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Adults Are Not Just Enormous Children: Type 2 Diabetes Mellitus in Adults With Congenital Heart Disease

Jason F. Deen, MD; Eric V. Krieger, MD

It has often been said that "children are not just tiny adults" to highlight the unique medical needs of children and to set the expectation that physicians who care for children should be trained and educated in pediatric medicine.[1] Presumably controversial in the past, this sentiment has risen to the level of axiom. Dedicated pediatric care is now available for nearly every medical subspecialty, and there has been a rapid expansion of dedicated children's hospitals.

A consequence of the successes of pediatric cardiology and pediatric cardiac surgery is an aging population of patients born with congenital heart defects.[2] It has been more than a decade since the number of adults with congenital heart disease (CHD) surpassed the number of children with CHD in the United States, and the proportion of adults continues to grow. The average age of patients seen in our CHD program in 2015, for example, was 35 years, and 26% were aged >40 years.

Adults with CHD experience premature morbidity and mortality, often from cardiovascular events and acquired comorbidities.[3,4] These chronic medical problems are similar to those seen in an adult population.[4] Chronic kidney disease is a strong predictor of death in adult CHD patients, and dementia, gastrointestinal bleeding, and chronic pulmonary disease also contribute to mortality in older patients with CHD.[4–6] A recent report from a German national registry detailed non-CHD–related deaths in a cohort of patients (mean age at death 57.6±20.5 years) and showed that adults with CHD die of malignancies, infections, neurological events, and liver disease.[7] Furthermore, traditional risk factors for atherosclerotic disease such as obesity,[8] hypertension,[9] glucose intolerance,[10,11] dyslipidemia,[11] metabolic syndrome, and sedentary lifestyle[12] are pervasive in the adult CHD population. We previously reported a 2-fold increased risk of metabolic syndrome in adults with CHD.[13]

Madsen and colleagues' study of type 2 diabetes mellitus (T2DM) in CHD in this issue of the *Journal of the American Heart Association* adds to the growing body of literature highlighting traditional cardiovascular risk factors in survivors of pediatric heart disease.[14] The authors use population-based cohort study of Denmark to determine whether those with CHD are at increased risk for the development of T2DM. The Danish National Registry of Patients uses unique personal registration numbers to provide patient-level information regarding diagnoses, inpatient and outpatient contacts, and medication usage. The authors use this database to identify 5149 Danish patients born between 1963 and 1980 with a diagnosis of CHD who were alive at age 30. They compare these participants with 49 968 age- and sex-matched Danish persons without CHD. The risk of developing T2DM is 1.35 (95% CI 1.14–1.61) higher in those with CHD compared with the control population.

The authors also report that the association between CHD and T2DM is strongest among those with cyanotic forms of CHD (hazard ratio 2.85, 95% CI 1.77–4.57) compared with controls. The authors propose that cyanotic patients have higher rates of T2DM because hypoxemia leads to impaired insulin secretion and insulin sensitivity; however, this explanation should be viewed with caution because the authors did not have information regarding the duration or severity of the cyanosis, and it can be assumed that the vast majority were repaired to normoxemia in infancy or early childhood. Although it is plausible that this relatively brief period of cyanosis could lead to impaired glucose metabolism decades later, such a novel hypothesis requires confirmation. The authors appropriately acknowledge alternative explanations

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Seattle Adult Congenital Heart Service, University of Washington Medical Center, Seattle, WA; Seattle Children's Hospital, University of Washington School of Medicine, Seattle, WA (J.F.D., E.V.K.).

Correspondence to: Eric V. Krieger, MD, Seattle Adult Congenital Heart Service, University of Washington Medical Center Box 356422. 1959 NE Pacific Street, Seattle, WA 98195. E-mail: ekrieger@u.washington.edu

J Am Heart Assoc. 2016;5:e003960 doi: 10.1161/JAHA.116.003960.

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for the increased prevalence of T2DM in cyanotic patients: a common genetic predisposition, exercise restriction leading to obesity and metabolic syndrome, or a type I error.

The primary finding of the report by Madsen et al, that those with CHD are at risk for T2DM, is important. Using a similar national database, researchers in Sweden explored the outcomes of adults with coexisting CHD and T2DM. Patients with CHD and T2DM had higher morbidity and mortality rates than those with T2DM alone.[15] It remains unknown, however, how the diagnosis of T2DM affects the outcomes of patients with CHD. The Danish data set used by Madsen et al seems well suited to determine whether the presence of T2DM increases morbidity, mortality, or health care utilization in the adult CHD population.

T2DM is strongly linked to obesity and metabolic syndrome, and it is unfortunate that the Danish registry does not contain anthropomorphic data. Consequently, it is unknown whether differential obesity rates explain the high prevalence of T2DM in patients with CHD. Similarly, data were insufficient to determine whether exercise restriction, which is common in children with CHD, contributes to a sedentary lifestyle, central obesity, and the development of T2DM. Although some studies have found that the prevalence of obesity in CHD patients likely matches that of the general population,[8,16] others reported that patients with complex forms of CHD have an increased higher rates of obesity.[17,18]

Are these data the proverbial canaries in the coal mine? Do they portend an accumulation of traditional cardiovascular risk in adult CHD patients? Because adults with CHD are becoming obese, with increased rates of metabolic syndrome and T2DM, professional societies are making an effort to combat these risks. It is now widely known that activity restriction contributes to obesity,[19,20] so recent policy statements have encouraged (rather than discouraged) increased physical activity in patients with virtually all forms of CHD.[12]

Just as children are not simply tiny adults, adult survivors of pediatric heart disease are not just enormous children; they have acquired cardiovascular disease that increasingly mirrors that of the general adult population. For that reason, those who care for adults with CHD should have expertise in both CHD care and adult cardiovascular medicine. Directed subspecialty training must ensure qualified medical providers. In recognition of this, the American Board of Internal Medicine, the American Board of Pediatrics, and the Accreditation Council for Graduate Medical Education established training guidelines and board certification for adult CHD specialists, emphasizing that cardiologists with a background in adult cardiology must have expertise in CHD and those with a background in pediatric cardiology must expertise in acquired cardiovascular disease in order to provide comprehensive care to the adult population with CHD.

Disclosures

None.

References

1. Time to be serious about children's health care. *Lancet*. 2001;358:431.
2. O'Leary JM, Siddiqi OK, de Ferranti S, Landzberg MJ, Opotowsky AR. The changing demographics of congenital heart disease hospitalizations in the United States, 1998 through 2010. *JAMA*. 2013;309:984–986.
3. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, van Dijk AP, Vliegen HW, Grobbee DE, Mulder BJ. Mortality in adult congenital heart disease. *Eur Heart J*. 2010;31:1220–1229.
4. Afilalo J, Therrien J, Pilote L, Ionescu-Ittu R, Martucci G, Marelli AJ. Geriatric congenital heart disease: burden of disease and predictors of mortality. *J Am Coll Cardiol*. 2011;58:1509–1515.
5. Dimopoulos K, Diller GP, Koltsida E, Pijuan-Domenech A, Papadopoulou SA, Babu-Narayan SV, Salukhe TV, Piepoli MF, Poole-Wilson PA, Best N, Francis DP, Gatzoulis MA. Prevalence, predictors, and prognostic value of renal dysfunction in adults with congenital heart disease. *Circulation*. 2008;117:2320–2328.
6. Alonso-Gonzalez R, Borgia F, Diller GP, Inuzuka R, Kempny A, Martinez-Naharro A, Tutarel O, Marino P, Wustmann K, Charalambides M, Silva M, Swan L, Dimopoulos K, Gatzoulis MA. Abnormal lung function in adults with congenital heart disease: prevalence, relation to cardiac anatomy, and association with survival. *Circulation*. 2013;127:882–890.
7. Engelings CC, Helm PC, Abdul-Khaliq H, Asfour B, Bauer UM, Baumgartner H, Kececioglu D, Korten MA, Diller GP, Tutarel O. Cause of death in adults with congenital heart disease—an analysis of the German National Register for Congenital Heart Defects. *Int J Cardiol*. 2016;211:31–36.
8. Moons P, Van Deyk K, Dedroog D, Troost E, Budts W. Prevalence of cardiovascular risk factors in adults with congenital heart disease. *Eur J Cardiovasc Prev Rehabil*. 2006;13:612–616.
9. Gaeta SA, Ward C, Krasuski RA. Extra-cardiac manifestations of adult congenital heart disease. *Trends Cardiovasc Med*. 2016; pii: S1050-1738(16)30021-4. doi: 10.1016/j.tcm.2016.04.004. [Epub ahead of print].
10. Ohuchi H, Miyamoto Y, Yamamoto M, Ishihara H, Takata H, Miyazaki A, Yamada O, Yagihara T. High prevalence of abnormal glucose metabolism in young adult patients with complex congenital heart disease. *Am Heart J*. 2009;158:30–39.
11. Martinez-Quintana E, Rodriguez-Gonzalez F, Nieto-Lago V, Novoa FJ, Lopez-Rios L, Riano-Ruiz M. Serum glucose and lipid levels in adult congenital heart disease patients. *Metabolism*. 2010;59:1642–1648.
12. Longmuir PE, Brothers JA, de Ferranti SD, Hayman LL, Van Hare GF, Matherne GP, Davis CK, Joy EA, McCrindle BW; American Heart Association Atherosclerosis H and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Y. Promotion of physical activity for children and adults with congenital heart disease: a scientific statement from the American Heart Association. *Circulation*. 2013;127:2147–2159.
13. Deen JF, Krieger EV, Slee AE, Arslan A, Arterburn D, Stout KK, Portman MA. Metabolic syndrome in adults with congenital heart disease. *J Am Heart Assoc*. 2016;5:e001132 doi: 10.1161/JAHA.114.001132.
14. Madsen NL, Marino BS, Woo JG, Thomsen RW, Videboek J, Laursen HB, Olsen M. Congenital heart disease with and without cyanotic potential and the long-term risk of diabetes mellitus: a population-based follow-up study. *J Am Heart Assoc*. 2016;5:e003076 doi: 10.1161/JAHA.115.003076.
15. Dellborg M, Bjork A, Pirouzi Fard MN, Ambring A, Eriksson P, Svensson AM, Gudbjornsdottir S. High mortality and morbidity among adults with congenital heart disease and type 2 diabetes. *Scand Cardiovasc J*. 2015;49:344–350.
16. Pinto NM, Marino BS, Wernovsky G, de Ferranti SD, Walsh AZ, Laronde M, Hyland K, Dunn SO Jr, Cohen MS. Obesity is a common comorbidity in children with congenital and acquired heart disease. *Pediatrics*. 2007;120:e1157–e1164.
17. Chung ST, Hong B, Patterson L, Petit CJ, Ham JN. High overweight and obesity in Fontan patients: a 20-year history. *Pediatr Cardiol*. 2016;37:192–200.

18. Pasquali SK, Marino BS, Pudusseri A, Wernovsky G, Paridon SM, Walker SA, Cohen MS. Risk factors and comorbidities associated with obesity in children and adolescents after the arterial switch operation and Ross procedure. *Am Heart J*. 2009;158:473–479.

19. Stefan MA, Hopman WM, Smythe JF. Effect of activity restriction owing to heart disease on obesity. *Arch Pediatr Adolesc Med*. 2005;159:477–481.

20. Morrison ML, Sands AJ, McCusker CG, McKeown PP, McMahon M, Gordon J, Grant B, Craig BG, Casey FA. Exercise training improves activity in adolescents with congenital heart disease. *Heart*. 2013;99:1122–1128.

Key Words: Editorial • adult congenital heart disease • diabetes mellitus