 78.0 (64.0-91.0)] and also than those in class A (only for VO_2peak/Kg) despite without reaching statistical significance. Moreover, it should be noted that, this not statistically, but clinically significant trend is detectable also between trained subjects in class C and untrained subjects in class B (VO_2peak/Kg and VO_2peak % of predicted) and A (only for VO_2peak/Kg).

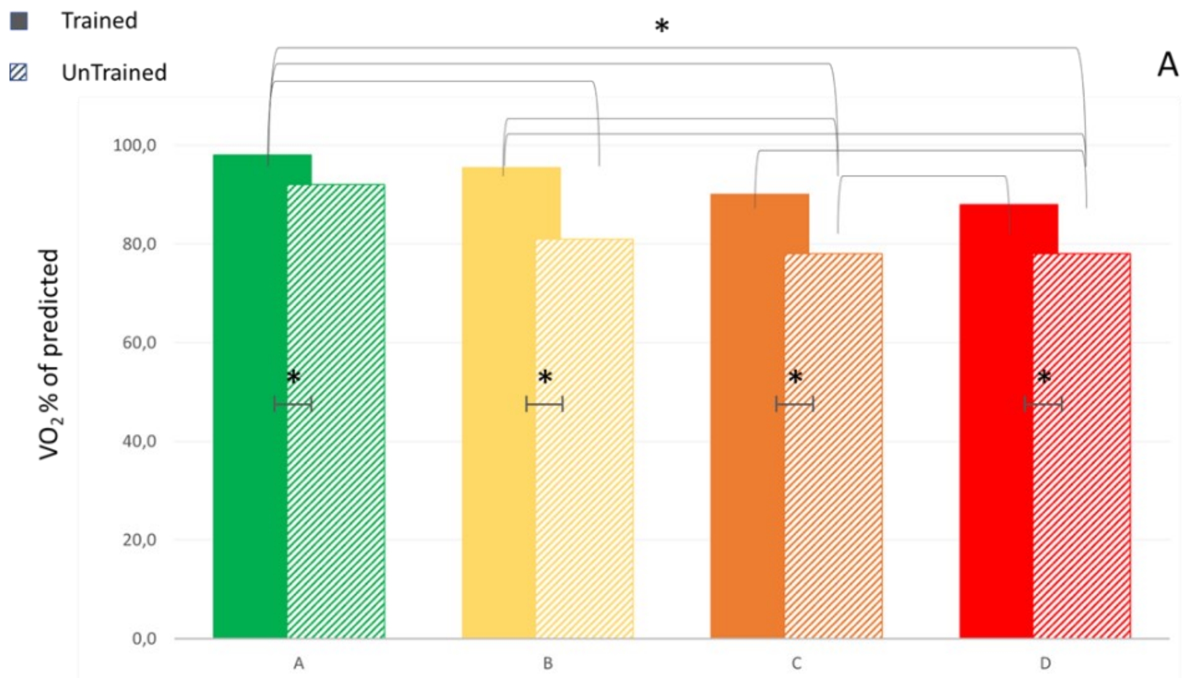

Figure 5A. *Differences in VO2 % of predicted among trained and untrained subjects belonging to different ESC2020 classes; represents the comparison between trained and untrained subjects in the same ESC2020 class and between different ESC2020 classes. Comparisons among only trained and untrained subjects, as well as the precise p-value of all the comparisons are reported in Supplementary table V. * p< 0.05*

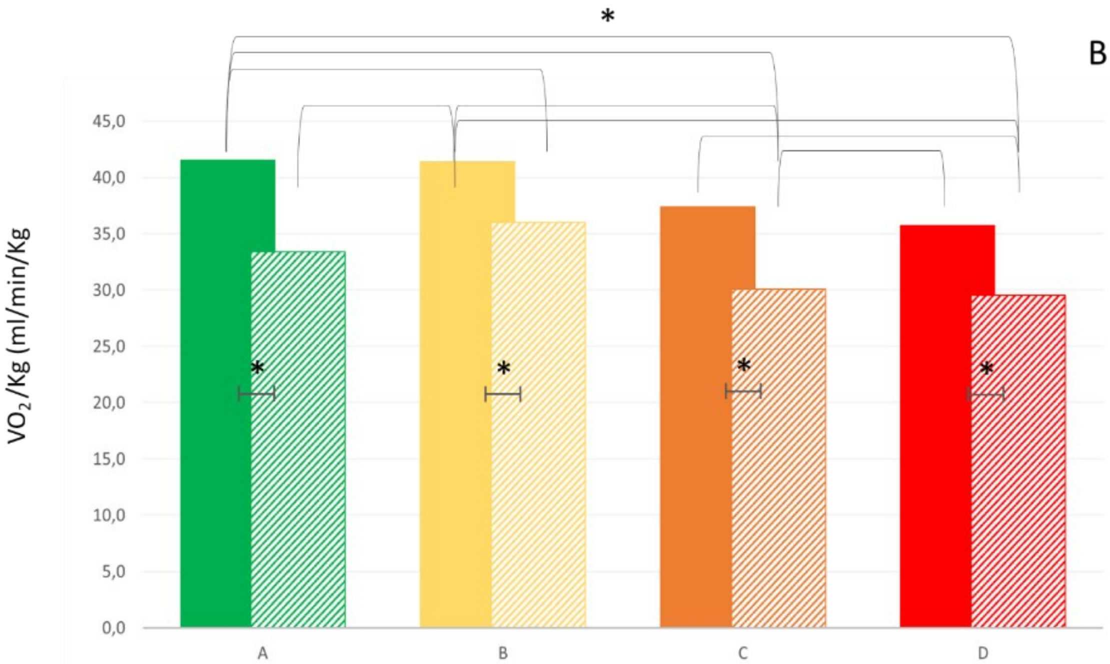

Figure 5B. *Differences in VO2/Kg of predicted among trained and untrained subjects belonging to different ESC2020 classes; represents the comparison between trained and untrained subjects in the same ESC2020 class and between different ESC2020 classes. Comparisons among only trained and untrained subjects, as well as the precise p-value of all the comparisons are reported in Supplementary table V. * p< 0.05*

Finally, in a stepwise multivariate linear regression analysis, the training resulted an independent determinant of cardiorespiratory fitness together with age, sex, TAPSE and end diastolic volume, while peripheral oxygen saturation, the type of CHD and the ejection fraction did not remain in the multivariable model (Table V).

	Beta	P
Male sex	0.296	< 0.001
End diastolic volume	0.274	< 0.001
Age	- 0.201	< 0.001
TAPSE	0.228	< 0.001
Training	0.179	0.001

Table V.

Multivariate stepwise linear regression analysis for independent determinant of VO_2/kg. Model 1: Type of CHD, ejection fraction, SPO2 at rest not significant.

Competitive sports eligibility according to COCIS 2017 and COCIS 2023 guidelines

In this study we also classified patients following the Italian protocols COCIS 2017 and the most recent COCIS 2023.
Figure 6A and 6B show the distribution of each CHD divided by COCIS 2017 eligibility, in which "cleared" represents patients eligible for all competitive sports, "skill" represents patients eligible only for skill-based sports and "not cleared" represents patients non-eligible for any competitive sport.
Concerning Tetralogy of Fallot (ToF) 54.4% of cases are not eligible for competitive sports, 16.6% are eligible for skill-based sports, and around 28.8% are suitable for all sports. Coarctation of the Aorta (CoA) shows that 54.4% of cases are not eligible for competitive sports, 12.2% are eligible for skill-based sports, and 33.3% are eligible for all sports. Patients with combination of anomalies include 59.6% of cases who are not eligible for competitive sports, 24.2% are suitable for skill-based sports, and 16% are eligible for all sports. TGA includes 65% of cases who are not eligible for any competitive sport, 13.3% only for skill-based sports and 21.6% eligible for all competitive sports. Patients who underwent Fontan correction for univentricular heart are mostly not-eligible for competitive sports (62.2%), 13.2% are eligible for skill-based sports and 24% for all sports. Among patients with bicuspid aortic valve, 53% was cleared for all sports, 6.6% was eligible only for skill-based sports and 40% for all kind of sports. DORV and DOLV shows similar percentages for cleared, skill, and not cleared, respectively 55.5%, 11.1% and 33.3%. LVOT obstructions 76.4%, 11.7% and 11.7%. Congenital pulmonary valve stenosis 50%, 6.2% and 43.7%. Finally, ASD/VSD shows that almost 70% is non-eligible, 15.3% is eligible only for skill sports and 15.3% is actually eligible for all sports.

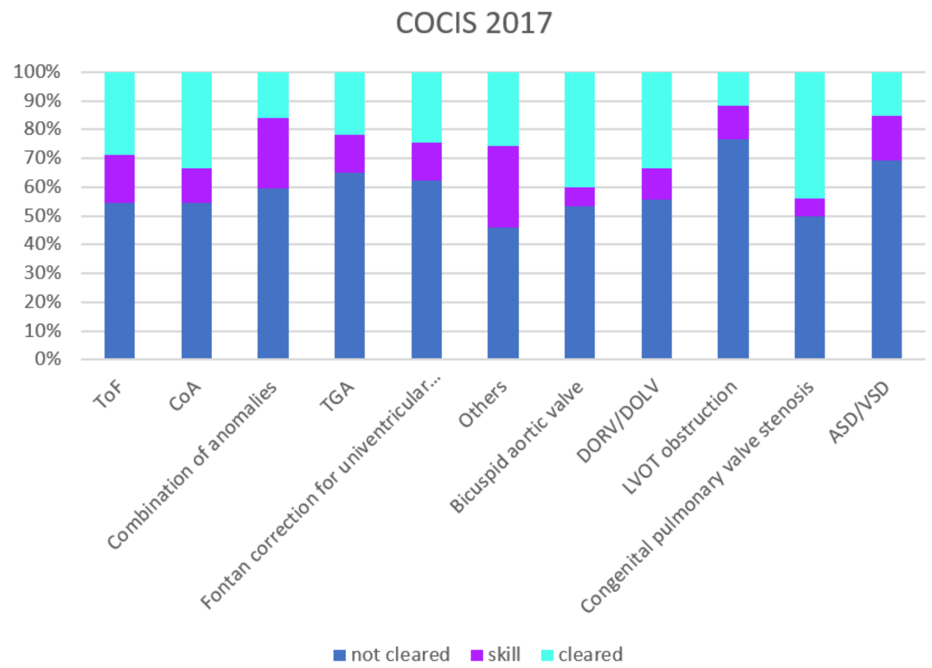

Figure 6A. *Distribution of patients (%) divided by CHD based on COCIS 2017 competitive eligibility class. ToF: Tetralogy of Fallot; CoA: Aortic Coarctation; TGA: Transposition of the Great Arteries; DORV/DOLV: Double Outlet Right Ventricle/Double Outlet Left Ventricle; LVOT: Left ventricle outflow tract stenosis; ASD-VSD: Atrial septal defect-Ventricular septal defect.*

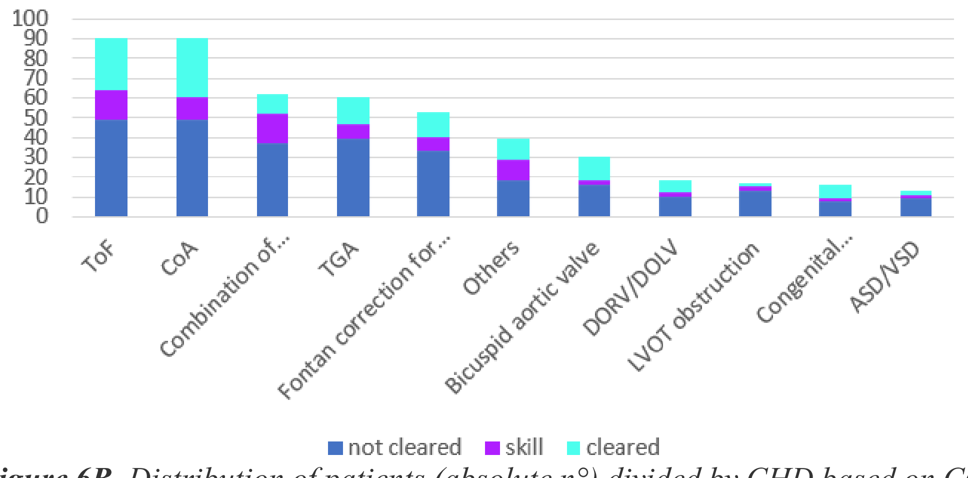

Figure 6B. *Distribution of patients (absolute n°) divided by CHD based on COCIS 2017 competitive eligibility class. ToF: Tetralogy of Fallot; CoA: Aortic Coarctation; TGA: Transposition of the Great Arteries; DORV/DOLV: Double Outlet Right Ventricle/Double Outlet Left Ventricle; LVOT: Left ventricle outflow tract; ASD-VSD: Atrial septal defect-Ventricular septal defect.*

The same procedure has been applied following the COCIS 2023 protocols, which includes a new category that we named "cleared by functional status", indicating that some patients previously considered eligible only for skill-based sports could eventually be considered eligible for all type of sports activity following a functional assessment through CPET, echocardiogram, and/or cardiac MRI.

Figure 7A and 7B shows these results.

ToF (Tetralogy of Fallot) show 56.32% of patients who cannot be eligible for any competitive sport activity, 8.05% for skill-based, 14.94% of eligible for all type of sports and 20.69% classified as cleared by functional status. CoA results are similar (55.06%; 6.74%; 11.24%; 26.97%). Patients with combination of anomalies (59.68%; 14.52%; 11.29%; 14.52%). TGA include 65% of patients not-eligible, 11.67% for skill based, 6.67% eligible for all sports and 16.67% eligible following functional evaluation. Patients who underwent Fontan correction for univentricular heart (63.46%; 7.69%; 5.77%; 23.08%). Bicuspid Aortic Valve (53.33%; 6.67%; 16.67%; 23.33%). DORV/DOLV (55.56%; 0% eligible only for skill-based sports; 16.67% for all sports and 27.78% only after functional assessment).

LVOT Obstruction (Left Ventricular Outflow Tract Obstruction) (76.47%; 11.76%; 11.76% and no patients eligible after functional assessment). Congenital Pulmonary Valve Stenosis (50%; 6.25%; 12.50%; 31.25%)

ASD/VSD (Atrial/Ventricular Septal Defect) (69.23%, no patients for skill-based sports, 7.69% for all sports, and 23.08% cleared by functional status evaluation.

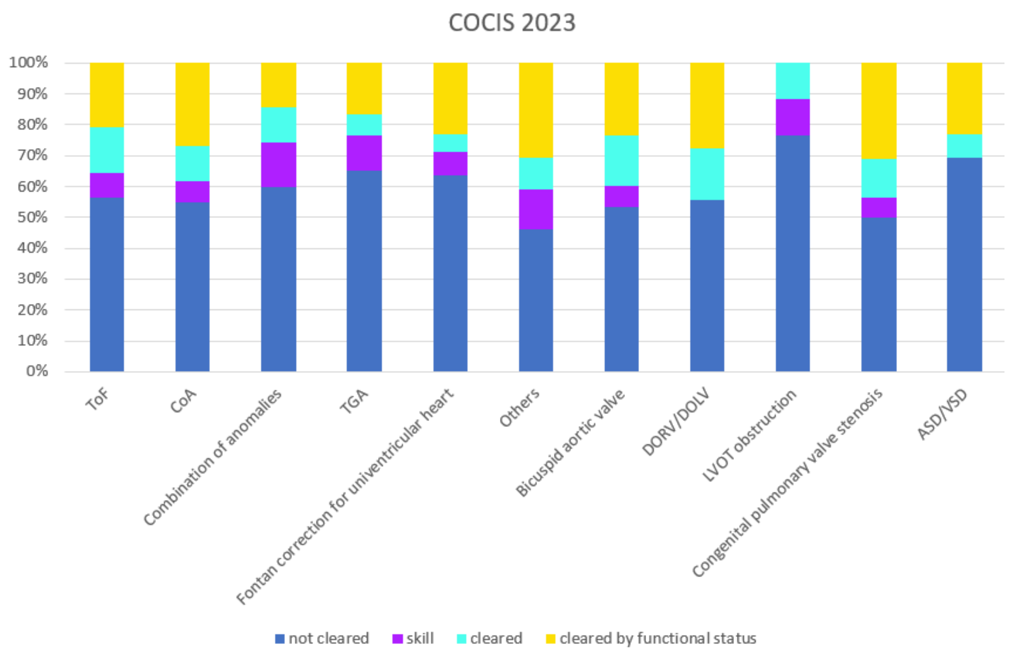

Figure 7A. *Distribution of patients (%) divided by CHD based on COCIS 2023 competitive eligibility class. ToF: Tetralogy of Fallot; CoA: Aortic Coarctation; TGA: Transposition of the Great Arteries; DORV/DOLV: Double Outlet Right Ventricle/Double Outlet Left Ventricle; LVOT: Left ventricle outflow tract stenosis; ASD-VSD: Atrial septal defect-Ventricular septal defect.*

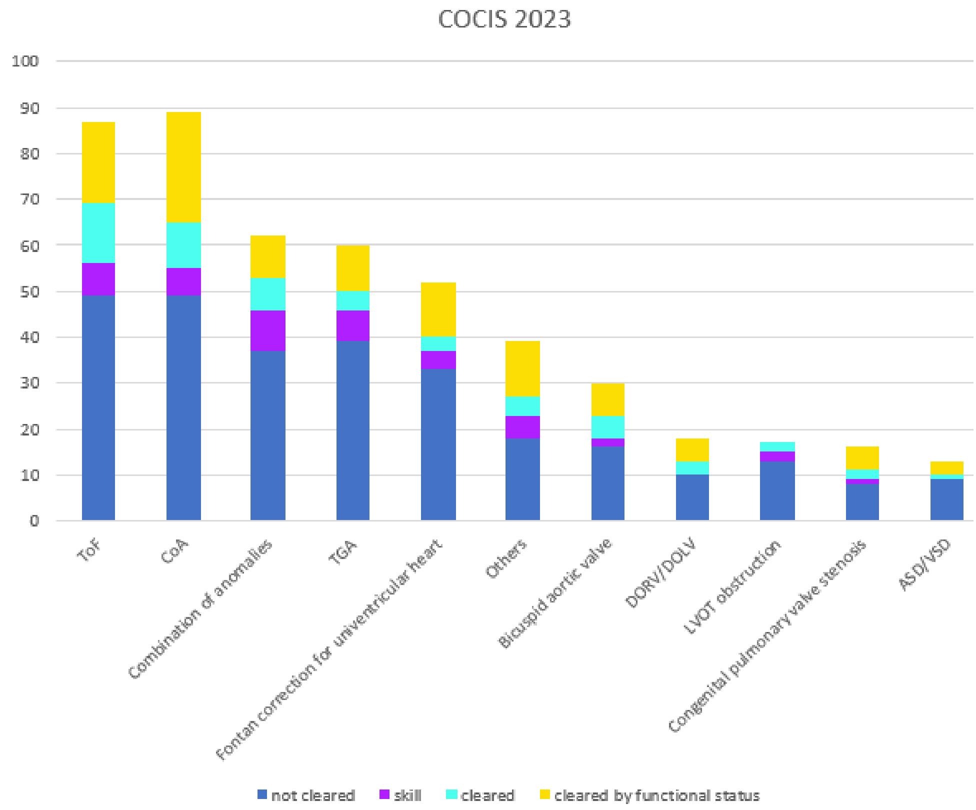

Figure 7B. *Distribution of patients (absolute n°) divided by CHD based on COCIS 2023 competitive eligibility class. ToF: Tetralogy of Fallot; CoA: Aortic Coarctation; TGA: Transposition of the Great Arteries; DORV/DOLV: Double Outlet Right Ventricle/Double Outlet Left Ventricle; LVOT: Left ventricle outflow tract stenosis; ASD-VSD: Atrial septal defect-Ventricular septal defect.*

Finally, we realized an alluvial diagram showing the class changes between COCIS 2017 and COCIS 2023 (Figure 8). It is relevant to notice that 23 patients classified by COCIS 2017 as eligible only for skill-based competitive sport activities are considered by COCIS 2023 potentially eligible for all sports following cardiopulmonary functional assessment. Consequently, potentially cleared patients become 159 instead of 135, if we consider that patients who were eligible for all sports by COCIS 2017 stay eligible for all sports by COCIS 2023. The chart shows also that all patients previously considered not eligible remain not eligible in COCIS 2023.

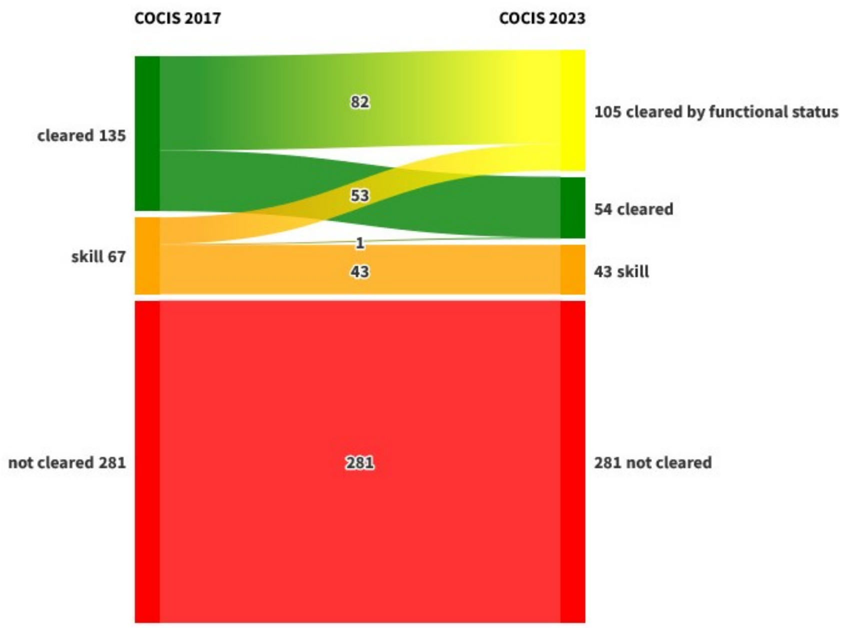

Figure 8. *Alluvial diagram showing the class changes between COCIS 2017 and COCIS 2023.*

8. Discussion

Cardiorespiratory fitness is one of the most important and independent predictors of mortality and disability in general population, and in chronic conditions, including CHD, as well as in young people [43,44]. Competitive sport participation is a key element not only for cardiorespiratory fitness improvement, but also for social inclusion, psychological development, mental health, and quality of life, particularly for children, adolescents and young people[45]. Nevertheless, for people living with CHD competitive sport participation for many years was banned due to a lack of solid scientific data, optimized therapeutic treatment, limited survival, and a tendency to overprotect these patients [46]. However, nowadays, surgical, and pharmacological treatments ensure excellent survival and quality of life for these individuals, also opening the possibility of structured exercise and even participation in competitive sports. The recent guidelines of the European Society of Cardiology provide detailed and evidence-based indications for adequate screening and professional guidance for these patients on whether or not to participate in competitive sports and, if so, which type of sport is most appropriate for their specific condition[47]. The 2023 Italian COCIS protocols for competitive sports eligibility represent a new assessment tool for patients with CHD, these are pathology-specific.

This is the first study that applies ESC 2020 guidelines and compares them with COCIS 2017 and the most recent 2023 version, on competitive sport eligibility in a such large population of patients with congenital heart disease, highlighting, furthermore, the difference in functional capacity among ESC 2020 and COCIS 2023 classes and the impact of training on functional capacity.

Only one third (31%) of these patients is ineligible for competitive sports (class D), and of those eligible (n=338), 28% can play any kind of sport at a competitive level. In our population, the congenital heart diseases most represented were aortic coarctation, tetralogy of Fallot and transposition of the great arteries. There was also a higher prevalence of males, who are known to be more commonly affected by congenital heart disease [48]. The clinical characteristics of our population define a group of subjects with congenital heart disease in whom the outcomes of cardiac surgery are excellent, and the course of clinical-instrumental parameters is clinically benign. This population could be indirectly selected since the subjects included are those patients who consecutively attend the sports medicine outpatient clinic and who, by definition, are in good hemodynamic compensation (NYHA classes I and II) and show no absolute contraindications to maximal exercise testing [49]. This may influence data interpretation, so it should be specified that the morpho-functional characteristics of these subjects refer to patients with congenital heart disease who are potential candidates for structured exercise or even competitive sport. Therefore, these data cannot be easily generalized to all subjects with congenital heart disease regardless of their severity, outcome of cardiac surgery, complications and medical history. Patients included in this study show on average either a normal functional capacity compared to a healthy subject of the same sex and age or slightly/moderately reduced and very rarely severely reduced. This data is in line with the articles that show the distributions of functional capacity in different congenital heart diseases of adults and children [50,51], but its interpretation should always consider the possible selection bias that accompanies this type of study which, by definition, cannot consider all subjects who are not able to undergo measurement of cardiorespiratory fitness via maximal cardiopulmonary testing.

It is known that people with CHD have higher risk of cardiovascular events due to both the anatomical condition, but also to frequent catheterization, interventions, medications and so on. In addition, the amounting of cardiovascular risk factors linked to lifestyle and ageing may accentuate atherosclerotic damage[52]. In this regard, it is good to note that the prevalence of ischemic signs on cardiopulmonary testing is low in this population.

In this study, there is evidence of a progressive reduction in functional capacity as one moves from class A to class D. This trend is to be expected as the classification involves downgrading based on the morpho-functional characteristics of the patients rather than simply the type of congenital heart disease they have. Moreover, even when considering the percentage of subjects with significant impairment in functional capacity, we can observe that these are absent in the first two classes (A and B), while they appear in the classes characterized by greater impairment. These results confirm what has been observed in the previous literature and are in line with the clinical characteristics of the subjects. It is known that also in patients with CHD regular physical exercise have several functional benefits. Very interesting is the effect of physical activity on the functional capacity of these patients. These data highlight that anatomical abnormality is not the only determinant of functional capacity because subjects who do regular structured exercise are characterized by better functional capacity, even at equal ESC2020 class. In other words, within the same ESC class, subjects who exercise regularly have a significantly higher mean value of maximal oxygen consumption than sedentary subjects. This finding is independent of the proportion of subjects practicing competitive activities and is observable in all ESC classes, even in class D in which no type of competitive activity is allowed and in which subjects with the most compromised morpho-functional characteristics are grouped. These findings suggest that whatever is the type of CHD and whatever is the type of training or structured exercise there is a significant effect on cardiorespiratory fitness. In previous studies, predominantly randomized controlled trials, the effects of exercise training on cardiorespiratory fitness were variable and less evident in subjects with Fontan[53]. Furthermore, it must be specified that in Trials populations are often selected, interventions are standardized, and highly specialized staff as well as the presence of very assiduous or even constant supervision. Our study has the relative “weakness” of having an observational design, but it has the strength of reporting data from real life. The fact that the effect of any type of structured exercise improves cardiorespiratory fitness regardless of CHD type and degree of impairment is scientific evidence that "every minute counts”. In addition, it should be noted that physical exercise adds many other benefits on global wellbeing such as the improving of perceived quality of life, improving of BMI and motor skills. These are all crucial points particularly for a population composed mainly of children and adolescents as they are often forbidden to participate in sports activities with major impacts on their mental and physical development[53] . Even more, surprising finding is that the functional capacity of trained subjects in class D is higher than that of non-exercising subjects despite the lacking in statistical significance. This finding supports the literature that encourages structured exercise of individuals with CHD, regardless of their complexity, because the possibility of adapting exercise is almost infinite, and unless there are important contraindications, exercise at the appropriate intensity relative to the risk profile improves cardiorespiratory fitness and reduces the risk of noncommunicable diseases for which individuals with CHD seem to be more susceptible [52]. Finally, in the present study, be physically active by performing regular structured exercise is an independent determinant of cardiorespiratory fitness in people with CHD. This finding might be obvious in a general population, but not in this particular group of people. In people with CHD, indeed, functional limitation should be primarily due to anatomical unchangeable characteristics, but the present study shows that on average there is a considerable range of intervention and a significant amount of functional capacity to be retrieved and, most importantly, that regular exercise is able to recruit much of the limitation associated with deconditioning both periphytic, pulmonary, and even cardiogenic. It is known that exercise training improves exercise capacity by increasing cardiorespiratory fitness, but also influencing motoric skills and muscular oxygenation, including respiratory muscles. This effect may lead also to a better ventilation efficiency and a lower fatigue of respiratory muscles especially at higher intensities, resulting, thus, in reduction in ventilatory limitation to exercise, as well as to improved exercise tolerance [54]. In addition, psychological status and quality of life are impressively improved in people with CHD engaging structured exercise and, last but not least, structured exercise is a key lifestyle component for preventing non-communicable diseases that may represent an increasing hazard for people living with CHD, in particular for sedentary [55].

In the context of Italian healthcare system, the Sports Physician has access to a series of protocols for the assessment of fitness for competitive sports (COCIS 2023). These protocols, similar to previous European and American recommendations, provide pathology-specific guidelines. The key aspects to evaluate are always ventricular function and morphology, the degree of valvular insufficiency, pressure gradients across shunts/valvular stenoses/outflow tracts, estimated pressures in the right ventricle, aortic dimensions, arrhythmic burden or atrioventricular conduction disturbances, signs of exercise-induced myocardial ischemia, and blood pressure behavior during exercise. Additionally, other conditions that may coexist with the underlying congenital heart disease and influence the final fitness judgment are also assessed (presence of mechanical or biological valves, prosthetic conduits, or ICD/PM). [36]

The role of CPET (Cardiopulmonary Exercise Testing) is fundamental in evaluating individuals with congenital heart disease.[41] In the Italian protocols, especially for more complex congenital heart diseases, aerobic capacity (peak VO2 > 80% of predicted for gender and age) and the assessment of ventilatory-perfusion mismatch signs (VE/VCO2 slope < 30) are required to formulate the fitness judgment for competitive sports.

Studies in the literature use peak VO2 values extrapolated from the general population, and it is universally accepted that peak VO2 correlates with prognosis and quality of life in individuals with congenital heart disease.[56–58] However, the use of the same reference values for peak VO2 valid for the general population can be misleading in the clinical and prognostic evaluation of subjects with congenital heart disease. Each congenital heart disease has different severity and complexity of presentation and various intrinsic cardiogenic, ventilatory, and peripheral limitations. For this reason, it would be more appropriate to use pathology-specific reference values as outlined by Kempny et al. for the adult population[59] and by Amedro et al. for the pediatric population.[60]

One of the objectives of this work was to compare the possibility of granting competitive sport eligibility according to the COCIS protocols with the ideal eligibility derived by applying the ESC recommendations algorithm.

It is important to note that in the COCIS, "fit for all sports" is stated without differentiating the hemodynamic demands of the discipline, except in certain contexts (e.g., exclusion of power sports in cases of hypertension, signs of ventricular hypertrophy, or aortic dilation). In the ESC recommendations, however, two large subgroups were created, placing all sports in Class A, while in Class B, endurance sports (e.g., swimming, long-distance running/cycling, rowing) are excluded, and team and power sports are retained. The exclusion of endurance sports has prognostic significance given the known cardiovascular remodeling effects that can result. The lack of specificity regarding the type of sport, combined with pathology-specific selection criteria, could explain the discrepancy between eligibility according to COCIS and ideal eligibility according to ESC in Group B. Noting that COCIS does not differentiate sports into endurance, mixed, and power categories, but uses the generic term "all sports," Classes A and B will be considered as a single group.

The COCIS 2017 chart displays the distribution of patients with various congenital heart anomalies based on their eligibility for sports activities. The categories are "not cleared" (not eligible for competitive sports), "skill" (eligible for skill-based sports), and "cleared" (eligible for all sports). The general trends are that the majority of patients across all categories are classified as "not cleared; moreover, a smaller percentage of patients fall into the "skill" and "cleared" categories. The implications of these results are that there is a high non-clearance rate (around 70%) for most congenital heart anomalies, suggesting that a significant number of patients with these conditions may face restrictions on competitive sports participation based on COCIS 2017. Moreover, a minority of patients are cleared

for all sports, indicating that only a limited subset of patients with congenital heart diseases can participate in all forms of competitive sports without restrictions. The COCIS 2017 highlights the variability in sports eligibility among patients with different congenital heart anomalies, precisely it considers every pathology on its own, emphasizing the importance of individualized assessments and recommendations based on each patient's specific condition and overall health status. This version of the guidelines appears more restrictive than the ESC 2020 protocols. The updated version of COCIS 2023 introduce the possibility to upgrade the eligibility of some patients previously declared eligible only for skill-based sports, to all type of sports following functional CPET, echocardiographic or cardiac MRI evaluation.
The categories are "not cleared" (not suitable for competitive sports), "skill" (suitable for skill-based sports), "cleared" (suitable for all sports), and "cleared by functional status" (cleared for all sports after specific functional assessment). The majority of patients across all categories are classified as "not cleared," similar to 2017. There is a notable increase in the "cleared by functional status" category compared to 2017. This change suggests that more patients are being re-evaluated and potentially cleared for all sports based on functional assessments. The increase in patients cleared by functional status reflects advancements in medical evaluations and treatments, allowing more individuals with congenital heart anomalies to participate in competitive sports. The data shows a shift towards more personalized assessments, potentially leading to better health outcomes and quality of life for these patients.

The number of patients classified as "not cleared" remains unchanged at 281 from COCIS 2017 to COCIS 2023. This indicates a stable group of patients whose conditions are severe enough to prevent them from participating in any competitive sports. The main causes of non-eligibility were reduced functional capacity, the presence of moderate or severe pulmonary insufficiency, hypertrophy and/or dysfunction of the right ventricle (RV), the presence of complex arrhythmias, and significant desaturation during exercise.

The main causes of non-eligibility according to ESC were the presence of pulmonary hypertension with RV dilation/dysfunction, complex arrhythmias, severe desaturation during exercise, volume overload with a dilated and dysfunctional RV, severe pressure overload, or a combination of these factors.

According to the COCIS protocols, subjects with univentricular hearts can never be considered eligible for any type of sport due to the varying degrees of complexity and severity of their underlying anatomical abnormalities. These individuals have reduced exercise capacity of multifactorial etiology, which is directly correlated with the risk of mortality and the development of other comorbidities.[61] Additionally, they possess unique compensatory mechanisms to increase cardiac output during exercise.

The ESC recommendations, however, state that having a univentricular morphology does not in itself contraindicate skill-based sports in the absence of other significant morpho-functional alterations. With this approach, half of our subjects could be considered fit for skill-based sports, while the remaining half were deemed unfit due to the presence of complex arrhythmias, inducible signs of myocardial ischemia, severe exercise-induced desaturation, severe systolic dysfunction, severe ventricular hypertrophy, or a combination of these factors.

From the comparison of Italian and European recommendations, it emerges that the presence of myocardial ischemia and/or inducible complex arrhythmias and severe exercise-induced desaturation are contraindications to any type of competitive sport for both sets of recommendations examined. The European recommendations appear more permissive than the Italian ones as they ideally grant competitive sports fitness for certain types of sports even in moderate-to-severe cases (mixed sports, skill-based sports), whereas under the Italian regulations, the presence of even mild alterations contraindicates competitive sports in almost all cases. What differs is the more clinical-instrumental approach in the ESC guidelines, whereas the COCIS is more pathology-specific. The ESC guidelines also provide greater differentiation by type of sport, while the COCIS tends to generalize competitive sports.

Italian protocols allow the granting of competitive sports fitness for all sports in less severe forms of congenital heart disease (atrial septal defects, ventricular septal defects, LVOT obstructions, bicuspid aortic valve, congenital pulmonary valve stenosis). For CoA, TGA, and ToF, eligibility for skill-based sports can generally be granted only if near-optimal morpho-functional criteria are met. Granting eligibility for mixed sports (typically team sports) is reserved for very select cases evaluated in specialized centers for congenital heart disease.

Functional capacity in terms of peak VO2 is a fundamental parameter to consider, but although the European recommendations emphasize its importance in the assessment of individuals with congenital heart disease, it is not included in the algorithm itself. In contrast, in the COCIS, functional capacity is often included among the criteria for judging a subject's eligibility.

Finally, in the context of the non-parametric analysis comparing the various fitness classes, it is evident that subjects in Class A have an advantage in terms of functional capacity compared to those in other classes. Specifically, the percentage of predicted peak VO2 for gender and age was significantly different between Class A and Classes C and D, confirming the literature that reduced oxygen consumption correlates with exercise intolerance. The difference in maximal METs between classes also directly correlates with functional capacity.

Therefore, it is crucial to investigate if the alteration in functional capacity is only related to the underlying pathology or also due to inactivity. In this case, a physical activity program tailored to the specific case could not only improve the patient's overall condition and exercise tolerance but also potentially reduce morbidity and mortality. Naturally, functional capacity is not the only determinant of the clinical condition of these patients. Consequently, even patients with mild-to-moderate reductions in functional capacity may be eligible for high-intensity sports, while those with normal or only slightly reduced functional capacity may have a clinical condition that precludes them from engaging in high-impact cardiovascular activities.

9. Limitations and perspectives

This is an observational, cross-sectional study that can be considered as a starting point for a longitudinal observation on long-term outcomes. The information in this study would take on much greater value if supported by longitudinal data regarding the role of structured exercise on survival in these subjects. In this regard, the use of quantitative measures of exercise and training level could clarify the weight of individual components of an exercise program on the health of subjects with CHD. This work is an observation on the morpho-functional and clinical characteristics of a large population of patients with CHD and is based on the clinical routine for which the setting is standardized, but for clinical purposes and not exclusively for research. As previously reported, the results of this study are not generalizable to all CHD patients as the population studied suffers from a selection bias linked to their ability to perform exercise as they all performed a maximal cardiopulmonary test. Nonetheless, it would be interesting to study the effects of structured and adapted exercise even in subjects with greater limitations. Obviously in these subjects the precaution should be much greater, and the volumes and intensities should be precisely calibrated so as not to create greater damage than the possible benefit, but the results could represent an important therapeutic perspective for the well-being and general performance of these subjects.

10. Conclusions

ESC 2020 guidelines applied to a real large population of people with CHD, show that only about one third of subjects should avoid every type of competitive sport. However, it should be pointed out that also people unable to participate in competitive sports may receive individualized exercise prescription aiming to preserve and improve functional capacity. Cardiorespiratory fitness is higher in classes of subjects enabled to perform competitive sport with a significant decrease from class A to class D.

Subject that regularly perform structured exercise have higher cardiorespiratory fitness both in the same and between different ESC2020 classes. Structured exercise resulted an independent determinant of cardiorespiratory fitness independently from age, sex and morpho-functional characteristics in this large population of people with CHD. These findings coming from a real-life and cross-sectional observational study suggest that individualized and structured exercise prescription may have a significant impact on CRF level of people living with CHD.

Regarding eligibility for competitive sports, the Italian and European protocols are not mutually exclusive. The pathology-specific approach of the COCIS risks reducing the patient to a single altered value in an echocardiographic report, thereby losing a more general clinical perspective of the patient. This limitation is partially addressed by the updated COCIS 2023, and by the ESC 2020 recommendations which also aim to mitigate these risks by proposing a comprehensive, multiparametric, and individualized morpho-functional evaluation focused more to the subject, than only on the pathology. The new classification developed by the ESC is particularly useful because it does not rely on a disease-specific classification but instead assesses various morpho-functional aspects. This approach makes it easier to identify the presence or absence of conditions of eligibility or potential risk in practicing different types of competitive sports, even in the presence of a combination of associated clinical conditions. The update version of the COCIS guidelines in 2023, compared to the 2017 edition, is more permissive, introducing the possibility of upgrading some patients previously deemed eligible only for skill-based sports to be eligible for all competitive sports, thereby aligning better with the ESC 2020 guidelines.

What could be beneficial is integrating the two approaches to achieve a holistic clinical evaluation of the individual while not neglecting reference parameters that impact the progression of a specific congenital heart disease. It is essential to create synergy between cardiologists, cardiac surgeons, and sports physicians for the evaluation of an individual who wishes to engage in competitive sports without risking their underlying pathology.

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