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ORIGINAL ARTICLE

National database study of survival of pediatric congenital heart disease patients in Taiwan

Shu-Jen Yeh [a,b], Hui-Chi Chen [c], Chun-Wei Lu [d], Jou-Kou Wang [d], Li-Min Huang [b,d], Shin-Chung Huang [e], San-Kuei Huang [e], Mei-Hwan Wu [d,*]

[a] *Department of Pediatrics, Far Eastern Memorial Hospital, New Taipei City, Taiwan, ROC*
[b] *Graduate Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei City, Taiwan, ROC*
[c] *Genomics Research Center, Academia Sinica, Taipei City, Taiwan, ROC*
[d] *Department of Pediatrics, National Taiwan University Hospital and Medical College, National Taiwan University, Taipei City, Taiwan, ROC*
[e] *Taiwan Bureau of National Health Insurance, Taiwan, ROC*

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Background/Purpose: The incidence of congenital heart disease (CHD) and severe CHD is 13.08 and 1.51/1000 live births, respectively, in Taiwan, which has had national health insurance since 1995 and child health indices similar to those in the US. This study sought to further elucidate the fatality of CHD patients and their survival from a national database.
Methods: From the national health insurance database 2000–2010, we retrieved data from CHD patients who were diagnosed at age <6 years. The survival status at discharge was ascertained for estimation of survival.
Results: In total, 18,843 pediatric CHD patients were identified. The overall prevalence of CHD was 1288 per 100 000 live-births. Severe CHD (tetralogy of Fallot (4.4%), transposition of the great arteries (1.6%) and double outlet right ventricle (1.1%)) accounted for 11.5% of all cases. The 1-month/5-year survival in simple and severe CHD was 99.1%/97.5% and 90.2%/76.4%, respectively ($p < 0.0001$). The Kaplan-Meier survival at 5 years of age was lowest for hypoplastic left heart syndrome (19.7%), followed by transposition of the great arteries (66.7%), double outlet right ventricle (69.0%), and common ventricle (66.0%). The 5-year survival of the birth cohort in the same study period was 99.3%.

* Corresponding author. Department of Pediatrics, National Taiwan University Hospital, No. 7 Chung-Shen South Road, Taipei 100, Taiwan, ROC.
E-mail address: wumh@ntu.edu.tw (M.-H. Wu).

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Conclusion: This national database study revealed that the survival of children with simple CHD was still slightly lower than that of the general population and the survival of severe CHD patients, though only accounting for one-tenth of CHD cases, remained unsatisfactory. Such survival profiles are similar to those from Western reports and warrant a refined and dedicated medical care program for children with CHD.
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Introduction

Recent advances in postnatal cardiac intervention have greatly improved the outcomes of patients with congenital heart disease (CHD)[1–4]; however, data regarding overall survival rates are still scarce.[3–6] The incidence of CHD ranges from 4 to 12 per 1000 live births and is generally estimated to be approximately 10 per 1000 live births.[6–8] A Taiwanese national population study (2000–2006) showed that the overall incidence of CHD was 13.08 per 1000 live births, with severe and simple CHDs occurring at rates of 1.42 and 11.66 per 1000 live births, respectively.[9]

The survival of individuals with simple CHD, such as ventricular or atrial septal defects, is good and comparable to the normal population. However, for individuals with severe CHD, the prognoses vary considerably. Generally, individuals with CHD requiring single ventricular palliation, such as hypoplastic left heart syndrome (HLHS) or common ventricle, still have poor prognoses.[3,6] At the other end of the spectrum, patients with biventricular CHD, such as tetralogy of Fallot (ToF) or transposition of the great arteries (TGA), survive well if properly managed. Some studies have suggested that the long-term survival rate of ToF is approximately 85–90%.[10–13] The results from institutional studies vary significantly, however, and have multiple confounding factors. A population-based study using a registry database may avoid institutional bias and would provide a global view of outcomes for patients with CHD, which will be important references for relevant healthcare policy-making.

The healthcare system in Taiwan is deemed to be sound and the child health indices are similar to those in the USA.[14] National Health Insurance (NHI) is administered by the Bureau of National Health Insurance, Department of Health. More than 98% of Taiwanese nationals have been obligated, by law, to join the government-run, single-payer NHI program since 1995.[15] Using the NHI database, we investigated the overall survival rates of patients with CHD and, similarly, determined the rate for each subtype of CHD.

Patients and methods

Patient identification from the National Health Insurance database

The health care records for patients diagnosed with CHD before the age of 6, between January 1, 2000 and December 31, 2010, were retrieved for analysis. The patients enrolled in this survival study were born between 2000 and 2005 and were first diagnosed with CHD before turning 6 years old. The NHI database consists of the health records from each medical visit, including the date of birth, sex, dates of admission or outpatient department visits, reimbursement, and survival status upon discharge from the hospital. Each record was encoded with a scrambled identification number, preventing identification of the specific individual.

CHD classifications

The CHD diagnoses were identified according to the CHD codes of the International Classification of Diseases, Ninth Revision, Clinical Modification. The codes encompassing 'simple' CHD, included 745.4 (ventricular septal defect, VSD), 745.5 (secundum atrial septal defect, ASDII), 746.0 (anomalies of the pulmonary valve), 746.2 (Ebstein's anomaly), 746.3 (aortic valve stenosis, AS), 747.0 (patent ductus arteriosus, PDA), 747.1 (coarctation of the aorta, CoA), 747.3 (anomalies of the pulmonary artery), and 747.42 (partial anomalous pulmonary venous return). The diagnostic codes comprising 'severe' CHD were 745.0 (common truncus), 745.1 (TGA), 745.11 (double outlet right ventricle, DORV), 745.12 (congenitally corrected transposition of great arteries, ccTGA), 745.2 (ToF), 745.3 (common ventricle), 745.6 (endocardial cushion defect), 746.1 (tricuspid atresia and stenosis, TA), 746.5 (congenital mitral stenosis), 746.7 (HLHS), and 747.41 (total anomalous pulmonary venous return).[9] To avoid errors caused by incorrect tentative diagnosis and miscoding, patients were included who had been admitted to a hospital with a major diagnosis of CHD or who had visited the outpatient department with a major diagnosis of CHD at least 3 times before they reached the age of 6 years.

Statistical analyses

Data management and statistical analyses were performed using SAS version 9.2 (SAS, Cary, NC, United States). The patients diagnosed with a specific CHD under the age of 6 years (0–5 years old) were included to ensure adequate CHD detection and determine the mortality rates.

The total number of deaths occurring in children under 5 years of age, and the mean and median ages at death, were determined. The numbers of deaths were classified into the following age groups: $<$1 month, 1 month–1 year, and those who were 1, 2, 3, and 4 years of age. The Kaplan-Meier estimates of survival at 1-month, 1-year, and 5-years were determined. Survival estimates and 95% confidence intervals were computed using the Kaplan-Meier method. The aggregate survival curves of simple, severe and all CHD cases, in addition to the survival curves for each specific CHD, were plotted. The log rank test was performed to examine the differences between simple and severe CHDs, using the two-sided method at an alpha level of 0.05.

Results

The results of this study indicated that: (1) severe CHD accounted for 11.5% of all CHD cases in Taiwan, with the three leading diagnoses being ToF, TGA, and DORV; (2) the 5-year survival of patients with severe CHD (76.4%) was much lower than that of patients with simple CHD (97.5%); and (3) most of the deaths in CHD patients occurred before 2 years of age.

A total of 18,843 patients were identified with CHD within the first 6 years of life, and constituted the study population. The distribution of each type of CHD is summarized in Table 1. ASDII (31.4%) was the most common CHD, followed by VSD (29.6%), PDA (15.4%), anomalies of the pulmonary valve (7.1%), and ToF (4.4%). Patients with severe CHD accounted for 11.5% of the total CHD patient population. There were three types of severe CHD that accounted for more than 1% of the total number of CHD cases: ToF (4.4%), TGA (1.6%), and DORV (1.1%). The proportion of CHD cases that required single ventricle palliation (HLHS, TA, and common ventricle) accounted for 1.4% of CHD patients.

Table 1 The distribution of congenital heart disease.

ICD-9-CM	CHD type	Group	Number (%)
7450	Common truncus	S	158 (0.7)
7451	Transposition of great arteries (TGA)	S	351 (1.6)
74511	Double outlet right ventricle (DORV)	S	239 (1.1)
74512	Congenitally corrected transposition of great arteries (ccTGA)	S	38 (0.2)
7452	Tetralogy of Fallot (ToF)	S	983 (4.4)
7453	Common ventricle	S	141 (0.6)
7454	Ventricular septal defect (VSD)	E	6604 (29.6)
7455	Ostium secundum type atrial septal defect (ASD II)	E	7021 (31.4)
7456	Endocardial cushion defect (ECD)	S	360 (1.6)
7460	Anomalies of pulmonary valve (aPV)	E	1575 (7.1)
7461	Tricuspid atresia or stenosis (TA/TS)	S	74 (0.3)
7462	Ebstein's anomaly	E	79 (0.4)
7463	Aortic stenosis (AS)	E	167 (0.7)
7465	Congenital mitral stenosis (MS)	S	23 (0.1)
7467	Hypoplastic left heart syndrome (HLHS)	S	122 (0.5)
7470	Patent ductus arteriosus (PDA)	E	3429 (15.4)
7471	Coarctation of aorta (CoA)	E	433 (1.9)
7473	Anomalies of pulmonary artery (aPA)	E	405 (1.8)
74741	Total anomalous pulmonary venous connection (TAPVR)	S	87 (0.4)
74742	Partial anomalous pulmonary venous connection (PAPVR)	E	43 (0.2)

E = simple CHD; S = severe CHD.

The event-free survivals (95% CI) of all CHD patients at 1 month, and at 1, 2, 3, 4, and 5 years ranged from 98.1% (97.9—98.2%) at 1 month to 95.1% (94.5—95.4%) at 5 years. Fig. 1 shows that the survival for simple CHD ranged from 99.1% at 1 month to 97.5% at 5 years; the corresponding survival rates for severe CHD were significantly lower, falling from 90.2% to 76.4%, respectively, ($p < 0.0001$, log rank test). The 5-year survival of each specific CHD is plotted in Fig. 2. Over the course of the study period, the general birth population had a 5-year survival rate of 99.3%.

Table 2 shows detailed information with respect to the age distribution of deaths and the cumulative fatality for each CHD subtype. The major contributors to CHD-related death were: VSD ($n = 135$), ToF ($n = 119$), TGA ($n = 116$), HLHS ($n = 98$), and DORV ($n = 73$). Most of the deaths occurred within the first 2 years of life. For patients with TGA, HLHS, Ebstein's anomaly, and CoA, more than half of the deaths occurred within the first month after birth. The 1-month survival was lowest for HLHS (31.1%), followed by TGA (76.6%), Ebstein's anomaly (82.3%), and DORV (84.9%). Patients with these four CHDs also had the worst 1-year survival rates. Common ventricle (75.9%), ccTGA (76.3%) and partial anomalous pulmonary venous return (79.1%) were the other CHDs with survival rates <80%. The 5-year survival was decreased to below 80% in patients with congenital mitral stenosis (73.9%), partial anomalous pulmonary venous return (76.7%), TA (78.4%), common truncus (79.1%), and total anomalous pulmonary venous return (79.3%). The 5-year survival was worst for patients with HLHS (19.7%), followed by common ventricle (66.0%), TGA (66.7%), ccTGA (68.4%), and DORV (69.0%).

Discussion

The proportion of patients with severe CHD (11.5%) was quite close to that reported in a previous study examining CHD in live births during the 2000—2006 period.[9] With the

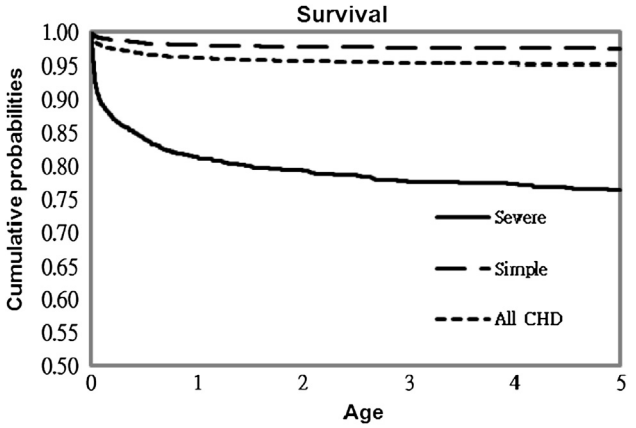

Figure 1 Survival of all cases of CHD, and those with simple and severe CHD. The 1-month, 1-, 2-, 3-, 4-, and 5-year survival of all CHD patients was 98.1%, 96.1%, 95.7%, 95.3%, 95.3%, 95.1%, respectively. The 1-month, 1-, 2-, 3-, 4-, and 5-year survival of simple CHD patients was 99.1%, 98.0%, 97.8%, 97.6%, 97.6%, 97.5%, respectively. The 1-month, 1-, 2-, 3-, 4-, and 5-year survival of severe CHD patients was 90.2%, 81.4%, 79.4%, 77.6%, 77.4%, 76.4%, respectively.

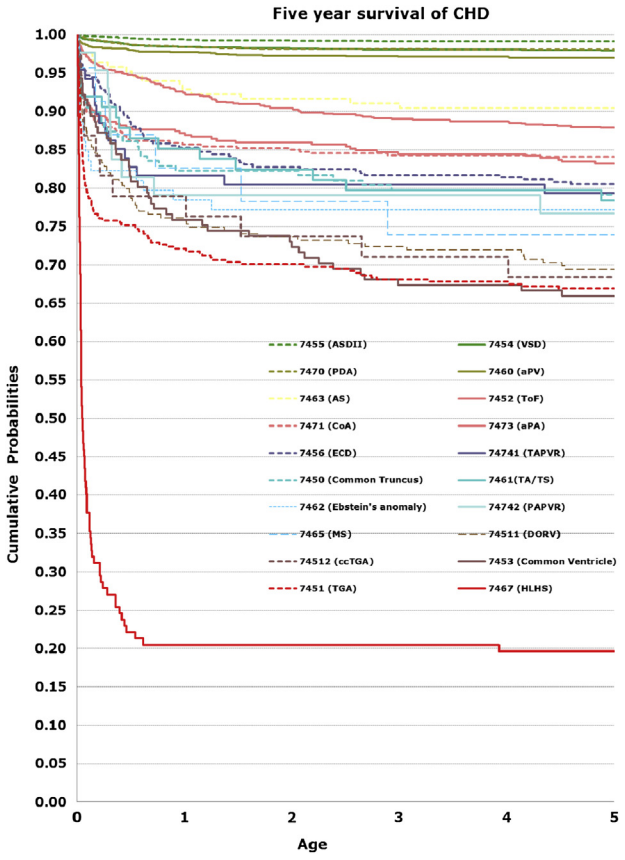

Figure 2 Survival of specific CHD, stratified by the International Classification of Diseases, Ninth Revision codes.

complete record of medical coverage available from the NHI database, the 5-year survival of CHD children in Taiwan during the decade spanning 2000–2010 was 97.5% and 76.4% for simple and severe CHD, respectively. The survival of patients with simple CHD was slightly lower than that of the general population (99.3%), but the survival rate of patients with severe CHD was far from satisfactory. Such medical challenges have also recently been reported in Belgium and England,[2,6] where the mortality rates for CHD patients were similar to those reported in Taiwan.[2,6] Nevertheless, a trend of improved outcome was still evident; the mortality rate declined when compared to that reported in the 1980s and 1990s.[16–18]

As shown in Table 2, the median age of death is consistently less than the mean age. The highest proportion of CHD-related deaths, particularly for severe CHD patients, was observed within the first 2 years after birth. Early fatalities have also been observed in other studies.[3,6] Most patients with TGA, HLHS, anomalies of the pulmonary artery, anomalies of the pulmonary valve, and CoA died within the first month, reflecting the natural history of the disease and intervention-related complications. For simple lesions, such as ASDII and VSD, CHD-related deaths may occur later, in adulthood.[3]

As shown in the present study, the major contributors towards CHD-related deaths included VSD, ToF, TGA, HLHS, and DORV. In the United States, HLHS was the largest contributor to CHD deaths before the age of 6, followed by ToF, TGA, pulmonary atresia, and PDA.[3] VSD is the CHD most commonly associated with chromosome anomalies or syndromic combinations, and patients with these disorders were not excluded form the current analyses. The VSD-related deaths might therefore be overrepresented within

Table 2 The age distribution of deaths in patients with congenital heart disease below the age of 5 years.

Disease		Total number of deaths	Age at death (year)		Number of deaths						Kaplan-Meier estimate of survival (%)		
		(<5 y)	Mean	Median	<1 mo	1 mo–1 y	1	2	3	4	<1 mo	<1 y	<5 y
7450	Common truncus	33	0.92	0.23	14	14	0	4	0	1	99.9	82.3	79.1
7451	TGA	116	0.6	0.06	70	28	7	7	1	3	76.6	71.8	66.7
74511	DORV	73	0.92	0.2	29	28	6	3	1	6	84.9	74.9	69.0
74512	ccTGA	12	0.84	0.19	5	3	2	1	0	1	86.8	76.3	68.4
7452	ToF	119	1.16	0.69	26	48	20	14	3	8	96.3	92.2	87.8
7453	Common ventricle	48	1	0.49	12	22	4	8	0	2	89.4	75.9	66.0
7454	VSD	135	0.86	0.39	39	66	12	9	2	7	99.3	98.4	97.9
7455	ASD II	63	0.86	0.5	12	33	9	5	3	1	99.8	99.3	99.1
7456	ECD	70	0.85	0.4	18	35	9	4	1	3	94.4	85.3	80.6
7460	aPV	47	0.82	0.13	21	15	7	2	2	2	98.3	97.7	97.0
7461	TA/TS	16	0.91	0.38	6	5	2	2	0	1	91.9	85.1	78.4
7462	Ebstein's anomaly	18	0.22	0.04	12	5	1	0	0	0	82.3	78.5	77.2
7463	AS	16	1.3	0.56	4	8	2	1	1	0	96.4	92.2	90.4
7465	MS	6	0.94	0.56	1	2	1	0	0	0	95.6	82.6	73.9
7467	HLHS	98	0.13	0.04	72	25	0	0	1	0	31.1	20.5	19.7
7470	PDA	66	0.61	0.32	17	37	9	2	1	0	99.4	98.4	98.1
7471	CoA	69	0.42	0.05	42	20	3	3	0	1	88.9	85.7	83.8
7473	aPA	68	0.81	0.1	34	18	5	6	0	5	89.9	86.7	83.2
74741	TAPVR	18	0.5	0.19	1	15	1	0	0	1	92.0	81.6	79.3
74742	PAPVR	10	0.71	0.31	1	8	0	0	0	1	97.7	79.1	76.7

the overall CHD population. The 1-, 2-, and 5-year survival rates of ToF patients in the present study were 92.5%, 90.7%, and 87.8%, respectively, which is better than the results reported from Belgium (83%, 83%, and approximately 80%, respectively).[6] Since the incidence of ToF is generally higher in Western countries,[6] the relatively high number of deaths from ToF in the current study may be related, at least in part, to the high number of newborns with ToF in Taiwan. The current study also reported much worse survival rates of HLHS (20.5% and 19.7% at 1 and 5 years, respectively) than that reported in the Belgian study.[6] Since the incidence of HLHS in Taiwan is only approximately one-fourth of that observed in Western countries, difficulties in learning how to treat this CHD may explain the poor outcomes.[8,9]

For patients with ToF and TGA, differences were noted between the institutional reports and the present study. In this national database study, the 5-year survival was 87.8% and 66.7% for ToF and TGA patients, respectively. These estimates are lower than those of the institutional reports, which have estimated the long-term survival rate for ToF to be 90.5% and for the 2-year survival rate TGA patients to be 89%.[11,19] Further studies to determine the determinants of outcomes may be required.

Study limitations

Despite using the NHI nationwide database, some CHD patients without NHI coverage could not be assessed in this study. Moreover, some CHD patients may die before admission due to sudden collapse or by being refractory to resuscitation. These patients are included in our study, leading to a potential overestimation of the survival of pediatric CHD patients. As the NHI coverage in Taiwan was more than 98% and medical resources are easily accessible, we believe that the influence of the abovementioned limitations on our results should be minimal. However, we were unable to access the National Death Registry due to the law concerning the protection of privacy. Furthermore, we could not validate the specific details of the CHD by chart review to re-confirm the diagnosis and the exact cause of death, which is another limitation of our nationwide database study.

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