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New Diagnostic Criteria for Marfan Syndrome Published in Journal of Medical Genetics

*New Guidelines Facilitate Accurate Diagnosis of
Life-Threatening – but Treatable – Genetic Disorder*

PORT WASHINGTON, NY, July 1, 2010 – An international panel of experts in the diagnosis and management of Marfan syndrome, a potentially fatal genetic disorder, has published new diagnostic criteria for the disorder, thus simplifying the evaluation process for physicians. The new diagnostic process – which continues to be based primarily on a multi-system clinical examination – will provide patients with a more accurate diagnosis and better medical management. The new criteria for Marfan syndrome were published in the *Journal of Medical Genetics* (*J Med Genet* 2010;47:476-485)

“The diagnostic evaluation for Marfan syndrome is unavoidably complex due to the highly variable presentation of affected individuals, the age-dependent nature of many of its manifestations, absence of gold standards and its extensive differential diagnosis,” said Bart Loeys, MD, Center for Medical Genetics, Ghent University Hospital, Ghent, Belgium, who spearheaded the panel. “While diagnostic criteria should emphasize simplicity of use and the desire for early diagnosis, the highest priority in developing these guidelines was accuracy.”

Marfan syndrome and related connective tissue disorders affect approximately 200,000 Americans. Because connective tissue makes up the entire body, the disorder manifests itself in many body systems, including the skeletal system, eyes, lungs, blood vessels and heart. Many people with Marfan syndrome experience an expansion of the aorta. It is essential for affected people to be diagnosed and managed properly. Without proper monitoring and medications to reduce the stress on the aorta, affected people are at high risk for aortic dissection or rupture, which could result in sudden death. With an accurate diagnosis and proper medical treatment, they can live a normal lifespan.

The new nosology provides a method for evaluating a patient by deriving a systemic score, with various features of Marfan syndrome assigned a numeric value; the diagnosis depends on the total systemic score. This is a change from the previous nosology which relied on evaluation of features as “major” or “minor.” A web-based diagnostic tool for the application of the new criteria is available for physicians at the National Marfan Foundation website, www.marfan.org.

The scoring system reflects three significant changes in the way Marfan syndrome is diagnosed:

- The two cardinal features of Marfan syndrome – aortic root dilatation/dissection and ectopia lentis (dislocated lens of the eye) – are weighted more heavily than other characteristics.
- There is a more precise role for molecular testing.
- Less specific manifestations of Marfan syndrome are either removed or given much less weight in the evaluation process.

The diagnostic criteria have been defined for those with a family history of the condition and for those who may be a sporadic case; that is, they are the first in their family to be affected.

Specific guidelines are also given for children (less than 20 years of age), with different scenarios proposed for those with family history and those without family history. For those who do not meet the diagnostic threshold for Marfan syndrome or a related condition, the nosology employs the diagnosis of “non-specific connective tissue disorder,” which fosters ongoing monitoring of the aortic size and function, until such a time when a specific diagnosis can be made.

The nosology also offers additional diagnostic considerations and recommends more testing if a patient has sufficient findings of Marfan syndrome but, additionally, shows other unexpected features. The differential diagnosis and management for alternative diagnoses, such as Loeys Dietz syndrome, vascular Ehlers Danlos, mitral valve prolapse syndrome, familial aortic aneurysm and more, are outlined.

“These new diagnostic criteria will be of great benefit to both physicians, particularly those who do not see many cases of Marfan syndrome, and patients,” said Carolyn Levering, President and CEO of the National Marfan Foundation, Port Washington, NY. “It addresses the practical challenges that diagnosing the condition presents to physicians and, at the same time, protects patients by balancing the use of diagnostic categories with a discussion of ongoing risk and the need for follow-up and management.”

Methodology

The revised nosology was based on critical review of clinical characteristics in large published patient cohorts, the experience and opinions of the panel members with extensive experience in applying the former criteria, the differential diagnosis of Marfan syndrome, and the strengths and limitations of molecular genetic testing. The guiding principals for revising the diagnostic criteria were: maximal use of evidence-based decision-making; attention to practical implications; a focus on features and criteria that distinguish Marfan syndrome from other disorders; and definition of purposeful thresholds for diagnosis.

In addition to Dr. Loeys, the panel was comprised of the following Marfan syndrome experts: Harry C. Dietz, MD, and Paul Sponseller, MD, Johns Hopkins University School of Medicine; Alan C. Braverman, MD, Washington University School of Medicine; Bert L. Callewaert, MD, Julie De Backer, MD, and Anne M. De Paepe, MD, Ghent University Hospital; Richard B. Devereux, MD, Weill Cornell Medical College; Yvonne Hilhorst-Hofstee, MD, Leiden University Medical Center (the Netherlands); Guillaume Jondeau, MD, Hopital Bichat (Paris, France); Laurence Faivre, MD, Children’s Hospital, (Dijon, France); Dianna M. Milewicz, MD, PhD, University of Texas Medical School; Reed E. Pyeritz, MD, PhD, University of Pennsylvania; and Paul Wordsworth, MD, Nuffield Orthopaedic Center (Oxford, UK).

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