ORIGINAL RESEARCH

Adult Congenital Heart Disease in a Nationwide Population 2000–2014: Epidemiological Trends, Arrhythmia, and Standardized Mortality Ratio

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***Background*—**The adult congenital heart disease (ACHD) population will grow with medical advances, but data are limited. We investigated the epidemiological profile of ACHD in Taiwan, a country with a congenital heart disease program since 1955, population of 23 million, and easily accessible high-standard medical care.

***Methods and Results*—**ACHD patients, born after 1954, were identified from the nationwide database 2000–2014. The ACHD prevalence in the population aged 18 to 59 was 140.53, 157.08, 182.45, and 217.00 per 100 000 in 2000, 2005, 2010, and 2014, respectively (increasing time trend, $P<0.0001$). Percentage of severe ACHD also increased over time ($P<0.0001$) and was 11.70% in 2014. The 5 leading ACHD diagnoses were ventricular septal defect, secundum atrial septal defect, patent ductus arteriosus, pulmonary stenosis, and tetralogy of Fallot. Freedom from tachyarrhythmia at age 50 years was 0.574 and 0.710 for severe and simple ACHD, respectively. Cardiac causes accounted for the majority of deaths, followed by malignancy in simple ACHD and external causes/sudden death/out-of-hospital death in severe ACHD patients. The proportion of unexpected death was 10%. Compared with the general population, the standardized mortality ratio was higher not only in severe ACHD (3.164; 95% confidence interval, 2.664–3.664), but also in women with simple ACHD (1.704; 95% confidence interval, 1.499–1.909), with a higher proportion of cardiac, labor, and sudden death as causes of death.

***Conclusions*—**We demonstrated an increasing trend in ACHD prevalence and medical complexity. They are at risk of tachyarrhythmia, higher mortality, and unexpected deaths, suggesting a gap in their medical care. **(*J Am Heart Assoc*.2018;7: e007907. DOI: 10.1161/JAHA.117.007907.)**

Key Words: adult congenital heart disease • arrhythmia • epidemiology • mortality rate

With medical advances, most patients with congenital heart disease (CHD) may survive into adulthood.[1,2] However, epidemiological data are still limited. Prevalence of adult CHD (ACHD) depends on incidence of CHD in live birth, timing of implementation of the CHD program, and quality, accessibility, and affordability of the CHD program. Open heart surgery for CHD was first performed in the 1940s in North America. According to administrative database, prevalence of ACHD in Quebec was 4.09 per 1000 adults in 2000 and 6.12 per 1000 adults in 2011.[3,4] Data of ACHD prevalence may also be estimated from CHD incidence at birth and survival estimate for each type of CHD. By using this approach, prevalence of ACHD was estimated to be between 1.77 and 4.91 per 1000 adults in 6 high-income countries between 2001 and 2011.[2,5–7] Prevalence of ACHD is generally lower than incidence of CHD at birth for the following reasons: (1) case mortality; (2) loss of follow-up because of spontaneously resolved CHD or asymptomatic surgically repaired CHD; and (3) poor adherence to medical follow-up schedules. Although outcomes of repaired CHD are generally satisfactory, repeated intervention or intervention for late complications, such as stenting for stenosis, pacemakers for conduction disturbances, or even defibrillators for ventricular arrhythmias, are sometimes required. Disease burden and medical demand may increase in the future, which would be a primary medical concern.

In Taiwan, the National Health Insurance (NHI) program, which covers more than 99% of the Taiwanese population (≈23 million), was implemented in 1995. The NHI provides highly accessible high-standard medical care. Furthermore,

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Clinical Perspective

What Is New?

- This nationwide adult congenital heart disease (ACHD) study disclosed an increasing trend of ACHD prevalence and percentage of severe ACHD (217.00 per 100 000 and 11.7% in 2014, respectively).
- Freedom from tachyarrhythmia at age 50 years was 0.574 and 0.710 in severe and simple ACHD. Cardiac causes accounted for the majority of deaths, followed by malignancy in simple ACHD and external causes/sudden death/out-of-hospital death in severe ACHD.
- Standardized mortality ratio is higher not only in severe ACHD (3.164), but also in women simple ACHD (1.704), with higher proportions of cardiac, labor, and sudden death as causes of death.

What Are the Clinical Implications?

- The increasing trend of ACHD prevalence and the medical complexity is expected and is up to the timing of the implementation of structured congenital heart disease program and its accessibility/affordability in each country.
- Given that the ACHD patients are at risk of higher mortality from ACHD per se and relatively higher proportion of unexpected death, interdisciplinary collaboration and timely risk stratification/intervention are mandatory particularly in an ACHD center.
- Medical needs (eg, treatment for tachyarrhythmia) are distinct medical issues, of which treatment can only be optimized by future studies.

the NHI waives copayment for patients with CHD and provides affordable care for children with CHD from birth. Child health indices in Taiwan are similar to those in the United States.[8] The practice of pediatric cardiology in Taiwan was started relatively early, with the first cardiac repair of CHD performed in 1954 and the first Blalock-Taussig shunt performed in 1965. In the past 2 decades, more than 10 medical centers have provided advanced cardiac care, including cardiac surgery and transcatheter interventions. Therefore, a nationwide database covering a 15-year period is adequate for obtaining state-of-the-art epidemiology data for ACHD, including trends and outcomes.

Methods

Our institutional research board approved this study. All data used are deidentified; thus, each individual's consent is waived.

Data, analytical methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Patient Cohort

Patients were selected from the healthcare records of the NHI database between January 1, 2000 and December 31, 2014 based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes (*ICD-9* codes: 745.0–747.42).[9] Thus, we created a population-based CHD database containing data files of all patients diagnosed with CHD who had used the healthcare system in Taiwan. There were few people with incomplete data attributed to, possibly, emigration, immigration, etc. At every time point, adult patients were considered as those aged ≥18 years. Because the CHD program in Taiwan was implemented in 1954, adults born after January 1955 were studied. Such criteria may overlook the confounding effects of other diseases commonly encountered in old age and represent the ACHD epidemiology after implementation of the CHD program. To avoid errors from tentative diagnoses, we excluded patients who had made fewer than 3 outpatient clinic visits for a major diagnosis of CHD. The CHD population was further grouped as having simple CHD and severe CHD. Severe CHD included tetralogy of Fallot (TOF), transposition of great arteries, double outlet of right ventricle, endocardial cushion defect, total anomalous pulmonary venous return, tricuspid atresia, congenitally corrected transposition of the great arteries, common truncus, and common ventricles.[4,9] Simple CHD includes the other CHD diagnoses.

Each health record had a scrambled identification number and comprised information such as date of birth, date of visit, sex, type of admission or outpatient department visit, diagnosis and treatment codes, reimbursement fees, and survival status at discharge. Occurrence of arrhythmias was identified from the coexisting diagnosis of *ICD-CM* codes for each type of arrhythmia. Patients who received pacemaker therapy and an intracardiac defibrillator converter were identified using the procedure codes and device reimbursement codes. Survival was confirmed using the survival status at discharge and further confirmed using patients' insurance status on December 31, 2014. Causes of death were defined by the diseases listed at the first and second main diagnoses at the final admission or final emergency service visit during which the patient died.

Statistical Analysis

We performed statistical analyses using SPSS (Version 20.0; SPSS, Inc, Chicago, IL) or SAS (Version 9.4; SAS Institute Inc, Cary, NC). Prevalence was defined as the proportion of individuals in a population who had a disease at a specific time point. We measured the observed prevalence of CHD corresponding to the number of patients from the database between 2000 and 2014 in a given single year of age between

18 and 59 years for each calendar year divided by Taiwan's population of the same in a given single year of age between 18 and 59 years for each calendar year. Pop(a,t) as the Taiwanese population and ACHD(a,t) as the number of ACHD cases in age a and calendar year t, the prevalence of ACHD was defined as ACHD(a,t)/Pop(a,t)×100 000. Because CHD was present since birth, a patient would contribute to the prevalence in all the years of his or her life. Absolute numbers and prevalence are reported on the basis of a patient's age each year. The yearly trend was then examined using the Poisson regression model. Kaplan–Meier analysis was used for the estimate for freedom from events. Mortality data in the general population were accessed from the Taiwan National Vital Statistics from 2000 to 2014. Because of the annual mortality data in the general population from our National Vital Statistics were presented by age groups in every 10 years, the comparison of annual mortality between ACHD and general population was made in the population between 20 and 59 years by age groups in every 10 years. To compare the mortality between the general population and ACHD population, standardized mortality ratios (SMRs) were used and calculated using the following formula: SMR=observed number of deaths (O)/expected number of deaths (E). The 95% confidence interval (95% CI) for SMR was calculated using the formula, 95% CI=SMR±1.96×SE, where SE SMR=SMR/$\sqrt{O}$=$\sqrt{O}$/E.[10]

Results

Prevalence of ACHD

A total of 122 518 patients with CHD were identified, of which 33 212 (44.3% male) were aged >18 years in 2000, 2005, 2010, and 2014. These patients composed the ACHD cohort. Prevalence of CHD in 2000, 2005, 2010, and 2014 was estimated, respectively, under the different definition of population at risk. After considering the birth cohort, the population at risk were aged 18 to 45 years in 2000 (N=10 602 098), 18 to 50 years in 2005 (N=12 204 825), 18 to 55 years in 2010 (13 818 080), and 18 to 59 years in 2014 (N=15 027 897), respectively. Prevalence of ACHD was 140.53 (95% CI, 138.27–142.78), 157.08 (95% CI, 163.7–168.4), 182.45 (95% CI, 180.2–184.7), and 217.00 (95% CI, 214.64–219.35) per 100 000 adults in 2000, 2005, 2010, and 2014, respectively (Table 1). An increasing trend was observed for ACHD prevalence in each year as well as the prevalence of most specific types of ACHD (Table 1). The annual increment for ACHD was 2.4%, 3.2%, and 4.7% in 2005, 2010, and 2014, respectively. The 5 leading ACHD diagnoses in 2014 were ventricular septal defect, secundum atrial septal defect, patent ductus arteriosus, pulmonary stenosis, and TOF, followed by coarctation of the aorta, aortic stenosis, endocardial cushion defect, transposition of great arteries, and Ebstein's anomaly. Prevalence of all other CHD diagnoses was below 1 per 100 000 adults. Only the prevalence of hypoplastic left heart syndrome, subaortic stenosis, and cor triatriatum remained constant. Percentage of severe ACHD in the whole ACHD cohort increased with time (P<0.0001) and was 10.20% and 11.70% in 2000 and 2014, respectively (Figure 1A). From 2000 to 2014, increases in prevalence of severe and simple ACHD were 77.2% (from 0.14 per 1000 to 0.25 per 1000 individuals) and 51.8% (from 1.26 per 1000 to 1.92 per 1000 individuals), respectively. Female dominance was observed in prevalence of secundum atrial septal defect, patent ductus arteriosus, pulmonary stenosis, pulmonary atresia, Ebstein's anomaly, endocardial cushion defect, and common truncus, whereas male dominance was noted in prevalence of TOF and transposition of great arteries.

Arrhythmias in ACHD

Tachyarrhythmias were observed in 2396 (7.22%) patients, including atrial flutter or fibrillation in 1369 (median onset age, 41.34; 39.06±11.54 years), supraventricular tachycardia or Wolff–Parkinson–White syndrome in 904 (median onset age, 25.43; 26.96±13.23 years), and ventricular tachycardia or ventricular fibrillation in 515 (median onset age, 33.34; 32.88±13.31 years). In 389 of these patients, tachyarrhythmia occurred before age 18. Freedom from tachyarrhythmias was 0.965, 0.924, 0.821, and 0.697 at the ages of 30, 40, 50, and 59 years, respectively. Patients with severe ACHD were more likely to develop arrhythmias than were those with simple ACHD (P<0.0001; Figure 1B). Freedom from tachyarrhythmias was 0.574 and 0.710 at the age of 50 years in patients with severe and simple ACHD, respectively. In each type of ACHD, patients with complex CHD, common ventricle, Ebstein's anomaly, and tricuspid atresia had higher risk of tachyarrhythmia (Table 2). Almost half of these patients are expected to develop tachyarrhythmia by the age of 40 or 50 years. Freedom from tachyarrhythmia in patients with TOF was 0.734 and 0.599 at the ages of 50 and 59 years, respectively. Furthermore, patients of all types of ACHD were at a >10% risk of experiencing tachyarrhythmia by age 50. Electrophysiology with or without ablation was performed in 513 (21.4% of patients with tachyarrhythmia) patients at a median age of 28.81 (30.49±13.55) years. Implantable cardioverter-defibrillators were administered to 33 patients (6.5% of those who had survived ventricular tachycardia or ventricular fibrillation episodes).

Bradyarrhythmias were observed in 306 (0.99%) patients, including complete atrioventricular block in 193, sick sinus syndrome in 104, and both in 9.

Table 1. Prevalence and the Trend of Adult Congenital Heart Disease in Taiwan Population Aged 18 to 59 Years 2000–2014 (Number/100 000) and the Trend Over the Time Point 2000, 2005, 2010, and 2014

Diagnosis	2000 (95% CI)	2005 (95% CI)	2010 (95% CI)	2014 (95% CI)	*P* Value (Sex Dominance)	*P* Value (Trend)
Severe	14.33 (13.61, 15.05)	17.53 (16.78, 18.27)	21.41 (20.64, 22.19)	25.4 (24.59, 26.21)	0.50	<0.0001
TOF	8.89 (8.32, 9.45)	11.04 (10.45, 11.63)	13.27 (12.67, 13.88)	15.53 (14.9, 16.16)	0.0016 (M)	<0.0001
ECD	2.38 (2.08, 2.67)	2.65 (2.37, 2.94)	3.15 (2.85, 3.44)	3.47 (3.18, 3.77)	<0.0001 (F)	<0.0001
TGA	0.99 (0.8, 1.18)	1.25 (1.05, 1.45)	1.72 (1.5, 1.93)	2.14 (1.91, 2.38)	<0.0001 (M)	<0.0001
Common truncus	0.48 (0.35, 0.61)	0.52 (0.4, 0.65)	0.61 (0.48, 0.74)	0.86 (0.71, 1.01)	<0.0001 (F)	0.0001
Tricuspid atresia	0.37 (0.25, 0.48)	0.48 (0.35, 0.6)	0.64 (0.5, 0.77)	0.83 (0.68, 0.97)	0.99	<0.0001
DORV	0.33 (0.22, 0.44)	0.44 (0.32, 0.56)	0.65 (0.52, 0.79)	0.75 (0.61, 0.89)	0.53	<0.0001
TAPVR	0.22 (0.13, 0.31)	0.33 (0.23, 0.43)	0.48 (0.37, 0.6)	0.63 (0.5, 0.75)	0.18	<0.0001
Common ventricle	0.29 (0.19, 0.4)	0.36 (0.25, 0.47)	0.45 (0.34, 0.56)	0.59 (0.47, 0.72)	0.08	0.0002
Complex CHD	0.19 (0.11, 0.27)	0.25 (0.16, 0.33)	0.3 (0.21, 0.4)	0.44 (0.33, 0.55)	0.12	0.0002
HLHS	0.15 (0.08, 0.22)	0.18 (0.1, 0.26)	0.14 (0.08, 0.21)	0.15 (0.09, 0.21)	0.0034 (F)	0.7236
Simple	126.2 (124.06, 128.34)	139.55 (137.46, 141.65)	161.04 (158.92, 163.15)	191.6 (189.39, 193.81)	<0.0001 (F)	<0.0001
VSD	45.13 (43.85, 46.41)	53.2 (51.91, 54.49)	64.01 (62.68, 65.34)	76.72 (75.32, 78.12)	0.0003 (M)	<0.0001
ASDII	48.76 (47.43, 50.09)	50.64 (49.37, 51.9)	55.89 (54.64, 57.14)	66.01 (64.71, 67.31)	<0.0001 (F)	<0.0001
PDA	16.82 (16.04, 17.6)	17.87 (17.12, 18.62)	19.44 (18.7, 20.17)	22.6 (21.84, 23.36)	<0.0001 (F)	<0.0001
PS	10.55 (9.94, 11.17)	12.4 (11.78, 13.03)	15.83 (15.17, 16.5)	20.54 (19.81, 21.26)	<0.0001 (F)	<0.0001
CoA	2.11 (1.84, 2.39)	2.64 (2.35, 2.93)	3.42 (3.11, 3.73)	4.21 (3.88, 4.53)	0.21	<0.0001
AS	3.28 (2.94, 3.63)	3.5 (3.17, 3.83)	3.76 (3.44, 4.09)	4.2 (3.87, 4.53)	<0.0001 (M)	<0.0001
Ebstein	1.52 (1.28, 1.75)	1.58 (1.36, 1.8)	1.69 (1.47, 1.9)	1.9 (1.68, 2.12)	<0.0001 (F)	0.014
SAS	0.43 (0.31, 0.56)	0.42 (0.3, 0.53)	0.5 (0.38, 0.62)	0.53 (0.41, 0.64)	<0.0001 (M)	0.1822
PA	0.19 (0.11, 0.27)	0.21 (0.13, 0.29)	0.35 (0.26, 0.45)	0.45 (0.34, 0.55)	0.0141 (F)	<0.0001
Cor triatriatum	0.22 (0.13, 0.31)	0.22 (0.14, 0.3)	0.21 (0.13, 0.29)	0.25 (0.17, 0.33)	0.27	0.6019
Total	140.53 (138.27, 142.78)	157.08 (154.86, 159.3)	182.45 (180.2, 184.7)	217 (214.64, 219.35)	<0.0001 (F)	<0.0001

AS indicates aortic stenosis; ASDII, secundum atrial septal defect; CI, confidence interval; CoA, coarctation of aorta; DORV, double outlet of right ventricle; ECD, endocardila cushion defect; HLHS, hypoplastic left heart syndrome; PA, pulmonary atresia; PDA, patent ductus arteriosus; PS, pulmonary stenosis; SAS, subaortic stenosis; TAPVR, total anomalous pulmonary venous return; TGA, transposition of great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

Mortality in ACHD

During follow-up for 395 783 patient-years, 685 deaths (2.06%) occurred. Among them, 645 deaths occurred in patients aged ≧20 years of age. Annual mortality in each age-group–specific mortality was higher in older age groups in the simple and severe CHD groups (Figure 2A). Annual mortality among patients with TOF, the most common form of severe CHD, was almost twice as high as that among patients with secundum atrial septal defect and ventricular septal defect, the most common forms of simple CHD (Figure 2B). In patients with ACHD, cardiac causes accounted for the majority of deaths, followed by malignancy in patients with simple ACHD and external causes, sudden death, or out-of-hospital death in patients with severe ACHD (Table 3). Sudden death, out-of-hospital death, and death after cardiopulmonary resuscitation by emergency services accounted for ≈10% of all the deaths.

Comparison With the General Population

Annual mortality in each age group in the general population was substantially lower than that in patients with severe ACHD (Figure 2A). Therefore, SMRs were calculated using the Taiwan reference population's age at diagnosis-, sex-, and time-of-follow-up–adjusted mortality rates (Table 4). SMR was

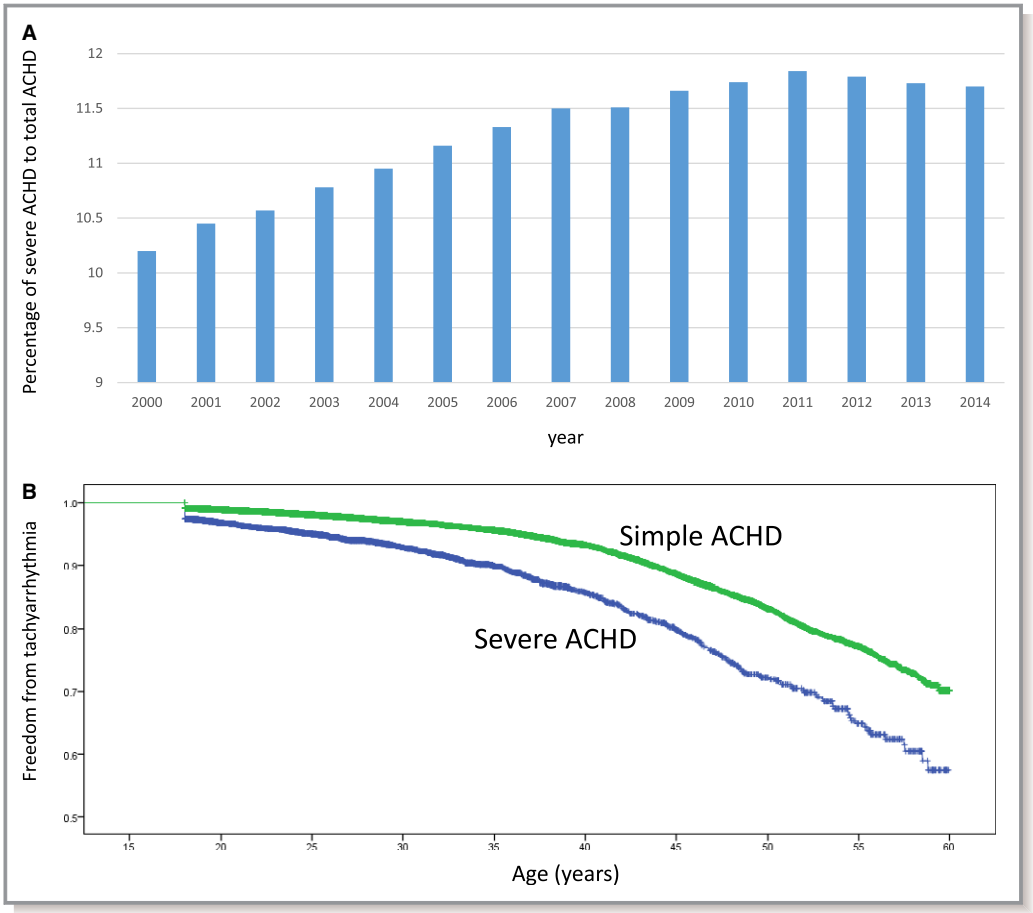

Figure 1. A, Percentage of severe adult congenital heart disease in the whole adult congenital heart disease cohort from 2000 to 2014. B, Freedom from tachyarrhythmia in simple adult congenital heart disease (simple ACHD) and severe adult congenital heart disease (severe ACHD) cohorts.

higher not only in patients with severe ACHD (3.164; 95% CI, 2.664–3.664), but also in women with simple ACHD (1.704; 95% CI, 1.499–1.909). In each specific type of ACHD, we observed an excess mortality in all types of severe ACHD, but only in women for the most common types of simple ACHD (ventricular septal defect, secundum atrial septal defect, patent ductus arteriosus, and pulmonary stenosis).

To elucidate the reasons for the excessive mortality in ACHD, we compared the causes of death in age comparable groups between ACHD and the general population (Table 4). The proportion of cardiac death was substantially higher in the ACHD group than in the general population and was essentially attributed to ACHD per se. Moreover, the proportion of labor as the cause of death was much higher in patients with ACHD (1.32%) than in the general population (0.04%) and may account for the excessive mortality in women with simple ACHD. In addition, the proportion of sudden death as the cause of death was higher in patients with simple and severe ACHD than in the general population.

Discussion

From a national database covering a period of 15 years, we obtained the latest epidemiological data of a population aged 18 to 59 years in an era of advanced CHD interventions. The main findings were as follows. (1) ACHD prevalence and percentage of severe ACHD increased over time and were 2.170 per 1000 adults and 11.7%, respectively, in 2014. (2) Tachyarrhythmia is common in ACHD, and freedom from tachyarrhythmia by the age of 50 years was 0.574 and 0.710 in patients with severe and simple ACHD, respectively. (3) Mortality among patients with ACHD increased with age and the SMR adjusted to the general age population was substantially higher in patients with severe ACHD and women with simple ACHD. (4) Excessive mortality in ACHD patients may be related to ACHD per se; but ACHD patients more likely died of sudden death or labor compared with the general population.

This is the first nationwide cohort study to investigate the prevalence, outcomes (arrhythmia and mortality), and trends

Table 2. In the Adult Congenital Heart Disease Patients Aged 18 to 59 Years, the Freedom From Tachyarrhythmias at Each Age Point in Each Type of Adult Congenital Heart Disease

	Age (y)				
Disease (Case No.)	20	30	40	50	59
Complex CHD (74)	0.808 (0.046)*	0.745 (0.055)	0.533 (0.099)	0.000 (0.000)†	NA
Ebstein's anomaly (298)	0.858 (0.021)	0.777 (0.026)	0.620 (0.034)	0.390 (0.040)	0.265 (0.053)
PA (68)	1.0	0.936 (0.036)	0.688 (0.112)	0.516 (0.171)	0.258 (0.202)
Tricuspid atresia (128)	0.920 (0.024)	0.790 (0.047)	0.695 (0.060)	0.542 (0.109)	0.406 (0.143)
Cor triatriatum (41)	1.0	0.864 (0.063)	0.864 (0.063)	0.549 (0.120)	0.439 (0.137)
DORV (123)	0.908 (0.027)	0.869 (0.034)	0.803 (0.055)	0.750 (0.073)	0.500 (0.210)
Common ventricle (100)	0.866 (0.035)	0.784 (0.048)	0.599 (0.086)	0.539 (0.096)	0.539 (0.096)
TGA (334)	0.949 (0.012)	0.871 (0.023)	0.832 (0.029)	0.657 (0.060)	0.564 (0.083)
TOF (2524)	0.980 (0.003)	0.946 (0.005)	0.880 (0.011)	0.734 (0.022)	0.599 (0.052)
ECD (538)	0.974 (0.007)	0.957 (0.010)	0.895 (0.019)	0.776 (0.033)	0.576 (0.059)
TAPVR (97)	0.989 (0.011)	0.989 (0.011)	0.930 (0.057)	0.744 (0.126)	0.638 (0.146)
Common truncus (135)	0.970 (0.015)	0.939 (0.026)	0.859 (0.051)	0.723 (0.085)	0.643 (0.107)
SAS (86)	0.988 (0.012)	0.937 (0.031)	0.828 (0.053)	0.720 (0.069)	0.648 (0.092)
AS (643)	0.991 (0.004)	0.973 (0.007)	0.944 (0.012)	0.839 (0.023)	0.672 (0.053)
PS (3118)	0.984 (0.002)	0.974 (0.003)	0.953 (0.006)	0.855 (0.018)	0.676 (0.047)
ASDII (10 086)	0.985 (0.001)	0.962 (0.002)	0.918 (0.004)	0.808 (0.007)	0.668 (0.015)
PDA (3465)	0.993 (0.001)	0.982 (0.003)	0.957 (0.005)	0.883 (0.011)	0.727 (0.048)
PS (3119)	0.984 (0.002)	0.974 (0.003)	0.953 (0.006)	0.855 (0.018)	0.676 (0.047)
HLHS (24)	1.0	0.955 (0.044)	0.955 (0.044)	0.795 (0.150)	0.795 (0.150)
CoA (644)	0.991 (0.004)	0.975 (0.007)	0.935 (0.017)	0.865 (0.028)	0.797 (0.048)
VSD (11 703)	0.991 (0.001)	0.976 (0.002)	0.945 (0.003)	0.870 (0.007)	0.781 (0.016)

AS indicates aortic stenosis; ASDII, secundum atrial septal defect; CoA, coarctation of aorta; DORV, double outlet of right ventricle; ECD, endocardila cushion defect; HLHS, hypoplastic left heart syndrome; PA, pulmonary atresia; PDA, patent ductus arteriosus; PS, pulmonary stenosis; SAS, subaortic stenosis; TAPVR, total anomalous pulmonary venous return; TGA, transposition of great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

*Data are shown as freedom from the event (SE).

†Last patient developed atrial flutter/fibrillation at the age of 43 years.

of ACHD in the recent 15 years. The study results revealed that prevalence of ACHD rapidly increased at an annual increment of 2.4% in 2000–2005 and 4.7% in 2011–2014. Such an increase might continue until the prevalence is close to the incidence of CHD at birth adjusted by optimized survival. In 2014, the prevalence of ACHD in our study was 2.17 per 1000 adults, which is within the previous reported estimated range (1.7–6.12 per 1000).[1,3–6] In most high-income countries in which care for ACHD is increasingly structured, prevalence of severe ACHD would increase over time.[3,4,11] As revealed in the report from Quebec, severe ACHD accounted for 9% and 10.13% of the CHD population in 2000 and 2010, respectively.[3,4] The percentage of severe CHD in our cohort in 2014 was even higher (11.7%), suggesting a future increasing trend in both ACHD and its medical complexity.

Because of the residual hemodynamic and electrophysiological disturbances, tachyarrhythmia in repaired TOF is common.[12–14] According to data from the Alliance for Adult Research in Congenital Cardiology, tachyarrhythmia occurred in 29.9% of adult TOF patients and in a higher percentage of older patients. In the current study, freedom from tachyarrhythmia decreased with age and was 0.734 and 0.599 at the ages of 50 and 59 years, respectively, in adult TOF. Risk of tachyarrhythmia was 26.6% at age 50 and 40.1% at age 59. However, the highest risk of tachyarrhythmias was observed in patients with complex CHD, followed by those with Ebstein's anomaly. All patients with complex CHD and 61% of those with Ebstein's anomaly might have tachyarrhythmia by age 50. Such a risk can be attributed to the common association between conduction system abnormalities in these patients.[15–18] However, tachyarrhythmias are common to all ACHD types. Even in simple ACHD, more than 10% of the patients were estimated to have tachyarrhythmia by age 50. The mechanisms for such increased risks of tachyarrhythmia are related to structural alterations and

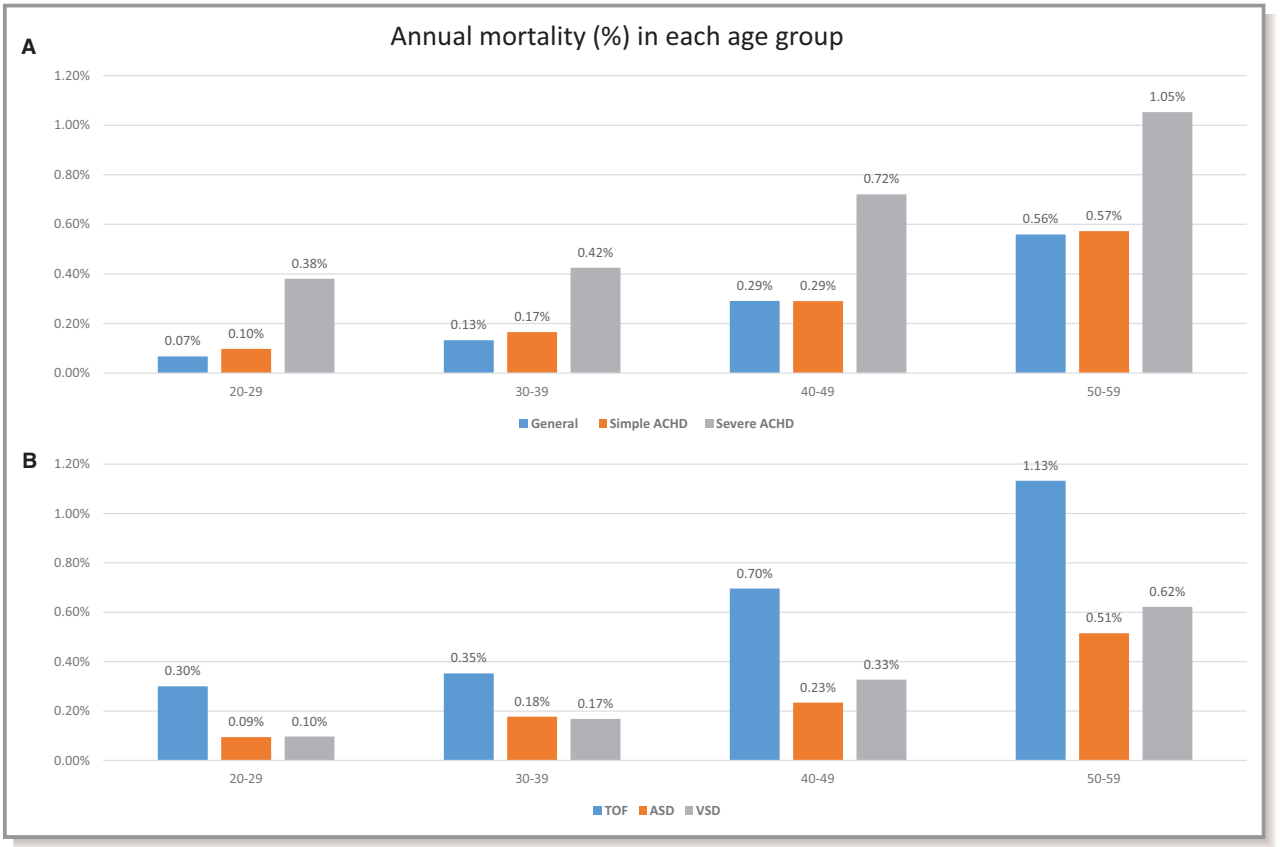

Figure 2. A, Age-group–specific mortality in general population, simple adult congenital heart disease (simple ACHD), and severe adult congenital heart disease (severe ACHD) patients. B, Age-group–specific mortality in adult patients with tetralogy of Fallot (TOF), secundum atrial septal defect (ASDII), and ventricular septal defect (VSD).

electrophysiological remodeling; however, additional studies on each type of ACHD are warranted to completely elucidate these mechanisms.

Table 3. Causes of Death in Adult Congenital Heart Disease and General Population Aged 20 to 59 Years of Age During the Study Period 2000–2014

Causes of Death	ACHD			General Population
	Severe	Simple	Total	
Cardiac	61.14%	37.33%	43.42%	9.35%
Malignancy	3.43%	12.97%	10.53%	34.53%
External causes	4.57%	6.68%	6.14%	18.27%
CVA	3.43%	4.91%	4.53%	5.24%
SD	4.57%	4.13%	4.24%	0.14%*
Labor complication	0.57%	1.57%	1.32%	0.04%
Out of hospital death	4.57%	6.48%	5.99%	NA
ES CPR	0.63%	0.57%	0.58%	NA
Others	18.85%	27.11%	25%	32.43%

CVA indicates cerebrovascular accident; ES CPR, cardiopulmonary resuscitation in emergency service; SD, sudden death.
*Data 2007–2014.

Survival of patients with ACHD was less favorable than that of the general population, and the identified risk factors included cyanosis, univentricular physiology, genetic disorders, ventricular dysfunction, residual hemodynamic lesions, and acquired late complications.[19] However, overall survival was reduced irrespective of the level of complexity, repair status, or underlying CHD.[19] Mortality among our patients with severe ACHD was 3.164-fold higher than that among the general population. However, we also observed excessive mortality in patients with simple ACHD, but only in women, with 1.889-fold higher mortality. We observed that labor accounted for 1.57% of the causes of death in patients with simple ACHD. In severe ACHD patients, labor accounted for 0.57% of the causes of death. By contrast, labor accounted for only 0.04% of the causes of death in the general population. The higher proportion of labor as the causes of death in simple ACHD patients compared with severe ACHD patients may simply reflect the fact that so few of the severe ACHD patients were able or advised to carry a pregnancy. Maternal cardiac and neonatal complication rates were extremely high in pregnant women with CHD.[20] Labor may, at least partially, account for the excessive mortality in women with simple ACHD. Furthermore, sudden death accounted for a higher

Table 4. Standardized Mortality Ratios (Adjusted to the General Population by Age and Sex) in the Study Period 2000–2014

Population Aged 20 to 59 y	Subgroup	Gender	Standardized Mortality Ratios (% CI)	*P* Value
ALL ACHD		Total	1.279 (1.181, 1.378)	<0.001
		Male	1.13 (1.007, 1.253)	0.0274
		Female	1.889 (1.683, 2.096)	<0.001
Simple CHD		Total	1.078 (0.983, 1.174)	0.094
		Male	0.89 (0.774, 1.006)	0.08
		Female	1.704 (1.499, 1.909)	<0.001
	VSD	Total	1.187 (1.016, 1.357)	0.0194
		Male	0.855 (0.684, 1.026)	0.1247
		Female	2.065 (1.638, 2.491)	<0.001
	ASDII	Total	0.994 (0.851, 1.137)	0.937
		Male	0.892 (0.692, 1.091)	0.314
		Female	1.542 (1.253, 1.832)	<0.001
	PDA	Total	1.347 (1.04, 1.654)	0.01
		Male	1.386 (0.853, 1.918)	0.095
		Female	2.018 (1.441, 2.595)	<0.001
	PS	Total	0.929 (0.607, 1.251)	0.678
		Male	0.604 (0.23, 0.978)	0.107
		Female	1.727 (1.005, 2.449)	0.009
	CoA	Total	1.855 (0.916, 2.793)	0.015
		Male	1.716 (0.652, 2.78)	0.084
		Female	2.24 (0.277, 4.204)	0.064
	Ebstein	Total	1.31 (0.402, 2.218)	0.443
		Male	1.118 (0.022, 2.213)	0.824
		Female	1.976 (0.04, 3.912)	0.165
	AS	Total	0.772 (0.316, 1.228)	0.39
		Male	0.403 (0.05, 0.757)	0.036
		Female	1.898 (0.379, 3.417)	0.11
Severe CHD		Total	3.164 (2.664, 3.664)	<0.001
		Male	2.987 (2.396, 3.578)	<0.001
		Female	3.887 (2.869, 4.904)	<0.001
	TOF	Total	2.844 (2.225, 3.463)	<0.001
		Male	2.583 (1.874, 3.292)	<0.001
		Female	3.666 (2.354, 4.977)	<0.001
	TGA	Total	2.712 (1.031, 4.393)	0.001
		Male	2.276 (0.59, 3.963)	0.025
		Female	3.455 (−0.455, 7.364)	0.022
	DORV	Total	8.422 (3.202, 13.642)	<0.001
		Male	11.394 (3.498, 19.289)	<0.001
		Female	5.159 (−1.991, 12.309)	0.01
	Tricuspid atresia	Total	5.042 (1.008, 9.077)	<0.001
		Male	3.512 (−0.462, 7.485)	0.02
		Female	9.016 (−1.187, 19.219)	<0.001

Continued

Table 4. Continued

Population Aged 20 to 59 y		Subgroup	Gender	Standardized Mortality Ratios (% CI)	*P* Value
		ECD	Total	2.031 (1.118, 2.944)	0.002
			Male	2.292 (0.995, 3.589)	0.003
			Female	2.182 (0.566, 3.798)	0.034

AS indicates aortic stenosis; ASDII, secundum atrial septal defect; CoA, coarctation of aorta; DORV, double outlet of right ventricle; ECD, endocardila cushion defect; HLHS, hypoplastic left heart syndrome; PA, pulmonary atresia; PDA, patent ductus arteriosus; PS, pulmonary stenosis; SAS, subaortic stenosis; TAPVR, total anomalous pulmonary venous return; TGA, transposition of great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

percentage of causes of death in simple and severe ACHD (4.24% in ACHD versus 0.14% in the general population).[21] Collectively, the proportion of unexpected death (sudden death, out-of-hospital death, and death after resuscitation by emergency services) was high (10%), indicating a gap in the medical care program for ACHD. As suggested in previous studies, sudden death from ACHD may be associated with ventricular dysfunction, QRS prolongation, and QT dispersion; however, 10% of sudden deaths still occurred in patients with simple septal defects (including 2 unrepaired because of insignificant shunt).[22]

Study Limitations

Although our findings were robust, this study had certain limitations. First, to avoid the inclusion of patients who had received tentative CHD diagnoses, we excluded patients who visited the outpatient clinic less than 3 times because of CHD diagnoses. Therefore, we may have underestimated ACHD prevalence among patients with ACHD who poorly adhered to medical visiting schedules. Second, the presence of CHD sometimes was not discovered until adolescence or even until adulthood and the intervention time course may be different, these variables may have affected the mortality data. Third, we may have underestimated the risk of sudden death and the associated arrhythmias of those who died before arriving at the hospital. Furthermore, because we could not directly assess the hemodynamic data, we could not analyze the association between these parameters and the outcome. Additional studies with selected institutional databases may provide insights into this association.

Conclusions

This nationwide population study demonstrated that the prevalence of ACHD was 2.17 per 1000 adults in 2014 and revealed an increasing trend in the prevalence and medical complexity. In addition, the findings indicated the significant risk of tachyarrhythmia in each type of ACHD. Moreover, the proportion of unexpected deaths (sudden death, out-of-hospital death, and death after resuscitation by emergency services) was high (10%), indicating a gap in the medical care program of ACHD.

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Disclosures

None.

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Adult Congenital Heart Disease in a Nationwide Population 2000–2014: Epidemiological Trends, Arrhythmia, and Standardized Mortality Ratio

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