



Cardiovascular Risk Factors and Adults with a Congenital Heart Defect! Should we be More Careful?

Nazanin Khadem (MD)¹, Behzad Alizadeh (MD)², Shirin Sadat Ghiasi (MD)^{3*}

¹ Student Research Committee, Urmia University of Medical Sciences, Urmia, Iran

² Associate Professor of Pediatric Interventional Cardiology, Pediatric Department, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

³ MD, Research Fellow, Pediatric and Congenital Cardiology Division, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

ARTICLE INFO

Article type

Review article

Article history

Received: 24 Dec 2023

Revised: 11 Mar 2024

Accepted: 17 Mar 2024

Keywords

CHD

Cardiac Disorder

Obsession

Physical Activity

ABSTRACT

Introduction: Congenital Heart Disease (CHD) is a common condition affecting 8 in 1,000 live births and is no longer limited to pediatric cases due to advances in medical techniques. Thus, the increase of chronic diseases and the development of comorbidities become noticeable and the evaluation of cardiovascular risk factors in patients is necessary.

Methods: A systematic review of English and Persian literature was performed by electronic search in databases of Scopus, PubMed, Science Direct, Up-to-date, and ProQuest from 2000 to 2021. The study focused on all articles on risk factors for congenital heart disease in adults. Initially, 200 articles were extracted and evaluated by the research team according to the inclusion criteria, and 74 articles were finally selected. The association between adults with congenital heart disease and the risk of cardiovascular disease by conducting a narrative was evaluated.

Results: Out of six groups of risk factors that were recognized for adults with congenital heart disease, the level of physical activity is highly impressive. The findings showed that while women were less active and more likely to be obese, male patients had a greater prevalence of smoking and high blood pressure. Although age is discussable specifically based on the other medical factors, sex was not individually determined for the self-effective risk factor.

Conclusion: Cardiovascular risk factors remain the remarkable leading obsession across time in the world. Alarmingly, the increasing rate of CHD in adults requires the best healthcare investments.

Please cite this paper as:

Khadem N, Alizadeh B, Sadat Ghiasi Sh, Cardiovascular Risk Factors and Adults with a Congenital Heart Defect! Should we be More Careful?. Rev Clin Med. 2024;11(1): 1-7.

Introduction

The demographics of patients with severe adult congenital heart disease (ACHD) have changed in recent years. Severe congenital heart disease (CHD) is estimated to occur in approximately 8 per 1,000 live births (Goeddel et al. 2020). CHD is the most common isolated congenital organ malformation. Worldwide, 1.35 to 1.5 million children are born with CHD each year, about 45% of them with moderate or complex heart defects

and the remaining 55% with simple heart defects (Neidenbach et al. 2018).

Congenital heart disease is not limited to pediatric clinical practice. Medical and surgical improvements have resulted in most children with congenital heart disease surviving to adulthood. Unfortunately, many patients with congenital heart disease require further evaluation and some form of surgical intervention, as well as medical treatment and

***Corresponding author:** Shirin Sadat Ghiasi,
Pediatric and Congenital Cardiology Division, Faculty of
Medicine, Mashhad University of Medical Sciences, Mashhad,
Iran

E-mail: shirin.ghiasi@gmail.com

Tel: + 985131802024

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

lifelong follow-up. (Lane, Lip, and Millane 2002).

It is currently estimated that over 90% of infants born with CHD will live to adulthood. These patients are more likely to develop chronic problems and comorbidities as they age. For example, chronic heart failure is known to affect 25% of patients with CHD by the age of 30. This incidence increases with age. CHD patients are also more likely to develop acquired cardiovascular diseases, as 80% of young adults with CHD have at least one cardiovascular risk factor. (Neidenbach et al. 2018).

Some children with congenital heart disease (CHD) still suffer from long-term cardiovascular complications, despite remarkable success in surgical and medical management of CHD (Wang et al. 2019).

In this research, we are investigating whether adults have the same cardiovascular risk factors as other healthy individuals without congenital heart disease.

Materials and Method

We conducted a review (narrative) study by electronically searching the Scopus, PubMed, Science Direct, Current and ProQuest databases for English and Persian language literature from 2000 to 2021. The databases were searched using the keywords “congenital heart disease” and “risk factors” or “predisposing factors” or “predictive factors” and “biological agents” or “social factors” or “pathophysiology” or “hormonal factors” or “lifestyle” and “cardiovascular”. For the PubMed database evaluation, keywords were selected according to the MeSH system. Cross-sectional, cohort, case-control, intervention and review articles on risk and predisposing factors of congenital heart disease in adulthood were included.

After removing the authors' names, 200 article abstracts were extracted from the initial evaluation of article titles and assessed for inclusion criteria by the research team. If there was disagreement between the two reviewers about the presence of inclusion criteria, the article abstract was given to the third reviewer, whose opinion was decisive for the inclusion of the article in the review. In this review article, we conducted a comprehensive evaluation of the included studies to ensure high-quality and reliable results. The quality of the articles was assessed using established criteria such as study design, sample size and representativeness, data collection methods, risk of bias, and statistical analysis.

This process was designed to assess the internal validity, reliability, and overall methodological

rigor of the included studies. After article adjudication, 74 articles were identified as eligible. The full texts of the available articles then were prepared. In the case of articles with unavailable full text, correspondence was conducted with the authors to request them to send the full text of the article after explaining the purpose of the study.

The articles were assessed by three members of the research team with regard to the criteria for inclusion. If the inclusion criteria were met, the article was reviewed and the content related to the topic was extracted. This allowed the main findings of each study to be noted in the article specifications under the title concerned. After the collection, the material and content were categorized according to the scientific content in their respective subgroups. Our aim in this study was to evaluate the association between adults with congenital heart disease and the risk of cardiovascular disease using a narrative approach.

Results and Discussion

Analysis of the articles identified five groups of risk factors for adults with congenital heart defects: psychological, obstetric, biological and hormonal, social, and lifestyle. Age, gender, high blood pressure, type 2 diabetes, physical activity, BMI, smoking, and contracting the COVID-19 infection are some of the risk variables that we have listed.

Covid 19

The COVID-19 pandemic poses a significant challenge to the care of patients with serious chronic diseases, including ACHD. The virus has a direct effect on the cardiovascular system, and pre-existing cardiovascular disease is a major risk factor for morbidity and mortality in this setting.

Even though ACHD patients have significant cardiovascular disease, not all patients with CAD should be considered high risk because of their younger age and the heterogeneity of anatomy and physiology across the spectrum of CAD. Based on the anatomy of the significant cardiac lesion and additional physiological considerations such as symptoms. The conflicting statistics regarding risk stratification for ACHD are shown in Figure 1.

For practical reasons, Radke et al. 2020 divide patients into three risk categories: low risk, medium risk, and high risk. Low-risk patients would not be prevented from carrying out their normal activities, including those in healthcare. Intermediate-risk patients are advised to reduce physical contact with customers and co-workers, and healthcare Jobs involving minors

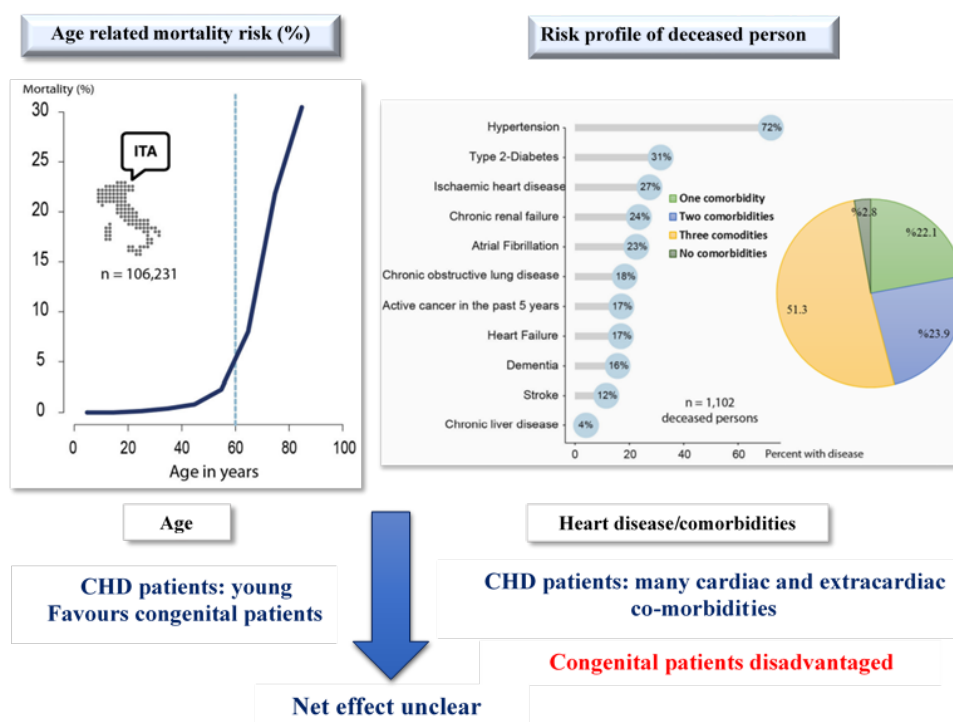


Figure 1. Data from over 100,000 affected patients in northern Italy show that severe COVID-19 and death are typically associated with advanced patient age. Conversely, the majority of ACHD patients are young (Marelli et al. 2014), which would imply a reduced risk. However, in our dataset, the majority of non-congenital COVID-19 patients who died had one or more comorbidities, mostly of a cardiovascular nature. According to this data (Dataset Minichini, Kaggle, based on Italian Civil Protection Department data, 21 April 2020), pre-existing cardiac involvement (as observed in ACHD) is a significant risk factor for a poor outcome. Therefore, it is currently unknown how these conflicting elements may ultimately affect the outcome of ACHD. Congenital heart disease is referred to as CHD or adult congenital heart disease (Radke et al. 2020).

or patients with COVID-19 who are not able to comply with infection control procedures are not recommended.

Self-isolation at home and individualized work exemptions are recommended for patients at high risk. It is worth noting that the treatment of patients with ACHD should be based on patient risk and clinical status if SARS-CoV-2 testing results are positive. Figure 2.

Physical Activity

The general consensus is that children with CHD have lower levels of PA than their healthy peers (Longmuir et al. 2013). This is based on earlier research conducted more than 25 years ago that assessed PA levels in children with severe CHD. Since then, at least 18 publications have compared PA levels in children with CHD to a healthy population (Casey, Craig, and Mulholland 1994). The majority of research studies included adolescent patients, but four included younger school-aged children (Casey, Craig, and Mulholland 1994; Leitch et al. 2000; Massin et al. 2006; Barbour-Tuck et al. 2020) and one had a preschool population (Stone et al. 2015). The percentage of female subjects ranged from 32 (Brudy et al. 2020) to 76 percent (Ewalt et al.

2012), and the number of patients with CHD ranged from 7 (Leitch et al. 2000) to 316 (Chen et al. 2007). In most studies, individuals had a wide range of cardiac diagnoses. Three studies also included heart transplant recipients (Barbour-Tuck et al. 2020; Lunt et al. 2003; Voss et al. 2017). In three studies, only patients with Fontan circulation were included (McCrinkle et al. 2007; Hedlund et al. 2016; Härtel et al. 2020). The remaining 4 studies compared PA levels with previously published normative data from healthy cohorts, whereas the remaining 14 included a control group of healthy age-matched children (Lunt et al. 2003; Voss et al. 2017; McCrinkle et al. 2007; Ray, Green, and Henry 2011). Daily PA levels have been assessed using a variety of techniques, including objective measures and self- and parent-reported questionnaires (van Deutekom and Lewandowski 2021). For objective measurements, accelerometry was most commonly used. Two studies used the doubly labeled water method (Leitch et al. 2000) and heart rate monitors (Massin et al. 2006). All studies provided information on PA levels, defined as time spent in PA, frequency of activity, PA scale score, or energy expenditure. In addition, eight studies (Massin et al. 2006; Stone

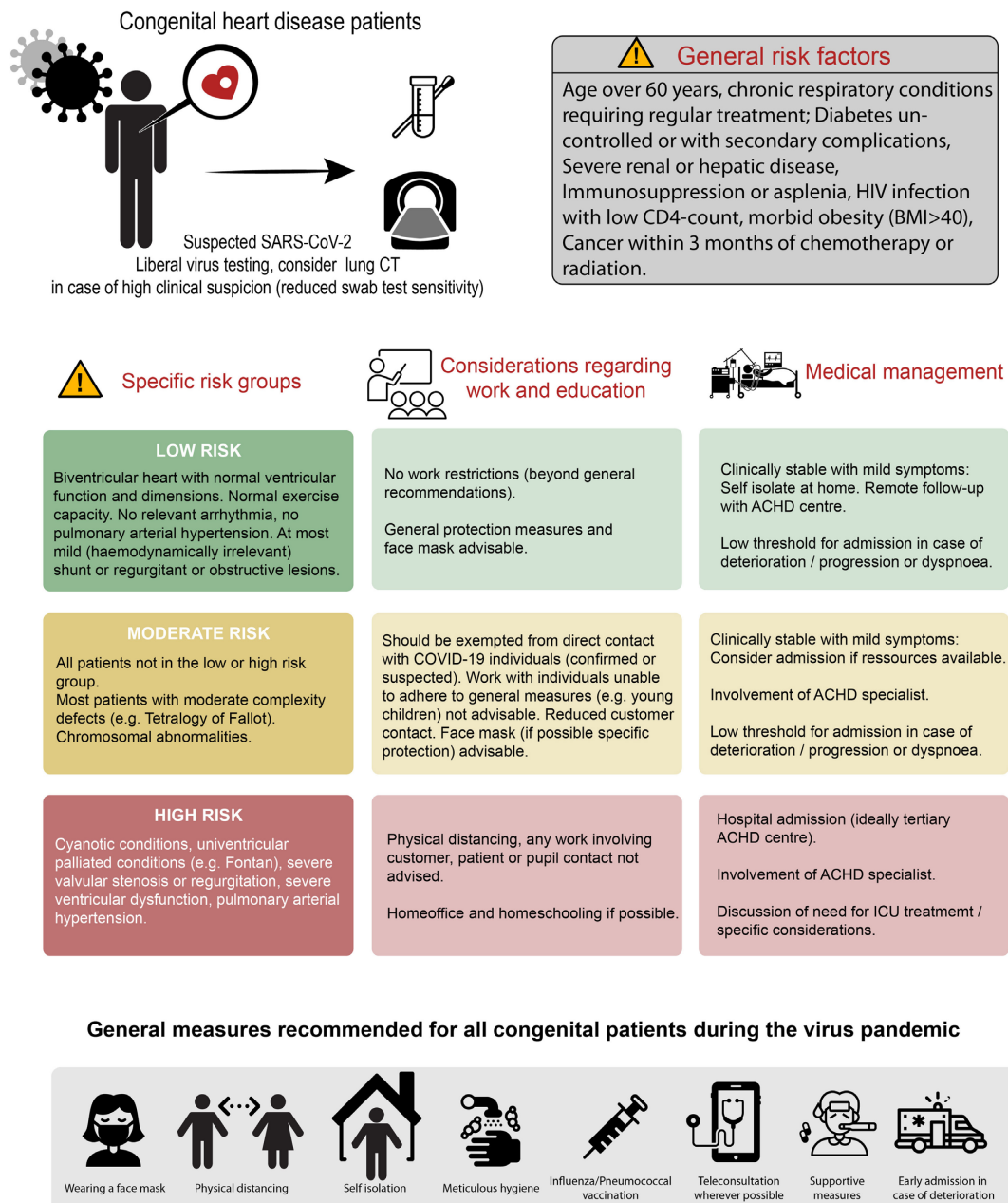


Figure 2. Our unique institutional strategy for clinical management of ACHD patients and preventive actions. The underlying heart defect anatomy and related physiology/complications are the basis for risk categorization. BMI is for body mass index. CD4 refers to cluster of differentiation 4. ICU stands for critical care unit. SARS-CoV-2 stands for severe acute respiratory syndrome coronavirus 2 (Radke et al. 2020).

et al. 2015; Brudy et al. 2020; Ewalt et al. 2012; Voss et al. 2017; Härtel et al. 2020; Arvidsson et al. 2009; Ray and Henry 2011) described the percentage of people meeting national or international PA recommendations, and six studies also included information on the amount of time spent sitting (Stone et al. 2015; Ewalt et al. 2012; Voss et al. 2017; Hedlund et al. 2016; Härtel et al. 2020; Ray and Henry 2011). There were no statistically significant differences in PA levels between children with CHD and age-matched healthy peers in 9 of the 18 studies (50 percent)

(Leitch et al. 2000; Stone et al. 2015; Chen et al. 2007; Brudy et al. 2020; Ewalt et al. 2012; Lunt et al. 2003; Voss et al. 2017; Härtel et al. 2020). Four of the nine remaining studies found that children with CHD were often less active than controls or normative data (Casey, Craig, and Mulholland 1994; Massin et al. 2006; Moschovi et al. 2020; Ray, Green, and Henry 2011). The results of the other studies were equivocal or limited to certain subgroups. For example, two studies found that while there were no differences in girls, boys with CHD had lower PA

levels as measured by accelerometry than healthy boys. In contrast, a study of 147 adolescents with a Fontan circulation found that while boys were largely unaffected, girls were affected. PA levels were significantly lower than those of healthy children (Fredriksen, Ingjer, and Thaulow 2000; Kao et al. 2009). Interestingly, Arvidsson et al. (2009) found that compared with peers of the same age and sex, only females with CHD aged 9 to 11 years had lower PA levels than girls or boys without CHD.

The method of measurement may be the reason for the apparent differences between the studies. In five (Casey, Craig, and Mulholland 1994; Hedlund et al. 2016; Ray, Green, and Henry 2011; Moschovi et al. 2020; Kao et al. 2009) of the eight (Barbour-Tuck et al. 2020), (Chen et al. 2007), and (Lunt et al. 2003) studies with self-reported or parent-reported outcomes, children with CHD had significantly lower PA levels. In contrast, none of the nine studies that used accelerometers to measure PA found differences between cases and controls (Stone et al. 2015; Brudy et al. 2020; Ewalt et al. 2012; Voss et al. 2017; Hedlund et al. 2016), and only three of the nine studies found lower PA levels in patient subgroups (Arvidsson et al. 2009; Fredriksen, Ingjer, and Thaulow 2000; Kao et al. 2009). The Amherst Health and Activity Study's healthy children and adolescents served as the control group in the only accelerometer study to find that children with CHD generally had lower PA levels than healthy children and adolescents (McCrinkle et al. 2007). The study by (Hedlund et al. 2016), which measured PA levels simultaneously with an accelerometer and a questionnaire in adolescent Fontan patients, is of particular interest.

The researchers found that, in comparison with healthy controls, teenagers with CHD exercised less frequently and less intensely. However, the amount of time spent in moderate to vigorous PA and accelerometer-measured activity levels did not differ between adolescents with CHD and controls (Hedlund et al. 2016).

BMI

The current system for categorizing obesity is based on body mass index (BMI), and disciplines ranging from global surveillance to patient assessment make extensive use of the advantages of BMI (Prentice and Jebb 2001). Normotension was present in 62.1 and 70.1 percent of men and women, respectively. Nearly 50% of both male and female patients had a BMI within the normal range. Men accounted for 25% of the overweight population (BMI > 25-30 kg/m²) and women made up 11% of the

obese population (BMI > 30 kg/m²). 0.9 and 0.6 percent of men and women, respectively, had diabetes (Moons et al. 2006).

Diabetes

Diabetes was diagnosed in 0.9% of men and 0.6% of women. These results showed that while women were less likely to be physically active and more likely to be obese, male patients had a significantly higher prevalence of smoking and hypertension. Comparing these data with risk factor prevalence in the general Belgian population, the patients reported significantly less smoking and more exercise than the age-adjusted general population. In contrast, the patients were generally more obese and had higher levels of hypertension.

Compared to the general population, our patients seemed to have a significantly higher rate of isolated systolic hypertension. There was no change in diabetes. Combining these five risk variables, we found that only 218 male patients (20.4%) and 190 female patients (21.0%) had a completely heart-healthy lifestyle; these were the patients who had no risk factors (Moons et al. 2006).

Conclusion

Given the growing burden of CHD in adults, it is vital to prioritize robust investment in health care to address the rising rates of CHD in adults. These investments should focus on people's mental, obstetrical, biological and hormonal, social and lifestyle conditions. By prioritizing robust health investments, we can hope to reduce the burden of this disease and improve the overall cardiovascular health of people worldwide.

Conflict of interest

The authors declare no conflict of interest.

Authors' contributions

Conception and design (BA, SSG); Drafting of the manuscript (NK); screening the articles (NK); Writing last edition and critical revision (SSG); Intellectual content and double review (SSG, NK, BA).

Ethics approval and consent to participate

As this is a systematic review, all ethical approvals and consents for the articles used were checked. Laboratory animals, specific human diseases, and/or the use of human information were not involved in any aspect of this article.

Consent for publication

Not applicable

Availability of data and materials

The published article and its supplements contain all the data of the study.

Funding

No funding was received for conducting this study.

References

- Arvidsson, D, F Slinde, L Hulthen, and J Sunnegårdh. 2009. "Physical Activity, Sports Participation and Aerobic Fitness in Children Who Have Undergone Surgery for Congenital Heart Defects." *Acta Paediatrica* 98 (9). Wiley Online Library: 1475–1482.
- Barbour-Tuck, Erin, Natasha G Boyes, Corey R Tomczak, Dana S Lahti, Chantelle L Baril, Charissa Pockett, Shonah Runalls, Ashok Kakadekar, Scott Pharis, and Timothy J Bradley. 2020. "A Cardiovascular Disease Risk Factor in Children with Congenital Heart Disease: Unmasking Elevated Waist Circumference—a CHAMPS* Study* CHAMPS: Children's Healthy-Heart Activity Monitoring Program in Saskatchewan." *BMC Cardiovascular Disorders* 20 (1). BioMed Central: 1–10.
- Brudy, Leon, Julia Hock, Anna-Luisa Häcker, Michael Meyer, Renate Oberhoffer, Alfred Hager, Peter Ewert, and Jan Müller. 2020. "Children with Congenital Heart Disease Are Active but Need to Keep Moving: A Cross-Sectional Study Using Wrist-Worn Physical Activity Trackers." *The Journal of Pediatrics* 217. Elsevier: 13–19.
- Casey, F A, B G Craig, and H C Mulholland. 1994. "Quality of Life in Surgically Palliated Complex Congenital Heart Disease." *Archives of Disease in Childhood* 70 (5). BMJ Publishing Group Ltd: 382–386.
- Chen, Chi-Wen, Yueh-Chih Chen, Mei-Yen Chen, Jou-Kou Wang, Wen-Jen Su, and Huey-Ling Wang. 2007. "Health-Promoting Behavior of Adolescents with Congenital Heart Disease." *Journal of Adolescent Health* 41 (6). Elsevier: 602–609.
- Ewalt, Lauren A, Michael J Danduran, Scott J Strath, Victoria Moerchen, and Ann M Swartz. 2012. "Objectively Assessed Physical Activity and Sedentary Behaviour Does Not Differ between Children and Adolescents with and without a Congenital Heart Defect: A Pilot Examination." *Cardiology in the Young* 22 (1). Cambridge University Press: 34–41.
- Fredriksen, P M, E Ingjer, and E Thaulow. 2000. "Physical Activity in Children and Adolescents with Congenital Heart Disease. Aspects of Measurements with an Activity Monitor." *Cardiology in the Young* 10 (2). Cambridge University Press: 98–106.
- Goeddel, Lee A, Youn Hoa Jung, Prakash Patel, Patrick Upchurch, Rohesh J Fernando, and Harish Ramakrishna. 2020. "Analysis of the 2018 American Heart Association/American College of Cardiology Guidelines for the Management of Adults with Congenital Heart Disease: Implications for the Cardiovascular Anesthesiologist." *Journal of Cardiothoracic and Vascular Anesthesia* 34 (5). Elsevier: 1348–1365.
- Härtel, Julian Alexander, Ulrike Herberg, Thomas Jung, Christian Winkler, Johannes Breuer, and Nicole Müller. 2020. "Physical Activity and Heart Rate Monitoring in Fontan Patients—Should We Recommend Activities in Higher Intensities?" *Plos One* 15 (1). Public Library of Science San Francisco, CA USA: e0228255.
- Hedlund, Eva R, Bo Lundell, Li Villard, and Gunnar Sjöberg. 2016. "Reduced Physical Exercise and Health-related Quality of Life after Fontan Palliation." *Acta Paediatrica* 105 (11). Wiley Online Library: 1322–1328.
- Kao, Ching-Chiu, Pi-Chen Chang, Ching-Wen Chiu, Lee-Pin Wu, and Jen-Chen Tsai. 2009. "Physical Activity Levels of School-Age Children with Congenital Heart Disease in Taiwan." *Applied Nursing Research* 22 (3). Elsevier: 191–197.
- Lane, D A, G Y H Lip, and T A Millane. 2002. "Quality of Life in Adults with Congenital Heart Disease." *Heart* 88 (1). BMJ Publishing Group Ltd: 71–75.
- Leitch, Catherine A, Cheryl A Karn, Gregory J Ensing, and Scott C Denne. 2000. "Energy Expenditure after Surgical Repair in Children with Cyanotic Congenital Heart Disease." *The Journal of Pediatrics* 137 (3). Elsevier: 381–385.
- Longmuir, Patricia E, Julie A Brothers, Sarah D De Ferranti, Laura L Hayman, George F Van Hare, G Paul Matherne, Christopher K Davis, Elizabeth A Joy, and Brian W McCrindle. 2013. "Promotion of Physical Activity for Children and Adults with Congenital Heart Disease: A Scientific Statement from the American Heart Association." *Circulation* 127 (21). Am Heart Assoc: 2147–2159.
- Lunt, Dianne, Tom Briffa, N Kathryn Briffa, and James Ramsay. 2003. "Physical Activity Levels of Adolescents with Congenital Heart Disease." *Australian Journal of Physiotherapy* 49 (1). Elsevier: 43–50.
- Marelli, Ariane J, Raluca Ionescu-Iltu, Andrew S Mackie, Liming Guo, Nandini Dendukuri, and Mohammed Kaouache. 2014. "Lifetime Prevalence of Congenital Heart Disease in the General Population from 2000 to 2010." *Circulation* 130 (9). Am Heart Assoc: 749–756.
- Massin, Martial M, Hedwig H Hövels-Gürich, Paul Gérard, and Marie-Christine Seghaye. 2006. "Physical Activity Patterns of Children after Neonatal Arterial Switch Operation." *The Annals of Thoracic Surgery* 81 (2). Elsevier: 665–670.
- McCrindle, Brian W, Richard V Williams, Seema Mital, Bernard J Clark, Jennifer L Russell, Gloria Klein, and Joey C Eisenmann. 2007. "Physical Activity Levels in Children and Adolescents Are Reduced after the Fontan Procedure, Independent of Exercise Capacity, and Are Associated with Lower Perceived General Health." *Archives of Disease in Childhood* 92 (6). BMJ Publishing Group Ltd: 509–514.
- Moons, Philip, Kristien Van Deyk, Davy Dedroog, Els Troost, and Werner Budts. 2006. "Prevalence of Cardiovascular Risk Factors in Adults with Congenital Heart Disease." *European Journal of Preventive Cardiology* 13 (4). Oxford University Press: 612–616.
- Moschovi, Dimitra, Emmanouil I. Kapetanakis, Panagiotis G. Sfyridis, Spyridon Rammou, and Evangelia Mavrikaki. 2020. "Physical Activity Levels and Self-Efficacy of Greek Children with Congenital Heart Disease Compared to Their Healthy Peers." *Hellenic Journal of Cardiology* 61 (3). Hellenic Society of Cardiology: 180–186. doi:10.1016/j.hjc.2019.01.002.
- Neidenbach, Rhoia, Koichiro Niwa, Oeztekin Oto, Erwin Oechslin, Jamil Aboulhosn, David Celermajer, Joerg Schelling, Lars Pieper, Linda Sanftenberg, and Renate Oberhoffer. 2018. "Improving Medical Care and Prevention in Adults with Congenital Heart Disease—Reflections on a Global Problem—Part I: Development of Congenital Cardiology, Epidemiology, Clinical Aspects, Heart Failure, Cardiac Arrhythmia." *Cardiovascular Diagnosis and Therapy* 8 (6). AME Publications: 705.
- Prentice, Andrew M, and Susan A Jebb. 2001. "Beyond Body Mass Index." *Obesity Reviews* 2 (3). Wiley Online Library: 141–147.
- Radke, Robert M, Tim Frenzel, Helmut Baumgartner, and Gerhard-Paul Diller. 2020. "Adult Congenital Heart Disease and the COVID-19 Pandemic." *Heart* 106 (17). BMJ Publishing Group Ltd and British Cardiovascular Society: 1302–1309.

24. Ray, Trena D, Angela Green, and Karen Henry. 2011. "Physical Activity and Obesity in Children with Congenital Cardiac Disease." *Cardiology in the Young* 21 (6). Cambridge University Press: 603–607.
25. Ray, Trena D, and Karen Henry. 2011. "Self-efficacy and Physical Activity in Children with Congenital Heart Disease: Is There a Relationship?" *Journal for Specialists in Pediatric Nursing* 16 (2). Wiley Online Library: 105–112.
26. Stone, Nicola, Joyce Obeid, Rejane Dillenburg, Jovana Milenkovic, Maureen J MacDonald, and Brian W Timmons. 2015. "Objectively Measured Physical Activity Levels of Young Children with Congenital Heart Disease." *Cardiology in the Young* 25 (3). Cambridge University Press: 520–525.
27. van Deutekom, Arend W, and Adam J. Lewandowski. 2021. "Physical Activity Modification in Youth with Congenital Heart Disease: A Comprehensive Narrative Review." *Pediatric Research* 89 (7). Springer US: 1650–1658. doi:10.1038/s41390-020-01194-8.
28. Voss, Christine, Stephanie L Duncombe, Paige H Dean, Astrid M de Souza, and Kevin C Harris. 2017. "Physical Activity and Sedentary Behavior in Children with Congenital Heart Disease." *Journal of the American Heart Association* 6 (3). Am Heart Assoc: e004665.
29. Wang, Tingting, Lizhang Chen, Tubao Yang, Peng Huang, Lesan Wang, Lijuan Zhao, Senmao Zhang, Ziwei Ye, Letao Chen, and Zan Zheng. 2019. "Congenital Heart Disease and Risk of Cardiovascular Disease: A Meta-analysis of Cohort Studies." *Journal of the American Heart Association* 8 (10). Am Heart Assoc: e012030.