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Adult congenital heart disease: A paradigm of epidemiological change

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ABSTRACT

Increasing survival rates for patients with congenital heart disease (CHD) represent a major achievement of modern medicine. Despite incredible progress been made in diagnosis, follow-up, early treatment and management in adulthood, many patients are faced with long-term complications, such as arrhythmia, thromboembolism, heart failure, pulmonary hypertension, endocarditis and/or the need for reoperation. In parallel, half of the patients are female, most of childbearing age, and, thus warrant specialist reproductive counseling and appropriate obstetric care. It is not surprising therefore, that healthcare utilization has steadily increased for CHD in recent years. Furthermore, cardiology and other medical disciplines are now faced with new challenges, namely the provision of expert care and optimal, lifelong medical surveillance for these patients.

1. Introduction

A few decades ago, congenital heart disease (CHD) was considered as a paediatric disease as the majority of patients with severe lesions rarely survived into adulthood. However, advances in early diagnosis and cardiac surgery have shifted the burden of disease from paediatrics to adult medicine. Consequently, adult patients with congenital heart disease (ACHD) are a constantly growing patient group nowadays outnumbering by far paediatric patients [1,2]. In the context of this radical epidemiological change, age distribution of ACHD along with the evolving epidemiological and more complex anatomic case mix and gender related needs, such as pregnancy, constitute an area of growing interest.

Although modern healthcare for ACHD has been life prolonging, it is often non-curative; furthermore, complications, such as arrhythmia, heart failure, pulmonary hypertension, endocarditis and thromboembolism are not uncommon and may further complicate the clinical course of ACHD patients [3]. Half of the patients are female and their natural desire to have their own children represents a new challenge for both physicians and patients alike.

As ACHD patients grow older, the risk of complications increases; there is, therefore, an imperative for better understanding of their ongoing needs and this should be matched with appropriate resource allocation towards their lifelong care [4].

2. General epidemiologic data

2.1. Prevalence and age distribution

The precise prevalence of CHD remains challenging as based on studies that did not include echocardiographic assessment on all newborns and/or on general fetal all-inclusive echocardiography. As a result, atrial septal defects, patent ductus arteriosuses and other defects may have been missed. Moreover, diagnoses such as bicuspid aortic valve, Marfan syndrome, silent patent ductus arteriosus, isolated partial anomalous pulmonary venous connection and mitral valve prolapse were excluded in many studies [5].

The overall prevalence of congenital heart disease is approximately 8–9 per 1000 live births, which translates to 1.35 million infants with a CHD per year globally [6]. Moreover, 28% of congenital defects in infancy are attributed to congenital heart disease. The most frequent subtypes of congenital heart disease are septal defects with a predominance of ventricular septal defects (VSD) (Table 1). Interestingly, 85–90% of small VSDs close spontaneously during the first year of life [6].

The prevalence of ACHD is 3–6 per 1000 adults [1,7]. A systematic review demonstrated that the prevalence of ACHD is approximately 3000 per million adults. Nonetheless, the heterogeneity of the studies involved represents a significant limitation of this estimation [1]. More

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Table 1
Incidence of major forms of CHD per 1000 live births.

Ventricular septal defect	2.62
Atrial septal defect	1.64
Pulmonary valve stenosis	0.87
Tetralogy of Fallot	0.5
Aortic coarctation	0.34
Transposition of the great arteries	0.31
Aortic valve stenosis	0.22

recently, Marelli et al. published contemporary data from the Canadian registry on the prevalence of ACHD up to 2010. The prevalence of ACHD increased by 54% during 2000–2010 period reaching 6.12 per 1000 adults in 2010 [8].

The percentage of patients with severe disease has also increased from 9% to 14% from 2000 until 2010. Adults were 54% of the total congenital heart disease population in 2000 and 66% in 2010. Furthermore, 60% of patients with severe congenital heart disease were adults in 2010 versus 49% in 2000 [8].

The survival of patients with CHD has improved dramatically; 40 years ago, 85% of patients would die in childhood, whereas today at least 85%, if not more, are expected to reach adulthood. Specifically, 98% with mild, 96% with moderate and 56% with severe ACHD survived until adulthood in a recent national registry from Belgium [9]. In USA, the cumulative 10-year survival was 95%, 90% and 80% for these 3 groups, respectively [10]. The accuracy of diagnosis with modern imaging, the improvement of surgical techniques and the optimal postoperative care have contributed to this marked increase in survival [11,12]. Interestingly, the median age of patients with severe ACHD was 11 in 1985, 17 in 2000 and 25 years in 2010, with a further increase anticipated in the near future [8]. Recent data from the CONCOR Dutch registry suggest that median survival of severe ACHD was 53.4 years; should be noted, however that mean age at inclusion was 28 years, thus, excluding patients with earlier attrition [13].

2.2. Gender

The gender distribution of CHD differs slightly, as females constitute 52% of children and 57% of ACHD [2]. The prevalence of severe ACHD is higher amongst female, but not in paediatric patients. Concerning ACHD subtypes, atrial, ventricular and atrioventricular septal defects and patent ductus arteriosus are more often identified in female adults, whereas transposition of great arteries and aortic coarctation are more common amongst paediatric males [2]. Bicuspid aortic valve is three times more frequent in males [14]. ACHD females have a 35% higher probability to develop pulmonary hypertension. In contrast, endocarditis, aneurysms, dissection and aortic surgeries are more common amongst males [15,16]. Male ACHD patients seem to require an implantable cardioverter defibrillator 2.2fold more frequently than females. Finally, a difference in mortality between genders was reported in a European survey from 24 countries, where 5-year mortality was 4% in males compared to 3% in females, even after adjusting for age and type of defect [15].

2.3. Regional distribution

Differences in the prevalence of CHD have also been reported between various geographic regions. Asia displays the highest birth prevalence with 9.3 per 1000 live births. Notably, pulmonary stenosis and tetralogy of Fallot are more prevalent in Asia, whereas left ventricular outflow obstruction is less common. The prevalence of CHD in Europe is 8.2 per 1000, in North America 6.9 per 1000 live births, whereas the lowest prevalence has been reported in Africa (1.9 per 1000 infants). These figures should be interpreted with caution, as they do not account for missed diagnoses [6].

2.4. Etiology of congenital heart disease

Approximately 8–12% of CHD is attributed to environmental factors during pregnancy such as alcohol consumption, rubella infection, hydantoin and thalidomide intake, phenylketonuria and poorly controlled insulin dependent-diabetes [17]. The genetics of CHD are not fully elucidated yet; an increasing number of genes, however, are considered to play a key role in cardiac malformations. In the Dutch registry (CONCOR), 15% of CHD patients had a relative (6% of first degree) with congenital heart defect [12].

2.5. Mortality

Even though mortality has dramatically decreased in all age groups and primarily in infants [18], patients with congenital heart disease and especially those with severe forms, such as tetralogy of Fallot, transposition of great arteries, congenitally corrected transposition of great arteries, univentricular hearts and Eisenmenger syndrome have a significantly lower life expectancy than the general population [19]. In the Royal Brompton Hospital, where almost 7000 ACHD were studied recently, common causes of mortality were chronic heart failure (42%), followed by pneumonia (10%), sudden cardiac death (7%), cancer (6%) haemorrhage (5%) and perioperative death [20]. Reported differences in mortality may relate to variations of socioeconomic status, education, urbanization, climatological factors and other factors such as comorbidities, differences in lifestyle and in patient's perception of the disease. For instance, ACHD mortality in the Netherlands, is higher in north rural regions compared with the rest of the country. Furthermore, in USA the mortality between non-Hispanic blacks is higher than non-Hispanic whites, despite the fact that the prevalence of CHD in the former is much lower [21].

3. Specific epidemiological data

3.1. Pregnancy

Most of women with CHD are of childbearing age and thus, require and will benefit from specialist reproductive counseling; most of them are capable of giving birth to their own child. However, they are at higher risk of cardiac, obstetric and fetal complications compared to health controls [22].

A recent literature review suggested that 11% of pregnancies of women with ACHD had cardiac complications [23]. Heart failure was the most frequent amongst them (4.8%), particularly so in patients with Eisenmenger syndrome, cyanotic CHD and pulmonary atresia [23]. Arrhythmias, especially supraventricular, complicate 4.5% of pregnancies. Serious cardiovascular events (cardiovascular deaths, strokes) are more prevalent amongst pregnant patients with Eisenmenger syndrome and unrepaired or only palliated cyanotic CHD.

Preeclampsia and eclampsia in patients with pulmonary valve stenosis, aortic coarctation, transposition of great arteries and tricuspid atresia with ventricular septal defect exceed the expected rate of 2% to 3%. Furthermore, thromboembolic events are observed in 2% of pregnancies, a much higher incidence than the 1 event per 1000–2000 pregnancies observed in general population [23].

Finally, complications from the fetus are more prevalent in pregnancies of women with ACHD. Fetal mortality is 4%, at least 4 times more than in the general population, whereas prematurity is 4% higher. Cyanosis per se does not constitute an absolute contraindication for pregnancy; however, cyanotic women give birth to low-weight babies. When oxygen saturations are <85% the chances of successful pregnancy are diminished [23,24].