Canadian Journal of Cardiology 34 (2018) 1624–1630

Clinical Research

Patterns of Incidence Rates of Cardiac Complications in Patients With Congenital Heart Disease

Ketina Arslani, MD,[a,*] Nico Roffler,[a,*] Marzena Zurek, MD,[a,b] Matthias Greutmann, MD,[c] Markus Schwerzmann, MD,[d] Judith Bouchardy, MD,[e] Tobias Rutz, MD,[e] Niklas F. Ehl, MD,[b] Christine Attenhofer Jost, MD,[f] and Daniel Tobler, MD;[a] on behalf of the SACHER Investigators

[a] *Department of Cardiology, University Hospital of Basel, University of Basel, Basel, Switzerland*

[b] *Department of Cardiology, Kantonsspital St Gallen, St Gallen, Switzerland*

[c] *University Heart Center, Department of Cardiology, University of Zurich, Zurich, Switzerland*

[d] *Center for Congenital Heart Disease, Department of Cardiology, Inselspital, University of Bern, Bern, Switzerland*

[e] *Department of Cardiology and Cardiac Surgery (CHUV), Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland*

[f] *The Cardiovascular Center, Klinik im Park, Zurich, Switzerland*

ABSTRACT

Background: This study aimed to evaluate age at the first onset of cardiac complications and variation of frequency of complications between different congenital heart defects.

Methods: The analysis included participants of the **S**wiss **A**dult **C**ongenital **H**eart Disease **R**egistry (SACHER). For this study, cardiac complications up to the time of inclusion in SACHER were analysed. Complications included atrial fibrillation, atrial flutter, supraventricular tachycardia, ventricular tachycardia, complete heart block, heart failure, stroke, endocarditis, myocardial infarction, and pulmonary hypertension. Incidence rates (IR; incidence rate per 1000 patient-years) for different age categories and diagnosis groups were analysed.

RÉSUMÉ

Contexte : Cette étude visait à évaluer l'âge à l'apparition des complications cardiaques et la variation de la fréquence des complications d'une cardiopathie congénitale à l'autre.

Méthodologie : L'analyse portait sur les patients inscrits au **S**wiss **A**dult **C**ongenital **H**eart Disease **R**egistry (SACHER). Aux fins de la présente étude, les complications cardiaques survenues jusqu'au moment de l'inclusion du patient dans le registre SACHER ont été analysées. Au nombre des complications figuraient la fibrillation auriculaire, le flutter auriculaire, la tachycardie supraventriculaire, la tachycardie ventriculaire, le bloc cardiaque complet, l'insuffisance cardiaque, l'accident vasculaire cérébral (AVC), l'endocardite, l'infarctus du myocarde et l'hypertension pulmonaire. Les taux d'incidence

With the invention of cardiac surgery and better cardiology care, most clinically relevant congenital heart defects are amenable to repair. Particularly, the survival of patients with moderate and complex congenital heart disease (CHD) into adulthood has improved and is still increasing.[1] Morbidity and mortality of adult survivors with CHD is, however, substantial, and many patients suffer from cardiac complications during lifetime.[2] We aimed to describe the frequency of the occurrence of cardiac complications stratified for age categories and types of patients with CHD and to calculate the incidence rates in different age categories from patients included in the **S**wiss **A**dult **C**ongenital **He**art Disease **R**egistry (SACHER). We hypothesized that cardiac complications predominantly occur in adult life and that incidence rates increase with age.

Methods

Study population and data collection

From SACHER (ClinicalTrials.gov Identifier NCT2258724) we analysed all patients included up to December 2016. SACHER includes patients with structural congenital heart defects or hereditary aortopathies. The detailed design of SACHER has previously been published.[3] The following baseline characteristics were analysed for this study: age at inclusion into SACHER, prior cardiac surgery

Received for publication June 20, 2018. Accepted September 19, 2018.

*These authors contributed equally to this work.

Corresponding author: Dr Daniel Tobler, Department of Cardiology, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland. Tel.: +41-61-265-25-25; fax: +41-61-279-98-23.

E-mail: daniel.tobler@usb.ch

See page 1629 for disclosure information.

https://doi.org/10.1016/j.cjca.2018.09.010

Results: Of 2731 patients (55% male, mean age 34 ± 14 years, 92,349 patient-years), a total of 767 (28%) had experienced at least 1 cardiac complication. The majority of complications (550; 72%) occurred in adulthood (> 18 years). Apart from perioperative stroke (IR: 1.77 in age group ≤ 4 years) and complete heart block (IR: 2.36 in age group ≤ 4 years), IR were much lower in childhood (IR < 1 for all complications between 5 and 17 years). Incidence of cardiac complications increased during adult life with highest IR for atrial fibrillation and atrial flutter in the age group ≥ 50 years (IR: 17.6 and 9.7, respectively). There were important variations of the distribution of complications among different diagnosis groups.

Conclusions: Cardiac complications are frequent in congenital heart disease. Apart from perioperative stroke and complete heart block, IR are low in childhood but the incidence increases during adult life. These data underscore the need of lifelong follow-up and may help for better allocation of resources maintaining follow-up.

Résultats : Sur 2731 patients (55 % de sexe masculin, âge moyen de 34 ± 14 ans, 92 349 années-patients), 767 au total (28 %) avaient eu au moins 1 complication cardiaque. La majorité des complications (550; 72 %) étaient apparues à l'âge adulte (> 18 ans). À l'exception de l'AVC périopératoire (TI : 1,77 dans le groupe d'âge ≤ 4 ans) et du bloc cardiaque complet (TI : 2,36 dans le groupe d'âge ≤ 4 ans), les TI étaient beaucoup moins élevés pendant l'enfance (TI < 1 pour toutes les complications entre 5 et 17 ans). L'incidence des complications cardiaques augmentait au cours de la vie adulte, avec un TI atteignant un maximum pour la fibrillation auriculaire et le flutter auriculaire dans le groupe d'âge ≥ 50 ans (TI : 17,6 et 9,7, respectivement). Des variations importantes de la distribution des complications ont été observées entre les différents groupes de diagnostic.

Conclusions : Les complications cardiaques sont fréquentes chez les patients atteints d'une cardiopathie congénitale. À l'exception de l'AVC périopératoire et du bloc cardiaque complet, les TI sont peu élevés pendant l'enfance, mais augmentent au cours de la vie adulte. Ces données mettent en lumière l'importance du suivi tout au long de la vie et pourraient contribuer à améliorer l'affectation des ressources permettant un tel suivi.

(defined as the main intracardiac repair procedure), palliative interventions (defined as each procedure [surgery or percutaneous intervention]) before the main repair, > 1 cardiac intervention (defined as having had a subsequent procedure after the main repair [surgery or percutaneous interventions]), valve surgery, implantation of a ventricular to pulmonary artery conduit, and device implantation (defined as the implantation of a pacemaker, an intracardiac defibrillator, or a cardiac resynchronization device). Within SACHER, lesions were grouped within different lesion categories, including shunt lesions, valve lesions (stratified for repair status), hereditary aortopathies, complex left ventricular outflow-tract obstructions, right heart lesions, and cyanotic and other complex lesions. Each category was further divided into subcategories: atrial septal defects (ASD II), sinus venosus defects with and without anomalous pulmonary connections, ventricular septal defects and patent ductus arteriosus (shunt lesions); unrepaired and repaired or replaced simple valve lesions (valve lesions); aortopathies including arch anomalies and patients with Marfan syndrome or other syndromes associated with aortopathies (excluding patients with a bicuspid aortic valve who were included in the category of valve lesions); repaired and unrepaired aortic coarctation and sub- and supravalvular aortic stenosis (complex obstruction of the left ventricular outflow tract); Ebstein anomaly, repaired tetralogy of Fallot and pressure-loaded ventricles including the double-chambered right ventricle and isolated branch pulmonary stenosis (right heart lesions); implantation of ventricular to pulmonary artery conduits, arterial switch, systemic right ventricle (including atrial switch and congenitally corrected transplantation of the great arteries), Fontan palliation, cyanotic heart disease (defined as Eisenmenger syndrome or unrepaired complex cyanotic heart disease). For all patients included in SACHER, the age at the first onset of the following cardiac complications were obtained from the chart review at the time of inclusion: atrial fibrillation, atrial flutter/intra-atrial re-entrant tachycardia, supraventricular tachycardia, ventricular tachycardia or fibrillation, complete heart block, infective endocarditis, stroke, myocardial infarction, congestive heart failure, and pulmonary hypertension.

Statistics

Data analysis was performed using SPSS software (Version 22.0; SPSS Inc, Chicago, IL). Data were described as medians with ranges or means with standard deviations, as appropriate. Comparisons of continuous or categorical variables were performed with the χ^2 test or Fisher exact test and Student's *t*-test or Mann-Whitney *U* test as appropriate. A *P* value of < 0.05 was considered significant. Six different age categories were created reflecting meaningful life stages: 0-4 years (young children, comprising the age of reparative surgery for the majority of patients), 5-17 years (older children and teenager), 18-29 years (young adults), 30-39 years (adults), 40-49 years (middle-aged adults), and ≥ 50 years (older adults). In each age category, the number of patient-years was calculated by multiplying the number of patients in the specific age category with the number of years of follow-up. The number of the first events of each cardiac complication in the specific age group was divided by the patient-years of follow-up in the specific age group and reported as events per 1000 patient-years (incidence rate). Patients with a first event have been censored in the specific complication for the next coming age categories.

Results

Frequency of cardiac complications

Of 2731 patients enrolled in SACHER from May 2014 to December 2016, we identified 767 (28%) patients with a history of cardiac complications (Table 1). The frequency of cardiac complications in different lesion groups and lesions are summarized in Figure 1 (detailed data are shown in

Table 1. Patient characteristics

	No complication (n = 1964)	Complications (n = 767)	HF (n = 72)	Stroke (n = 153)	MI (n = 24)	Endocarditis (n = 115)	AVB (n = 110)	AF (n = 177)	AFlut/IART (n = 204)	VT/VF (n = 102)	SVT (n = 117)	PHT (n = 107)	*P* value*
Male, n (%)	1075 (55)	422 (55)	37 (51)	81 (53)	14 (58)	71 (62)	59 (54)	107 (61)	117 (57)	63 (62)	62 (53)	49 (46)	0.464
Age at inclusion, *y*	31 ± 13	41 ± 16	48. ± 15	43. ± 14	47 ± 18	37 ± 14	38 ± 15	52 ± 15	42 ± 15.0	43 ± 14	38.9 ± 14.6	42.3 ± 16.6	< 0.001
Prior cardiac surgery (%)	1330 (68)	637 (83)	57 (79)	131 (86)	17 (71)	93 (81)	99 (90)	149 (84)	189 (93)	93 (91)	100 (86)	62 (58)	< 0.001
Palliative interventions (%)	316 (16)	203 (27)	25 (35)	45 (29)	6 (25)	28 (24)	25 (23)	40 (23)	81 (40)	39 (38)	40 (34)	19 (18)	< 0.001
> 1 cardiac intervention (%)	484 (25)	430 (56)	42 (58)	78 (51)	10 (42)	67 (58)	89 (81)	106 (60)	154 (76)	74 (73)	71 (61)	31 (29)	< 0.001
Valve surgery (%)	271 (14)	202 (26)	21 (29)	39 (25)	6 (25)	58 (50)	37 (34)	57 (32)	57 (38)	32 (31)	27 (33)	11 (10)	< 0.001
Mechanical	80 (4)	75 (10)	10 (14)	22 (14)	3 (13)	24 (21)	16 (15)	24 (14)	18 (9)	10 (10)	6 (5)	5 (5)	
Bioprosthesis	131 (7)	87 (11)	8 (11)	11 (7)	2 (8)	28 (24)	11 (10)	23 (13)	24 (12)	19 (19)	12 (10)	4 (4)	
Reconstruction	60 (3)	40 (5)	3 (4)	6 (4)	1 (4)	6 (5)	10 (9)	10 (6)	15 (7)	3 (3)	9 (8)	2 (2)	
RV/LV to PA conduits (%)	182 (9)	114 (15)	9 (13)	17 (11)	0 (0)	34 (30)	14 (13)	30 (17)	37 (18)	26 (26)	11 (9)	6 (6)	< 0.001
Device implantation (%)	25 (3)	168 (22)	18 (25)	24 (16)	2 (8)	17 (15)	83 (75)	49 (28)	49 (24)	48 (47)	22 (19)	12 (11)	< 0.001

AF, atrial fibrillation; AFlut, atrial flutter; AVB, total atrioventricular block; HF, heart failure; IART, intra-atrial re-entry tachycardia; MI, myocardial infarction; PHT, pulmonary hypertension; RV or LV to PA, right ventricle or left ventricle to pulmonary artery; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia.

* *P* value between patients with and without complication.

Supplemental Table S1). With the exception of atrial fibrillation ($P = 0.15$) the frequency of cardiac complications differed between lesion groups ($P = 0.008$ for heart failure and $P < 0.001$ for all other cardiac complications). The highest prevalence of any complication (with the exception of endocarditis and complete heart block) was found in patients with cyanotic and other complex heart disease. Endocarditis was most prevalent in patients with replaced valves and right ventricle to pulmonary artery conduits; complete heart block was most prevalent in patients with atrioventricular septal defects, Ebstein anomaly, and systemic right ventricles. The number of patients with prior myocardial infarction was small (n = 24).

Distribution of the first onset and incidence rates of cardiac complications

The mean age of the first onset differed between cardiac complications ($P < 0.001$) and was lowest for complete heart block (22 ± 19 years) and highest for atrial fibrillation (43 ± 16 years). The majority of all complications (550; 72%) occurred in adult age (> 18 years) with the exception of perioperative complete heart block, as illustrated in Figure 2.

When calculated for different age categories, 4 different time patterns of incidence rates were found: (a) increasing incidence rates with ageing, (b) highest incidence rates in early childhood and older adults (U-curve), (c) decreasing incidence rates after early childhood and only increasing after age 30 years with the highest incidence rates in older adults (J-curve pattern), and (d) highest incidence rates in young adults; decreasing in the older population (Fig. 3).

Discussion

In this study, we demonstrated important differences in incidence rates of various cardiac complications in patients with CHD. Overall, apart from perioperative strokes and atrioventricular block, complications were exceedingly rare in childhood, but for most complications, increasing incidence rates were documented in adult life.

Four distinctive patterns of incidence rates could be elaborated: (a) increasing incidence rates with ageing, (b) highest incidence rates in early childhood and older adults (U-curve), (c) J-curve pattern, and (d) highest incidence rates in young adults.

As expected, cardiac complications differed between lesions and lesion groups. Overall, cardiac complications were most common in patients with complex and cyanotic lesions and infective endocarditis was most prevalent in patients with prosthetic heart valves.

Time pattern: (a) increasing incidence rates with ageing

Several studies have demonstrated increasing incidence rates of tachyarrhythmia in patients with CHD during adulthood.[4-7] In line with these observations, we found in SACHER that the first onset of tachyarrhythmias typically occur in adulthood. This is particularly true for atrial fibrillation: in 87% of cases with atrial fibrillation, the event occurred after age 18 years with a steady increase with ageing and incidence rates in patients older than 50 years were 100

Figure 1. Frequency of patients with cardiac complications. Frequency (in %) of patients with cardiac complications among different lesions. **Pink bars**: shunt lesions. **Blue bars**: valve lesions. **Green bars**: aortopathies. **Orange bars**: complex left ventricular outflow tract obstructions. **Purple bars**: right heart lesions. **Brown bars**: cyanotic and other complex lesions. ASD II, atrial septal defects; AVSD, atrioventricular septal defect; IART, intra-atrial re-entry tachycardia; LVOT, left ventricular outflow tract; PA, pulmonary artery; PDA, patent ductus arteriosus; PVR, pulmonary valve replacement; RV, right ventricle; SVD, sinus venosus defect; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

times higher compared with children and adolescents. In general cardiology, atrial fibrillation is the most common cardiac arrhythmia and becomes more prevalent with ageing.[8-12] In the Anticoagulation and Risk Factors in Atrial Fibrillation study (United States), the overall prevalence of atrial fibrillation in the general population was 1%, much lower compared with the SACHER cohort (6.5% of patients).[12] In the Manitoba Follow-up Study, the incidence rate among 3983 male air crew recruits observed over 44 years rose from less than 0.5 per 1000 person-years before age 50 years to 9.7 per 1000 person-years after age 70 years.[13] In our cohort, the incidence rate was 8 per 1000 patient-years in

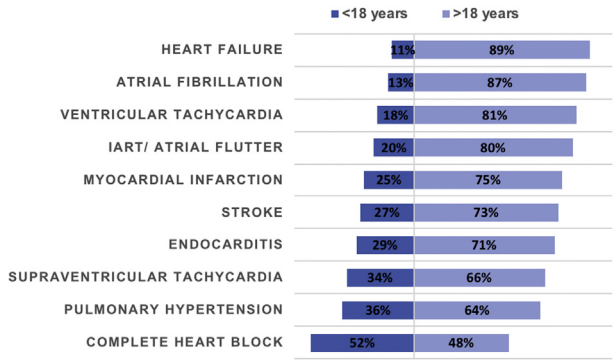

Figure 2. Distribution of the first cardiac complication before and after the age of 18 years. Percentage of first events stratified by age 18 years. Dark blue bars: percentage of patients in the cohort with a particular complication who were less than 18 years of age at the first onset. Light blue bars: percentage of patients in the cohort with a particular complication who were above 18 years of age at the first onset. IART, intra-atrial re-entry tachycardia.

the age category 40-50 years and rose to 17.6 per 1000 patient-years in patients over age 50 years, which is similar to incidence rates of patients in the age group of 80-85 years in the Rotterdam study, a large European population-based study.[11] We believe that incidence rates will further increase in the CHD population with ageing of patient cohorts particularly in those with complex repaired lesions. In our cohort, atrial fibrillation was common across all lesions and equally distributed among different lesion types and lesion groups. In contrast, other types of tachyarrhythmias, such as intra-atrial re-entrant tachycardia and monomorphic ventricular tachycardia, were predominantly found in patients with repaired complex defects and repaired right heart lesions, likely reflecting the notion that most of these arrhythmias are scar related and determined by the type of surgical repair and concomitant residual haemodynamic lesions.

Time pattern: (b) highest incidence rates in early childhood and older adults (U-curve)

Whereas all types of tachyarrhythmia occurred predominantly in adulthood, the first onset of complete heart block occurred predominantly in early childhood and older adults. Complete heart block in childhood can be either a lesion-specific complication mainly associated with congenitally corrected transposition of the great arteries[14] based on the anatomical features of this specific lesion or subsequently after open-heart surgery in early repair. The incidence of complete heart block after open-heart surgery for CHD is approximately 1% to 3% in older series.[15,16] Most of postoperative complete heart blocks are the consequence of procedures involving the closure of ventricular septal defect such as in tetralogy of Fallot, complete atrioventricular septal defect, or ventricular septal defect.[17] They usually occur immediately after surgery or early in the postoperative period, and in few cases, they also may occur many months or years after surgery. In line with these previous data, in SACHER, complete heart block is most prevalent in patients with repaired atrioventricular septal defect and congenitally corrected transposition of the great arteries.

Complete heart block in older adults may be the result of degenerative changes as seen in patients without CHD, may occur in patients with abnormal conduction system anatomy (atrioventricular septal defects and congenitally corrected transposition of the great arteries), or may be a consequence of operation/reoperation, particularly valve surgery.[18]

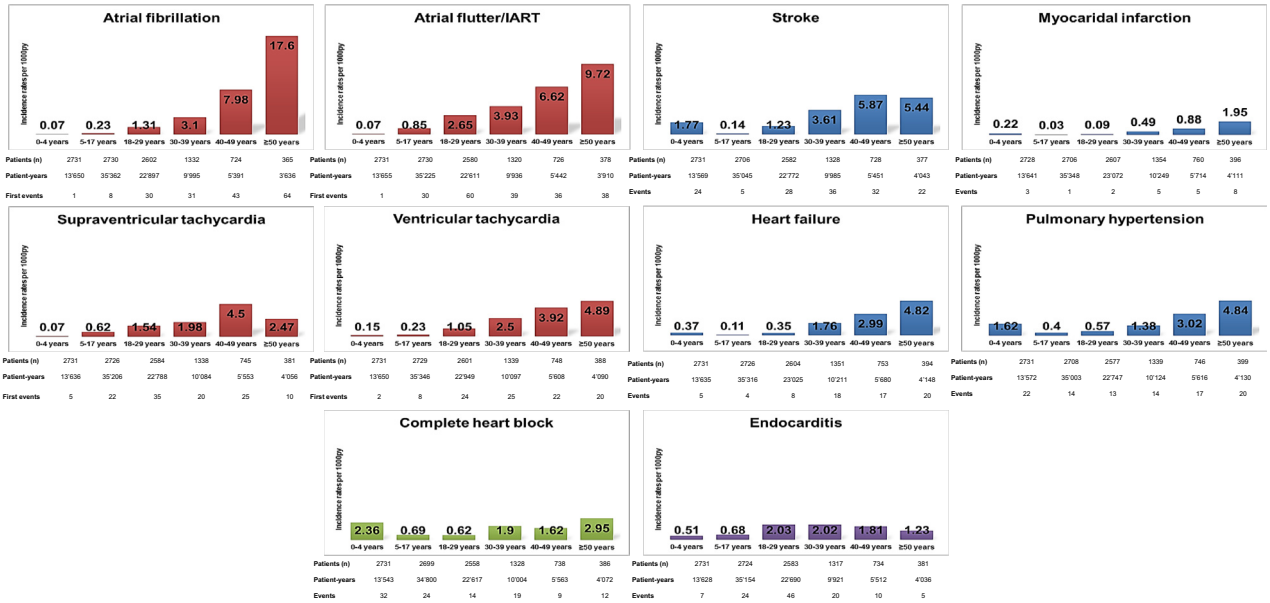

Figure 3. Incidence rates of cardiac complications in congenital heart disease per 1000 patient-years. **Red bars**: incidence rates are increasing with ageing. **Green bars**: highest incidence rates in young children and in older adults (U-curve). **Blue bars**: decreasing incidence rates after early childhood and only increasing after age 30 years with the highest incidence rates in older adults (J-curve pattern). **Violet bars**: highest incidence rates in young adults; decreasing in the older population. IART, intra-atrial re-entrant tachycardia.

Time pattern: (c) J-curve

The incidence rates of heart failure, stroke, myocardial infarction, and pulmonary hypertension showed a J-curve pattern. As described in literature, event rates of heart failure in CHD were increasing with age.[19,20] However, in SACHER, incidence rates of heart failure were 3 times higher in young children compared with adolescents. There are several explanations for this observation with perioperative failure and left-right shunting with subsequent volume overload in not corrected shunt lesions as the most possible ones. Whereas stroke and myocardial infarction are likely associated with peri-interventional accidents in childhood, pulmonary hypertension in childhood is mainly a sequela of untreated left-right shunt leading to elevated pulmonary arterial resistance and Eisenmenger syndrome. Later in adulthood, the prevalence of pulmonary hypertension is increasing, most probably due to left heart disease and the occurrence of postcapillary pulmonary hypertension.[21,22] We have previously demonstrated that the etiology of stroke in SACHER patients is only in approximately 50% of atrial arrhythmia—related origin.[23] Other etiologies of stroke were paradoxical emboli (air or thrombi) in 20%, peri-interventional in 17%, and of other etiology in 14% with septic emboli among others. These non—arrhythmia-related reasons are typically seen in children with stroke. Nevertheless, as the cohort of patients with CHD is still getting older, the incidence of atrial fibrillation and atrial flutter is further increasing. This will very likely lead to a higher incidence rate of cardioembolic strokes.

Myocardial infarction is still a rare complication in CHD. Of note are the 2 patients with an arterial switch operation, who had a myocardial infarction. Coronary events have been described as frequent as 7% in older series,[24] but seems less frequent in young adult patients.[25-27] In SACHER, we analyse only adult survivors, and children who deceased after an arterial switch operation will not be included into the registry and therefore will be missed.

Time pattern: (d) highest incidence rates in young adults

The time pattern of infective endocarditis was unique. We found the highest rates between age 18 and 40 years, whereas incidence rates were lower in children and older adults. Not surprisingly, 50% of the cases with an infective endocarditis occurred in patients with prosthetic valves. Patients with simple valve lesions and replaced (but not repaired) valves (17.6%), patients with a right ventricle to pulmonary artery conduit (12.5%), and patients with repaired tetralogy of Fallot and postpulmonary valve replacement (9.5%) were the most prevalent. The lower incidence rate of infective endocarditis in older adults is probably an artefact of our analysis as the majority of patients with high-risk conditions, such as prosthetic heart valves within our cohort, are < 50 years and simple lesions with low risk of endocarditis, such as ASD II, may be overrepresented in the older patient cohorts. Recent studies reported a higher incidence of infective endocarditis in bovine jugular vein grafts and percutaneously implanted pulmonary valves compared with homografts.[28,29] In the Dutch registry (CONCOR), the median age of adult patients with new onset of infective endocarditis was 37.8 years, similar to our data.[30]

Limitations

SACHER includes adult patients with CHD, and therefore, only prior complications of survivors of CHD could be analysed. Children with CHD who have died from tachyarrhythmia (eg, sudden death), heart failure (eg, undiagnosed child with aortic coarctation), myocardial infarction (eg, after the arterial switch operation), or stroke (eg, perioperative) are not included in the registry, and complications in deceased children have not been analysed in this study. Therefore, the incidence rates of cardiac complications may be underestimated in children. However, mortality has decreased dramatically in the previous decades, and even if slightly more events per patient-year occurred, it is unlikely that the time patterns of the incidence rates will significantly change. Another contribution to underestimation of cardiac complication in childhood is heart transplantation. However, in Switzerland, only 30 children have undergone heart transplantation in the last decade and many of them had non-congenital reasons (acute myocarditis, cardiomyopathy). Because of the retrospective study design, we had to rely on the reported cardiac complications by the attending physicians, but due to very regular follow-ups, in these patients nearly no relevant complications should be missed.

Patients with simple lesions such as bicuspid aortic valves or patients with ASD II are underrepresented in SACHER as many of these patients are followed by general cardiologists. Therefore, cardiac complications associated with these lesions may not have been represented adequately in this study.

Conclusions

Cardiac complications are frequent in CHD. Apart from perioperative stroke and complete heart block, incidence rates are low in childhood but the incidence increases during adult life. These data underscore the need of lifelong follow-up and may help for better allocation of resources maintaining follow-up.

Acknowledgement

We thank the clinical trial unit (CTU) of the University hospital Basel for their statistical support.

Disclosures

The authors declare that they have no relevant conflicts of interest to disclose.

References

1. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution. Circulation 2007;115:163-72.

2. Greutmann M, Tobler D, Kovacs AH, et al. Increasing mortality burden among adults with complex congenital heart disease. Congenit Heart Dis 2015;10:117-27.

3. Tobler D, Schwerzmann M, Bouchardy J, et al. Swiss Adult Congenital HEart disease Registry (SACHER)—rationale, design and first results. Swiss Med Wkly 2017;147:w14519.

4. Gatzoulis MA, Balaji S, Webber SA, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. Lancet 2000;356:975-81.

5. Bouchardy J, Therrien J, Pilote L, et al. Atrial arrhythmias in adults with congenital heart disease. Circulation 2009;120:1679-86.

6. Khairy P, Aboulhosn J, Gurvitz MZ, et al. Arrhythmia burden in adults with surgically repaired tetralogy of Fallot: a multi-institutional study. Circulation 2010;122:868-75.

7. Labombarda F, Hamilton R, Shohoudi A, et al. Increasing prevalence of atrial fibrillation and permanent atrial arrhythmias in congenital heart disease. J Am Coll Cardiol 2017;70:857-65.

8. Chugh SS, Blackshear JL, Shen WK, Hammill SC, Gersh BJ. Epidemiology and natural history of atrial fibrillation: clinical implications. J Am Coll Cardiol 2001;37:371-8.

9. Majeed A, Moser K, Carroll K. Trends in the prevalence and management of atrial fibrillation in general practice in England and Wales, 1994-1998: analysis of data from the general practice research database. Heart 2001;86:284-8.

10. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. Arch Intern Med 1995;155:469-73.

11. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J 2006;27:949-53.

12. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study. JAMA 2001;285:2370-5.

13. Krahn AD, Manfreda J, Tate RB, Mathewson FA, Cuddy TE. The natural history of atrial fibrillation: incidence, risk factors, and prognosis in the Manitoba Follow-Up Study. Am J Med 1995;98:476-84.

14. Connelly MS, Liu PP, Williams WG, et al. Congenitally corrected transposition of the great arteries in the adult: functional status and complications. J Am Coll Cardiol 1996;27:1238-43.

15. Bonatti V, Agnetti A, Squarcia U. Early and late postoperative complete heart block in pediatric patients submitted to open-heart surgery for congenital heart disease. Pediatr Med Chir 1998;20:181-6.

16. Weindling SN, Saul JP, Gamble WJ, et al. Duration of complete atrioventricular block after congenital heart disease surgery. Am J Cardiol 1998;82:525-7.

17. Ayyildiz P, Kasar T, Ozturk E, et al. Evaluation of permanent or transient complete heart block after open heart surgery for congenital heart disease. Pacing Clin Electrophysiol 2016;39:160-5.

18. Lev M. The pathology of complete atrioventricular block. Prog Cardiovasc Dis 1964;6:317-26.

19. Van Dijck I, Budts W, Cools B, et al. Infective endocarditis of a transcatheter pulmonary valve in comparison with surgical implants. Heart 2015;101:788-93.

20. Malekzadeh-Milani S, Ladouceur M, Iserin L, Bonnet D, Boudjemline Y. Incidence and outcomes of right-sided endocarditis in patients with congenital heart disease after surgical or transcatheter pulmonary valve implantation. J Thorac Cardiovasc Surg 2014;148:2253-9.

21. Kuijpers JM, Koolbergen DR, Groenink M, et al. Incidence, risk factors, and predictors of infective endocarditis in adult congenital heart disease: focus on the use of prosthetic material. Eur Heart J 2017;38:2048-56.

22. Piran S, Veldtman G, Siu S, Webb GD, Liu PP. Heart failure and ventricular dysfunction in patients with single or systemic right ventricles. Circulation 2002;105:1189-94.

23. Norozi K, Wessel A, Alpers V, et al. Incidence and risk distribution of heart failure in adolescents and adults with congenital heart disease after cardiac surgery. Am J Cardiol 2006;97:1238-43.

24. Oliver JM, Gallego P, Gonzalez AE, et al. Pulmonary hypertension in young adults with repaired coarctation of the aorta: an unrecognised factor associated with premature mortality and heart failure. Int J Cardiol 2014;174:324-9.

25. van Riel AC, Schuuring MJ, van Hessen ID, et al. Contemporary prevalence of pulmonary arterial hypertension in adult congenital heart disease following the updated clinical classification. Int J Cardiol 2014;174:299-305.

26. Arslani K, Notz L, Zurek M, et al. Anticoagulation practices in adults with congenital heart disease and atrial arrhythmias in Switzerland. Congenit Heart Dis 2018. https://doi.org/10.1111/chd.12627. Accessed November 5, 2018.

27. Legendre A, Losay J, Touchot-Kone A, et al. Coronary events after arterial switch operation for transposition of the great arteries. Circulation 2003;108(suppl 1):II186-90.

28. Tobler D, Williams WG, Jegatheeswaran A, et al. Cardiac outcomes in young adult survivors of the arterial switch operation for transposition of the great arteries. J Am Coll Cardiol 2010;56:58-64.

29. Kempny A, Wustmann K, Borgia F, et al. Outcome in adult patients after arterial switch operation for transposition of the great arteries. Int J Cardiol 2013;167:2588-93.

30. Khairy P, Clair M, Fernandes SM, et al. Cardiovascular outcomes after the arterial switch operation for D-transposition of the great arteries. Circulation 2013;127:331-9.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2018.09.010.