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EDITORIAL

EXERCISE, AGING AND FRAILTY: GUIDELINES FOR INCREASING FUNCTION

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The population is ageing worldwide at a phenomenal pace from 900 million ≥ 60 years old in 2015 to 2 billion in 2050 (1). The longer lifespan is due to advancement in public health, medical, social and economic development. However, healthspan has been slow to improve in most countries where the last decade of life is spent in poor health (2). Aging is associated with declines in functional capacity, and preserving function including lengthening healthspan is an increasingly important challenge for countries with a fast aging population. The World Report on Ageing and Health by World Health Organisation (WHO) defines healthy ageing as the process of developing and maintaining functional ability that enables wellbeing (3). The interaction between individual's intrinsic capacity and environmental characteristics are crucial to achieve the optimum trajectory which can be modified to maintain a person's functional ability and intrinsic capacity throughout the life course. We assert that greater knowledge of the effects of the exercise interventions on age-related amelioration of intrinsic capacity domains (i.e locomotion, vitality, cognition, psychological, sensory) that is present in the frail will allow a more coherent and holistic approach to treatment of the frail. This Viewpoint emphasizes the idea that the physiological bases underlying the assertions that exercise treatment of frailty directed at increasing muscle mass by pharmaceuticals in order to treat symptoms of frailty is an example of current medical, scientific and pharmaceutical industrial lack of appreciation of the role of exercise as a therapeutic agent having a major role both in the treatment and prevention not only of disease but also in functional capacity (4, 5).

Physical inactivity and social isolation accompanying ageing leads to decline in muscle strength, muscle mass and accelerates frailty, worsens chronic health issues, including hypertension, cardiovascular and cerebrovascular disease, diabetes, depression and dementia. Presently, there are no pharmacological agents (or combinations) or care standards known to slow down ageing. Physical activity including exercise training have been shown to influence key drivers of ageing even in the oldest-old including chronic inflammation, mitochondrial dysfunction, myokine release, autophagy, oxidative damage and insulin-like growth factor signaling (4, 6, 7). Exercise improves physical function and quality of life, reduces the burden of non-communicable diseases and premature overall mortality including cause specific mortality from cardiovascular disease, cancer, and chronic lower respiratory tract diseases (8-10). WHO has recently released guidelines on Physical Activity and Sedentary Behaviour strongly recommending moderate or greater intensity multicomponent physical activity on ≥ 3 days a week with emphasis on functional balance and strength training for improving functional capacity and preventing falls in older adults and those with chronic diseases (11). General physical exercise guidelines often focus on prevention of pathologies. Population level preventive efforts ideally before the onset of functional decline have been tried out and tested in many countries (12-16). Unfortunately, a limited amount of physical exercise strategies are planned to minimize exercise-related impact on function and/or ability to perform ADLs or in other domains of intrinsic capacity on older population, probably related to the scarcity of research in the area (4).

Aging is a risk factor for chronic diseases, frailty and dementia. Similarly, chronic disease can accelerate biological aging, frailty and dementia (17). Frailty is a dynamic clinical state of decreased functional reserve which increases individual's vulnerability to develop negative health-related events such as disability and/or mortality when exposed to external stressor (18). It is associated with a variety of negative outcomes including cognitive decline, falls, fear of falling, hospitalisation, increased healthcare utilisation, polypharmacy, institutionalisation, and mortality (19, 20). Frailty is not synonymous with disability or comorbidities, and almost half of frail older adults are still independent. Screening for frailty across a variety of healthcare settings including intermediate and long-term care settings and community is crucial to enable targeted personalised management (16, 18, 21-23). A few of the commonly used frailty screening tools include the Fried's Frailty Phenotype often known as the Cardiovascular Health Study (CHS) index, FRAIL scale, Frailty Index of Accumulative Deficits (FI-CD) and Clinical Frailty Scale (24-27). All of these tools are distinct but capture over-lapping

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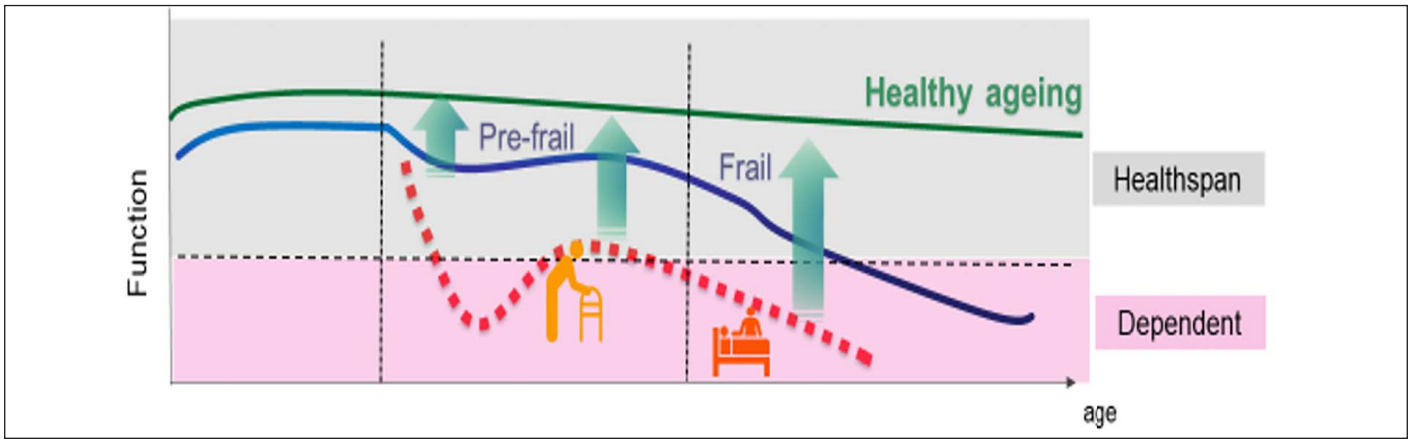
Figure 1
The Trajectory of Healthy Ageing, Frailty and Acute Illness / Hospital associated Disability



The ideal healthy ageing paradigm represented by thick green line. Frailty represented by blue line from a state of being physically robust to being at risk of disability and dependency and dying. Acute illness and / or hospitalization represented by dotted red line. Green arrows highlights benefit of exercise training and multicomponent interventions.

constructs and predicts poor functional outcomes. The FRAIL scale is fast, simple and convenient to use at the population level and has been validated in many countries (28). In a recent systematic review, the pooled prevalence of prefrailty ranged between 35% to 50%, and frailty 7% to 12%, increasing to 26% in those aged over 85 years (29, 30). Sarcopenia, the loss of muscle mass and strength, is the major cause of frailty (31, 32). One of the main challenges for the future is to use these scales which usually focus on identification of pathology or pathophysiology that accompany frailty to also monitor intrinsic domains (i.e locomotion, vitality, cognition, psychological, sensory) after multidomain non-pharmacological interventions (for example exercise or cognitive interventions).

Given the multidimensional nature of frailty comprising of physical, cognitive and social domains, reversing, preventing or slowing down progression of frailty requires a targeted multicomponent approach including physical exercise, management of polypharmacy, falls, nutrition, loneliness, cognitive impairment and depression for reversal and/or prevention of frailty (23, 33-35). Healthy and, even more so, chronically ill older adults are candidates for physical exercise strategies that will lessen the burden of comorbidity, disability and premature death caused by incident disease. A 10-year community-based multicomponent interventions (physical, nutrition and social encompassing group-based activities) in Kusatsu (Japan) improved functional status, reduced annual disability incidence, and prolonged active life expectancy at age 70 (36). Exercise interventions in nursing homes and long-term care facilities improve muscle strength and function (34, 35, 37-39). These benefits are lost after training cessation (35), especially in frail elderly patients with dementia after long-term physical restraint. In a recent study (38) on older adults (<75 years) living in nursing homes the Vivifrail multicomponent tailored exercise program (http://vivifrail.com/resources/) was very effective in the short-term (4 weeks) and prevented severe functional decline and strength loss in institutionalized older (i.e. physical frailty reversion and recovery of autonomy). Multicomponent exercise face-to-face interventions would seem advisable as an essential activity to protect older adults from severe functional decline (38).

The community-based approach is the best way forward and physical exercise is one of the main interventions with systemic effect proven to improve physical impairment related to frailty (low body mass, strength, mobility, physical activity level, energy) (5). Inter-individual variability and dose-response heterogeneity (subject-by-training interaction; 'individual response') in response to exercise is critical for defining threshold and optimal levels of activity that are necessary for health promotion and disease management. The type, intensity, frequency and duration of physical continues to be an area of research in frail older person (40). Twenty to thirty years ago, studies showed clear evidence that prolonged moderate-to-high intensity strength-training (i.e. 60-80% of maximum strength, 2-3 sets of 8-12 repetitions) would lead to large gains in maximal strength and power, muscle mass and functional ability (41, 42). Also, power training, including exercises in which daily activities are stimulated, are recommended including to optimize the functional capacity of frail individuals (43). Unfortunately, dose–response relationships between changes in fitness, function and better health outcomes have been defined for some, but certainly not for all, diseases and syndromes (44, 45). Some modalities or doses of exercise that are promoted for older adults (mild calisthenics, slow-paced walking) have little or no discernible effects on physical fitness but may possibly yield benefits in some domains. This area of investigation is critical for defining threshold and optimal levels of activity that are necessary for health promotion and disease management. Exercise and medical researchers have recognized the substantial variability in patient response to physical exercise interventions and have sought to understand these differences. Recently, it was reported that older patients performing an individualized exercise intervention showed

Figure 2

VIVIFRAIL Multicomponent Physical Exercise Program to Prevent Frailty and the Risk of Falls. Example of exercise wheels for each functional level that include the exercises, series and repetitions that should be done every week. Available at (53)

An example of exercise wheel type A (frail) for an older people who can walk with difficulty or help and type D for a robust person. (free download from http://vivifrail.com/resources/). Additionally, an App to perform the Vivifrail Test and to follow the exercise program corresponding to the degree of frailty and risk of falls is also available on Google Play or the App Store.

Figure 3

Poster to promote the participation in the VIVIFRAIL program of elderly people who come to centers and consultations. Step by step the way to participate in the exercise program that best suits the initial functional status is described. Available at (53)

a higher prevalence of responders and a lower prevalence of non-responders and adverse-responders for functional capacity, muscle strength, and cognitive function than those who were treated with usual care during acute hospitalization (46). An adverse response on functional capacity in older medical patients to physical exercise or usual care during hospitalization was associated with mortality at one year post-discharge. Moreover, the functional status presented at admission seems to be a cornerstone in the trajectory of patients during hospital stay and even more so at follow-up. These findings support the need for a shift from the traditional disease-focused approach in hospital acute care to one that recognizes functional status including gait speed as a clinical vital sign (46, 47).

Pre-frail and frail older adults are particularly vulnerable to adverse effects of hospitalisation especially functional decline and delirium as shown in Figure 1. In hospital, supervised exercise interventions have been shown to be safe and effective in attenuating functional decline and preventing cognitive decline (48-51). A multicomponent exercise program performed twice daily supervised and unsupervised for 20 minutes each during 5 to 7 consecutive days has shown to improve physical function with indirect effect on cognitive function (51). The exercises found to be beneficial included progressive resistance, balance, and walking training exercises aiming at 2 to 3 sets of 8 to 10 repetitions tailored to the individual's functional capacity with a load equivalent to 30% to 60% of the 1-repetition maximum. The type of exercises were based on clinical physical exercise guide, Vivifrail (http://vivifrail.com/resources/), involving mainly lower-limb muscles (squats rising from a chair, leg press, and bilateral knee extension), upper body (seated bench press), balance and gait re-training (semi tandem line walking, foot standing, stepping practice, walking

with small obstacles, proprioceptive exercises on unstable surfaces such as foam pads sequence, weight transfer from 1 leg to the other) (42, 52). Vivifrail has individual prescription passports for older adults depending on the older person's functional capacity level (serious limitation, moderate limitation and slight limitation as evaluated by the SPPB and a walking speed test) and the risk of falling (www.vivifrail.com) which can be implemented during unsupervised sessions (Figure 2 and Figure 3) (53).

Healthy ageing and lengthening healthspan should be a public health priority for every country. Physical activity including exercise training of low and/or moderate intensity have been found to be effective and safe in improving physical function even in the oldest old and frail older adults (54, 55). Community embedded program incorporating dual-task exercse to promote healthy ageing like the Healthy Ageing Promotion Program for You (HAPPY) has shown to improve cognition, physical function and frailty status, reduce social isolation and improve perceived health. Multicomponent physical exercise programs tailored to the persons functional capacity are fundamental to maintaining mobility, musculoskeletal function and optimal function of other body systems: neurological, cardiovascular, respiratory, and endocrine. However, a new era in the precision of the exercise prescription should also consider a priori the optimal exercise intervention being the more time-efficient but eliciting a smaller proportion of non-responder participants. Yet, exercise has not become fully integrated into usual primary or geriatric medicine practice and is still virtually absent from the core training of most medical doctors and other healthcare professionals.

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