

Safety of physical sports and exercise in ACHD

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ABSTRACT

An active lifestyle, including regular physical activity, is an important component of long-term health and wellbeing, including in patients with adult congenital heart disease (ACHD). In the past, however, safety concerns regarding ACHD patients engaging in exercise have led to overly restrictive advice from specialists. Over the past few decades, it has become clear that the vast majority of patients with ACHD can exercise safely within their own limits; moreover, exercise capacity is highly variable between patients and should be measured objectively when possible.

Cardiopulmonary exercise testing (CPET) is an essential part of ACHD surveillance and provides an integrative assessment of the cardiovascular, respiratory and muscular response to exercise. It allows an objective assessment of exercise tolerance, identification of the extent and mechanisms of exercise limitations, monitoring of disease progression and forms the basis of exercise prescription.

Exercise prescription in ACHD patients ideally follows evaluation in an expert center, incorporating clinical assessment and exercise testing, to identify specific risk factors for adverse events during exercise and allow individualized recommendations of safe limits for exercise. In cases where specific risks exist, the intensity of exercise should be adjusted with respect to its dynamic and static components. The exercise prescription should then be reviewed regularly and amended as risk factors emerge or are successfully treated.

This review highlights the benefits of physical activity in ACHD patients and discusses the main parameters that influence the risk of certain forms of exercise in some patients. CPET and exercise prescription for non-competitive sports are also discussed.

1. Introduction

At present, almost 97% of pediatric congenital heart disease (CHD) patients are expected to reach adulthood [1]. Many of these young adults have some form of long-term *sequela*, such as surgical scars or residual anatomic and hemodynamic lesions, which may overlap with acquired heart disease or other comorbidities developed throughout their adult years. Indeed, adult congenital heart disease (ACHD) patients have an increased likelihood of developing early cardiovascular (CV) risk factors, including obesity which affects up to a third of the population [2,3]. Physical inactivity is closely linked to obesity and other CV risk factors, and ACHD patients are more likely to be sedentary compared to the

general population [4,5].

Inactivity in the ACHD group has historical roots, and can be linked to three main causes:

- 1) Exercise intolerance resulting from the CHD itself,
- 2) Safety concerns about exercising,
- 3) Lack of healthy lifestyle choices.

It is, therefore, important to tackle each of these causes in order to promote healthy lifestyle choices for all ACHD patients in terms of physical activity.

Abbreviations: ACHD, adult congenital heart disease; AHA, American Heart Association; AS, aortic stenosis; BAV, bicuspid aortic valve; BP, blood pressure; CHD, congenital heart disease; CO, cardiac output; CPET, cardiopulmonary exercise test; CV, cardiovascular; d-TGA, Dextro-transposition of the great arteries; ECG, electrocardiogram; ES, Eisenmenger syndrome; ESC, European Society of Cardiology; ET, exercise training; FC, functional class; LVOT, left ventricle outflow tract; MI, myocardial infarction; PA, physical activity; PH, pulmonary hypertension; SCD, sudden cardiac death; VO₂, peak oxygen uptake.

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1.1. Benefits of exercise in ACHD

An active lifestyle, including regular physical activity, is an important component of maintaining long-term CV health, extending life expectancy and improving quality of life. The benefits of physical activity include: improvement in functional status, mental health and quality of life; weight control; reduction in CV disease, and in both early and late mortality [6]. There is a dose-response relationship between exercise and improved health; and the benefits of an active lifestyle are likely to be extensive to CHD patients. Moreover, the long-term benefits attributed to exercise in older adults without CHD (>65 years), such as a reduction in the risk of developing chronic conditions (e.g. certain types of cancer or progressive cognitive impairment) and better control over existent CV risk factors, may also apply to the ageing ACHD population [7].

Exercise intolerance (dyspnea or fatigue on exertion) is one of the most common complaints across the ACHD population, and is multifactorial, with important prognostic and quality-of-life implications [8]. Exercise intolerance can be assessed subjectively by the New York Heart Association (NYHA) classification or objectively using the cardiopulmonary exercise test (CPET), 6 min-walk or incremental shuttle walk tests, as appropriate. Routine exercise can improve exercise tolerance in ACHD patients by enhancing cardiopulmonary fitness. Exercising also benefits social and psychological health, along with self-esteem in this patient group [9,10].

While the majority of CHD patients may have objective signs of mild exercise intolerance, even in the absence of symptoms, certain diagnostic groups, including patients with Eisenmenger syndrome (ES), other cyanotic conditions, or single ventricle physiology tend to be more severely affected [8]. All patients can benefit from a suitable exercise routine, regardless of the severity of exercise limitation. In ES patients, severe exercise intolerance was linked to poor perceived quality of life, despite their chronic adaptation to activities to match their capabilities. Exercise benefits in this group include improvement of peak oxygen consumption (peak VO_2) and 6-min walk distance, as well as the physical domains of quality of life [11]. In Fontan patients, respiratory training can improve dyspnea, muscle strength and peak VO_2 [12]. Benefits of physical training in Fontan patients go beyond symptomatic relief; there is evidence that improving muscle strength can also help to increase cardiac output during exercise in this group [13].

1.2. Conundrums of exercise in ACHD

1.2.1. History is against us (but not the data)

In the past, CHD patients were instructed since infancy to avoid strenuous efforts and restrict exercise, both competitive and non-competitive (leisure) sports, with the rationale of preventing exercise-triggered cardiac events and sudden cardiac death (SCD). These recommendations have become obsolete in the last 20 years, as research has confirmed the safety of exercise in the ACHD population. Moreover, even though SCD accounts for up to 25% of the mortality in the CHD population, only ~10% of SCD is estimated to be exercise-related [14,15]. Therefore, an overly conservative, blanket approach to exercise prescription in pediatric and adult CHD patients carries the risk of causing confusion, fear and aversion towards all exercise, resulting in detraining and increasing the risk of obesity.

1.2.2. Many factors to consider

A major challenge for recommending and promoting exercise in ACHD is the anatomical and pathophysiological heterogeneity and varying complexity of each individual. Therefore, physicians need to consider multiple factors when they approach exercise prescription:

- 1) The main congenital cardiac diagnosis and its expected impact on exercise physiology;
- 2) Residual anatomical or hemodynamic lesions and surgical scarring, causing ventricular overload and predisposing to arrhythmias;

- 3) Comorbidities, (e.g., concomitant thoracic or other skeletal abnormalities, learning difficulties), implanted devices, need for long-term anticoagulation or medication that may impact the physiological response to exercise (e.g. beta blockers).

As a result, some ACHD physicians may find it difficult to produce a tailored exercise prescription or may tend to highlight risks over the benefits of physical activity when discussing with their patients, influencing patients' attitude towards sports [16,17]. Indeed, Bar-Mor and colleagues report that the cardiologist's attitude to exercise during a clinical visit has a direct impact on how adolescents with CHD evaluate their own exercise capability [18].

1.3. The best time to change attitudes and influence patient choices

In order to change patients' behaviors, a tailored exercise prescription and positive reinforcement from a reliable source are key factors. A critical time to reinforce a healthy lifestyle is the "transition" period (between ~12 and 22 years), when young patients should be educated about their condition, advised on developing healthy habits, and encouraged and empowered to make positive choices regarding their health. Exercise prescription in ACHD should follow a simple and step-wise approach, explaining to patients the rationale behind the recommendations provided, and educating them on the warning symptoms and signs they should look out for (e.g., exertional dizziness, persistent palpitations or chest pain).

2. Exercise prescription

To make exercise safer for ACHD patients, counseling should incorporate all of the components listed in Fig. 1.

2.1. Types of exercise and their physiological impact

According to the 2020 ESC Guidelines on sports cardiology and exercise in patients with CV disease, physical activity (PA) is defined as any voluntary bodily movement produced by the skeletal muscle that results in energy expenditure, while exercise training (ET) is a structured and repetitive physical activity with the objective to improve or maintain one or more components of physical fitness [19]. The concept of physical fitness integrates multiple components (cardiopulmonary endurance, muscular strength and endurance, body composition/morphology, motor capabilities and metabolic features), on which the individual's ability to perform exercise is dependent. While physical fitness establishes what patients can actually do, exercise training is closely linked to individual behavior, and incorporates what an individual is willing to do.

Exercise types and their physiology are best understood using a metabolic classification, i.e., aerobic versus anaerobic exercise. These types of exercise differ not only in terms of the duration and intensity of muscle contraction but, more significantly, on the metabolic substrate the muscle uses to produce energy and the efficiency of the process. During aerobic exercise, the muscle uses oxygen to extract energy from glucose and fatty acids. Aerobic training is usually achieved by endurance exercise (such as running, cycling or swimming), where large muscle groups perform rhythmic and repetitive movements at moderate intensity, which is ideal for improving cardiopulmonary fitness. During aerobic exercise, the heart meets the extra metabolic demand by increasing blood supply (i.e. cardiac output, CO) to ensure adequate tissue perfusion through enhanced myocardial contractility (positive inotropy) and heart rate (positive chronotropy). Heart function is facilitated by a relative reduction in afterload, mediated by peripheral autoregulatory mechanisms [20]. The maximal aerobic capacity is reflected by the maximal oxygen uptake/consumption (VO_2 max), which is the maximum amount of oxygen the body can utilize during strenuous exercise. The related measure of peak VO_2 is the highest value obtained during a CPET test and should approximate VO_2 max in incremental

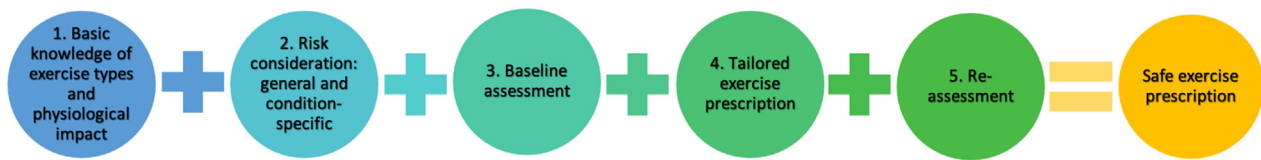


Fig. 1. Components of a safe exercise prescription.

exercise testing. The intensity of endurance training can be classified (and prescribed) according to the percentage of peak VO_2 , peak heart rate (HR) or heart rate reserve (HRR) achieved during exercise (Table 1) [19]. For example, performing endurance training at <40% of peak VO_2 would be considered low intensity. It is important to note higher intensity levels of endurance training require both aerobic and anaerobic metabolism to achieve the energetic requirements of the working muscles.

Resistance training or muscular fitness enhancement focuses on developing muscle strength, endurance and power and mostly relies on anaerobic metabolism: the brief and intense movements performed by a specific muscular group require fast energy delivery achieved by anaerobic glycolysis. Unlike aerobic exercise, where the heart has to adapt to an increased volume load, resistance training leads to a different set of physiological changes due to the pressure load placed on the heart. These differences are greater with shorter efforts of more forceful muscular contraction (i.e. fewer repetitions). During heavy resistance training, the cardiac output and stroke volume are relatively unchanged, mainly due to the acute increase in afterload generated by high intraabdominal and intrathoracic pressures, with contribution from a Valsalva maneuver [21]. The increase afterload is also a consequence of the elevation of vasoactive substances in the blood, secondary to tissue hypoxia and lactic acidosis [22]. The raised afterload consequently reduces the systemic venous return and thus ventricular preload. As the weight is reduced and the duration increases (more repetitions), CO starts to increase as with aerobic exercise. Examples of strength and power sports are weightlifting and sprinting. The intensity of resistance exercise is classified by calculating the repetition maximum (RM) for each specific exercise, which is the maximum amount of weight a subject is able to lift once (i.e., a single repetition); the intensity is then classified as a percentage of the RM. Anaerobic exercise burns fewer calories (does not utilize fat) and is less beneficial to cardiopulmonary fitness, but does enhance muscular strength, improves bone strength and mineral density, and can increase lean mass. At moderate levels, resistance training is beneficial for CV risk factor modification, reduces pain and disability, and can be beneficial for mental wellbeing [23].

Muscle training can be further classified according to muscle work, distinguished in isometric (static, no/very little change in muscle length during contraction) or dynamic (with length change during contraction). Static exercises can trigger Valsalva maneuvers, resulting in an increase in blood pressure and cardiac afterload. Classifying sports according to endurance/resistance and dynamic/static components can be challenging and, depending on the intensity level, most types of exercise

include a combination of both types. By considering the main type of muscle work, most sports can be categorized into endurance, strength, mixed (combination of endurance and strength) or skills sports. A skills sport, such as golf or table tennis, may involve minimal demand on the cardiopulmonary system. A summary of sports disciplines can be found in Fig. 2, based on the European Society of Cardiology sports classification [19,24].

Regular low/moderate-intensity aerobic exercise training (such as walking, swimming or cycling) is largely safe and effective for most ACHD patients [19,25]. Exercises with a predominant static/resistance component can also be beneficial, but recommendations should be individualized, as the afterload increase may trigger cardiovascular events in certain cohorts (e.g. in patients prone to aortic complications, and in those with severely obstructive lesions or severe systemic ventricular systolic dysfunction).

2.2. Risks associated with exercise in ACHD

Risks associated with exercise can be divided into cardiovascular and non. The most frequent complications associated with exercise are indeed non-cardiac, such as musculoskeletal injuries and soft tissue trauma, which largely depend on the intensity and duration of the exercise, prior fitness levels and skills. Cardiac complications associated with physical activity are most commonly related to the following 5 mechanisms (alone, or in combination): arrhythmias, acute myocardial ischemia, heart failure exacerbation, inability to increase cardiac output during exertion and aortic dissection or rupture. All of these mechanisms can potentially culminate in the most feared complication associated with exercise, sudden cardiac death.

Alarming and/or prodromal symptoms during exercise include dizziness and pre-syncope episodes, chest pain, and excessive/disproportionate palpitations or dyspnea. Clarifying the underlying mechanism associated with a specific symptom is challenging. For example, exertional syncope may be related to a malignant arrhythmia in patients with arrhythmogenic substrates (such as tetralogy of Fallot), but can also be caused by left-sided obstructive lesions (e.g. severe aortic stenosis, as in bicuspid aortic valve disease or following a prior aortic valve replacement) or by worsening cyanosis (e.g. in Eisenmenger syndrome). Whilst chest pain is more commonly associated with myocardial ischemia (due to ischemic heart disease, ventricular hypertrophy or increased end-diastolic ventricular pressures) or aortic dissection/rupture, it can also be also a manifestation of tachyarrhythmia. It is that important that physicians interpret exercise-induced symptoms in the light of the underlying cardiac condition, including previous interventions and residual lesions. Fig. 3 provides an outline of the mechanisms responsible for complications during exercise in relation to the most common types of ACHD and potential diagnostic tools.

2.2.1. Arrhythmias and SCD

Arrhythmogenic triggers are assumed to be especially relevant in SCD and responsible for more than 50% of the SCD cases in ACHD patients [26]. The risk of late SCD in certain ACHD cohorts, including patients with left-sided obstructive lesions and cyanotic heart disease, has been estimated at between 50 and 200 times that of the general population. SCD affects patients with both repaired and unrepaired CHD and the risk persists several decades after reparative surgery. During exercise, the increase in sympathetic tone and myocardial oxygen demands combined

Table 1

Relative intensity levels in endurance training and associated training zones.

Intensity levels	Max VO_2 (%)	HR max (%)	HRR (%) ^a	RPE Scale	Training zone
Low intensity/ light exercise	<40	<55	<40	10–11	Aerobic
Moderate	40–69	55–74	40–69	12–13	Aerobic
High	70–85	75–90	70–85	14–16	Close to the AT
Very High	>85	>90	>85	17–19	Above the AT

Adapted from Pelliccia et al. [19]. Acronyms: AT, anaerobic threshold; HR, heart rate; HRR, heart rate reserve; Max VO_2 , maximal oxygen consumption; RPE, rate of perceived exertion (or Borg scale).

		Exercise Type			
		Skill 	Power 	Mixed 	Endurance 
Isometric Component		+/-	+++/++++	++/+++	++/+++
Dynamic Component		+/-	+/++	++/+++	+++/++++
Intensity	Low	• Golf • Sailing • Table tennis • Shooting • Curling • Bowling	• Discus (recreational) • Alpine skiing (recreational)	• Football/soccer • Basketball (adapted) • Handball (adapted)	• Jogging (<6 mph) • Long distance walking • Swimming (recreational)
	Medium	• Sailing / yachting • Equestrian	• Judo / karate • Discus (competitive) • Alpine skiing (competitive) • Shot putting • Short distance running	• Tennis (doubles) • Volleyball	• Speed walking • Middle- / long-distance running • Style dancing
	High		• Weightlifting • Wrestling • Boxing	• Hockey / Ice hockey • Rugby • Tennis (singles) • Water polo • Football/soccer (competitive) • Basketball (competitive) • Handball (competitive)	• Cycling (road) • Rowing • Mid- / long-distance swimming • Canoeing • Triathlon • Long distance skating

Fig. 2. Sports classification accordingly with predominant component (endurance, power, mixed and skill), muscular work (isometric and dynamic) and intensity of exercise. Adapted from Pelliccia et al. [19,24]. Acronyms: mph, miles per hour.

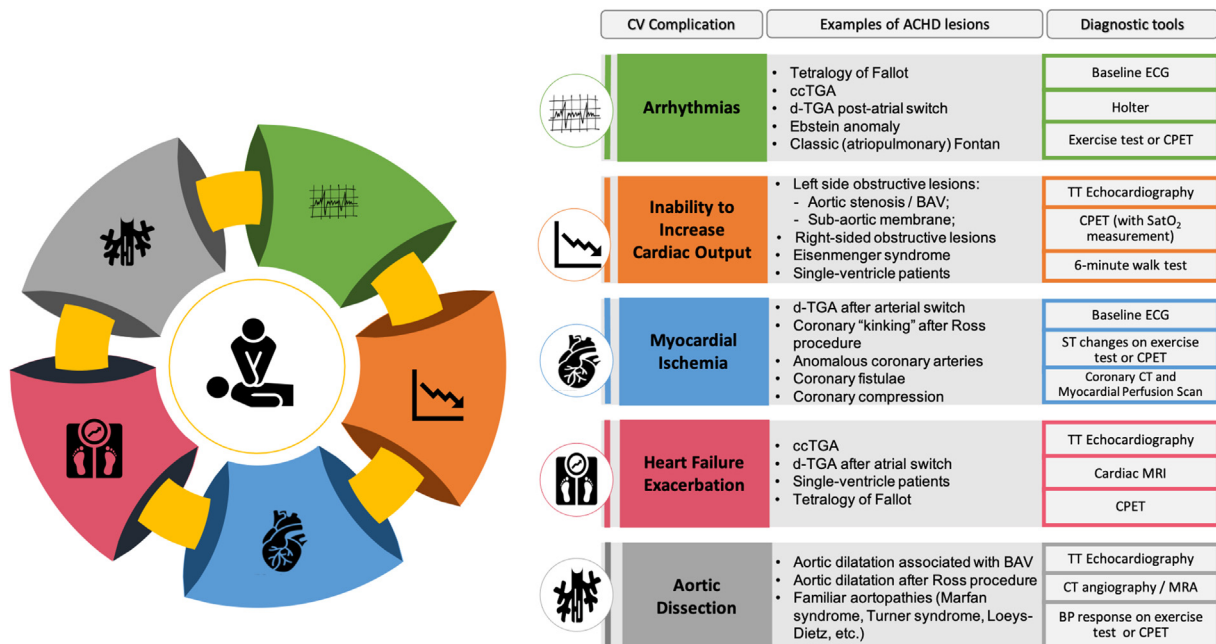


Fig. 3. Main cardiovascular risks associated with exercise in ACHD, congenital lesions associated with each complication and the major diagnostic tools. Acronyms: ACHD, adult congenital heart disease; BAV, bicuspid aortic valve; BP, blood pressure; ccTGA, congenitally corrected transposition of the great arteries; CPET, cardiopulmonary exercise test; CT, computed tomography; CV, cardiovascular; d-TGA, dextro-transposition of the great arteries; ECG, electrocardiogram; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; SatO₂, oxygen saturation; TT echocardiography, transthoracic echocardiography.

with a pre-existent structural substrate can trigger ventricular tachycardia (VT). Particular attention should be given to:

- Patients with tetralogy of Fallot, especially after late repair, with large ventriculotomy scars and a transannular patch [14]: the electrophysiological isthmus caused by surgical scarring and the patch

predisposes patients to fast macro-reentrant monomorphic VT, which can be fatal even in the presence of preserved ventricular function [27].

- In patients with d-transposition of the great vessels (d-TGA), surgical ventricular septal defect patches have been linked to monomorphic VT. Moreover, spontaneous or exercise-induced intra-atrial reentrant

tachycardias associated with extensive atriotomy and the construction of baffles (in patients after a Mustard or Senning procedure) are common, and can degenerate into VT, especially in patients with significant systemic ventricular dysfunction [28].

- Ebstein anomaly of the tricuspid valve is often associated with right-sided accessory pathways. SCD is not uncommon in this cohort and is associated with previous episodes of VT and tricuspid valve intervention [29].
- Atrial arrhythmias are very common in Fontan patients, especially those palliated with an atriopulmonary Fontan operation. Risk factors for SCD in Fontan patients include the type and timing of the operation (late repair at >16 years) and atrial arrhythmias postoperatively [30]. Ventricular arrhythmias are less common, but even atrial arrhythmias can lead to rapid hemodynamic deterioration and death in these patients, especially in those with a “failing Fontan” circulation. Arrhythmias can also trigger thrombosis and pulmonary emboli, further compromising the function of the Fontan circulation.

Not all arrhythmias associated with SCD in ACHD are tachycardias. Bradyarrhythmias are also common, e.g., in patients with repaired ventricular or atrioventricular septal defects, and those with congenital corrected TGA.

In patients with new arrhythmias at rest, the exercise test should be postponed until the arrhythmia is treated (rhythm or rate control). Patients belonging to the high-risk categories described above should only undergo exercise testing when there are strong clinical indications and should be supervised closely during the test by appropriately trained healthcare professionals. Exercise testing in this setting can be useful to unmask a potential rhythm disturbance triggered by exertion, whilst in a safe and controlled environment.

2.2.2. Inability to increase cardiac output in the presence of normal ventricular function

2.2.2.1. Left- and right-sided obstructive lesions. The most frequent causes of left ventricular outflow tract (LVOT) obstruction in CHD patients include congenital aortic stenosis (typically due to a bicuspid aortic valve) or subaortic stenosis. Both result in an increased ventricular afterload, but CO is maintained as long as the systemic ventricle can compensate by increasing its contractility. When the LV fails to overcome the obstruction, the patient can suffer a drop in CO and blood pressure, which can cause syncope and results in coronary hypoperfusion, and may lead to malignant arrhythmias [19,31]. For this reason, vigorous exercise (especially with a high isometric component) and competitive sports are contraindicated in patients with symptomatic severe LVOT obstruction. In patients with asymptomatic severe aortic stenosis, a CPET may be helpful to unmask symptoms, but the test should be carefully monitored and immediately stopped if symptoms or other alarming signs appear (e.g. drop or “flattening” of the blood pressure response to exercise, arrhythmias or significant ST changes). Hence, patients with severe LVOT obstruction should not participate in competitive or vigorous leisure sports but should remain active through low-intensity activities with a low isometric component, especially when LV systolic function is preserved and exercise testing has been reassuring, with a normal blood pressure response and no other complications. In mild and moderate LVOT obstruction, more intensive physical activity may be appropriate [32].

For the same reason, patients more than mild (>30 mmHg) right-side obstructive lesions, such as pulmonary stenosis or double-chamber right ventricle, should also avoid intense endurance or resistance sports [25].

2.2.2.2. Cyanosis and pulmonary hypertension. Patients with Eisenmenger syndrome have severely raised pulmonary artery pressures and an intra- or extra-cardiac communication with shunt reversal (right-left shunting). The shunt is responsible for chronic cyanosis but may act as an

“relief” mechanism for the pressure-overload RV and allows patients to increase cardiac output during exertion, at the expense of worsening cyanosis. Both the pulmonary hypertension and the decline in systemic oxygen saturations contribute to severe exercise intolerance and can lead to exertional syncope in Eisenmenger patients. Despite this, even patients with Eisenmenger syndrome should be encouraged to exercise within their abilities, prescribing exercise that is carefully tailored, based on a thorough expert clinical assessment, including objective measures of exercise capacity (e.g. gentle CPET or 6-min walk test). The 2020 ESC ACHD guidelines recommend low-intensity exercise with a low static component, while pediatric guidelines are less restrictive, and accept endurance training of moderate intensity 3–7 times a week (such as 60 min of walking) or interval training (e.g., 10–30 min of cycling) with short intervals of high intensity [25]. Competitive sports and scuba diving are contraindicated.

2.2.2.3. Single ventricle physiology. In patients with a Fontan circulation, the absence of a sub-pulmonary ventricle results in a chronically reduced systemic ventricular preload. Moreover, the cardiac output depends on systemic ventricular and valve function, the presence of obstruction to flow in the systemic or Fontan circulation (e.g. a restrictive ventricular septal defect in patients with transposed great arteries or stenosis of the Fontan pathway or pulmonary arteries), pulmonary vascular resistance, presence of a fenestration etc. Hence, exercise intolerance is common in Fontan patients and depends on the state of the Fontan circulation, presence of complications (e.g. arrhythmias) and levels of (de)training. During exercise, Fontan patients are often unable to increase their cardiac output sufficiently, experience a rise in systemic venous pressures and pulmonary vascular resistance, may become (more) cyanosed (in the presence of a fenestration, veno-venous or arteriovenous collaterals) and may develop arrhythmias [33]. Chronotropic incompetence and Fontan-associated-myopathy have also been described.

A systematic review of different exercise types (aerobic, low resistance and respiratory training) found that exercise was, overall, safe in Fontan patients and led to improvements in exercise capacity and quality of life, although only half of the patients experienced an increase in peak VO_2 [34]. Current guidelines recommend leisure activity, while competitive sports should be limited to low-to-moderate dynamic and low static components [25]. As with all ACHD patients, an individualized approach to exercise prescription is advisable, based on the anatomic features, past medical history and results of exercise testing. While SCD during exercise is not a common occurrence in this population, arrhythmias are frequent and can cause rapid hemodynamic deterioration. Dehydration should be avoided.

2.2.3. Heart failure exacerbation

Systemic ventricular function and the ventricle's ability to increase and maintain the cardiac output through a rise in contractility and heart rate are key components of the CV response to exercise. Systolic and/or diastolic ventricular dysfunction are common in ACHD and may occur as a result of past or ongoing hemodynamic lesions, anatomic abnormalities (e.g. systemic right ventricle, single ventricle, non-compaction), myocardial ischemia, previous multiple operations etc. Moreover, chronotropic incompetence is also common, and is often due to intrinsic abnormalities of the conduction system, medication or permanent pacing. Patients with Mustard and Senning operation for d-TGA are often unable to increase systemic ventricular preload due to the non-compliant (“stiff”) pulmonary venous pathway.

The above limitations become markedly manifest during exertion, with an acute rise in ventricular filling pressures and low cardiac output. During resistance/isometric exercise, the sudden excessive upsurge in blood pressure and rise in afterload can be very poorly tolerated and may even trigger malignant arrhythmias. However, appropriate levels of exercise with a combination of dynamic and low-level static components should be encouraged after a comprehensive baseline assessment.

2.2.4. Ischemic heart disease

Vigorous exercise can trigger myocardial ischemia and myocardial infarction [35], either due to coronary artery pathology (e.g. atherosclerosis with acute plaque rupture during exercise) or mechanisms unrelated to the epicardial coronaries (e.g. imbalance between myocardial oxygen consumption and delivery in pathologically hypertrophied ventricles). After the age of 35 years, atherosclerosis should always be considered as a possible cause of chest pain and coronary heart disease in ACHD patients.

Congenital coronary abnormalities are present in 5% of the general population, and are the second commonest cause of SCD in young athletes in the US [22,36]. High-risk features include [36,37]:

- a left main coronary artery from the right sinus of Valsalva with an intra-arterial course between the aorta and pulmonary artery,
- a long intramural course (5–15 mm) with an origin at an acute angle and slit-like ostium (independent of the artery affected), or
- the presence of ischemic symptoms.

Other coronary abnormalities in ACHD include coronary fistulas, coronary kinking after surgical procedures (such as a Ross procedure or after an arterial switch in d-TGA) and external coronary compression due to a dilated pulmonary artery (in patients with pulmonary hypertension or large long-standing left-right shunts).

Patients with high-risk features should be thoroughly assessed and considered for surgical correction, while sports should be discouraged until repaired. Again, an individualized approach is required, depending on the anatomical lesion and results of functional and/or invasive assessment.

2.2.5. Aortic dissection and other aortic complications

Acute type A dissection or aortic aneurysm rupture accounts for 2–3% of SCD in athletes and 4% in the overall population [35]. Different CHD pathologies can be associated with progressive aortic dilatation, such as aortopathy related to a bicuspid aortic valve, tetralogy of Fallot, d-TGA (after atrial or arterial switch procedures) and coarctation of the aorta. Patients after a Ross procedure should also be monitored for autograft dilatation [38]. However, the risk of aortic dissection/rupture is generally lower in ACHD patients compared to those with familial aortopathies (e.g. Marfan syndrome, Turner syndrome, Loeys-Dietz), or acquired aortic aneurysms [19].

In order to assess the risk of aortic complications during exercise, a comprehensive assessment of the underlying aortopathy is needed, including aortic diameter (current size and rate of progression), family history of dissection or SCD (recognized risk factor), pre-existing fitness levels and blood pressure response during exertion. With the exception of patients with a bicuspid aortic valve and an aorta <40 mm, all patients with congenital or genetic associated aortopathies should avoid high intensity sports, contact and “power” sports. Exercise with a high isometric component should also be avoided, as they can cause a sudden significant rise in blood pressure. In high-risk patients (familial aortopathies with ascending aorta diameter >45 mm; bicuspid aortic valve and tetralogy of Fallot >50 mm) all vigorous sports are contraindicated, but patients should remain active through low intensity dynamic activity [19].

2.3. Exercise safety assessment and CPET

Prior to exercise prescription in ACHD patients, a comprehensive review should be undertaken, starting with a detailed medical history and fitness background, and completed with baseline investigations, including an electrocardiogram (ECG), transthoracic echocardiogram and exercise testing, ideally a CPET. In patients with arrhythmic substrates, a Holter monitor may also be considered.

Incremental exercise testing is key to unmask symptoms on exertion and expose potential complications, e.g. rhythm abnormalities, ischemic

ECG changes, and an abnormal blood pressure and/or HR response, that are often not obvious during daily activities. In addition, the CPET provides a wealth of information, including objective assessment of exercise capacity, potential causes for exercise limitation and the safety of exercise. The VO_2 formula from the Fick equation shown below, demonstrates that the increased oxygen consumption during exercise requires the cardiac, respiratory, vascular and muscular systems to work in concert to deliver oxygen from the air to the peripheral tissues (i.e. the muscles cells at work). The CPET can help to assess the relative contribution of each system and assess the underlying mechanisms involved in any exercise intolerance.

$$\begin{aligned}\text{VO}_2 &= [\text{CO}] \times [\text{oxygen extraction}] \\ &= [\text{HR} \times \text{SV}] \times [\text{C}_a\text{O}_2 - \text{C}_v\text{O}_2] \\ &= [\text{HR} \times \text{SV}] \times [1.36(\text{Hb})(\text{S}_a\text{O}_2 - \text{S}_v\text{O}_2)]\end{aligned}$$



Cardiac



Non-cardiac

Where C_aO_2 is the arterial oxygen content, C_vO_2 is the venous oxygen content, Hb is the serum hemoglobin concentration, S_aO_2 is the arterial oxygen saturation and S_vO_2 represents the venous oxygen saturation. The non-cardiac portion of the equation equates to the respiratory system's ability to obtain oxygen, the vascular system's capacity to deliver oxygen and the muscle's ability to extract and use it. Acronyms: CO, cardiac output; HR, heart rate; SV, stroke volume; VO_2 , oxygen uptake/consumption.

2.3.1. CPET – practical considerations

Exercise testing reproduces an incremental effort within a safe, controlled environment, using either a treadmill or a stationary cycle ergometer. Cycle ergometry requires less space and is preferred in patients with mobility restrictions or severe exercise intolerance, while also allowing blood gas measurements and better blood pressure and ECG readings. Nevertheless, early leg muscle (mainly quadriceps) fatigue can be a limiting factor on the bicycle and is most accurate in assessing exercise capacity in patients who regularly use a bicycle. A treadmill test is deemed more “physiological”, as it mimics ordinary day-to-day activities that involve walking on the flat and uphill, carrying one's weight, hence recruiting more muscle groups and achieving higher HR responses and a 10–20% higher peak VO_2 compared to cycle ergometry [39]. However, the amount of work performed is dependent on body weight and there is a greater risk of falls or injury on the treadmill [40]. An Arm Crank Ergometer is an alternative for patients with reduced leg mobility, and usually follows a similar protocol to the bicycle ergometer, but at lower workloads.

On CPET, a mask or mouthpiece is used to measure ventilation (VE), oxygen uptake (VO_2) and carbon dioxide production (VCO_2). With the right exercise protocol, a “steady-state” may be assumed, hence metabolic parameters measured at the lungs can be taken to reflect metabolic processes happening in the periphery (i.e. the working muscles), e.g. identifying the time of onset of anaerobic metabolism (anaerobic threshold). Peak VO_2 , the VE/VCO_2 slope, VO_2 at anaerobic threshold and oxygen pulse are important parameters commonly reported during CPET; they provide important info on the physiology of exercise and mechanisms of exercise intolerance and also have prognostic implications in ACHD [8]. This information is summarized in Table 2. Of note, peak VO_2 is reduced across the ACHD spectrum and to various degrees in major CHD cohorts; therefore, exercise capacity should be interpreted in relation to “normality” thresholds (expected values) for each CHD diagnosis [41].

2.3.2. CPET safety

Exercise testing is usually considered safe and serious cardiac events

Table 2

Main parameters measured during cardiopulmonary exercise testing and their clinical relevance in ACHD.

Parameter	Definitions and normal values	Implications in ACHD
Peak VO_2	- It is defined as the highest value of oxygen uptake measured (usually expressed in mL/kg/min). - It approximates the maximal aerobic power of each individual on maximal exercise. - It is determined by: the maximal cardiac output, the arterial oxygen content, the fractional distribution of the cardiac output to the exercising muscle and peripheral oxygen extraction. - Normal values: >80% predicted of individuals with similar age, gender and height. - Each ACHD category has its own range of normal values (nomogram) [41].	- It tends to be reduced in all ACHD groups (even in asymptomatic patients), but its reduction accompanies greater CHD severity [8]. - It has a linear relationship with functional class measured by NYHA functional class in ACHD [8]. - Peak VO_2 is an independent predictor of a combined endpoint of all-cause mortality and hospitalization, patients with a peak $\text{VO}_2 < 15.5$ mL/kg/min being at a 3-fold increased risk [8]. - It correlates with maximal heart rate, FEV1, pulmonary arterial hypertension and cyanosis [8].
VE/VCO_2 slope	VE/VCO_2 represents the gas exchange efficiency during exercise, i.e., the amount of ventilation needed ("breathed air") to eliminate a certain amount of carbon dioxide. - The VE/VCO_2 slope is a simplification of the complex relation between ventilation and CO_2 production. - It is independent of maximal exertion. - It reflects pulmonary perfusion, the degree of physiological dead space and ventilation/perfusion mismatch, as well as ventilatory reflex sensitivity. VE/VCO_2 slope >33 is considered an abnormal response.	- Cyanosis had a significant impact on the ventilatory response to exercise. - While this parameter tends to be raised in all ACHD groups, patients with Eisenmenger syndrome have the most disproportionately high VE/VCO_2 slopes (mean value 71.2) [45]. - In noncyanotic CHD patients, a slope of >38 or above resulted in a 10-fold increased risk of mortality at a mean follow-up of 2 years [45].
Anaerobic threshold (AT)	- AT is defined as the level of oxygen consumption above which aerobic metabolism is supplemented by anaerobic processes. Above the anaerobic threshold, lactate accumulates and is buffered by plasma bicarbonate, causing an increase in CO_2 production (VCO_2). - It can be assessed by two methods: V-slope method (using the VCO_2 versus VO_2 slope) or the ventilatory equivalent methods (ventilation vs VO_2 and VCO_2 slopes). - In normal subjects the AT should happen at around 70–80% of the peak VO_2.	- ACHD patients have an AT below normal (usually around 45–60% of peak VO_2), and it is particularly reduced after Fontan surgery [46]. - Some patients might not even reach the AT during the test due to muscle weakness, deconditioning, heart failure or cyanosis [47]. - It is one of the strongest predictors of death from any cause or HF hospitalization in d-TGA patients who achieved AT at lower heart rates (<95bpm) [48].
Heart rate-derived parameters	- Peak HR: maximal HR recorded during exercise - HR reserve: difference between peak and resting heart rate	- Heart rate response to exercise is often blunted in ACHD. - Chronotropic incompetence is related to the severity of exercise intolerance, plasma

Table 2 (continued)

Parameter	Definitions and normal values	Implications in ACHD
	- HR recovery: difference between peak heart rate and heart rate at a specific recovery time. - Chronotropic incompetence is the inability to increase the HR appropriate to the degree of effort and metabolic demands (normally >85% of the age-expected maximum HR during exercise [49]).	- natriuretic peptide levels and peak oxygen uptake. - The reduction of peak HR, HR reserve and HR recovery have shown to be predictors of mortality in ACHD [50].

Adapted from Dimopoulos et al. and Mantegazza et al. [51,52]. Acronyms: ACHD, adult congenital heart disease; CHD, congenital heart disease; CO_2 , carbon dioxide; FEV1, forced expiratory volume in 1 second; HF, heart failure; HR, heart rate; FC, functional capacity; NYHA, New York Heart Association.

during the test, such as death, myocardial infarction, arrhythmia, hemodynamic instability, and musculoskeletal injury, are rare (<1–5 per 10,000 tests, mortality <0.5 per 10,000 tests) [42]. The pre-test risk of complications is widely dependent on the cardiovascular background; patients with non-revascularized ischemic heart disease or significant left ventricular tract obstruction are at high risk of exercise-induced complications.

In the CHD setting, there is limited information on the rate of CPET complications. In our experience, major complications (including death, cardiac arrest, syncope, symptomatic or sustained VT, symptomatic or persistent supraventricular tachycardia, myocardial infarction or need for immediate hospital admission) are rare. Patients with complex unrepaired defects, severe pulmonary hypertension, significant ventricular dysfunction and moderate-severe aortic stenosis or other obstructive lesion are considered to be higher risk, hence the American Heart Association (AHA) recommends physician supervision [43]. The response to exercise differs between CHD patients with different anatomy and physiology (even within the same diagnostic group) and it is important that the healthcare professionals supervising the test are familiar with CHD and potential complications during vigorous exertion.

To minimize the risks associated with exercise testing in ACHD:

- 1) All tests should be carried out by qualified health professionals, physicians or physiologists, familiar with CHD, potential complications and their management.
- 2) Exercise test requests should be screened for very high-risk patients who should receive direct physician supervision.
- 3) When the test is supervised by non-CHD physicians, easy access to a physician trained in CHD is advisable.
- 4) All test supervisors should be certified on advanced cardiopulmonary resuscitation (CPR) maneuvers.
- 5) The Exercise Lab should be equipped with a "help" button (calling for assistance around major complications) and an easily accessible "crash" (resuscitation) cart, including a defibrillator and oxygen. This equipment should be reviewed regularly (ideally at the start of each working day).
- 6) The resuscitation team should be easily contactable and aware of the location and facilities of the Exercise Lab. The laboratory should have adequate space for resuscitation maneuvers and the entire resuscitation team.

2.4. Prescribing exercise in ACHD

The European Society of Cardiology recommends that exercise prescription in ACHD should be based on hemodynamics and arrhythmogenic risk, both for leisure and competitive sports [19,54] (Fig. 4). In this review, we focus on the recommendations for non-competitive/leisure

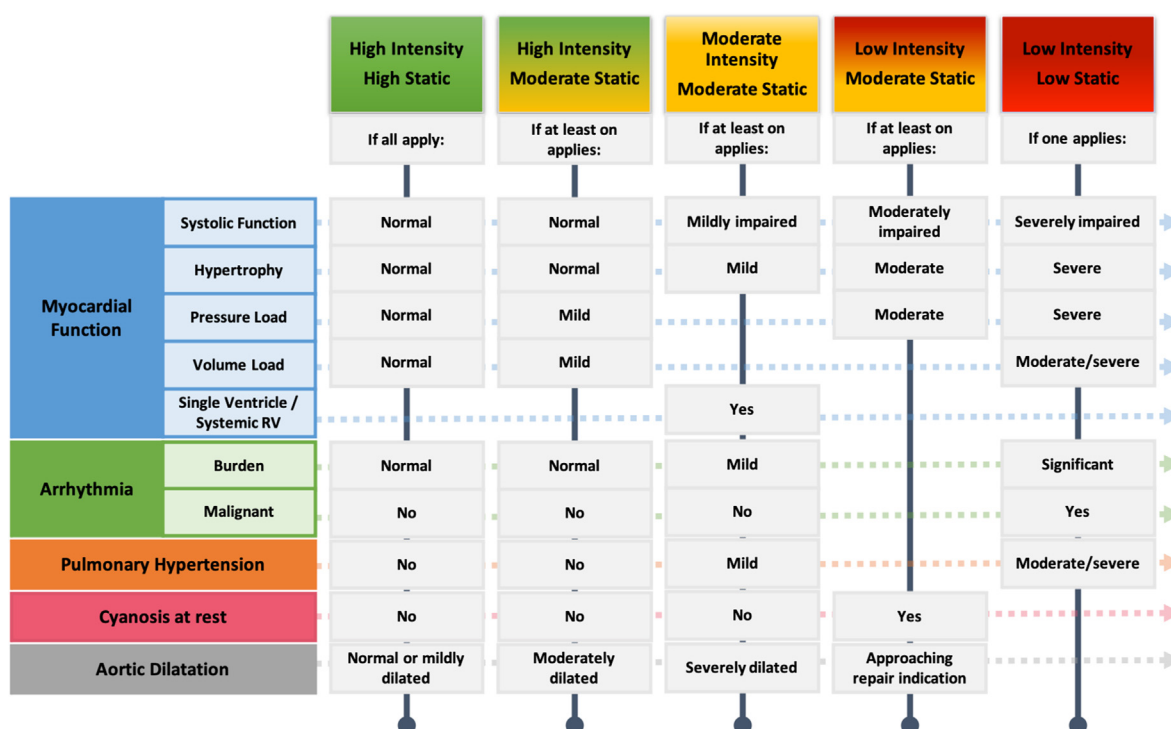


Fig. 4. Recommendations on the amount of static exercise and intensity of exercise for non-competitive sports based on 5 baseline parameters, adapted from Pelliccia et al. [19]. Acronym: RV, right ventricle.

sports in ACHD. Therefore, a careful investigation of 5 parameters at baseline (ventricular function, pulmonary artery pressures, aortic size, arrhythmias and oxygen saturation at rest and on exercise) is necessary. The peak VO_2 , peak HR and exercise time on CPET can be used to determine the intensity and duration of exercise prescribed. If no abnormalities are found during the initial assessment, patients can engage in high-intensity training with exercises or sports that include both high dynamic and static components. In patients with moderate aortic dilatation or mild LV pressure or volume overload, exercise with no more than a moderate static component is advised. In patients with severe systemic ventricular dysfunction, elevated pulmonary artery pressures or a significant arrhythmic burden, both endurance and static components should be performed at low intensity. Every exercise prescription should provide the type, frequency, duration and intensity of the exercise training. These components are summarized in Table 3. After exercise prescription, regular follow-up is advised to adjust the exercise prescription, especially in patients with high-risk features. Competitive sports should be reserved for patients with a good functional class (NYHA I or II) without any high-risk features, and patients should be reassessed every year clinically and by ECG, echocardiography and exercise testing [54].

Improving patients' compliance is also important, and can be enhanced by [16]:

- Reminding patients of the importance of exercise at every follow-up visit, adopting a positive attitude towards exercise, focusing on its benefits and discussing how it can be performed safely and be incorporated into their daily routine.
- Discussing any concerns, anxieties and fears regarding exercise training.
- Highlighting the benefits of exercise, not only in terms of prognosis, but also the more immediately tangible benefits of reduced symptoms, improved mobility, increased independence, weight loss and mental wellbeing.
- Promoting self-monitoring (for example through fitness wearables) and data sharing with their healthcare center, which may motivate

patients, and allows them to adjust their levels of training and detect complications (e.g. arrhythmias) [44].

3. Special considerations

3.1. Devices

A significant proportion of ACHD patients have permanent pacemakers for sinus node dysfunction (e.g. common in left atrial isomerism) or atrioventricular block. While permanent pacemakers are nowadays rate-responsive, the response is often suboptimal for younger individuals, limiting their ability to augment their cardiac output on exertion [8]. As the maximal HR is limited by the device, not by the patient's physical conditioning, the exercise prescription in patients with pacemakers should be based on the Borg scale (Fig. 1) rather than % maximum achieved HR. In patients with implantable cardioverter defibrillators (ICDs), the target HR should be lower than the ICD discharge threshold, in order to avoid inappropriate shocks during exercise. A pacing physiologist should ideally be present to adjust the PPM/ICD settings based on the results of the exercise test [19].

During sports, PPMs and ICDs should be protected to minimize the risk of direct collision, and certain high-intensity contact sports are contraindicated.

3.2. Anticoagulation

ACHD patients often have indications for temporary or lifelong anticoagulation. In patients taking anticoagulants, contact or collision sports should be discouraged, and the risk of intracranial bleeding discussed clearly.

4. Conclusions

Exercise is safe in the vast majority of ACHD patients and is essential for counteracting the detrimental effects of detraining on exercise capacity, quality of life and prognosis. A thorough assessment in an expert

Table 3
Components of exercise prescription.

Exercise prescription components to be discussed at every visit	
Type “What kind?”	Endurance versus resistance/strength (see Fig. 2)
Frequency “How often?”	Overall exercise volume measured in sessions per week, for example [53]: With intent to compete: - Competitive athletes (defined as >6 hours per week) - Recreational athletes (>4 h per week) With goal to physical fitness: - Exerciser: ≥ 2.5 h/week - Physical inactive: <2.5 h/week
Time/Duration “For how long?”	Recommended (in healthy individuals and simple forms of CHD) ^a : - Endurance: minimum 150 minutes/week of moderate intensity exercise - Resistance/Strength: 2–3 times per week
Intensity “How hard?”	Endurance prescription should be based on: Absolute intensity: energy expenditure during exercise (expressed in kcal/min or metabolic equivalents, METs^b) Relative intensity: % peak aerobic capacity (i.e., % peak VO₂ based on CPET) % maximal HR recorded during a CPET % HRR based on the Karvonen formula: % of maximal HRR (the difference between maximal HR and resting HR) added to resting HR Rate of perceived exertion (RPE) or Borg scale Intensity Levels: See Table 1 Resistance prescription should be based on: % RM: 1 RM is defined as the maximum amount of weight a person can lift throughout a range of motion for one repetition. 5 RM (maximum weight lifted during 5 repetitions) is a good representation of maximal strength % maximal HR or % HRR if exercise is mixed Intensity levels: - Light training: < 20% of 1RM - Moderate training intensity: 30–50% 1RM with 15–30 repetitions - Higher training intensities: 50–70% of 1RM with 8–15 repetitions

Adapted from Pelliccia et al. and Riebe et al [6,19]. Acronyms: HR, heart rate; HRR, heart rate reserve; max VO₂, maximal oxygen consumption; MET(s), metabolic equivalent(s); RM, repetition maximum.

^a For moderate or complex lesions, recommendations specific to the type of CHD may apply.

^b 1 MET is defined as the amount of oxygen consumed while sitting at rest, equal to 3.5 mL O₂/kg//min.

center, incorporating exercise testing, is recommended prior to exercise prescription. The intensity of the dynamic and static components of the exercise recommendation should be adjusted according to individual assessment and patients reviewed regularly to adjust the exercise prescription.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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