Researchers nationwide ask for new focus on 'sudden death' heart disorder

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(PHILADELPHIA) An abrupt, fatal heart attack in a young athlete on the playing field is a tragedy destined to repeat itself over and over until more is understood about hypertrophic cardiomyopathy (HCM), a genetic disorder that is the most common cause of sudden death in young people but which affects people of all ages. So says a task force of cardiologists and cardiac biologists, headed by Thomas L. Force, M.D., James C. Wilson Professor of Medicine at Thomas Jefferson University, in the September 14th online edition of the journal *Circulation*.

Their special report is the culmination of a 1.5-year effort to sum up the relatively little that is known, and much that remains a mystery, about HCM, and to list what future research priorities should be - all with a goal of developing novel treatments. All 21 researcher-physicians, from institutions around the country, participated in an HCM working group convened by the National Heart, Lung, and Blood Institute. HCM is believed to affect 1 in 500 people, yet without a detailed family and genetic history, many people may not know they are at risk for sudden death, says Dr. Force, who, as a nationally-known cardiology investigator, had led a number of symposiums and study groups to focus on causes and novel therapies for patients with sickened hearts.

"Unbelievably to me, this problem is still not understood or even known to exist by many people, and it remains a very challenging disease to treat," he says. "The medical management of HCM has changed very little over the past decades."

HCM, a thickening of the heart muscle which makes it more difficult for it to pump blood, often manifests itself when it's too late, he says. "The reason it can be deadly is because people with the disease are often unaware that they have it and physical exertion - such as sports - can bring on the sudden, fatal series of events that causes the heart to go into arrest," Dr. Force says.

HCM patients can also be significantly disabled by heart failure, and atrial and ventricular tachyarrhythmas. A few medical therapies such as implanting a cardiac defibrillator exist for selected, high-risk patients, but most medical therapies have largely focused on alleviating symptoms of the disease, not on altering its natural history, he says.

Because so little is known about HCM, some have lobbied for mass screening of young athletes, but most physicians feel it is impractical and would lead to a lot of false positives. "A cardiac exam in a general practitioner's office is not very precise, and more detailed examinations such as routine ECGs would likely be prohibitively expensive and might still miss a significant number of children or could needlessly alarm parents and children," he says. "Some children with HCM have only a minor amount of hypertrophy in their hearts but they are still prone to sudden death, and people can experience sudden death before any symptoms of heart trouble occur. Again family history becomes very important in identifying potentials at risk"

Given these issues, the recommendations of the task force are important in identifying mechanisms and, ultimately, developing novel therapies, Dr. Force says.

Among them are to:

- Define all genetic causes: HCM is caused by hundreds of

different mutations in genes that encode components of the sarcomere, the contractile apparatus of cardiac muscle. But knowledge of the full spectrum of genes and mutations in HCM is needed to explain how the disease develops and, thus, how it can be treated. For example, Dr. Force says some mutations lead to heart failure, while others lead to sudden death with little evidence of heart damage.

- Study the natural history of the disease: Establish a multi-center prospective observational cohort study of HCM that represents a range of mutations. This will provide insights into the diagnosis and progression of HCM that will refine clinical practice.

- Support clinical trials: When potential therapeutic strategies are identified in pre-clinical studies and early clinical trials, a randomized, placebo-controlled multi-center clinical trial should test the therapies. A major goal in treatment of HCM is to limit the life-threatening consequences of arrhythmia, the researchers say.

- Prevent mutant gene expression: Pharmacologic therapies may only alleviate symptoms, so in order to impact patient survival, strategies are needed that significantly reduce or eliminate expression of HCM mutant genes, the task force says.

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