Arrhythmic burdens in patients with tetralogy of Fallot: A national database study

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BACKGROUND Tetralogy of Fallot (TOF) is a common cyanotic congenital heart disease with increasingly recognized late morbidity.

OBJECTIVE The purpose of this study was to explore the long-term outcome by using a national database of Taiwan, a country with national health insurance and easily accessible medical care.

METHODS Data on TOF patients were retrieved from database records from 2000 to 2010. Complications and therapies were identified by their respective codes.

RESULTS We identified 4781 TOF patients (prevalence 0.63/1000 in pediatric patients and 0.06/1000 in adult patients). Arrhythmias were identified in 219 patients (8.3% for adult patients and 2.8% for pediatric patients): 160 tachycardia and 59 bradycardia (4 with tachy–bradycardia syndrome). The occurrence of arrhythmias was associated with higher mortality (excluding cardiac surgical death, 15.6% vs 8.6%, $P = .001$). Patients with atrial fibrillation were the oldest (median age 44.3 years), followed by those with tachy-bradycardia syndromes (32.4 years) and atrial flutter (31.5 years). The incidence of nonperioperative tachycardia increased with age (1.4%, 1.7%, 3.3%, 5.2%, 10.2%, and 16.9% in age group 0–9, 10–19, 20–29, 30–39, 40–49, and $\geq$50 years, respectively). Tachycardia therapy (ablation and implantable cardioverter-defibrillator) was administered in 20.4% (annually 2.4%) of patients with nonperioperative tachycardia. In the subgroup born 2000–2010 with complete postnatal data, mortality was 15.1% (296/1960), and 1-, 5-, and 10-year survival was 0.911, 0.826, and 0.788, respectively. Risk of atrioventricular block requiring a pacemaker was 0.6%.

CONCLUSION Arrhythmias are common in TOF patients and increase mortality risk. Medical needs because of tachycardia often appear late in adulthood.

KEYWORDS Tetralogy of Fallot; Arrhythmia; Survival

ABBREVIATIONS **AF** = atrial fibrillation; **AFL** = atrial flutter; **AVB** = atrioventricular block; **ICD** = implantable cardioverter-defibrillator; **NHI** = National Health Insurance; **RFCA** = radiofrequency catheter ablation; **SSS** = sick sinus syndrome; **SVT** = supraventricular tachycardia; **TOF** = tetralogy of Fallot; **VF** = ventricular flutter/fibrillation; **VT** = ventricular tachycardia

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Introduction

Tetralogy of Fallot (TOF) is the most common form of cyanotic congenital heart disease.[1] According to the Taiwan national health insurance database from 2000 to 2006, the incidence was 0.63 per 1000 live births, which is higher than that reported in a U.S. study (0.23 per 1000 live births).[2,3] The first cardiac repair of TOF was successfully performed in 1955 in the United States and in 1965 in Taiwan.[4,5] According to our institutional 30-year database comprising 819 TOF patients, acute surgical mortality was 3.3% and 30-year survival was 90.5%, which is considerably close to that reported in recent Western studies.[5–7] However, a substantial number of patients remain at risk for arrhythmias and sudden death during long-term follow-up.[5,8–11] The burden of arrhythmias in TOF patients varies with the duration of postoperative follow-up and the study population. Based on an adult cohort from the Alliance of Adult Research of Pediatric Cardiology, the arrhythmia burden was as high as 43%.[11] However, these reports are mostly institutional or multi-institutional studies. Patients with congenital heart disease tend to adhere less to medical follow-up after they start school and frequently present with emergency conditions, such as arrhythmias. Therefore, the true long-term outcomes and medical needs may not be presented accurately by these institutional studies.

In Taiwan, after the 1995 implementation of the National Health Insurance (NHI) program, which covers >99% of the population, almost every TOF patient was eligible to receive full medical service. The medical care system has been widely reported as efficient. The child health indices in

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Taiwan are similar to those in the United States.[12] TOF has been the leading type of cyanotic congenital heart disease in Taiwan, and medical treatment of children exhibiting cardiac diseases is easily accessible.[2] Therefore, our national health insurance database comprises an appropriate study cohort to investigate the long-term outcomes of TOF patients and their current medical needs, particularly when focusing on arrhythmia events.

Methods

NHI database and patient identification

All health care records between January 1, 2000, and December 31, 2010, were retrieved from the complete computerized database of the NHI program. Based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* codes, patients diagnosed with TOF (745.2) were selected. Each health record comprises a scrambled identification number and information such as date of birth, dates of visits, sex, type of admission or outpatient clinic visit, diagnosis and treatment codes, reimbursement fees, and survival status at discharge. Survival status was confirmed by the patient's insurance status in 2012. To avoid including patients with a tentative diagnosis, those who had an outpatient clinic visit under the TOF diagnosis ≤ 2 times were excluded.

Definition of arrhythmic events and interventions

Until December 31, 2010, identified patients were observed for any complications and interventions detailed in the following. The occurrence of arrhythmias was defined in terms of the following disease codes: *bradycardia:* complete atrioventricular block (426.0), atrioventricular block (AVB) (426.1), and sick sinus syndrome (SSS) (427.81); and *tachycardia:* supraventricular tachycardia (SVT) (427.0), ventricular tachycardia (VT) (427.1), unspecified paroxysmal tachycardia (427.2), atrial fibrillation (AF) and atrial flutter (AFL) (427.3), and ventricular fibrillation and flutter (VF) (427.4).

Radiofrequency catheter ablation (RFCA) intervention was determined if any of the treatment codes (33091A or 33091B) were reimbursed. Permanent pacemaker or device implantation was determined if any of the treatment codes (68012B or 68041B) were reimbursed. Patients who received implantable cardioverter-defibrillator (ICD) therapy were identified by reimbursement for the device. Cardiac surgery and vascular/shunt operation were identified by the respective treatment codes.

Statistical analysis

The Statistical Package for Social Sciences (SPSS version 15.0, SPSS Inc, Chicago, IL) was used for analysis. Continuous variables are given as mean $\pm$ SD and categorical data as sample proportions. The Kaplan–Meier survival curve was adopted for survival analysis. The overall prevalence was calculated from the populations from 2000 to 2010, which were adopted from the Statistical Yearbook of the Interior, Department of Statistics, Ministry of the Interior.

Results

Epidemiologic data

Prevalence of TOF

We identified 4781 (51.8% male) TOF patients. The average pediatric (<20 years) and adult (≥ 20 years) populations between 2000 and 2010 were 5 890 060 and 16 875 475, respectively. Thus, the prevalence of TOF in pediatric and adult populations was 0.63 per 1000 and 0.06 per 1000, respectively.

Survival in the subgroup of TOF patients born between 2000 and 2010

To avoid the error of overestimating event-free survival, Kaplan–Meier survival analysis was performed in the subgroup of 1960 patients born between January 2000 and December 2010 and therefore exhibited complete postnatal data in our database. Among these patients, 296 deaths occurred (mortality 15.1%). Survival at the age of 1, 5, and 10 years was 0.911, 0.826, and 0.788, respectively.

Arrhythmias in the whole TOF cohort

A total of 219 of the 4781 patients (4.6%) received medical care for arrhythmias during the study period of 11 years, including 160 (73.1%) with tachycardia and 59 (26.9%) with bradycardia (including 4 with tachycardia and bradycardia syndrome). The incidence was 8.3% in adults and 2.8% in pediatric patients. There were 40 deaths; 7 of these were cardiac surgical deaths. The mortality of those with arrhythmias was 22.3%. If cardiac surgical deaths were excluded, the mortality still was significantly higher in TOF patients if they exhibited arrhythmia (15.6% [33/212] vs 8.6% [381/4038], $P = .001$). The demographic data for each arrhythmia group are summarized in Table 1.

Tachycardia

All tachycardias. The incidence of all tachycardia was 3.3% in the TOF patients (6.6% in adults and 1.8% in pediatric patients). SVT accounted for 44%, followed by AF (29%), VT (18%), AFL (6.9%), and VF (3.1%). The proportion of males was higher in patients with VF (80%) and VT (68%). The age at final follow-up was highest in the AF group, followed by the tachycardia and bradycardia syndrome and AFL groups.

Nonperioperative tachycardia

Incidence. Nonperioperative tachycardia accounted for 92% of the tachycardia cases. The incidence of all types of nonperioperative tachycardia in the individual birth year group revealed an increasing trend of tachycardia with age, particularly AF, AFL, and VT (Figure 1). The chances of requiring medical care for nonperioperative tachycardia was 1.4%, 1.7%, 3.3%, 5.2%, 10.2%, and 16.9% in the age group 0–9, 10–19, 20–29, 30–39, 40–49, and ≥ 50 years projected by 2010, respectively. Mortality at the latest follow-up for