



SYMPOSIUM ABSTRACT BOOK

Innovative Ways to Support Mobility into Old Age: An Interconnected Musculoskeletal Strategy

Nestlé Health Science Satellite Symposium
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Society (EuGMS) - Helsinki, Finland

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FOR HEALTHCARE PROFESSIONALS ONLY

AGENDA

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CHAIRPERSON

Dr. Luigi Ferrucci, MD, PhD

Scientific Director, Chief of the Longitudinal Studies Section, National Institute on Aging, NIH, Maryland, USA.



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Prof. Eva Topinková, MD, PhD

Head and Chair of the Department of Geriatric Medicine, Charles University and General University Hospital, Prague, Czech Republic.



Optimal Nutrition and Physical Activity Interventions to Support Mobility in Community-Dwelling Older Adults

Prof. José Viña, MD, PhD

Full Professor and Freshage Research Group Leader, Department of Physiology and Medicine, University of Valencia, Spain.



Pain as a Main Hurdle for Mobility in Joint Issues: Evidence-Based Approaches

Dr. Nicola Veronese, MD

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Summary and Actionable Guidance for Healthcare Professionals to Assess, Prevent and Manage Elements of Mobility Decline

Dr. Luigi Ferrucci, MD, PhD

Scientific Director, Chief of the Longitudinal Studies Section, National Institute on Aging, NIH, Maryland, USA.





Dr. Luigi Ferrucci, MD, PhD

Introduction

Chair biography

Dr. Luigi Ferrucci is a geriatrician and an epidemiologist who conducts research on the causal pathways leading to progressive physical and cognitive decline in older persons. He has made major contributions in the design of many epidemiological studies conducted in the U.S. and in Europe. Dr. Ferrucci received a Medical Degree and Board Certification in 1980, Board Certification in Geriatrics in 1982 and Ph.D. in Biology and Pathophysiology of Aging in 1998 at the University of Florence, Italy. Between 1985 and 2002 he was Chief of Geriatric Rehabilitation at the Department of Geriatric Medicine and Director of the Laboratory of Clinical Epidemiology at the Italian National Institute of Aging. In September 2002, he became the Chief of the Longitudinal Studies Section at NIA. From 2002 to 2014 he was the Director of the Baltimore Longitudinal Study on Aging. Dr. Ferrucci is currently the Scientific Director of NIA, since May 2011.



Abstract

Understanding that health in older persons is best assessed through the evaluation of physical and cognitive function rather than through the simple enumeration of disease diagnosis is perhaps the most important accomplishment of the geriatric research field. Loss of mobility is the most important factor affecting the decline of quality of life with aging. Research on mobility, however, has still been focused on the different medical conditions that can affect mobility, such as osteoarthritis, sarcopenia, osteoporosis, loss of aerobic capacity and neurological control. The most paradigmatic example is the search for a clinical definition of sarcopenia. Years of discussion about what threshold of skeletal muscle mass, muscle strength or walking speed, and in what combination should be used for the definition of sarcopenia and it has been discussed in hundreds of meetings and scientific papers. But this enormous effort resulted in very little progress in this field, no agreed upon definition, and no clear path for the development of effective interventions.

Where do we go from here? Perhaps, it is time to change perspective and consider that, according to the geroscience hypothesis, the impairment of the different physiological dimensions that affect mobility performance are all affected at the same time, although with different combination of severity, by the biology of aging. This hypothesis has two very important implications:

- 1) The different physiological dimensions that affect mobility are mutually compensating. For example, in the presence of a balance problem, the amount of muscle strength required to walk is much higher than in the absence of any balance problems. Thus, a standard definition of a threshold of what is "enough" strength cannot be established because such threshold depends on the presence and severity of other impairments.
- 2) Interventions that target only one physiological factor that affect mobility may not be effective depending on the presence of other impairments, reciprocal combinations, and severity.

This hypothesis calls for a precision geroscience approach to the diagnosis of mobility loss that quantifies the contribution of different physiological dimensions and based on such diagnostic process identifies subgroups of patients most likely to respond to different interventions. Gerotherapeutics by targeting at the same time the various dimensions of mobility loss may be particularly effective in prevention and treatment of mobility loss in older persons.



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Introduction Dr. Ferrucci:

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Prof. Eva Topinková, MD, PhD

Uncovering the Major Determinants Behind Declining Mobility

Speaker biography

Prof. Eva Topinková, MD, PhD, is a Head of the Department of Geriatrics, First Faculty of Medicine in Prague, and Chair of the Geriatric Medicine Department at the General Faculty Hospital in Prague since 2005. As a Full Professor of Internal Medicine, Geriatric Medicine and Social Sciences her broad clinical and research interest involves a wide range of geriatric and general aging research topics, including but not limited to clinical geriatrics, healthy aging and health system research to integrate and optimize elderly care through a person-specific approach.

She is a leading national expert in geriatric medicine, Board member of the Czech Society of Geriatrics and Gerontology, past president of IAGG European Region Clinical Section and former IAGG Europe Scientific Secretary, Czech representative in UEMS-Geriatric Medicine, member of EUGMS SIG groups on frailty, sarcopenia, pharmacology, falls, geriatric rehabilitation, incontinence. Her research experience involves many clinical trials and European research projects ADHOC, CLESA, NUTRI-SENEX, PREDICT, SHELTER, MID-Frail, MPI-AGE, and more recently SPRINTT and SO-NUTS focusing on nutrition, physical activity and lifestyle contributing to healthy aging and disability prevention.



Abstract

Maintaining optimal physical functioning until very old age and prevention of mobility disability are core goals for healthy aging. Mobility and independent locomotion are important pillars of independence and the intrinsic capacity concept. Epidemiological studies report mobility limitations in about 35% of persons aged 70 and most persons over 85 years. Mobility limitations have been associated with an increased fall, disability, hospitalization, and mortality risk as well as with decreased quality of life, and poor psycho-social wellbeing. A low physical activity (PA) level has been linked to sarcopenia, and to mobility limitations which is a hallmark of physical frailty^{1,2}. However, most people in developed countries do not meet the recommended PA level.

Mobility is understood as "one's ability to move independently around their environment". However, in the broader sense mobility includes not only psychosocial, cognitive, and physical determinants but expands to the transportation and environmental, financial, cultural and gender aspects. In the broader definition: *Mobility is the ability to move oneself around freely and independently, to participate in activities of daily living and one's social life without any restrictions and have access to life spaces and surrounding*. The broader definition supports the need for a holistic approach to mobility and involvement of interdisciplinary perspective such as health care, medicine, human movement and sport sciences, biomechanics, nursing, rehabilitation, psychology, and other. However, there is no single universally accepted definition of mobility.

Results from a European cross-sectional study in older adults showed that the most powerful predictors of mobility limitations were age, chronic conditions (arthritis, stroke, diabetes, and obesity), poor health status, physical inactivity, and demanding environment³.

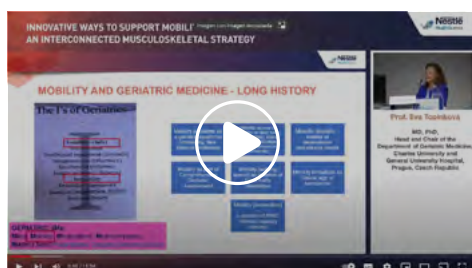
Early identification of older people with the (risk of) mobility limitations enables clinicians target interventions preventing further decline in mobility, and development of disability and dependence. When addressing mobility decline, proper and standardized assessment tools recording mobility domains and contextual factors is key (such as physical: gait, balance, strength, frailty, multimorbidity, cognitive, neuromuscular, and psychological: motivation, participation, QOL, life satisfaction) to screen for and diagnose mobility problems and to monitor changes longitudinally. PROMS in mobility studies should be defined.

Concrete measures in public health domain and health care, environmental design and security, transportation, and services infrastructure should address the modifiable determinants of mobility disorders. In the lecture we will present selected results of multimodal intervention for prevention of mobility disability in physically frail elderly (the SPRINTT project⁴) and the use of a web app promoting healthy behaviour (nutrition and physical activity) in the critical period around the retirement (the SO-NUTS project⁵).



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Prof. José Viña, MD, PhD

Optimal Nutrition and Physical Activity Interventions to Support Mobility in Community-Dwelling Older Adults

Speaker biography

José Viña studied Medicine at the University of Valencia, Spain, where he obtained his PhD after doing research work with Hans Krebs in Oxford, UK. Dr. Viña is Professor of Physiology at the University of Valencia, where he combines teaching with research, the latter in two main lines, aging and exercise. José Viña leads a successful research group called FRESHAGE that works on different aspects of aging, including healthy aging, exercise, and Alzheimer's disease. He has numerous publications (over 350 publications in prestigious international journals) on glutathione, mitochondria, oxidative stress, free radicals, nutrition, and exercise. Prof. Viña has received numerous awards and distinctions, including the Albert Struyvenberg Medal, awarded by the European Society for Clinical Research (ESCI) 2017, the "Onda Cero" Science Award in 2018, and the Research Trajectory Award from the Council of the University of Valencia 2019. Dr. Viña gave a lecture at the 2018 Gerontological Society of America presidential address and has given a lecture at the Nobel Prize Foundation session on aging in 2019. Dr. Viña is an Editor of "Free Radical of Biology and Medicine" and also a member of the Royal Academy of Medicine of the Valencian Community. In addition, he has been awarded two honorary doctorates, University of Buenos Aires (Argentina) and University of Rennes (France). Dr. Viña was President of the Society for Free Radical Research International (SFRR-I) 2020-21.

Dr. Viña's work has been recognized by his colleagues. Dr. Viña's articles (including book chapters) have been cited more than 20,800 times, giving an h-index of 77 and an extended h-index (including book chapter citations) of 84.

Dr. Viña was the author of the most cited article in the Biochemical Journal 1978, also in the Free Radical Biology and Medicine in 2003 and in the Journal of Gerontology in 2013. He was the most cited author in Free Radical Research 2008. He was the second most cited author in IUBMB Life in 2000, in the Biochemical Journal in 1980 and in Free Radical Biology and Medicine in 2019 (data taken from: <https://exaly.com/author/2255005/jose-vina/rankings>).



Abstract

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Nutritional recommendations have evolved from the 20th century idea of the minimal requirements, which are based on pioneering work by Frederick G. Hopkins to that of the 21st century, which intends to reach optimal nutrition. Minimal requirements for growth are not sufficient anymore when we want to promote longevity and especially healthspan, which in clinical terms is also defined as prevention of frailty^{1,2}.

Bruce Ames and his co-workers have analysed in detail the deficiencies in micronutrients that are found in American and, in general, western populations and have shown that a very significant proportion of individuals, especially after the age of 65, show substantial deficiencies in micronutrients³. It is important to underpin that 40% of the European population over 65 are deficient in protein. This is due to lack of appetite, dental problems and, in general, the lack of energy that is required to maintain daily life activities. This low protein intake is worrisome as it's contrary to expert recommendations for older adults to consume more protein (1.0-1.2g/kg bw/day for healthy adults >65y), which is particularly important to help overcome anabolic resistance and support muscle health^{4,5}.

On the other hand, physical exercise is of the utmost importance to maintain health and prolong life⁶.

This is of particular importance for the elderly population. We performed a clinical trial in which a multicomponent personalised social exercise programme was performed by a group of frail individuals for a period of six months, after which participants were significantly less frail, less depressed and visited the primary care centre significantly less than controls (who went to the exercise centre but did not perform exercise)⁷. Moreover, we have recently confirmed this by a real life intervention study⁸.

However, the possible synergistic effect of nutritional supplementation, especially in terms of proteins and micronutrients, together with exercise on the delaying of frailty has not been studied in sufficient detail.

We report here the results of a clinical study on frail individuals with regard to their nutritional habits (MNA: Mini Nutritional Assessment) and also their exercise habits, which were virtually non-existent at the beginning of the study. Within-subject comparisons were established, and well as comparisons to a group of individuals who did not perform exercise.

Methods: this is a prospective randomised clinical study involving 74 community-dwelling frail individuals at risk of malnutrition (age ≥70). They were divided into three different groups: control (CG), nutritional supplementation (SG) and nutritional supplementation plus a multicomponent exercise training programme (ESG) described in⁶. The nutritional supplementation consisted of a daily intake of two 200 ml bottles of Meritene. Each of these



bottles contains 16 g of proteins, 3.6 g of lipids and 25 g of carbohydrates. A mixture of vitamins and minerals are also included. Exercise was performed three days a week for six months, and it was personalised and supervised.

Results

We have determined up to 27 different parameters that may be classified as: physical and biochemical parameters; psychological parameters; socio-sanitary parameters; and determinants of malnutrition and frailty.

The general outlook of these measurements is that exercise, together with a nutritional supplement, results in a very significant improvement in the majority of these parameters and leads to the prevention of an increase in biological age (determined using the methylome) of the individuals involved.

Many of the parameters improved significantly when individuals were treated with exercise together with a nutritional supplement. Prominent among these are improvements in abdominal girth, fat mass and lean mass.

As far as biochemical parameters are concerned, formic acid and vitamin D3 were significantly higher in the individuals treated than in controls. We, however, did not observe changes in lipid peroxidation as determined by malondialdehyde measured using ultra high-pressure liquid chromatography.

With regards to the psychological parameters, ESG significantly improved the EQ-5D analogue scale that describes the self-perception of life quality and significantly improved the Yesavage scale, which is indicative of geriatric depression. Slight improvements in the minimal state were also observed.

Regarding the socio-sanitary parameters, ESG very significantly lowered the number of visits to the primary care centre (leading to a 50% reduction). In a similar fashion, the number of visits to the emergency wards was very significantly lowered when, and only when, exercise and supplements were administered. Another important clinical parameter determined was the number of falls, which were significantly reduced in the ESG individuals. Finally, disability, as determined by the Barthel scale, was significantly lower in the ESG individuals.

Malnutrition and frailty determinations: Both the ESG and the SG improved on the Mini Nutritional Assessment (MNA) scale, while the CG worsened it. We have determined two major parameters that were described by Linda Fried and her colleagues: one is the gait speed which is significantly improved in ESG. The same occurs with the hand grip which is significantly improved after six months of treatment. With all parameters included (also taking into consideration the general feeling of wellbeing as well as the involuntary weight loss) we have observed that exercise supplemented with a calorie-containing drink with vitamins, minerals and proteins lowers frailty as determined by the Linda Fried criteria.



Concluding remarks

Achieving optimal nutrition is a major goal for the gerontologists and geriatricians of the 21st century. The minimal requirements that were usually studied in the 20th century have been overtaken by the newer concept of optimal nutrition to achieve maximal healthspan. Here we report results of a clinical intervention study in which we have administered a nutritional supplement (Meritene) together with a well-controlled exercise programme.

These interventions have resulted in significant improvements in parameters of frailty and very importantly, in a 50% reduction in the number of visits to the primary care centre and emergency wards during the period of study. A number of other health risk factors also improved including quality of life, nutritional adequacy, body composition, falls and disability, and indicators of psychological health.

The general conclusion that may be drawn from these studies is that it is strongly recommended for the general population to include controlled, personalised, social exercise as part of the normal health care of elderly individuals, and in the significant proportion of older adults at-risk of or with signs of sub-clinical malnutrition, exercise must be accompanied by a nutrition supplement containing proteins and micronutrients.

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Dr. Nicola Veronese, MD

Pain as a Main Hurdle for Mobility in Joint Issues: Evidence-Based Approaches

Speaker biography

Dr. Nicola Veronese, MD, is a certified trained geriatrician, currently working as Senior Researcher in Geriatrics at the University of Palermo, Italy. His research is mainly epidemiological and focused on the most common diseases affecting older people. In particular, his interest areas are osteoarticular, metabolic (including obesity and diabetes) and cardiovascular diseases, as well as nutrition. He is the author of more than 600 articles published in national and international scientific journals, and of numerous abstracts accepted by national and international congresses.

He has several positions in European societies such as member of the executive board of the European Interdisciplinary Council on Ageing and of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases, leader of the Special Interest Group in Systematic Reviews and meta-analyses of the European Geriatric Medicine Society. In this latter society, he is also involved as a member of the Committee for the Guidance for Guidelines Procedures. Finally, Dr. Veronese is Associate Editor of Age and Ageing and Aging Clinical Experimental Research and member of the editorial board of Experimental Gerontology and Journal of the American Medical Directors Association. Nicola Veronese is one of the Top Italian Scientists, Clinical Sciences and named as one of the world's leading experts in frailty, comprehensive geriatric assessment, magnesium, meta-analysis and ranked among the World's Top Medicine Scientists, Rising Stars (40 worldwide).



Abstract

Osteoarthritis (OA) is the most common form of arthritis, being characterized by joint pain and stiffness leading to functional decline and loss in participation and quality of life. Since the risk factors for OA are increasing (e.g., obesity, physical inactivity and others), its incidence is dramatically increasing. As widely known, OA is associated with several negative outcomes in older people including disability, poor functional recovery, and probably others such as depression and cardiovascular diseases. OA is a highly expensive condition: for example, in the United States it is estimated that each year \$ 65.5 billion are directly used for this condition.

One of the most salient characteristics of OA, particularly when affecting the knee, is pain. In knee OA, pain may have several sources and causes such as muscle spasm, subchondral bone marrow damage, synovitis, stretching of the joint capsule, tendonitis, and ligament enthesopathy. In the attempt to have a step-by-step algorithm that may practically help the physician in managing pain and function, the ESCEO (European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases) proposed in 2019 some recommendations based on the literature¹. In these guidelines, oral nonsteroidal anti-inflammatory drugs (NSAIDs) are traditionally listed among first-line medications in people with knee OA, but in recent years concerns regarding safety are arising. In particular, in the ESCEO guidelines, the use of oral NSAIDs should be based on the patient's renal, cardiovascular, and gastrointestinal risk profile.

For overcoming these potential limitations, complementary medicines with COX-independent pain-relieving and anti-inflammatory effects, e.g., oral enzyme combination (OEC) combining the natural compounds trypsin, bromelain, and rutoside trihydrate has become increasingly popular among OA patients. Regarding knee OA, in an individual patient-level pooled reanalysis of patient-reported data from six prospective, randomized, double-blind, parallel-group studies in adult patients with moderate-to-severe knee OA treated for at least 3 weeks with OEC or diclofenac, OEC showed a similar efficacy and a superior tolerability/safety profile associated with a significantly lower risk of adverse events². Several hypotheses have been proposed for explaining this positive effect. In particular, it seems that alpha-2-Macroglobulin, a plasma proteinase inhibitor with inflammatory properties that regulate the distribution and activity of many cytokines, is associated with the proteases present in the OEC, finally modulating the effect of several pro-inflammatory cytokines³.

Another intervention that we should consider in patients with knee OA is physical exercise. A recent network meta-analysis has shown that physical exercise has a similar effect to NSAIDs on pain and function, mainly mediated by its anti-inflammatory action⁴.

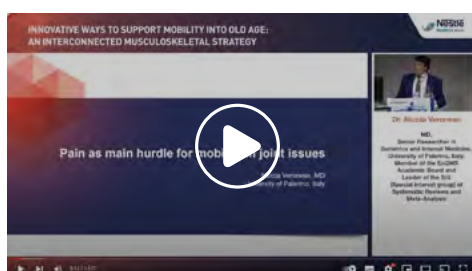
In conclusion, we must remember that pain is one of the most important characteristics in knee OA, that often precedes the onset of disability. Several medications are available for treating pain in knee OA, but safety profiles are important. In this sense, OEC therapy,



containing the proteolytic enzymes bromelain and trypsin in addition to the plant flavonoid rutin in patients with OA, seems to be as effective as NSAIDs, but with a superior side effect profile. Physical exercise is also important and must be recommended to all patients with knee OA due to its anti-inflammatory action.

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Dr. Luigi Ferrucci, MD, PhD

Summary and Actionable Guidance for Healthcare Professionals to Assess, Prevent and Manage Elements of Mobility Decline.

Abstract

A new prospective to support mobility in older persons.

The focus on the preservation of physical and cognitive function is one of the main tenants of Geriatric medicine. The traditional approach to understand mobility impairment is to identify the specific tissue pathology primary responsible of the functional loss and prescribe interventions that specifically address such pathology. While this approach is quite effective in younger persons that typically develop disability from an acute disease, trauma, or genetic predisposition, it is much less effective in the elderly in whom mobility problems are typically multifactorial, including a combination of dysfunction in the central and peripheral nervous system, muscle, joint and energetics. It is becoming more and more evident that the most effective approach to preserve mobility is to implement behavioral interventions early in life that include among others factors physical activity, adequate and healthy nutrition as well as maintaining a healthy weight.

A robust body of literature suggests that adequate nutrition is particularly important but is also complex. Healthy dietary patterns, such as the Mediterranean diet, appear to be more strongly related to prevention of mobility loss and mortality prevention than intake of single nutrients. There is emerging evidence that past level of physical activity affects age trajectories of mobility, whereas current physical activity may be influenced by impairments. Obesity is important not only because of the strain of carrying a higher weight but also because obesity is associated with inflammation, dysfunctional and inefficient energetics, and the continuous trauma imposed to the joint cartilages. Inflammation and cartilage thinning, and degeneration cause chronic pain that complicate the clinical picture.



Because of the complexity of mobility impairment in older persons, developing interventions that target the multiple cause of mobility impairment may be the most effective path to prevention and cure. Incidentally the behavioral intervention mentioned above all are beneficial to neurological control, muscle and joint health as well as energetic metabolism. The emerging field of geroscience suggest that gerotherapeutics, by targeting the intrinsic mechanisms of aging biology therefore beneficially affecting the functionality and integrity of multiple physiological systems, may be particularly effective in the treatment of complex geriatric syndromes, such as mobility loss. Clinical trials are currently in the field aimed at testing this hypothesis. In the meantime, clinicians play an instrumental role in screening, assessing and optimizing patient care related to risk factors for mobility decline.



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