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MEETING REPORT

Lessons from the FNIH-NIA-FDA sarcopenia consensus summit

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Meeting Report from the FNIH-NIA-FDA Sarcopenia Consensus Summit, Baltimore, MD, USA, 8–11 May 2012

Introduction

Dr Irwin Rosenberg coined the term 'sarcopenia' in 1988, which was fundamental in bringing needed attention to a pathological condition that has very serious consequences to individuals and society. But 24 years later, sarcopenia remains largely undiagnosed and undertreated, why?

Just 2 months ago, a group of around 100 scientists from all parts of the globe gathered in Baltimore, USA for the Sarcopenia Consensus Summit to debate and discuss, among other things, the elusive working definition of sarcopenia. Skeletal muscles are very complex in nature, which is compounded by the complexities of aging itself making this disease difficult to be precisely defined.

This 4-day consensus definition conference was co-organized by the Foundation of National Institutes of Health (FNIH), National Institutes of Aging (NIA) and the Federal Drug Adminstration (FDA), and was co-sponsored by five pharmaceutical companies (Abbott, Amgen, Eli Lilly, Merck and Novartis). Importantly, a consensus definition of sarcopenia, is gradually being enabled through the FNIH Biomarkers Consortium Sarcopenia Project, led by Dr Stephanie Studenski, that has been acting as a neutral convener for academia, industry, FDA, NIH and related professional societies. The Sarcopenia Project came to the 2012 Sarcopenia Consensus Summit prepared with data from thousands of individuals on several major aging longitudinal studies conducted in the United States in the past several decades in hopes of facilitating the definition of sarcopenia.

Defining Sarcopenia

For a clinician that two decades ago moved into the areas of muscle biophysics/physiology and is now going back to human studies, it is quite reassuring to see the concept of muscle weakness being invoked without the traditional view that sarcopenia is the loss of muscle mass, as it is the overall quality of the muscle that is affected and not necessarily the size or quantity of muscle.[1]

Thus, in my own attempt to define sarcopenia, I have concluded that: sarcopenia is the loss of muscle quality during aging characterized by a decline in muscle strength that if untreated can lead to weakness, disability, an increased risk of falls and loss of independence. While genetic and epigenetic factors seem to contribute to sarcopenia, proper diet and physical activity can be effective in at least minimizing the progression and severity of sarcopenia. Also integral to its definition is the recognition that there are grades of sarcopenia that range from sub-clinical to frailty.

For the individual, his family and the clinician, perhaps the most important fact is that the sarcopenic individual is becoming weaker. In fact, grip strength, one of the best functional indicators of muscle weakness, strongly correlates with disability, morbidity and mortality in the elderly.[2–4] There must be much more to strength and power than muscle diameter alone. In fact, in a number of studies,[5–8] the gain in strength following exercise training far exceeds the gain in muscle mass, suggesting that intrinsic adaptations to muscle can overcome its size limitations. Understanding these intrinsic mechanisms could lead to new treatments for sarcopenia and other muscle diseases.

Summary of Sarcopenia Project Key Findings

Setting the tone. In her opening remarks, Dr Stephanie Studenski (Division of Geriatric Medicine, University of Pittsburgh and Director of the FNIH Sarcopenia Project) emphasized the urgent need for a gold standard criteria for the diagnosis of sarcopenia and said that distribution-based definitions will not work anymore. She argued that to properly define sarcopenia, we must think like clinicians, as ultimately clinicians will either treat or not treat sarcopenia. The available data from the Sarcopenia Project should be used to better define sarcopenia, and to engage all interested parties on this subject to move this field forward and to give clinicians the tools necessary to prevent and treat sarcopenia.

The NIA insight. Dr Luigi Ferruci, NIH—National Institutes of Aging: It was clear from day 1 that the goals of NIA were the same goals of the conference. NIA pointed out that sarcopenia is much more than the old anatomical definition of muscle loss. Dr Ferruci shared very intriguing data for 24-h creatinuria that clearly strengthened the association between reduced muscle mass and poor muscle function, suggesting that elevated levels of creatinuria could be a potential biomarker for sarcopenia. Why a panel of serum proteins could not be used along with determination of muscle mass and function to diagnose sarcopenia?

FDA insights. Dr Dragos Roman (FDA Team Leader) stressed that the FDA does not have an official policy on sarcopenia. Currently, there is no approved sarcopenia indication, but since 1964, several products have been approved for cachexia-related syndromes (oxadrin, menace, serostin; see also CRF 201.57). He emphasized that clinical trials will need to address the following questions: what is the clinical meaningful benefit of a drug or intervention? Does it improve mobility and muscle strength? Does it reduce the risk of fractures? Does it reduce mortality?

Sarcopenia, cachexia and frailty. Dr John Morley (Division of Geriatrics, School of Medicine, Saint Louis University) introduced key concepts on differences between these three conditions (sarcopenia, cachexia and frailty). He also made a very strong point that the science of nursing must be changed if sarcopenia is to be properly treated. Then, he shared the good news that protein supplementation is at least partially effective in preventing some of the muscle loss with age.

Muscle dysfunction and disability. Dr Roger Fielding (Jean Meyer USDA Human Nutrition Research Center on Aging, Tufts University) stressed that almost all new drugs in the pipeline to potentially treat sarcopenia are all designed to target muscle mass. He reminded the audience that the current consensus definition postulates that if gait speed is less than $1.0\,m\,s^{-1}$ and appendicular muscle mass is less than $7.23\,kg\,m^{-2}$ for males and less than $5.67\,kg\,m^{-2}$ for women, an evaluation of sarcopenia is warranted. The European Consensus definition of sarcopenia proposed a 'case-finding algorithm' that could become useful in implementing a final strategy for sarcopenia diagnosis and treatment.[9]

Lessons from osteoporosis. Dr Steve Cummings (California Pacific Medical Center Research) reasoned that the arbitrary decision in 1992 to diagnose osteoporosis with a *T*-score of -2.5 was critical for the area of bone diseases, as bone mineral density osteoporosis became a recognized disease with an ICD. It also led to additional research and the critical and essential participation of the pharmaceutical industry in the development of different medications to treat bone diseases.

Summary of key findings. The last 2 days of this conference were waited with great anticipation, as the data from the following studies would be presented and summarized: In Chianti (Dr Dawn Alley, Univ. of Maryland Medical School); MrOs and SOF studies (Dr Peggy Cawthon, Califronia Pacific Medical Center); Rancho Bernardo Study (Dr Tien Dam, Columbia University); The Framingham Study of Cohorts (Dr Robert McLean, Harvard Medical School); The Boston Puerto Rican Health Study (Dr Carmen Sceppa, Northeastern University); Health ABC and AGES-Reykjavik (Dr Tamara Harris, National Institute of Aging). In addition, Dr Anne Kenny (UCONN Center of Aging) presented data on Clinical Trials, Dr Maren Fragala (College of Education, University of Central Florida) elaborated on lower extremity strength association to low gait speed, and Drs Karen Mahoney and Laurie Burke on the perspectives from the FDA on Sarcopenia and Treatment Benefit and clinical outcome assessment. A corollary of these presentations is how strongly well-positioned grip strength rose as a strong indicator of muscle weakness, mobility disability and morbidity. These studies also confirmed the need for additional studies in populations that might represent the extreme conditions of no sarcopenia and frail sarcopenia and also on non-caucasian. An important finding based on the Baltimore Longitudinal Study on Aging Paradigm is that muscle strength is critical for mobility, and that in fact there is a very large disagreement between muscle function and muscle mass, and that mass alone can only explain less than half of the functional loss (for a recent review, see Brotto and Abreu[10]).

Final remarks. A feasible explanation for the disparity between mass and function is that other adaptations occur in muscle cells. It is possible that in some individuals the loss of muscle mass induces compensatory changes at the excitation–contraction coupling machinery that makes it more effective and force per unit of cross-bridges is actually enhanced, whereas in others maladaptation leads to loss of function.

An intriguing fact that was raised during the Summit is; one in two women and one in four men over the age of 50 years will have an osteoporosis-related fracture in his or her remaining lifetime. Is this higher incidence of fractures in women a reflection of their intrinsic lower muscle mass?

Thus, it is conceivable that any loss of muscle mass in women could have a higher impact than similar losses in men, given this intrinsically lower muscle mass and a normally higher ratio of muscle/fat in women. Such knowledge should help lead into new policies that further stimulate sports and exercise practice among women, particularly at an early age.

In conclusion, the FNIH-NIA-FDA Sarcopenia Summit represented an important step towards a better understanding of sarcopenia that should help to define this condition as a human disease that should be prevented and treated.

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