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How Knowing the Genetics Affects Management of Cardiomyopathy

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Cardiomyopathies are hereditary heart muscle conditions. The advances in technology in recent decades have allowed the identification of a number of genes that encode information for specific proteins of the heart muscle. Some mutations in these genes are considered to be responsible for the inherited heart conditions.

Knowledge of the genes has already helped in the understanding of a number of ultrastructural changes associated with these conditions and their clinical expression. At a clinical level, the genetic information could influence the management of a condition if it could provide a good understanding of the development of a disease, enable the clinician to predict who will be affected and when, and allow the course of the condition and the symptoms to be modified. This would require a strong and reproducible association between the genetic changes and the clinical condition.

In many cases though, a number of factors affect how the gene mutations manifest themselves. These factors can be environmental, developmental, other genes, and translators of the genes within the cells. For example, the lifestyle and the amount of exercise that one engages in can affect the age of appearance and the severity of expression of a genetic condition. Additionally, the presence of more than one mutation in the genes encoding heart proteins can have a synergistic role in how the disease presents. In this increasingly complex situation, we might not know all the genetic contributors.

Another merit of the genetic information would be to rule out from lifelong screening the relatives who do not carry the mutation. To exclude unaffected relatives from further evaluation requires solid information that the genetic change is the one that caused the condition.

Another application of the knowledge of the genetic status in certain conditions is to enable the individual or the parents of a child to make some informed choices on issues such as career or lifestyle. For example, if a condition is more likely to present earlier or in more severe form in mutation carriers who exercise at a very competitive level, then it is important to advise accordingly.

In everyday clinical practice, before interpreting the genetic changes in patients, the mandatory step remains the consideration of the context provided by the clinical information. Therefore, it is always wise to combine the genetic results with the results of the clinical tests.

In arrhythmogenic right ventricular cardiomyopathy, families and individuals with the same gene mutation have very different phenotypes. In hypertrophic cardiomyopathy, new gene mutations are frequently found that have not been seen before and we cannot easily predict the disease expression. In dilated cardiomyopathy, a large variety of genes may be involved and so genetic testing has not proved very helpful. Despite all this, there are genes that have been statistically linked with a higher prevalence of complications or even sudden death. One example is the gene encoding the Lamin protein, which is related to a subtype of dilated cardiomyopathy more frequently associated with sudden death at young or middle age and heart failure.

At present, genetic therapies with modification of the genetic information in one's DNA tailored to specific conditions are not available for cardiomyopathies, but research is active in the field and it is possi-

ble that this will be one of the clinical applications of genetic testing in the future.

In conclusion, genetic information in cardiomyopathies has helped and is still helping enormously in the understanding of the conditions and the research. However, its clinical application in the management of cardiomyopathies remains limited and has to be adjusted to the specific condition, gene and person.