Proceedings of the 4th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/61/20241460

# Progress in the Diagnosis and Treatment of Congenital Heart Disease (CHD)

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**Abstract.** Congenital heart disease (CHD) is currently the highest incidence of congenital malformation, and there are many types, some children may be combined with a variety of malformations, and symptoms vary, some may be asymptomatic for life, serious people are born with serious symptoms such as the hypoxia, shock and even death. Even if the child is not stillborn, usually within 1 year after untreated, it will eventually die due to the severe or complex malformations. Therefore, early diagnosis and intervention are particularly important. With the increasing of the diagnostic methods and techniques, the accuracy of diagnosing complex CHD is getting higher and higher. With the continuous in-depth clinical research on CHD, interventional therapy has been further developed in the treatment of this disease, while new materials and new instruments are emerging in an endless flow, and imaging technology innovation has expanded from simple and common congenital heart disease to some rare and difficult complex congenital heart disease, promoting the qualitative leap in the field of interventional therapy for congenital heart disease. In this paper, the epidemiological characteristics, disease burden, risk factors, ultrasound assessment, interventional therapy, etc. of children with CHD were systematically reviewed, aiming to provide clinical reference for clinicians to manage and treat related children.

**Keywords:** Congenital heart disease, diagnosis, intervention.

## 1. Introduction

Congenital heart disease (CHD) refers to the abnormal cardiac development of the fetus during the embryonic period, usually accompanied by macrovascular dysplasia, with high mortality and disability rates, and generally poor prognosis. The incidence of CHD is 0.7% ~ 0.9%, and about 160,000 new children with CHD are diagnosed in China every year [1]. With rapid advances in early diagnosis and cardiac surgery, survival rates have improved dramatically, but CHD remains one of the leading causes of infant death. Up to now, more than 90% of children have survived to adulthood. However, with the increasing age and changes in physical and psychological functions, children still face risks of arrhythmia, heart failure and premature death after treatment until adulthood [2,3]. Existing data shows that many factors affect the occurrence and development of CHD, such as genetic factors and environmental factors, while its specific pathogenesis is still not completely clear [4,5]. There are many ultrasound methods for clinical screening of CHD, and how to choose the best examination method or how to combine other auxiliary examination measures to obtain more accurate examination results is also an urgent concern in clinical practice. Interventional therapy has been well developed in

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cardiovascular diseases and is widely used in clinical practice with the characteristics of less trauma and faster recovery. However, there are many clinical studies on the interventional therapy of CHD, but there are differences in the conclusions of existing studies, and there is no uniform standard [6]. This article mainly reviews the progress of diagnosis and treatment of CHD, providing more theoretical basis for the clinical diagnosis and the treatment of CHD.

## 2. Epidemiology and disease burden

The 2019 Global Burden of Disease (GBD) results tool was used to retrieve CHD-related data in China from 1990 to 2019 (the data of GBD 2019 China Burden of Disease study were mainly from the National Disease Surveillance system, the China Maternal and Child Health Surveillance System and the China Disease Prevention and Control Information System).The results showed that in the past 30 years, the incidence of CHD in China generally increased first and then decreased. Compared with the standardized incidence of 50.2/100 000 in 1990 (53.7/ 100 000 in males and 46.3/100 000 in females), the standardized incidence of CHD in 2019 was 49.0/100 000 (51.5/ 100 000 in males, 46.1/ 100 000 in females) fell by 2.4%. From 1990 to 2019, the average incidence of CHD in newborns (⩽28 days) was 24,97.9 per 100,000, the average incidence of CHD in children under 1 year old was 26266/100,000, and the incidence of CHD in people aged 1 year and above was 0. The CHD mortality rate decreased with age. The CHD mortality rate of children under 5 years old was 101.67/100,000 person-years, and the mortality rate of people aged 5 years and above decreased. However, the mortality rate of people aged 55~<60 years increased temporarily [7,8]. An epidemiological survey of 58,262 children aged 3 to 14 years (from 252 schools in 11 ethnic groups) in Yunnan Province found that 404 children were diagnosed with CHD, with a total prevalence of 6.96‰, including 6.42‰ males and 7.5‰ females [9].

In the process of CHD children's medical treatment, there is not only a direct medical disease economic burden, but also a direct non-medical disease economic burden such as room and board expenses and transportation expenses for accompanying relatives and friends, and an indirect disease economic burden such as loss of labor time caused by their family members or guardians. In a retrospective analysis, parents of CHD children who underwent thoracotomy or interventional surgery in three hospitals in Xinjiang Province were interviewed by telephone using a self-designed questionnaire, and multiple linear regression model was used to analyze the factors affecting the economic burden of disease. The results showed that the median total economic burden of CHD was 44,140 yuan. It is higher than the average level of per capita disposable income of Xinjiang residents in 2020-2022, with direct economic burden of 41,000 yuan and medical economic burden of 38,000 yuan; The total economic burden of the disease was tetralogy of Fallot, pulmonary stenosis, ventricular septal defect, and atrial septal defect in descending order. The results of multiple linear regression show that the number of days in hospital is an important factor affecting the indirect economic burden and the total economic burden, which means that the longer the number of days in hospital, the longer the working time loss of the parents of the children, thus increasing the total economic burden. Family monthly income is an important factor affecting the direct economic burden and the total economic burden, which may be related to the waiting time for bed, the longer the waiting time, the more the family monthly income loss. It may due to the families with high monthly household income pursue relatively better medical services and more comfortable accommodation conditions [10].

## 3. Risk factors

### *3.1. Genetic factor*

CHD patients have a tendency of family aggregation, and the prevalence rate of children with CHD in one family is higher than that with normal family in both families, suggesting that genetic factors play an important role. Aneuploidy is the earliest identified genetic factor of CHD, which is manifested by the abnormal number of chromosomes. Copy number variation (CNV) is the variation caused by genomic rearrangement. In a clinical study, children with non-syndromatic CHD had a 7.1% higher load of potentially pathogenic CNV than healthy controls ($P < 0.05$), and copy number variation was closely

DOI: 10.54254/2753-8818/61/20241460

associated with an increased risk of death and transplantation (2.55 times) [11]. Nkx2.5 gene plays an important role in the heart development. The mutation and the abnormal expression of single or multiple genes of the gene may lead to the abnormality of the heart structure and also the function. A meta-analysis proved that abnormality of this gene increased the risk of CHD [12].

### *3.2. Environmental factor*

Many epidemiological investigations have shown that CHD is associated with exposure to a variety of environmental factors, common environmental factors include maternal environmental exposure during pregnancy and external environmental teratogenic factors.

Preconception diseases or acute infections during pregnancy, as well as medications taken before and during pregnancy, may affect the birth outcome of the fetus. A 34-year cohort study involving 2 million newborns showed that early gestational diabetes was associated with a 4-fold increase in the risk of CHD in the offspring, and the cause was not directly caused by high levels of glucose, while may ultimately increase the risk of CHD through the signaling pathway regulating insulin sensitivity [13]. A birth cohort study based on data from Fujian (n=21345) showed that pregnancy accompanied by higher levels of triglyceride, low-density lipoprotein and apolipoprotein B increased the risk of CHD in offspring, while low high-density lipoprotein was negatively correlated with the occurrence of CHD [14]. External environmental factors include chemical factors such as environmental toxins and teratogens, such as tobacco, alcohol and air pollution, as well as physical factors such as high temperature, high altitude hypoxia and exposure to environmental radiation sources. A case-control study involving 749 children with CHD and 880 healthy control children to examine the association between the exposure of maternal smoking and CHD during pregnancy, it found that the longer the exposure period, the higher the risk of congenital heart disease in the offspring [15]. A case-control study based on national surveillance that analyzed association between the CHD and the maternal PM2.5 exposure in 1,434,998 newborns from more than 30 provinces or municipalities showed that for every 10 $\mu g/m^3$ increase, offspring had a 2% increased risk of CHD (OR=1.02), with VSD being the most affected (OR=1.04) [16]. In a recent research, evidence shows that the effect of smoking in Cytochrome P450(CYP450) on its susceptibility would further on increase the possibility of CHD and the form of false cardiac structure.

## 4. Diagnostic evaluation

At present, the common method of CHD examination is ultrasound, especially the prenatal non-invasive ultrasound technology, may improve the accuracy of the diagnosis. In addition, the method has no damage to the fetus, has good repeatability, and can effectively check the fetal heart structure, and confirm whether the fetus has large blood vessel malformation or heart malformation as early as possible. The best application time is mid to late pregnancy or early pregnancy. Color Doppler ultrasound is an emerging technology, and compared with conventional ultrasound technology, it may improve the detection rate of CHD and is usually used in the middle and late pregnancy [17]. In a retrospective analysis, clinical data of 86 suspected children with CHD were included, and the results showed that the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of color Doppler ultrasound in diagnosing CHD in children were 96.05%, 80.00%, 94.19%, 97.33% and 72.73%, respectively [18].

Of course, only one examination method is often not enough, clinical diagnosis can be combined with other auxiliary examination measures, such as fetal magnetic resonance examination, fetal ultrasound and interventional prenatal diagnosis, can make the examination results more perfect.

Nanotechnology utilizes the unique properties of nano-materials to provide new strategies for the diagnosis and also treatment of CHD. These properties make the advanced imaging, biosensing, targeted drug delivery and inflammation possible. Nanotechnology can detect cardiac injury markers faster, more sensitively, and more accurately. Electrochemical and optoelectronic biosensors using nano-materials can detect biomarkers at concentrations below those detected by traditional methods, providing reference for early diagnosis and treatment of CHD.

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## 5. Interventional therapy

In 1966, Rashkind performed an atrial septostomy on children with complete transposition of the great arteries using balloon catheters, which marked the initial exploration stage of interventional treatment of CHD.

Interventional treatment of CHD began in 1980s in China. In 1981, Professor Zhou Aiqing and others from Shanghai Children's Medical Center successfully carried out atrial septostomy. Since then, interventional closure of atrial septal defect, patent ductus arteriosus, percutaneous balloon pulmonary valve dilation, and percutaneous balloon angioplasty after coarctation of the aorta have been carried out successively in China. percutaneous balloon pulmonary valvuloplasty (PBPV) is a method for treating simple congenital pulmonary stenosis. According to a 2018 data, 58 cases of PBPV were performed in 14 international centers, with a success rate of 71%. The in-hospital survival rate of live infants who received intrauterine treatment was higher than that of those who did not receive FCI treatment (91% vs. 75%) [19]. In 1989, Maxwell's team used intrauterine balloon aortic valve dilation (PBAV) for the first time to treat fetal severe aortic stenosis (AS), two cases were successfully operated, while the prognosis was poor, which initially confirmed that fetal surgery was feasible, which means there were still many shortcomings [20]. Echocardiography-guided PBAV in the treatment of severe congenital AS is feasible and safe. Some scholars have shown that the success rate of balloon dilatation for neonatal severe aortic stenosis is higher, and the mortality rate is significantly reduced. The application of new arterial sheath for transthoracic aortic valve balloon dilatation is safer than that of traditional arterial sheath. However, long-term follow-up showed that the reoperation was still high. The reason may be that perivalvular structure is elastic and elastic retraction occurs after dilation. Therefore, in the clinical application of this operation, neonatal femoral artery injury should be avoided as much as possible [21].

In recent years, with the increasing maturity of 3D printing and the imaging development, it has been widely used. The equal-scale individualized 3D printing model may accurately restore the anatomical morphology of related diseases, enabling doctors to clearly and intuitively understand the specific anatomical conditions of relevant parts of patients before surgery, and deepen their understanding of anatomy on the basis of imaging analysis [22]. Although interventional closure is the preferred treatment for atrial septal defect (ASD), inferior vena cava type ASD is still considered a contraindication for interventional closure. Because it is close to the inferior vena cava opening, composed of the entrance of the inferior vena cava and the lower wall of the left atrium, with few residual lower edges and insufficient defect edges to fix the conventional ASD occluders on the atrial septa. However, 3D printing model can determine the location of ASD and the details of the surrounding edges and evaluate whether it can be adequately used for fixation of the occluders. The selection of appropriate occluder can ultimately achieve the purpose of individualized diagnosis and treatment, so that the criterion of contraindication has more space for exploration, while its effectiveness and safety still need to be further explored clinically [23].

## 6. Conclusion

CHD is a lifelong chronic disease. With the rapid development of the echocardiography technology, CHD in the neonatal period may be correctly diagnosed at an early stage. At the same time, identifying the genetic cause through genetic testing is of great significance for the early diagnosis and early treatment and prevention of CHD. Since the 1990s, interventional treatment of CHD has formed a new field, and countries around the world have successively formulated guidelines and quality control standards for the treatment of CHD patients, so that the interventional treatment of CHD tends to be standardized, but the therapy still needs continuous development, especially the VSD, which has been the difficulty of interventional treatment, such as the anatomical site of the defect is special, difficult to place the umbrella, the operation time is long, the influence of radiation is great, and the probability of umbrella closure failure, occluding device displacement, postoperative arrhythmia and atrioventricular block is high. In the future work, people should actively develop and optimize domestic plugging devices, increase professional training for interventional physicians, do a good job in case registration and long-term follow-up evaluation, carry out large-scale studies with higher quality evidence-based

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evidence, constantly sum up experience and improve the level, and strive to overcome the problem of CHD as soon as possible.

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