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The role of the geneticist and genetic counselor in an ACHD clinic

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ABSTRACT

There is a growing population of adults surviving with congenital heart disease due to the advancements in surgical repair and medical management. At the same time, the understanding of the genetic basis of both syndromic and isolated congenital heart disease has grown tremendously and is being rapidly translated into changes in clinical care, resulting in an increasing need for incorporation of genetic expertise into the care of adult congenital heart disease patients. Here we review the importance of delivery of genetic information to the adult congenital heart disease population and highlight the shared and distinct roles of clinical geneticists and genetic counselors in provision of services. The adult congenital heart disease patient population has unique needs and clinical geneticists and genetic counselors can play an important role in the diagnostic evaluation and assessment of these patients to provide an accurate etiologic diagnosis and to counsel regarding genetic testing, recurrence risk, family screening, and prenatal diagnosis.

1. Introduction

There is a growing population of adults surviving with congenital heart disease due to the advancements in surgical repair and medical management. At the same time, the understanding of the genetic basis of both syndromic and isolated congenital heart disease has grown tremendously. Advancements in genetic technologies now allow more precise diagnosis. Furthermore, an improved understanding of epidemiology, human genetics, and cardiac development has identified subclasses of cardiovascular malformations with increased heritability. Therefore, at a time when many patients with congenital heart disease are reaching childbearing age, there are substantial new insights into causation that may be relevant to their own medical condition as well as their recurrence risk. Medical genetics professionals can play an important role in the diagnostic evaluation and assessment of ACHD patients to provide an accurate etiologic diagnosis and to counsel regarding genetic testing, recurrence risk, family screening, and prenatal diagnosis.

2. Genetics care providers in the clinic

A clinical geneticist is a physician who has specific subspecialty training in medical genetics. In the United States, clinical geneticists are board certified through the American Board of Medical Genetics. Physicians must have 2 years of training in an ACGME accredited residency program in another specialty and 2 years in an ACGME-accredited residency in clinical genetics. Training may also be accomplished as a residency combined with pediatrics, internal medicine, or obstetrics and gynecology (www.abmg.org). Most clinical geneticists obtain board certification in two specialties, most commonly pediatrics and clinical genetics. Clinical geneticists receive training in the diagnostic evaluation, management, and genetic counseling of patients with genetic disorders and their families.

A genetic counselor is a graduate level trained healthcare professional who receives training in both medical genetics and counseling. The National Society of Genetic Counselors describes genetic counseling as the process of helping people understand and adapt to medical, psychological, and familial implications of genetic contributions to disease. This process integrates: 1) interpretation of family and medical histories to assess the chance of disease occurrence or reoccurrence, 2) education about inheritance, testing, management, prevention, resources and research and 3) counseling to promote informed choices and adaptation to the risk or condition [1].

3. Rationale for involvement of genetics

The 2007 American Heart Association Scientific Statement on the genetic basis for congenital heart defects outlined four important reasons for making a genetic diagnosis in patients with congenital heart disease [2]. First, there may be other important organ system involvement for which screening or surveillance is indicated and which can be proactively managed. Second, there may be prognostic information for clinical outcomes. Third, there may important genetic reproductive risks. Fourth, there may be other family members for whom genetic testing (or other medical surveillance) is appropriate. The first reason presented in the AHA statement may appear to be geared

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toward a pediatric population and less relevant for the ACHD patient population. However, it is not uncommon to encounter ACHD patients for whom diverse medical problems have never had a unifying diagnosis. Providing this information not only guides future management and therapy but is also frequently a source of relief for patients and allows increased understanding and engagement in their health care needs.

Current ACHD patients may not have been evaluated by genetics at the time of diagnosis. Those who were evaluated did not have access to the significant advances that have occurred in genetic testing in the interim. As described in more detail in the section on genetic testing, chromosome microarray analysis, fluorescence in situ hybridization (FISH), multiplex ligation-dependent probe amplification (MLPA), and the majority of single gene sequencing tests have only been available within the last 5–15 years. In many centers, newborns with complex cardiovascular malformations now routinely undergo genetic testing. For example, the 2007 AHA consensus statement advocates FISH testing for 22q11.2 deletion syndrome for all infants with interrupted aortic arch type B or truncus arteriosus; tetralogy of Fallot associated with absent pulmonary valve, aortic arch anomalies (including right aortic arch), pulmonary artery anomalies, or aortopulmonary collaterals; perimembranous ventricular septal defect and associated aortic arch abnormalities; or infants with isolated aortic arch abnormalities [2]. Recommendations for testing in the ACHD population have not been developed, but it is clear that the genetic testing now considered standard of care was not available when this patient population was first diagnosed.

The accuracy of genetic counseling about recurrence risk is determined by the accuracy of the patient's diagnosis. Based on epidemiologic studies such as the Baltimore–Washington infant study and the Danish National epidemiologic study, syndromic cardiovascular malformations comprise at least 25% of all cardiovascular malformations [3–5]. With the improvements in diagnostic yield with more sophisticated genetic testing, it is possible to identify a higher percentage. To our knowledge, no specific study on the yield of genetic testing in an unselected ACHD population has been performed. However, it is not rare to make a syndromic diagnosis in an adult. Geneticists are well trained to evaluate patients for possible genetic syndromic conditions including those conditions with markedly variable expressivity or decreased penetrance. In addition, geneticists can evaluate family members for other syndromic features and facilitate appropriate genetic testing or referrals.

Recent human genetic studies have also identified subclasses of cardiovascular malformations which show familial clustering and are highly heritable or more likely associated with underlying genetic causes [3,6]. Multiple epidemiologic studies show that isolated cardiovascular malformations show familial clustering and have high heritability. A recent Danish population-based study investigating absolute and relative recurrence risk of congenital heart disease strongly suggests that gene mutations are the underlying cause [3]. Three of the classes of defects with the highest relative risk of recurrence of the same heart defect phenotype were heterotaxy, with a relative risk of 79.1 (95% CI 32.9–190), right ventricular outflow tract defects, with a relative risk of 48.6 (95% CI 27.5–85.6) and left ventricular outflow tract obstructive (LVOTO) defects, with a relative risk of 12.9 (95% CI 7.48–22.2). Familial clustering of dissimilar types of heart defects also had an elevated relative risk of 3.02 [7], suggesting that common pathways that involve shared susceptibility genes may underlie a continuum of heart defects.

These findings are important because they alter information on recurrence risk based on type of cardiovascular lesion. Further, they suggest the importance of additional screening in first degree family members. For example, LVOTO defects including bicuspid aortic valve (BAV), aortic valve stenosis (AVS), coarctation of the aorta (CoA), and hypoplastic left heart syndrome (HLHS) have been shown to be highly heritable and multiple genetic loci have been mapped [8–10]. The presence of an LVOTO lesion increases the risk of identifying BAV in a parent or children (relative risk 5.05) [11]. The high heritability of these malformations has been established with recurrence risks ranging from 5% risk of BAV in first degree family members of individuals with AVS, CoA, or HLHS to 22% recurrence risk of cardiovascular malformations in siblings of patients with HLHS [8,11,12]. These findings lead to a recommendation for echocardiographic screening in first degree relatives of an individual with AVS, CoA, or HLHS.

Current guidelines recommend counseling about recurrence risk for patients with ACHD. One recent study addressed the knowledge of ACHD patients regarding their diagnosis, family risk, and recurrence risk [13]. Over 50% of patients did not estimate recurrence risk in the correct range of magnitude. Additional information about inheritance of CHD was desired by 41% of patients. One-third of patients recalled receiving information from their cardiologists whereas 13% had been evaluated by a clinical geneticist. Approximately 60% of patients seen by a geneticist reported that the information was clear as compared to 29% receiving information from a cardiologist or nurse. Likewise, 60% reported receiving information about recurrence risk of CHD as compared to 28% receiving information from a cardiologist or nurse. While additional data are needed, these results indicate that genetic evaluation and genetic counseling are important components of ACHD care and developing improved methods for communicating genetic information and education in this patient population is important.

4. Role of the genetic counselor in the ACHD population

In the adult congenital heart disease clinic, the genetic counselor functions in several capacities, including obtaining a detailed family and medical history and interpreting that history for risk assessment; counseling the patient on recurrence risk associated with congenital heart disease and/or on risk for a specific genetic syndrome; facilitation of genetic testing and interpretation of results; and finally providing psychosocial support and counseling related to this genetic information. In the ACHD clinic, a genetic counselor may take on an additional role of triaging patients that should be referred for a complete genetic evaluation with a geneticist as well as suggesting other subspecialty referrals based on medical history.

4.1. Family and medical history

Genetic counselors aid in the process of genetic evaluation by obtaining detailed family and medical histories, beyond those histories routinely obtained due to time constraints of physicians involved in the care of patients seen in the ACHD clinic. This information should include focus on congenital heart disease as well as other possible associated non-cardiac concerns. Evaluation of a family history should begin with obtaining a pedigree. Standard pedigrees should include at least 3 generations and document family history of not only congenital heart disease but also other birth defects, learning disabilities, multisystem disease, and consanguinity. The detailed patient medical history obtained should include documentation of non-cardiac disease, particularly those which may be associated with genetic syndromes (Tables 1 and 2).

4.2. Counseling on recurrence risk and risk for a genetic syndrome

Interpretation of the family and medical history for assessment of recurrence risk or risk for a genetic syndrome is a key component of the genetic counseling process. One role of the genetic counselor in this patient population, after interpretation of the obtained family and medical history, is to explain inheritance patterns to a family. Possible inheritance patterns associated with congenital heart disease, both isolated and syndromic, include autosomal dominant, autosomal recessive, X-linked, and multifactorial. Genetic conditions following