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SPECIAL ARTICLE

HIGHLIGHTS FROM THE 2019 INTERNATIONAL CONGRESS ON FRAILTY AND SARCOPENIA RESEARCH

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Introduction

The International Conference of Frailty and Sarcopenia Research was held in Miami, Florida, in February of 2019 (1). The 9th edition of this conference had the highest attendance rate since its debut and is now a major venue that attracts the best key opinion leaders in the field of sarcopenia and frailty. Approximately 400- 500 delegates from around the world shared their results across the spectrum of research, from animal studies targeting novel mechanisms to large clinical trials for improving function, reducing disability, and improving quality of life in aging persons. With the recent implementation of ICD-10 code for sarcopenia (2), more and more industry leaders are looking for novel strategies and treatments counteracting the decline of skeletal muscle and physical function. By identifying sarcopenia as a disease (2) and the increasing number of older adults in the world (3), targeting and understanding the process of sarcopenia will be essential for geriatricians and gerontologists in the coming years. This paper will present the major highlights of this conference.

Characterizing people at risk of sarcopenia and frailty

In 2018, the European Working Group on Sarcopenia in Older People (EWGSOP) refined their definition for sarcopenia, based on knowledge gap since 5 years (4). The panel from this group presented to researchers and clinicians the new definition for its diagnosis. The updated definition puts muscle strength at the forefront as an indicator of probable sarcopenia, uses more precise cut-offs (instead of decimals) and focuses on severity by measuring physical performance tests after sarcopenia detection. As such, including a more precise measurement of sarcopenia for geriatric assessments will increase the likelihood of detecting impairments at early stages and introduce better personalized care for the management of this disease. This new definition will also simplify the work for clinicians for the assessment of sarcopenia in their geriatric evaluation. Finally, these updates regarding sarcopenia's classification of a disease and its new definition reiterates critical role in the development of dependence in older adults.

In line with this, the so-called ICOPE (Integrated Care for Older People) (5) has been presented. This model proposes a shift in clinical care towards a community-level approach in the prevention of intrinsic capacity decline. The final goal is to longitudinally observe the trajectories of the individual's intrinsic capacity adopting a life-course approach. In the clinical care setting, clinicians mostly react to a disease when it manifests. This process will thus help at developing personalized interventions for enhancing the individual's capabilities (regardless of age, diseases, socio-demographic characteristics, and specific clinical phenotypes). For this, intrinsic capacity was presented. Briefly, intrinsic capacity is defined by the composite of all of the physical and mental capacities of an individual (6). Five domains define intrinsic capacity: cognition, locomotion, psychological, sensory, and vitality (7). These five domains capture the key functions most influencing the health status and independent life of the aging individual. In order to translate this theoretical framework into an objective operational instrument, specific research has been conducted under the coordination of the World Health Organization and ad hoc clinical tools will shortly be published.

Physiological processes related to sarcopenia and frailty

The ICSFR conference also provided new data regarding biomarkers and physiological processes that seems affected during sarcopenia and frailty. First, deuterated creatinine (D3-creatine) has been presented a technique providing a quite direct quantification of muscle mass. Cawthon and colleagues (8) showed that D3-creatinine was associated with physical performance and functional outcomes in older adults. Consistently with previous papers, they also demonstrated how the appendicular lean mass quantified by dual X-ray

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absorptiometry (DXA) has a modest association with functional outcomes. Nonetheless, a discussion raised about the clinical feasibility and large-scale implementation of the technique in the assessment of sarcopenia older persons. In particular, it was discussed whether this technique (which is surely more accurate at quantifying the amount of muscle mass than other instruments) may be applicable over the large-scale and in the clinical setting (where more frequently available alternatives as DXA or bioelectrical impedance analysis are already available).

Furthermore, other presentations focusing on different biomarkers as a function of the physiological process of sarcopenia and frailty were shown. For example, mitochondrial dysfunction, which is known to be associated with the pathophysiology of aging (9), is now in the sights of researchers as a promising causal mechanism of sarcopenia and frailty (10, 11, 12, 13). Surely, the inflammation pathway represents a major (direct and/or indirect) contributor of these processes (10, 14). A study by Walston and colleagues has, in fact, showed that rodents with chronic inflammation had reduced mitochondrial autophagy and presented reduced muscle function (11). In other words, inflammation and mitochondrial dysfunction can produce an acceleration of the age-associated decline of the skeletal muscle. If this hypothesis is confirmed in the near future,intervention trials on the topic are needed.

Advances in translational research

Recent advances in translational research has been presented at the ICSFR conference. To begin, Dr LaDora Thompson presented a mouse model that matches frailty in humans; they found that the mice with a frail phenotype had lower survival ages and lower functional status (15). In keeping with this, it is important to better translate results from mice to human studies and that mouse models should use similar biomarkers as humans. Gait speed is a well-known marker for negative outcomes in older adults, but it is not yet clear whether its trajectory is comparable between mice and humans. Results were presented during the ICFSR conference showing that gait speed decreases non-linearly in both species, but humans had shortened step length whereas mice tend to rather present a reduced cadence (16).

Additionally, presentations on longevity and caloric restrictions were also discussed. Briefly, de Cabo and colleagues found that in caloric restricted mice, animals fed with lard had 40% increased life span compared to those following a soy bean oil diet during caloric restriction (17). Furthermore, the same intervention group showed improvements in muscle mitochondrial function and mass (18). These interesting studies suggest a potential relationship of the composition of fatty acid saturation with mitochondrial function and longevity in a specific mice model. In line with these studies, a ketogenic diet (which is a diet that relies basely on fat and proteins) has been shown to increase lifespan in mice (19). However, future studies are needed to replicate and confirm these findings in other species.

Novel treatments against sarcopenia and frailty

In this context, urolithin A, a bioactive compound derived from pomegranate, seems to prevent losses in mitochondrial dysfunction by inducing selective mitophagy in worms and rodents and improve muscle function in the latter (13). Studies are also on the way to develop specific treatments against sarcopenia. Sarconeos (BIO101), which activates the Mas receptor of the renin angiotensin system (20) seems to inhibit muscle wasting. Also, interesting findings from an exerkine called apelin for the prevention of sarcopenia have been presented. In particular, Dray et al. have presented their results showing that apelin production during exercise is lower during aging and that apelin treatment may exert hypertrophic and regenerative effects on older muscle (12). Allogeneic stem cells are also gaining momentum as possible future treatment of physical frailty. Dr Joshua Hare et al. presented data from their laboratory showing that stem cell injection increased muscle function in older adults with physical frailty (21). A phase III randomized controlled trial is currently ongoing.

Studies in the field of exercise have shown again some promising results. In obese older adults, combined aerobic and resistance training plus diet is the best strategy to improve physical function (22). Also, high-intensity interval training has shown to significantly improve functional capacity in obese older adults compared to moderate intensity exercise, providing supporting evidence for this type of intervention (23). Moreover, Dr Eduardo Feriolli provided evidence that resistance training combined with fish oil had significant improvements in muscle strength and size in sarcopenic women. Dr Shalender Bashin presented preliminary results showing that protein intake higher than the recommended daily allowance (RDA) may not be always needed for improving muscle mass and function in older adults (24). Finally, new and interesting studies are underway for treating sarcopenia and frailty in older adults, such as the DO-HEALTH trial (25) and the SPRINTT study (26), with results presented in the coming year.

Conclusions and future perspectives

In all, the 2019 ICSFR conference in Miami gathered clinicians and researchers with special interest in the fields of sarcopenia and frailty. Nonetheless, there are still some challenges ahead regarding the measurement of lean mass and muscle mass. More studies are needed to validate the capacity of currently used and new markers to measure muscle mass and to try and tease out its relationship with muscle function. Also, the prevalence of sarcopenia and frailty is still poorly recognized in life-threatening diseases such as cancer and heart disease.

For the World Health Organisation (WHO), healthy aging

is not a life without diseases, but should enable older people to maintain functional capacities in order to do what they value. It is important that medicine goes forward targeting frail older subjects, because this condition can be reversible and it greatly increase the risk of dependency. Strategies should be implemented in early aging (between 45 and 75yrs) to maintain the highest level of physiological reserves. After the age of 75, it is important to monitor functions regularly by using assessment tools and information and communications technology (ICT) devices to intervene as soon as possible once declines are detected. In the future, research on biomarkers of aging will help us select subjects who are at risk of both losing intrinsic capacity and dependency, thus allowing us to design novel therapies to maintain functional capacities. Prevention strategies still need several years and will be only possible if senior citizens themselves are involved in the preventive strategies as actors of their own health promotion program. Therefore, self-management is one of the top priorities for research and care for the future by the National Institute of Aging (NIA).

The Next ICSFR conference will be held in Toulouse France between 11-13 March of 2020 under the scientific leadership of the collaborative program developed between the Gerontopole W.H.O Collaborative center for Frailty, Clinical research and Geriatric Training (Pr Bruno Vellas, Pr Yves Rolland), the U.S.D.A HNRCA Tufts University Boston (Pr Roger fielding) and the University of Milano (Pr Matteo Cesari). More information regarding the registration and abstract submission is available on https://frailty-sarcopenia.com We look forward seeing you in Toulouse for the 10th anniversary of the ICSFR congress.

Conflict of Interest: None

Ethical standard: No humans participated in this study.

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