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SPECIAL ARTICLE
Congenital heart disease

Acquired cardiovascular disease in adults with congenital heart disease

A call to action for timely preventive measures—a clinical consensus statement of the European Society of Cardiology Working Group on Adult Congenital Heart Disease in collaboration with the European Association of Preventive Cardiology and the European Association of Percutaneous Cardiovascular Interventions

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Abstract

Rates of successful surgical repair and life expectancy for patients with congenital heart disease have increased dramatically in recent decades. Thanks to advances in diagnosis, treatment, and follow-up care, an ever-increasing number of individuals with congenital heart disease are reaching advanced age. The exposure to cardiovascular risk factors during their lifetime is modifying the outlook and late clinical trajectory of adult congenital heart disease (ACHD). Their disease burden is shifting from congenital to acquired, primarily atherosclerotic cardiovascular disease (ASCVD) with worrisome consequences. In addition, the complex background of ACHD often curbs appropriate preventive strategies by general practitioners or adult cardiologists. Comprehensive guidance for the prevention and management of acquired heart disease in ACHD patients is currently not available, as this topic has not been covered by the European Society of Cardiology (ESC) guidelines on cardiovascular disease prevention or the ESC guidelines for the management of ACHD. In this document, a state-of-the-art overview of acquired heart disease in ACHD patients and guidance on ASCVD prevention for both ACHD specialists and non-ACHD cardiologists are provided. The aim is to provide a clinical consensus statement to foster the development of a sustainable strategy for the prevention of ASCVD in a practical and simple-to-follow way in this ever-growing cardiovascular cohort, thus reducing their cardiovascular burden.

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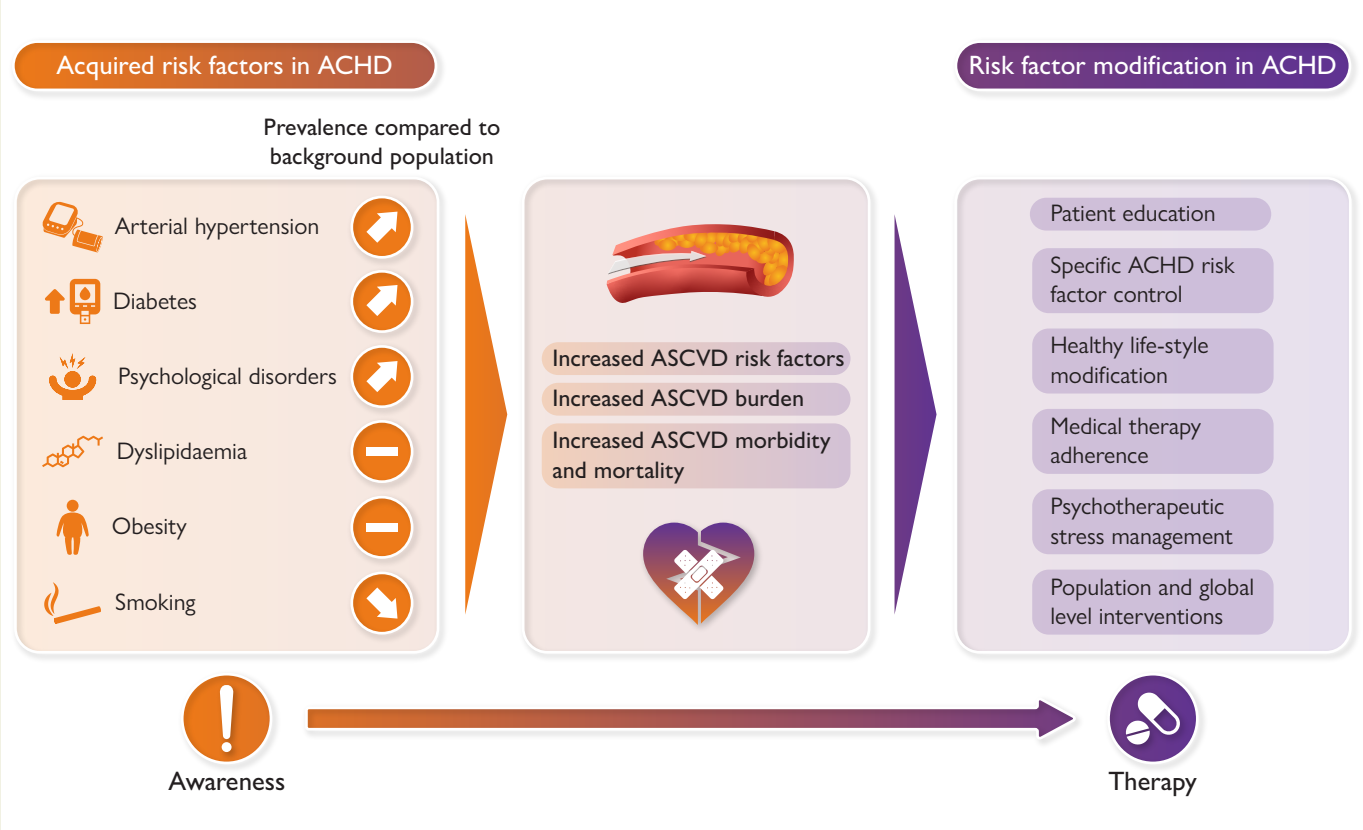
Graphical Abstract



Acquired cardiovascular disease in adults with congenital heart disease. Acquired cardiovascular risk factors are prevalent in ACHD and they are associated with increased ASCVD risk, ASCVD burden, and ASCVD morbidity and mortality in this population. Timely addressing and modifying acquired cardiovascular risk factors is paramount in ACHD. ACHD, adult congenital heart disease; ASCVD, atherosclerotic cardiovascular disease.

Keywords Adult congenital heart disease • Cardiovascular prevention • Cardiovascular risk factors • Transition medicine

Introduction

Altogether, ~90% of patients with mild, 75% with moderate, and 40% with complex congenital heart disease now reach the age of 60 years.[1] These numbers are expected to further increase in the coming years.[2] Continuous improvements in the diagnosis and treatment of adult congenital heart disease (ACHD) have brought about a growing population of older individuals with unique healthcare needs. In these patients, burden of morbidity and mortality has shifted from congenital towards acquired, primarily atherosclerotic cardiovascular disease (ASCVD) and their risk factors, even within the complex ACHD spectrum. Acquired heart disease not only represents the leading cause of death at the global general population level but also is a growing concern in ACHD. These patients are at increased risk for premature ASCVD, where treatment and outcome are more complex and severe due to underlying congenital heart disease.[3] Multiple reasons for accelerated ASCVD may include abnormal coronary artery anatomy, inflammation, scarring of the coronary arteries from surgical manipulation or the abnormal anatomy underlying congenital heart disease, reperfusion injuries during cardiac surgery, hypertension (coarctation patients), ventricular hypertrophy or dilation, aortopathy with dilated aorta and increased aortic stiffness, and associated genetic syndromes.[4–6]

When compared with the general population of similar age, patients with ACHD show (i) more pronounced risk factors for ASCVD[7,8]; (ii) earlier onset of ASCVD[3]; (iii) higher burden of ASCVD, even amongst patients with lower-complexity congenital heart disease[3,7,9,10]; and, finally, (iv) increased morbidity and mortality following cardiovascular events.[3,9] This excess cardiovascular risk in ACHD remains even after adjustment for conventional cardiovascular risk factors and, for example, includes a two-fold increased risk of acute coronary syndrome.[3,7] The 2020 European Society of Cardiology (ESC) guidelines for the management of ACHD represent a comprehensive report; however, there is scarce information on the risk factors and acquired heart disease management in this ageing population. Moreover, the 2021 ESC guidelines on cardiovascular disease prevention do not address the ACHD population; there is, in fact, no mention of the 'congenital heart disease' term in the prevention guidelines.[2,11]

Due to the alarming body of evidence regarding the prevalence and impact of ASCVD in ACHD, we aim to herewith provide our clinical consensus statements regarding conventional and ACHD-specific risk factors and suggest appropriate screening strategies and therapeutic goals for the ACHD population.

Risk factors for atherosclerotic cardiovascular disease and their association with adult congenital heart disease

The relationship between conventional risk factors and ASCVD is well established. In an ageing cohort of ACHD with abnormal anatomy, function, and physiology, the effect of these superimposed cardiovascular risk factors may well be amplified since these patients are often already at risk of systemic ventricular dysfunction, arrhythmia, and overt heart failure (HF). At least one modifiable risk factor is present in up to 80% of ACHD,[12] with overweight/obesity and systemic hypertension being the most prevalent.[13]

Overweight/obesity

Overweight and obesity have emerged as a growing global menace involving up to 40%–50% of ACHD patients,[14,15] a prevalence similar to the general population.[16] Overweight and obese ACHD patients have higher prevalence and severity of hypertension, hyperlipidaemia, and diabetes.[17] For example, obese patients who underwent arterial switch repair for transposition of the great arteries (TGA) for which coronary artery excision and re-implantation is an important component of surgery and potential risk factor for coronary abnormalities have increased markers of early cardiovascular disease including high blood pressure, left ventricular mass, increased carotid intima-media thickness, and higher triglyceride and lower high-density lipoprotein (HDL) cholesterol levels.[18]

Obesity in ACHD may be the result of interplay among multiple factors. During infancy, parental overprotection with overfeeding, representing false sense of better health in worried parents and historical recommendations of exercise restriction in this population, potentially contributed to a low level of physical activity and obesity. Education regarding appropriate healthy lifestyle is often inadequate; unhealthy diet with excessive intake of ultra-processed foods[19] and sedentary lifestyle are an early threat. In a sample of almost 4000 ACHD patients around the globe, only 31% achieved the World Health Organization's recommended level of physical activity.[20] Patients' uncertainty regarding the safety or benefit of regular physical activity represents an important barrier to physical activity.[21,22]

Systemic hypertension

The prevalence of systemic hypertension amongst ACHD patients is higher than in the general population,[8,23–25] spanning the entire age spectrum, encompassing both low complexity disease with essential hypertension[7,23] and specific conditions linked to secondary hypertension, such as aortic coarctation or Williams–Beuren syndrome. Adult congenital heart disease–related factors that may contribute to the multifactorial genesis of hypertension include arterial stiffness, altered endothelial function, renal disease (especially in cyanotic patients), and sleep apnoea.

Dyslipidaemia

Adult congenital heart disease patients seem to have lower total cholesterol but also lower HDL cholesterol in comparison with age- and gender-matched controls.[26] However, the impact of dyslipidaemia in ACHD is often underestimated.[8] A case-control study showed that ACHD patients are less likely than their peers to receive guideline-directed prescription of lipid-lowering agents.[26] Multiple reasons have been hypothesized, including lower awareness of hyperlipidaemia amongst paediatricians and lower acceptance of younger individuals to initiate a lifelong treatment. Within ACHD, patients with Fontan circulation with a chronic liver disease have a particular form of dyslipidaemia characterized by low cholesterol levels and low HDL cholesterol,[27] reflecting significant liver dysfunction with important prognostic implications, and associated increased clinical risk. In contrast, cyanotic ACHD patients often exhibit low cholesterol levels, a potentially protective factor[28–30] that can be explained by genetic determinants of cyanosis, hypoxaemia, erythrocytosis, and other related factors.

Diabetes and metabolic syndrome

Type 2 diabetes mellitus and metabolic syndrome are more prevalent in ACHD in comparison with the general population.[8,24,31,32] Beyond traditional risk factors, cyanosis seems to be an independent risk factor for diabetes in ACHD, probably caused by the negative impact of hypoxia on glucose metabolism.[32] According to the International Diabetes Federation, metabolic syndrome is 1.8-fold more common in ACHD than in matched controls;[33] some subpopulations such as patients with Turner syndrome exhibit an even higher risk.[34,35] Patients with Down syndrome have a four-fold increased risk for developing type 1 diabetes compared with the general population.[36,37] However, they usually have better metabolic control, despite lower insulin doses, and lower rates of diabetes-related complications.[36]

Cigarette smoking

Tobacco is the strongest behavioural risk factor for ASCVD. However, its prevalence among ACHD is lower than in the general population.[38] The highest rate of smokers was observed in functionally limited patients in whom smoking seems to be a coping mechanism.[39] Smoking in ACHD was associated with increased mortality in patients with coronary artery disease,[40] TGA,[41] and emergency department visits.[42]

Psychological disorders

Psychological disorders in ACHD can occur due to multiple factors including psychological trauma related to the history of cardiac surgeries and interventions, need for multiple hospitalizations, haemodynamic disorders, neurological insults, and associated genetic syndromes. Adult congenital heart disease patients face unique stressors across their lifespan, contributing to higher risk of mood and anxiety disorders. It is estimated that as many as one in two ACHD patients experience a mood or anxiety disorder at some point in their lives.[43,44] Significant anxiety and depression are associated with increased morbidity and mortality risk amongst ACHD.[45,46]

Inflamm-aging in adult congenital heart disease

Being born with congenital heart disease often implies a life path characterized by repeated exposure to multiple stressors related to the underlying congenital heart defect itself and its direct haemodynamic consequences, the stress related to the surgical treatment/s and the unique anatomy often including prosthetic material. One of the consequences of repeated stimuli, starting early in life, is possible activation of the inflammasomes. The inflamm-aging concept,[47] immune changes contributing to accelerated aging in response to a lifelong stress influenced by both the genetics and the environment, may be especially relevant in ACHD.[48] Low-grade chronic inflammation can increase the risk of atherosclerosis and insulin resistance which are, in turn, the leading mechanisms in the development of ASCVD. Increasing evidence points at chronic

Table 1 Specific congenital heart disease and associated risk for acquired heart disease

Underlying congenital heart disease	Considerations on the relevant risk
Shunt lesions	Increased risk of paradoxical embolism with stoke or embolic coronary obstruction.
Cyanotic lesions	Increased risk for diabetes. Arrhythmia propensity. Generally identical or possibly reduced risk of ASCVD due to a variety of underlying pathophysiologic factors including hypocholesterolaemia, hypoxaemia, up-regulated nitric oxide, low platelet counts, and hyperbilirubinaemia.
Aortic coarctation, LVOT obstructive lesions	Increased risk of ASCVD, including premature coronary artery disease due to arterial hypertension, co-existent endothelial dysfunction, or higher propensity to develop neointimal hyperplasia.
TGA after the arterial switch operation	Increased risk for coronary complications due to type of surgical repair and potentially accelerated coronary artery disease which may be asymptomatic due to cardiac denervation at surgery.
Congenitally corrected TGA and TGA after atrial switch operation (systemic right ventricle)	Myocardial perfusion mismatch in oxygen supply and demand with one/right coronary artery supplying the hypertrophied systemic right ventricle. Myocardial perfusion defects of unclear clinical relevance. Frequent arrhythmias. Heart failure of the systemic right ventricle.
Abnormal origin of the coronary artery	Anatomical risk factors for ischaemia and sudden cardiac death: interaortic–pulmonary pathway, intramural course, orifice anomalies (slit-like, acute-angle take-off or orifice >1 cm above the sino-tubular junction).
Previous valve replacement (surgical or interventional)	Increased risk of endocarditis with possible embolic coronary obstruction. Bioprosthetic valve degeneration over time. Mechanical valve risk of thrombosis.
Ebstein anomaly of the tricuspid valve	Often with ASD/PFO, risk of paradoxical embolism with stoke, or embolic coronary obstruction. Increased risk of heart failure. Increased risk of arrhythmia.
Fontan circulation	Dyslipidaemia with low cholesterol levels and low HDL cholesterol may reflect severe liver dysfunction and increased clinical risk.

ASCVD, atherosclerotic cardiovascular disease; ASD/PFO, atrial septal defect/patent foramen ovale; HDL, high-density lipoprotein; LVOT, left ventricular outflow tract; TGA, transposition of the great arteries.

inflammation state and immune alterations as relevant culprits for the progressive worsening of myocardial function in ACHD patients.[49–52] Inflammatory pathways, such as those related to tumour necrosis factor, the ubiquitin–proteasome system, nuclear factor-kappa B, interleukin-6, and glucagon-like peptide-1 (GLP-1), are also known to be involved in tissue wasting processes and cachexia, common among aging ACHD.[53]

Risk stratification assessment for atherosclerotic cardiovascular disease in adult congenital heart disease

In order to develop and implement appropriate systematic screening tools for ACHD, we advocate that screening for ASCVD risk factors is implemented at the general practitioner level and at each cardiology visit.

Are current cardiovascular risk scores directly applicable to ACHD populations? Various risk scores have been developed and validated. However, none has been validated in ACHD nor accounts for the specific underlying congenital heart disease risk factors in this complex population. Specific subgroups of ACHD (*Table 1*) seem to be at different risk for ASCVD consequent to their underlying congenital heart defect.[30,54–59] Epidemiologic data in line with pathophysiological models suggest an increased risk of coronary artery disease in patients with aortic coarctation,[58] left ventricular outflow tract obstruction, and/or hypertrophy.[60] Nevertheless, currently recommended scores for the general population may be helpful to guide risk stratification and ACHD patient counselling in the absence of tailored tools. The ESC guidelines on cardiovascular disease prevention recommend the use of the Systemic Coronary Risk Estimation 2 (SCORE2) and Systemic Coronary Risk Estimation 2-Older Persons (SCORE2-OP) in people <70 years and ≥70 years of age, respectively, for primary prevention.[11] Based on gender, age, smoking status, systolic blood pressure, and cholesterol, the estimation of 10-year fatal and non-fatal ASCVD risk is made and, consequently, patients are categorized into being at low, moderate, high, and very high ASCVD risk, which provides the basis for treatment strategies.[11] By extrapolation, these risk scores should be applied to all ACHD patients. Cardiovascular risk factors and appropriate risk modifications need to be addressed at each clinical visit at least as proactively in ACHD patients as in the general population and potentially even more vigorously given the presence of underlying heart disease and higher cardiovascular complication risks.

Risk factor management for atherosclerotic cardiovascular disease in adult congenital heart disease

Historically, patients with congenital heart disease have been mainly cared for by paediatric cardiologists who had limited exposure to ASCVD. As the ACHD population is aging, ASCVD burden becomes more prominent. Current priorities are to (i) increase patients' awareness about acquired heart disease and prevention strategies and (ii)

Table 2 General preventive measures regarding acquired heart disease for adult congenital heart disease

General measures
Patient education
• Discuss conventional, major risk factors, and potential consequences of ASCVD providing incidence and percentage.
• Discourage binge drinking, cigarette smoking, e-cigarettes, and recreational drug use.
• Explore treatment adherence and discuss 'false myth' regarding drug side effects; simplification of pharmacological treatment should be kept in mind to improve lifelong adherence.
• Educate regarding possible negative consequences of an unhealthy behaviour as well as provide in-depth explanation of positive aspects of implementing healthy lifestyle choices.
• Emphasize the importance of oral and skin hygiene to minimize the risk of infective endocarditis.
Lifestyle counselling
• Provide healthy lifestyle examples giving practical advices for everyday life: reduce daily screen time, take daily walks, take the stairs, cook healthy meals, reduce red meat intake, discuss benefits of Mediterranean diet, avoid 'comfort food', and limit coffee/tea consumption.
• Encourage regular exercise training for at least 30 min of exercise 4–5 times a week.
• Elaborate a personalized diet/exercise plan with the support of dietary/training specialists.
• Refer to a smoking cessation program, if relevant.
• Organize and promote informative patient group meetings and webinars.
Patient re-assessment
• Assess patient general mood, diet, quality of sleep, physical activity, adherence to treatment, cigarette smoking, and alcohol intake.
• Consider employing a questionnaire to monitor progress.
Assess for symptoms suggestive of atherosclerosis or conditions of increased risk
• Actively search for symptoms suggestive of angina, claudication, transient ischaemic attacks, and sleep apnoea.
• Perform appropriate diagnostic tests in case of symptoms or increased risk.
Blood pressure measurement
• Measure blood pressure at each clinical visit and encourage patients to self-measure at home (always on the right arm; upper and lower extremities in patients with aortic coarctation).
Psychological support
• Facilitate specialist support in case of coping difficulties and anxiety/depression symptoms.
Wearable devices
• Use of personal wearable devices on smartphones may be helpful to monitor physical activity and progress and stimulate further healthy lifestyle.
• Setting of daily activity goals may assist patients to maintain a healthy lifestyle.
• Often in young individuals, an invaluable help can come from the use of smart watches or phone health apps, warning them that their day has been too sedentary or that they did not reach the targets agreed; it may also apply to older individuals.
• When available, interrogate wearable devices to obtain biometric data trends.
Yearly
• Measurement of weight and body mass index; consider waist circumference for obese patients.
• Consider basic laboratory test screening including blood cell count, renal and liver function, electrolytes, lipid panel, and glycaemia.
• Oral hygienist appointment.
• Calculate the 10-year fatal and non-fatal cardiovascular disease risk using SCORE2 if <70 years and SCORE2-OP if ≥70 years and make a guideline-directed management of risk factors in primary prevention.
• Advise influenza, pneumococcal, and COVID-19 vaccination (especially in cyanotic patients and in patients with complex congenital heart disease, including patients with right atrial isomerism).

Continued

Table 2 *Continued*

2-year interval
• Consider exercise/cardiopulmonary exercise testing to assess exercise tolerance, cardiorespiratory adaptation to exercise, and stress-related symptoms and determine individualized training thresholds through a tailored exercise programme.
• In case of symptoms or ECG and/or blood pressure abnormalities during exercise, initiate further investigations.
3-year interval
• Perform diabetes screening including HbA1c or fasting blood glucose.
• Perform 2 h 75 g oral glucose tolerance test for all ACHD patients with altered fasting plasma glycaemia and consider it in patients >40 years of age with body mass index ≥25 kg/m^2.
• Thyroid function screening.

ACHD, adult congenital heart disease; ASCVD, atherosclerotic cardiovascular disease; HbA1c, glycated haemoglobin; SCORE, Systemic Coronary Risk Estimation 2; SCORE2-OP, Systemic Coronary Risk Estimation 2-Older Persons.

educate ACHD specialists and general cardiologists on the importance of assessing and treating risk factors. In *Table 2*, we propose general preventive measures regarding ASCVD for ACHD patients, whereas in *Table 3*, we provide expert opinion for screening and management of conventional major risk factors in ACHD.

Patient education and healthy lifestyle modifications

Education

Health-related education represents an essential component in efforts to engage, empower, and improve the lives of ACHD patients.[61] Adult congenital heart disease patients are relatively young, motivated, and technologically savvy, have a lifelong disease, and should be interested in assuming joint responsibility for their life and care. Clinicians' responsibility is to take a proactive role to educate, encourage, and support patients to make healthy life choices, which primarily include adequate physical activity, good diet, risk factor reduction, medication adherence, and stress management. Education regarding possible negative consequences of an unhealthy behaviour, as well as in-depth discussion of the positive effects of healthy lifestyle choices, should be addressed at each visit.

Physical activity

Positive results from exercise have been well demonstrated; physical activity reduces all-cause mortality and decreases cardiovascular risk factors regardless of underlying disease, age, or gender.[62] More specifically, exercise provides beneficial effects on functional and mental health status, cardiorespiratory fitness, muscle strength, and metabolic profile and is of great value in the fight against obesity. The current ESC guidelines on sport and exercise recommend participation in regular moderate exercise in ACHD individuals; hence, the focus has shifted from historical exercise restriction to exercise promotion.[63] For most ACHD patients, physical activity can be unrestricted and should be strongly encouraged; only very few patients will have disease that necessitates activity restrictions (such as risk of ventricular arrhythmia).[64] Sudden cardiac death in congenital heart disease is rare (<0.1% per year), and only 8% of deaths occur during exercise.[63] In this respect, assessing high-risk patients with formal cardiopulmonary exercise testing may be of value. In most instances, cardio-protective and beneficial mental effects of physical activity far outweigh risks of sudden cardiac death.[65] Adult congenital heart disease patients are known to be less active and have poorer aerobic capacity with the majority, including those with simple defects, having reduced peak oxygen uptake at maximum exercise (VO_2) as compared with healthy controls.[21,22]

Convincing patients to exercise

Uncertainty about the benefits and risks of physical activity in ACHD has long confined patients to a sedentary lifestyle. Compared with the general population, this sedentary lifestyle has been in place often since childhood. A crucial initial step is reassuring patients of the benefits and safety of physical activity.

Advise physical activity according to the cardiovascular status and pre-existing level of physical fitness

Advice regarding the type and intensity of physical activity depends on the current level of physical activity and the underlying cardiac pathology with potential residual lesion/s. Other considerations, such as the presence of a pacemaker/defibrillator or the use of anticoagulants, are relevant when choosing activity, and avoidance of contact sports is advised.

The six steps on practical physical activity approach include (i) medical and surgical history and physical examination, (ii) assessment of five baseline parameters (ventricular function, pulmonary artery pressure, aorta, arrhythmia, and oxygen saturation at rest and during exercise), (iii) cardiopulmonary exercise testing, (iv) recommendation for type of exercise, (v) recommendation for relative intensity, and (vi) follow-up.[66] The results of the exercise test help determine the relative intensity, taking into consideration pre-existing level of physical activity, peak VO_2, saturations, arrhythmia propensity or conduction abnormality, and blood pressure response to exercise.

Patient-tailored prescription of physical activity

Based on the assessment, physical activity prescription should specify frequency, intensity, duration, type, and progression.[63,66,67] It is important to discuss ways to incorporate physical activity within other demands and expectations of patients' daily lives (e.g. studies, employment, and family responsibilities). Patient choice in specific activities is essential as enjoyment helps to maintain a regular exercise regimen. Physical activity can be classified according to its static component and its dynamic component; in general, dynamic exercise is more suitable than static exercise. A strong static component, which characterizes an isometric contraction, such as weightlifting and rowing, strongly increases the arterial pressure and therefore the ventricular afterload. Conversely, a dynamic component, such as

Table 3 Proposed systematic screening for and management of conventional major risk factors for atherosclerotic cardiovascular disease in adult congenital heart disease

Overweight/obesity
Screening
• Monitor BMI at least annually.
• Use current general cut points to identify ACHD patients with overweight (BMI 25.0–29.9 kg/m^2) and obesity (BMI ≥30 kg/m^2).
• Screen for diabetes, measuring HbA1c, arterial hypertension, and dyslipidaemia annually for overweight and obese ACHD patients.
• Assess for and promptly treat obstructive sleep apnoea that is common among obese ACHD patients.
Management
• Patient education is crucial, including information about the direct correlation between BMI and the risk of ASCVD, type 2 diabetes, and all-cause mortality.
• Patient education. Counsel overweight and obese adults with other cardiovascular risk factors (arterial hypertension, hyperlipidaemia, and hyperglycaemia) that lifestyle changes that produce even modest weight loss (3%–5%) produce clinically meaningful health benefits, which are further exaggerated with greater weight loss.
• Advise food intake of 1200–1500 kcal/d for women and 1500–1800 kcal/d for men aiming towards a reduction of 500 kcal/d.
• Advise Mediterranean diet rich in fruit, vegetables, oilseeds, fish, olive oil, and cereals.
• Sugar consumption needs to be limited to 10% of daily intake.
• Alcohol consumption needs be limited to 100 g/week.
• The use of a dietician is advisable and beneficial for the long-term management.
• Bariatric surgery may be an option in clinically stable ACHD patients with a BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 with obesity-related comorbid conditions, who are motivated to lose weight and who have not responded to behavioural treatment to improve health.
Arterial hypertension
Screening
• Screen for hypertension all ACHD patients at each outpatient clinic visit and by means of periodic home blood pressure monitoring.
• Patients with native or repaired aortic coarctation require screening at least yearly with measurements taken on the right arm and on the lower limb to check for upper/lower limb pressure gradients suggestive of re-coarctation.
• In case of systemic to pulmonary anastomosis which involves a subclavian artery, blood pressure measurements are to be taken on the opposite arm.
Management
• In general, in ACHD patients target blood pressure <130/80 mmHg.
• In patients with increased risk of aortic dilation and rupture (i.e. aortic coarctation, aortopathies including Marfan and Turner syndromes, bicuspid aortic valve, TGA after arterial switch operation, and tetralogy of Fallot with dilated aorta), consider a lower threshold for therapeutic intervention targeting blood pressure <120/80 mmHg.
• In patients with systolic ventricular dysfunction (systemic right or left ventricle and single ventricle), consider a lower threshold for therapeutic intervention targeting blood pressure <120/80 mmHg.
• Ambulatory blood pressure monitoring can be employed in adult patients with aortic coarctation and other conditions both for hypertension screening and for monitoring response to therapy.
• Testing physically active adults with aortic coarctation for exercise-induced hypertension may be helpful for further management.
• Educate patients regarding lifestyle measures that have been shown to reduce blood pressure including salt restriction, regular physical activity, high consumption of vegetables and fruits, and maintenance of optimal body weight.
• Use of combination therapy of at least two antihypertensive drugs in a 'single pill' is preferred over monotherapy, especially in younger patients, to improve adherence and therapeutic success and reduce the risk of individual drug side effects.
Dyslipidaemia
Screening
• Screen for dyslipidaemia at least every 5 years.
• Consider obtaining standard serum lipid profile, measuring the concentration of total cholesterol, HDL-C, triglycerides, and LDL-C in men >40 years old and in women >50 years of age or post-menopausal.

Continued

Table 3 ***Continued***

Dyslipidaemia
• Regularly assess cardiovascular risk and LDL-C levels to inform and timely adapt lipid-lowering treatment.
• Adult congenital heart disease patients with ASCVD, i.e. stroke, peripheral arterial disease, diabetes with target organ damage, or at least three major risk factors, or severe chronic kidney disease (eGFR <30 mL/min/1.73 m^2) are considered at very high risk, target ≥50% LDL-C reduction from baseline or an LDL-C of <1.4 mmol/L (<55 mg/dL).
• Patients with vascular abnormalities, such as aortic coarctation or TGA after arterial switch operation, may benefit from a stringent lipid control.
• Test liver function yearly in patients with Fontan circulation or in patients with Ebstein disease on statin therapy.
Management
• Educate patients regarding healthy lifestyle benefits on dyslipidaemia; physical activity is proven to reduce total cholesterol and increase HDL-C levels.
• Nutraceuticals, such as red yeast rice, might have a role for the initial treatment of young patients at low risk.
• Prescribe high-intensity statin up to the highest tolerated dose to reach the LDL-C goals, and combine with ezetimibe in case the goals are not achieved.
• In very high-risk cases, employ a triple combination of a maximum tolerated dose statin, ezetimibe, and anti-PCSK9 monoclonal antibodies if the objectives are not reached.
Diabetes
Screening
• Perform at 3-year intervals fasting blood glucose or HbA1c.
• Screen annually ACHD patients with concomitant Down syndrome.
• Diagnosis is based on HbA1c ≥ 6.5% (48 mmol/mol) or fasting blood glucose ≥7.0 mmol/L (126 mg/dL) and based on oral glucose tolerance test, if still in doubt.
Management
• Patient education regarding lifestyle changes including smoking cessation, low saturated fat and high-fibre diet, reduction in energy intake, and physical activity are the most important initial steps since they can lead to significant improvement in glucose levels.
• Inform patients regarding monitoring systems that allow more frequent glucose measurements by simply placing their smartphone close to the sensor, with the additional benefit to transfer results to their family doctors or diabetologists to optimize treatment without continuously pricking the patients' fingers; especially younger ACHD patients, reluctant to disrupt their day and stop their activities to repeat glucose measurements, may benefit from this technique.
• In vast majority of ACHD patients, metformin still represents initial therapy; consider the addition of GLP-1RA or SGLT2i to reduce cardiovascular and/or cardiorenal adverse outcomes.

ACHD, adult congenital heart disease; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated haemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9; SGLT2i, sodium-glucose co-transporter 2 inhibitor; TGA, transposition of the great arteries.

cycling, running, or swimming, increases arterial pressure moderately and gradually. Regular moderate-intensity aerobic exercise, that is, training with a heart rate of 60%–75% of achieved maximum heart rate during cardiopulmonary exercise test, with a goal of at least 30 min of exercise 4–5 times a week, is largely safe and effective for most ACHD patients. The use of personal wearable devices may help monitor progress and stimulate further investment. In practice, for individuals who are unable to monitor their heart rate or have chronotropic incompetence or atrial fibrillation, the use of 'if you can talk while exercising rule' could be applied to approximate moderate relative exercise intensity.[66]

How to start and maintain physical activity

The initiation of sport can be done by the patient himself, through a cardiac rehabilitation centre, or with the assistance from an adapted sport professional. In cooperation with the patient's cardiologist, it has been shown that the use of physical activity professionals leads to better results in terms of long-term practice, especially when management extends to include possible psychological barriers.[68] Home-based exercise in cooperation with a rehabilitation centre has also shown to be safe and more adapted to the life and constraints of adults in active life.[69]

Obesity prevention and management

Prevention of obesity, often a chronic condition, is a key objective; education of patients and their families should start from early childhood. Additional educational investment should be made at transition from paediatric to ACHD care. The importance of body weight control should be discussed at every clinical appointment, and body mass index (BMI) should be obtained at least yearly. Overweight and obese individuals need to aim for a weight reduction to reduce the risk of arterial hypertension, dyslipidaemia, and type 2 diabetes, thus improving their cardiovascular risk profile. Weight loss is achieved primarily through calorie restriction and physical activity. In general, a loss of 500 kcal/d

Table 4 Proposed preventive measures to reduce specific risk conditions in adult congenital heart disease

Heart failure
• Highlight the importance of adherence to medications.
• Pursue early recognition and treatment of iron deficiency and anaemia.
• Maintaining proposed physical activity may delay onset of decompensated HF and/or HF worsening.
• Avoidance of dehydration or volume overload.
• Protection from infections by means of healthy and safe lifestyle pursuits and employment of influenza, pneumonia, and COVID-19 vaccinations.
• Careful use or avoidance, when possible, of agents that put renal function at risk, especially in cyanotic congenital heart disease.
Arrhythmias
• Substances such as alcohol, cigarettes, drugs, and caffeine may trigger arrhythmia.
• Patients should be made aware that binge drinking and recreational drug use may trigger arrhythmia and should be discouraged.
• Patients' education regarding signs of arrhythmia such as palpitations and pre-syncopal or syncopal episodes should be provided.
• Patients should know to seek prompt medical help in case of sustained arrhythmia onset.
• Thyroid function should be tested regularly during follow-up, especially in patients on amiodarone.
• Periodic screening for arrhythmia using standard ECG is advisable; consider Holter ECG in ACHD patients known to be prone to arrhythmias.
Coronary artery disease
• Early diagnosis and treatment of traditional risk factors is mandatory to prevent atherosclerotic coronary artery disease.
• Patients should be educated regarding symptoms, such as precordial oppression or increased breathlessness, especially in diabetic patients.
• Adult congenital heart disease patients should have a copy of their resting 12-lead ECG (e.g. on their mobile phone) for comparison at each clinical or emergency department visit.
• Any changes in symptoms or changes from baseline ECG pattern should trigger further investigations.
Stroke and systemic embolism
• In ACHD with simple defects, CHA_2DS_2-VASc and HAS-BLED risk factor–based approach appears appropriate.
• In more complex congenital heart disease, careful evaluation with low threshold for additional investigations is advisable.
• In ACHD with atrial fibrillation or intra-atrial re-entrant tachycardia, stroke prevention should include well-controlled vitamin K antagonist dose; consider direct oral anticoagulation on an individual basis assessment.
Infective endocarditis
• All patients need to be educated regarding maintenance of meticulous dental and skin hygiene: discourage high-risk patients from tattoos, skin piercings, and nail biting.
• Patients at the high risk of infective endocarditis need to understand the potential merits of antibiotic prophylaxis prior to invasive procedures and apply accordingly.
• All patients need to be aware of signs and symptoms of infective endocarditis and refuse empiric antibiotic therapy before blood cultures are taken.
Frailty
• Importance of early recognition and management of potential physical and mental decline.
• The highest risk for frailty is amongst complex ACHD, primarily patients with a Fontan circulation and with cyanotic defects, who are less likely to suffer from overweight; caution is advised in case of unintentional weight loss and lower weight as it may represent a proxy for impaired pathophysiology (e.g. cardiac cachexia, protein-losing enteropathy, and hypoperfusion).

ACHD, adult congenital heart disease; ECG, electrocardiogram; HF, heart failure.

can be expected with a food intake of 1200–1500 kcal/d for women and 1500–1800 kcal/d for men.[70] The low-caloric diet can be personalized according to the patient's dietary preferences and heart disease; the advice of a dietician is recommended by practice guidelines and beneficial at the long term.[70,71] A Mediterranean diet rich in fruit, vegetables, oilseeds, fish, olive oil, and cereals with limited consumption of red meat, cold cuts, and dairy products is advised. Sugar consumption, in particular sugar-sweetened beverages associated with increase in cardiovascular disease,[72] should be limited to 10% of daily intake,[11] whereas alcohol consumption should be limited to 100 g/week.[11,73]

Patients should be informed that alcohol is energy-dense: it provides 7 kcal/g and no nutrients.[11] Severely obese patients or those with obesity-related comorbid conditions may benefit from bariatric surgery. The decision of undertaking a surgical procedure needs to be weighed against the risks of a surgical procedure in patients with residual cardiac lesions.[74] Patients who are willing to undergo bariatric surgery should optimally be operated at an ACHD tertiary-level centre.[74] Currently, there are no data on the safety and efficacy of novel promising medications for weight loss, primarily GLP-1 receptor agonists (GLP-1RA)[75] in ACHD patients.

Arterial hypertension management

Arterial hypertension, defined as office blood pressure values ≥140/90 mmHg, in ACHD should be managed similarly to the general population and in accordance with international guidelines beginning with lifestyle modifications aiming at a target ≤130/80 mmHg.[76] Standard routine blood pressure measurements should be obtained at each visit, and patients should be instructed on self-measurements. Special attention should be paid in case of aortic coarctation repair due to the risk of restenosis and recurrence/persistence of hypertension even in the absence of re-coarctation.[77] In general, if there is a history of aortic coarctation repair, right arm blood pressure and lower limb blood pressure measurements should be taken to exclude differential pressures suggestive of re-coarctation.[78] A lower optimal cut-off values may be set at 120/80 mmHg for special ACHD subsets with increased risk of aortic dilation and rupture (i.e. aortic coarctation; aortopathies including Marfan, Turner, and bicuspid aortic valve; TGA following arterial switch repair; and tetralogy of Fallot) or systolic dysfunction (i.e. systemic right ventricle and single ventricle).

In addition to lifestyle measures known to reduce blood pressure (salt restriction, alcohol avoidance, high consumption of vegetables and fruits, weight reduction, and regular physical activity),[76] most patients will require drug therapy to achieve optimal blood pressure control. The five major classes of drugs [angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), beta-blockers, calcium channel blockers (CCBs), and diuretics] form the basis of antihypertensive therapy. In patients with aortic coarctation and aortopathies, ACEI or ARB, which have been advocated to reduce the risk of progressive aortic dilatation,[79] and beta-blockers, in the absence of significant aortic regurgitation, should be considered as initial therapy.[11,80] The most effective evidence-based treatment strategy to improve blood pressure control is one that encourages the use of combination treatment in most patients, especially in the context of lower blood pressure targets; the approach enables the use of 'single-pill combination therapy' as initial therapy to improve adherence to treatment and reduce the likelihood of individual drug side-effect. Exception to this strategy are frail, older patients.[76] Uncontrolled hypertension should trigger additional diagnostics, for example, in aortic coarctation, appropriate imaging is needed to rule out significant re-coarctation before treatment uptitration. Vasodilators should be used with caution in those with significant re-coarctation to prevent pre-renal acute renal injury and in patients with Eisenmenger syndrome for their potential to augment right-to-left shunting. During pregnancy, ACEIs and ARBs are contraindicated, whereas alpha methyldopa, labetalol, nicardipine, and nifedipine are all good alternatives.[76]

Dyslipidaemia management

The first-line intervention in case of elevated lipid levels is promotion of physical activity, proven to reduce total cholesterol and increase HDL cholesterol levels. Nutraceuticals, such as red yeast rice, might have a role for the initial treatment of young patients at low risk.[81] Statin treatment initiation should follow a guideline-based stepwise approach, and total cardiovascular risk reduction should be individualized; this can be more specific if goals are defined. The use of goals can also assist patient–doctor communication. An ultimate low-density lipoprotein (LDL) cholesterol goal of <1.4 mmol/L (55 mg/dL), <1.8 mmol/L (70 mg/dL), <2.6 mmol/L (<100 mg/dL), and <3.0 mmol/L (<116 mg/dL) should be considered in patients with very high, high, moderate, and low cardiovascular risk, respectively.[82] High-intensity statins should be combined with ezetimibe when goals are not achieved with the maximum tolerated dose of statin.[82] Bempedoic acid, an oral cholesterol synthesis inhibitor, recently approved in several countries, is mainly considered in combination with ezetimibe in patients with statin intolerance but may be considered also in patients unable to reach LDL cholesterol goals in addition to the maximum tolerated dose of a statin.[83,84] In cases of very high cardiovascular risk including secondary prevention or/and familial hypercholesterolaemia, a combination of a maximum tolerated dose statin, ezetimibe, and anti-proprotein convertase subtilisin/kexin type 9 (PCSK9) monoclonal antibodies are encouraged if the goals are not reached.[11] Furthermore, inclisiran, a small interfering ribonucleic acid, shown to reduce LDL cholesterol by 50%–55% when applied subcutaneously twice a year,[11,85] may offer an appealing alternative for young ACHD patients. Liver function should be tested regularly in patients on statin therapy especially for those with a Fontan circulation and with chronic right-sided HF. Some ACHD patients with vascular abnormalities such as aortic coarctation and TGA after arterial switch repair or post Ross surgery may benefit from a more stringent lipid control.

Diabetes mellitus management

Type 2 diabetes has a long asymptomatic pre-clinical phase, which frequently goes undetected; regular screening, detection, and early treatment are the best strategies.[11] Screening and treatment should follow international guidelines for diabetes management with fasting blood glucose or glycated haemoglobin (HbA1c) (which can be done non-fasting) done at 3-year intervals, especially in those >40 years of age with BMI ≥25 kg/m^2.[86] Lifestyle changes are the most important initial step including smoking cessation, low–saturated fat and high-fibre diet, reduction in energy intake, and physical activity. For motivated, younger patients considerable weight loss with use of low-calorie diet followed by a weight maintenance phase early after the diagnosis can lead to diabetes remission and should be accentuated.[86] A target of HbA1c accepted for the majority of adults is <7.0% (53 mmol/mol); however, early in the course of diabetes, those who are not frail should target ≤6.5% (48 mmol/mol). In vast majority, metformin still represents the initial therapy, whereas in patients who have not reached their target HbA1c, addition of GLP-1RA and/or sodium-glucose co-transporter 2 inhibitor (SGLT2i) is helpful to reduce cardiovascular adverse outcomes.[87]

Psychotherapeutic stress management

Adult congenital heart disease patients are at the increased risk of mood and anxiety disorders due to health-related stressors such as the need for additional medical interventions and declining health status.[12] The diagnosis of acquired disease carries additional challenges. Known risk factors for ASCVD include unhealthy behaviours (e.g. tobacco use, poor diet, and sedentary lifestyle), emotional distress (e.g. depression and anxiety), stress (chronic, situational, and perceived),

social isolation, and loneliness.[88] Stress is a known risk factor for a new diagnosis, hospitalization, and mortality from coronary artery disease.[89] In contrast, positive emotional well-being (e.g. optimism, sense of purpose, and stress management) and supportive interactions between patient and medical professionals, family, and friends can all contribute to better outcomes.[88,90] Psychological interventions should target risk factors related to adherence with heart-healthy behaviours and psychosocial well-being including stress management.

Prevention of accelerated senescence

Prevention of accelerated senescence in patients with congenital heart disease over different life stages includes physiological, psychological, and behavioural predictors of accelerated aging to be identified. While there are no targeted interventions that could specifically be implemented, physical activity and nutrition have shown benefit in telomere maintenance.[91] Epigenetic modifications such as DNA methylation, histone modifications, and non-coding RNA can be chemically reversible and potential targets for rejuvenation strategies.[92] However, among currently available options, testosterone might be useful to counteract the development of HF and cachexia through the inhibition of inflammation and the direct stimulation of protein synthesis in the muscle.[93,94] Vitamin D supplementation might be helpful to protect muscle wasting.[95] However, these data need further confirmation before a final conclusion can be drawn. Regarding established cardiac medications, pre-clinical research suggested that ACEIs and ARBs may exert a favourable impact on insulin sensitivity, inflammation, and mitochondrial function, thereby contributing to muscle protection.[96] The effects of SGLT2i can counteract the development of myocardial fibrosis induced by pressure overload.[97] These might be beneficial in specific congenital heart defects, such as in systemic right ventricular failure.[98] In addition, since elimination of glucose through urine produces a net loss of calories, SGLT2i determines a systemic metabolic shift, positively affecting multiple pathways involved in aging, including inflammasome.[99,100] Further research on senescence in ACHD is clearly needed to promote the development of more effective and personalized preventive measures.[101]

Preventive measures for specific risk conditions in adult congenital heart disease to optimize cardiovascular health

In *Table 4*, we propose measures to reduce the specific risk conditions in ACHD.

Heart failure

Heart failure represents the leading cause of premature death in contemporary cohorts of ACHD[102] with the prevalence being the highest amongst patients with complex anatomy, such as systemic right ventricle or single ventricle physiology.[103] The mechanism of HF in ACHD is multifactorial and includes the underlying anatomic defect and/or residual haemodynamic lesions causing volume and/or pressure overload, systemic or pulmonary hypertension, cyanosis, myocardial ischaemia from either a supply and demand mismatch or coronary anomalies or injury, arrhythmias, dyssynchrony, and/or chronotropic incompetence. In an aging ACHD population, acquired cardiovascular factors such as arterial hypertension or atherosclerotic coronary artery disease further increase the risk of HF and aggravate its clinical presentation, management, and outcome.[3,7] Reducing HF risk and optimizing HF management requires patient education, adherence to medical therapy, self-care, and lifestyle advice to improve quality of life, lower hospital readmission rates, and reduce mortality.[104] Patients should understand the cause of HF, symptoms, and disease trajectory. In line with professional advice, indications and dosages of drugs and knowledge such as when to self-manage diuretic therapy and regulate fluid intake are more effective when clearly explained.

Arrhythmias

Arrhythmias are a common cause of morbidity and impaired quality of life and jointly with HF represent the leading cause of hospitalization and death in ACHD.[105] Patients with a Fontan physiology, systemic right ventricles, and Ebstein anomaly are particularly prone to arrhythmia. Careful assessment of clinical signs and symptoms, such as palpitations, pre-syncopal or syncopal episodes, and review of lesion specific risk factors, should be applied at each clinical visit in order to lead to timely action such as modifying drug therapy, catheter ablation, device insertion, and/or haemodynamic intervention as per need, to prevent further deterioration.

Coronary artery disease

Patients with congenital coronary artery anomalies, TGA after arterial switch repair and Ross or Ross-PEARS procedures, coarctation of the aorta, left ventricular outflow tract obstruction, and external compression of the left coronary ostium (as per dilated pulmonary artery in patients with Eisenmenger syndrome) and other patients with previous manipulation of coronary arteries during cardiac surgery have an increased risk of coronary artery disease. Systemic or pulmonary hypertension compression of the left main coronary artery between the pulmonary trunk and aorta can cause angina, dyspnoea, or sudden death, and this should also be taken into account. Moreover, although cyanotic conditions convey some protection from atherosclerotic coronary artery disease,[30] cyanotic patients are not immune to standard cardiovascular risk factors; such exposure appears to increase the risk of coronary artery disease for these patients to a similar extent as in the general population.[4] Many ACHD patients have abnormal baseline electrocardiogram (ECG) often with prolonged QRS duration, bundle branch block, signs of ventricular hypertrophy, and nodal or other rhythm disturbances that needs to be taken into consideration when assessing signs of ischaemia. Patients should have a copy of their baseline ECG in their mobile phone for reference purposes.

Stroke

Adult congenital heart disease patients, particularly those aged <60 years, have an increased risk of stroke and higher post-stroke mortality than the general population.[106,107] Previous shunt operations, residual/unrepaired septal defects, left-sided mechanical valves, and aortic coarctation are additional risk factors,[40,108] alongside HF, diabetes mellitus, recent myocardial infarction, and arrythmia.[106] Despite the fact that 25% of stroke cases are related to loss of sinus rhythm,[109] screening for atrial fibrillation still represents a challenge. Implantable event recorders may be helpful and complementary to Holter ECG in this setting. The use of wearable ECG devices, capable of long monitoring times, may facilitate to identify individuals with undiagnosed atrial fibrillation.[110] Appropriate and timely thromboprophylaxis and importance of adherence to it when indicated needs to be explained to patients to prevent stroke and other thromboembolism.

Thrombosis and thromboembolism

Thromboembolic complications seem to be 10–100 times more common in ACHD. Predisposing factors for thrombosis include dilated cardiac chambers with sluggish flow, tachyarrhythmias, intracardiac prosthetic material, pacemaker or defibrillator transvenous leads, intracardiac shunts, and associated hypercoagulable state.[111] Specific ACHD lesions showing a particularly high risk of thromboembolic complications include native atrial septal defects, Fontan circulation particularly when right-to-left shunts are present, uncorrected cyanotic heart disease, and Eisenmenger complex. Anticoagulation therapy options need to be assessed on the individual basis. Patients with central cyanosis have a higher risk of thromboembolism because of low cardiac output; however, they also have higher bleeding diathesis, posing additional challenges in treatment that must be taken into account.

Frailty

Recognition of frailty in ACHD patients is relevant, as it is associated with a faster clinical decline and higher clinical risk.[112] Traditionally associated to old age, it has become clear that frailty deriving from chronic disease has different indicators compared with age-related frailty. Patients with complex congenital heart disease are more frequently affected by dementia, HF, sarcopoenia, and reduced bone mineral content and density, even at relatively young age compared with the general population.[113,114] Currently employed criteria used to identify frailty, the physical frailty phenotype and the Frailty Index of Accumulative Deficits,[112] do not address the specifics of ACHD. Additional components should be added to existing frailty score systems, or dedicated ACHD scales should be developed, encompassing the heterogeneous landscape of ACHD, the stage of clinical evolution, and the disease history, including undertaken/planned interventions or clinical complications developed during the life trajectory of the individual ACHD patient. More precision would allow improved risk stratification but also the design of specific health interventions.[115]

Informed discussion

Shared, informed decision-making with the patient and family is vital to foster this bidirectional communication between the patient and the healthcare provider. Such a conversation aims to gain an in-depth understanding of patient's preferences, needs, and priorities, perform a structured benefit–risk assessment, formulate advice for ASCVD risk reduction, and reach consensus on actions to be taken.[116] Several elements should be included, such as personalized risk information, patient risk perception, level of self-efficacy/self-management expressed by patient, and potential competing priorities/needs. Patients often misperceive their ASCVD risk which may have a significant impact on patients' level of motivation;[117] healthcare providers need to recalibrate those misperceptions and are advised to use positive framing, focusing on the relative risks and potential benefits of risk-reducing actions as a mean of increasing patient's motivation.[118] To increase patient level of empowerment, risk factor modification ought to be discussed in light of patient ability to put the risk-reducing actions into practice. Multiple factors need to be considered including the patient's age, ethnicity, comorbidities, frailty status, life expectancy, beliefs, expectations, socioeconomics, family and occupational status, and willingness to consider change.[119]

Population- and global-level interventions

Efforts towards patient education, engagement, and empowerment should be expanded to the public and community, in addition to patients. Public health policy and advocacy towards a healthy lifestyle should account for the growing ACHD population and their specific needs. Health policies should focus on risk factors that have the greatest effects on averting ASCVD and death globally, with additional emphasis on risk factors of greatest importance in specific groups of countries.[120] A dedicated specific ACHD population strategy for ASCVD prevention represents the initial step, whereas the next step includes its implementation in practice. Monitoring and evaluation of this process at national and international levels is important for continuous improvement and for ensuring that such positive changes in life choices are sustainable.

Generation of clinical consensus statements

Steering committee

The steering committee was composed of two experts in ACHD (M.B. and M.A.G.), one expert in cardiovascular prevention (A.L.), and one interventional cardiologist (S.D.R.). The process was articulated in the following steps: (i) enrolment of the expert panel, (ii) generation of clinical statements based on gaps of evidence in the ACHD population, (iii) definition of consensus and agreement using a two-round Delphi approach, and (iv) generation of final wording for the statements supported by consensus. *Online survey form*. As the first step, an electronic form survey was developed by the steering committee to address the most relevant opened clinical issues not covered by evidence-based recommendations.

Expert panel

The expert panel that contributed to the rating was composed by a multidisciplinary group, including all 11 co-authors, with expertise in congenital heart disease, cardiovascular prevention, adult cardiology, cardiovascular interventions, and cardiovascular imaging, representing the ESC Working Group of Adult Congenital Heart Disease, the European Association of Percutaneous Cardiovascular Interventions, and the European Association of Preventive Cardiology. All experts received questionnaires by electronic form. Responses were collected from September to October 2022. *Generation of statements*. Based on the survey results, proposals of amendments of proposed statements were discussed. After discussion and final approval, 92 statements organized in 3 main sections were written and presented in *Tables 2–4*.

Rating process

For the first round, all experts received access to the online rating form and were asked to review the statements drafted by the steering committee and declare agreement or disagreement. In the latter case, experts were asked to indicate whether they disagreed and therefore proposed deleting of the statement or proposed alternative wording or an amended version of the original statement in case of partial disagreement. After the first round, statements were organized in textual form into three tables (*Tables 2–4*) and sent back to all experts for final

approval. For this second round, experts were invited to either accept or reject statements.

Conclusion

Early patient health education on the importance of healthy lifestyle choices and meticulous risk factor control are paramount to reduce the risk of acquired heart disease in adulthood for patients born with congenital heart disease (Graphical Abstract). This is highly relevant to an aging ACHD population, given the clinical complexity inherent to their condition and worrisome increase in prevalence of ASCVD amongst them. Hence, cardiovascular prevention merits vigilant attention and continuing investment from multiple disciplines, including paediatric cardiologists, general practitioners, adult cardiologists, ACHD specialists, and other specialities, including interventions at national and international levels to restrain the growing burden of acquired heart disease in ACHD and optimize further the life trajectory for these patients.

Supplementary data

Supplementary data are not available at *European Heart Journal* online.

Declarations

Disclosure of Interest

S.D.R. participated on a Data Safety Monitoring Board/Advisory Board for Sanofi, Amarin, Boehringer Ingelheim, Abbott Medical, Daiichi Sankyo, and Amgen. L.D.S. had support for attending meeting by Daiichi Sankyo. G.D. was supported by Janssen Global.

Data Availability

No data were generated or analysed for this manuscript.

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