Classification of Cardiomyopathies

Evolution or Revolution?

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"...I have attempted to maintain a proper balance between man and his instruments, between experienced opinion and statistics, between traditional views and heterodox, between bed-side medicine and special tests, between the practical and the academic, and so to link the past with the present."
—Paul Wood, OBE, MD (1)

Although it is not always appreciated, classification systems underpin virtually every aspect of our lives. The methods used to describe complex systems vary according to their primary purpose and the depth of understanding of the systems themselves, and necessarily evolve with the accrual of knowledge and changing needs in order to remain useful.

Classifications in medicine serve different purposes. Perhaps the best known, the World Health Organization International Classification of Diseases, is designed for morbidity and mortality reporting and in some countries is used for reimbursement purposes (2). By contrast, SNOMED Clinical Terms, or SNOMED CT, was created in 1999 from the merger of SNOMED Reference Terminology (SNOMED RT), developed by the College of American Pathologists, and the Clinical Terms Version 3, developed by the UK National Health Service in order to improve patient care through the recording of detailed clinical data and analysis of clinical processes (3). In this issue of the Journal, Arbustini et al. (4) propose a coding system inspired by these international standards for a very specific group of cardiac diseases—the cardiomyopathies. Their aim is to provide a precise, but adaptable, notation that links etiology with clinical phenotypes and, by inference, treatment and prognosis. As the classification of cardiomyopathies has been the subject of 2 other independent expert reviews in the United States and Europe relatively recently (5,6), the obvious question is why do we need a third report so soon?

Although much has been made about differences in terminology, there is broad agreement that the generic term cardiomyopathy refers to any disease of the myocardium that cannot be explained by coronary artery narrowing or abnormal loading of the ventricles. The arguments for the exclusion of these common causes of myocardial disease have been rehearsed elsewhere (5,6), but in essence, it is a pragmatic attempt to focus clinical attention on disorders that arise from within the cardiomyocyte or the extracellular matrix. Over the past few decades, it has become apparent that a substantial proportion of cardiomyopathies are caused by single-gene defects affecting different aspects of myocardial structure and function. With the exception of a few founder mutations, the prevalence of individual genetic mutations in most populations is relatively low, but in aggregate, the frequency of genetic cardiomyopathies is comparable to that of other common disorders, including many cancers. For 50 years, clinicians have grouped cardiomyopathies into subcategories on the basis of ventricular morphology and function. This approach has stood the test of time because it aligns very closely with clinical presentation and therapeutic strategies, but it is limited by the failure to consider etiology and by the exclusion of mild or intermediate phenotypes that do not meet conventional diagnostic criteria.

The system proposed by Arbustini et al. (4) is a valiant attempt to capture the pathophysiological complexity of cardiomyopathy in a single notation and represents a logical progression from an iterative diagnostic pathway proposed in a recent European Society of Cardiology working group position statement in which conventional cardiological assessments are combined with other noncardiac and molecular parameters in a cardiomyopathy-focused approach to diagnosis (7). At the heart of the scheme proposed by Arbustini et al. (4) is the idea that clusters of clinical features (or diagnostic “red flags”) can be used to identify specific genetic subtypes of cardiomyopathy that require individualized management strategies; the clinical cases used to support this argument represent some of the best examples of this.

The authors have clearly given much thought to the design of the scheme and its ability to evolve with advancing knowledge. However, there are number of aspects that need further consideration. The first is the category of morpho-functional class or “M,” which attempts to summarize informative phenotypic characteristics. At first glance, this is an innovative way of flagging diagnostic clues such as atrioventricular block and elevated serum creatine
phosphokinase, but examples such as the notation for an epsilon wave in arrhythmogenic right ventricular cardiomyopathy show how this approach could rapidly get out of hand. The clinical phenotype of arrhythmogenic right ventricular cardiomyopathy is highly complex and requires analysis of dozens of clinical measurements \(8\); inclusion of all such parameters in a single line of text, as implied by the notation, would be impractical, at least in everyday clinical practice. A related issue is the need for consistency in coding, particularly in patients or relatives with “early disease.” There is no doubt that many carriers of pathogenic mutations have mild or intermediate phenotypes that are not captured by standard definitions of disease. However, many of the clinical traits seen in such individuals are nonspecific or are conditional on factors such as age and sex (e.g., precordial T-wave inversion and mitral valve Doppler profiles). Universal adoption of the nomenclature requires that all users apply the same criteria, which in many cases have not been established.

Finally, the concept of “stage” is difficult to translate from the cancer context. In the grading of tumors, staging is used to plan treatment and to indicate prognosis. The challenge in cardiomyopathy is to find clinical parameters that fulfill the same aims. The authors propose use of the American College of Cardiology–American Heart Association stage (A through D) and New York Heart Association (NYHA) functional class (I to IV), but these are of limited use in some settings. For example, NYHA functional class III symptoms in a patient with hypertrophic cardiomyopathy and left ventricular outflow tract obstruction do not necessarily imply advanced end-stage disease with a poor prognosis. Similarly, a patient with mild dilated cardiomyopathy caused by a mutation in the lamin A/C gene may be at substantial risk of sudden cardiac death and yet be entirely asymptomatic. Staging based on symptoms alone is also challenged by the fact that functional status varies spontaneously or in response to treatment.

We live in an era of breathtaking scientific discovery driven by the ability to study complex systems using high-throughput technologies and sophisticated analytical tools. In the medical sciences, this is exemplified by emergence of whole new specialties such as genomics and proteomics. The scheme proposed by Arbustini et al. \(4\) represents a potential bridge between these new scientific disciplines and clinical medicine, but before it can be adopted, its primary purpose needs to be very precisely defined and its performance as a diagnostic and prognostic tool prospectively tested. For the moment, its most important contribution is to remind us that improvements in health come through the integration of basic science with the craft of clinical medicine.

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