Cardiogenetic counselling in a non-university hospital

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Background. Inherited heart disease is becoming a substantial part of everyday cardiology practice while genetic counselling still only takes place at university hospitals. In this study we review our seven-year experience with cardiogenetic counselling in a non-university hospital.

Methods. Retrospective analysis of patient records.

Results. A total number of 83 index patients were counselled. In 65 patients DNA tests were performed, resulting in 26 positive tests. In all patients with genotype confirmation of hereditary cardiovascular disease and in 32 families without a molecular diagnosis, family screening was advised. Out of 120 subsequently tested family members, 47 molecular genetic diagnoses were confirmed.

Conclusion. Although the number of patients reviewed was small, our data show that cardiogenetic diseases are part of daily cardiology practice. We believe counselling should be performed in more general hospitals. This is an excellent opportunity for collaboration between university and non-university hospitals, with immediate benefit for patients and their relatives. (*Neth Heart J* 2007;15: 412-4.)

Keywords: genetic counselling, heart disease (inherited), genetics

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The identification of the first gene for hypertrophic cardiomyopathy (HCM) in 1991¹ can be seen as the start of cardiogenetics, a field of cooperation between cardiologists and geneticists. Each year, more causal genes and disease-causing mutations for cardiomyopathies and primary electrical diseases are discovered^{2,3} and the field is rapidly expanding with major implications for patient care and management, even in asymptomatic people. At present, hereditary cardiovascular disease can be confirmed molecularly in patients and carriership can be detected in relatives. In persons at risk of developing fatal arrhythmias, treatment can be started in carriers who otherwise would not have been diagnosed yet.^{4,5} Cardiogenetic disorders have thus become a substantial part of daily cardiology practice, and are no longer limited to university hospitals. However, in the Netherlands genetic counselling and testing still takes places primarily in university hospitals.

The Medical Centre of Alkmaar (MCA) is a large non-university general hospital 50 kilometres north of Amsterdam. The cardiology department consists of 11 cardiologists, with a total of 28,462 outpatient visits in 2005, 5623 of which were new patients.⁶ It is the first Dutch centre where a cardiogenetic team from a university hospital holds outpatient clinics on a regular basis. In this article, we review our experience with this unique format since it was installed in 1999.

Methods

Since 1999, a specialised cardiogenetic team consisting of a clinical geneticist and a cardiologist, both based at the Academic Medical Centre of Amsterdam (AMC), has been counselling patients in Alkmaar. The frequency of the visits depended on demand. In the first years visits were scheduled monthly, which was ultimately reduced to visits every three to six months, depending on demand. All cardiologists working in our hospital independently referred patients with suspected inherited cardiac disorders to this team. Whenever DNA testing was advised by the cardiogenetic team, these tests were performed in the AMC's laboratory in Amsterdam. If the disease-causing gene could not yet be predicted or investigated, DNA was

Table 1. Prevalence of disease in all patients and results of genetic screening in patients and their relatives.

	All patients	DNA tested	DNA positive (% of tested)	Advice to screen family	Family members DNA tested	Family members with positive DNA
HCM	52	42 (81%)	20 (48%)	42 (81%)	108	45 (42%)
LQTS	6	6 (100%)	4 (67%)	5 (83%)	12	2 (17%)
BS	4	2 (50%)	1 (50%)	3 (75%)	0	0
ARVD	6	5 (83%)	1 (20%)	5 (83%)	0	0
DCM	5	4 (80%)	0	2 (40%)	0	0
Other arrhythmias	9	6 (67%)	0	1 (11%)	0	0
SCD	1	0	0	0	0	0
Total	83	65 (78%)	26 (40%)	58 (70%)	120	47 (39%)

The table lists the different proven or suspected diagnoses in referred patients, the number of patients in each subgroup in which DNA testing was performed and number of positive tests, and the results of family screening. HCM=hypertrophic cardiomyopathy, LQTS=long-QT syndrome, BS=Brugada syndrome, ARVD=arrhythmogenic right ventricular dysplasia, DCM=dilated cardiomyopathy, SCD=sudden cardiac death in family.

stored for future research and screening, if permitted by the patient. If a pathogenic mutation was detected in the proband, the team presymptomatically counselled family members with subsequent DNA testing when family members decided to undergo genetic screening. If DNA testing was not (yet) possible, most close relatives were advised to undergo cardiological screening in their neighbourhood. Further work-up, treatment and follow-up of probands was done by the cardiologists in the MCA.

For this review, we performed a retrospective analysis of all probands seen by the cardiogenetic team, based on the outpatient records in seven years, from 1999 till 2006.

Results

A total of 83 probands were seen by the cardiogenetic team. Records were available for all patients. Thirty-seven (45%) were male, mean age at first visit was 49 years (range 16-77 years). In 67 (81%) patients, the reason for referral was the cardiologist's suspicion of a genetic substrate based on the individual patient's signs and symptoms. In 14 (17%) patients, the family history and patient's clinical presentation were the reason for referral and in the remaining two (2%) patients, referral was at his or her own request.

The suspected or confirmed clinical diagnoses of referred patients are listed in table 1. Hypertrophic cardiomyopathy was the most frequent phenotype diagnosed.

DNA testing was performed in 65 (78%) patients. In 18 patients genetic testing was not performed. In ten patients the reason not to screen was because their phenotype was not suspicious for a genetic substrate, four patients refused to have DNA taken, in three patients a malignant form of hypertrophic cardiomyopathy was not suspected (which at that time was a reason only to store DNA and not perform genetic tests). In one patient, advice was given to perform DNA

testing in another family member whose genetic results could provide more valuable information to the family.

Table 1 also lists the results of DNA testing. In 26 patients molecular genetic screening revealed a putative disease-causing mutation: 20 had a gene mutation leading to hypertrophic cardiomyopathy (HCM), four mutations leading to long-QT syndrome (LQTS), one for arrhythmogenic right ventricular dysplasia (ARVD) and one Brugada syndrome (BS) related mutation. In our study 48% of patients with hypertrophic cardiomyopathy had positive DNA results, which is comparable with results found in previous studies.⁷⁻⁹

Cascade screening was advised for all 26 patients with a positive DNA diagnosis. In 32 patients without genetic confirmation (yet), the suspicion of hereditary cardiovascular disease was nonetheless still high. Therefore, clinical screening of family members was advised. In 120 family members DNA screening was performed, 47 (39%) molecular genetic tests were positive. We do not have complete data on cardiological screening of relatives, which may have been performed in another hospital.

Discussion

Molecular genetic testing can confirm a clinical diagnosis in an individual person, if the clinical picture or family history is not clear. Consequently, in families with a proven disease-causing mutation a negative test refutes the disease or the possibility of that disease developing in family members. Before performing a genetic test, some issues should be considered. Negative test results can provide feelings of relief in probands, but they should be aware that not all causal DNA mutations have been identified yet. Therefore, not finding a mutation does not necessarily mean that the disease is not genetic.

Positive test results, even in probands, can have a huge impact on someone's life. Not only the emotional

burden of proven genetic disease, including the risk for offspring, needs to be dealt with, but also possible financial consequences for health, life insurance and work, as well as lifestyle consequences for sports and work. Possible consequences of predictive test results for family members should be discussed as well. By screening family members, an asymptomatic person can be transformed into a 'patient' carrying a possibly fatal disease, sometimes needing invasive treatment and in most cases leading to lifestyle advice and regular cardiological screening. Family relationships can be affected in both a positive and a negative way because of the test results. These issues should be discussed with the patients and relatives before ordering a genetic test.¹⁰⁻¹²

It should be realised that the above considerations apply not only to molecular genetic testing, but also to cardiological investigations performed in asymptomatic individuals.

Since 1999, cardiogenetic counselling in our hospital has revealed 26 index cases of DNA-proven hereditary cardiovascular disease and a further 32 cases with a strong suspicion of an inherited disorder, although DNA confirmation was not (yet) available. When family-based genetic screening was advised, the cardiogenetic team invited relatives by a family letter. Cardiological screening of relatives was discussed with the proband and advised to the referring cardiologist. Despite efforts to stimulate relatives to undergo screening, in some families no relatives at all attended, although it is possible that family members decided to visit another hospital for cardiological screening without the knowledge of the cardiogenetic team. In the LQTS families only a small proportion were screened. Strikingly, in the HCM families the uptake was the highest, although the clinical picture of HCM is less severe (in most cases) than in primary electrical diseases, such as LQTS.

Since patients with suspected hereditary cardiac diseases have always been referred to university hospitals, there are no records of the incidence and prevalence of inherited cardiac disease at general hospitals in the Netherlands. Therefore, we do not know if our outpatient clinic for cardiogenetic counselling results in a better recognition of inherited diseases as compared with other non-university hospitals. However, the easy access to cardiogenetic counselling probably led to more frequent referrals, compared with a situation in which counselling is only possible in the university hospital itself. We believe this increase in referral leads to earlier diagnosis and improved treatment in these patients and their relatives.¹³

Furthermore, for the individual patient, it is more convenient when all outpatient visits can be done in the same hospital, instead of travelling to another city.

As cardiogenetics is a rapidly growing field in cardiology, we believe that collaboration between general and university hospitals offers an excellent opportunity to provide the best care for these patients. We therefore encourage other hospitals to integrate a structure as described in this article in their daily practice.

Conclusion

In this study, we have reviewed our initial experience with a cardiogenetic counselling team in a non-university hospital. Although it is not possible to determine whether easy accessibility of a cardiogenetic team leads to a significant difference in the frequency of diagnoses, we believe it leads to increased referral which in turn results in improved patient care. With the evolution of knowledge in cardiogenetics, cardiogenetic counselling should be implemented in all daily cardiology practice, not only in hospitals attached to universities, but also in non-university hospitals. More attention should be given, however, to uptake of predictive (cardiological or genetic) screening in relatives. ■

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