

The New Tsunami: Are we Heeding the Warning? The Challenges of Sarcopenia and Frailty in Older People

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Rec date: Jun 28, 2015; **Acc date:** Jul 20, 2015; **Pub date:** Jul 23, 2015

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Introduction

Worldwide, population ageing is constantly increasing, from 461 million people older than 65 years in 2004 to an estimated 2 billion by 2050 [1]. One of the critical challenges of population ageing is the clinical condition of frailty and the closely associated manifestation of sarcopenia. Frailty at its most basic level of definition has been defined as “a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency or death” [2]. Sarcopenia, on the other hand, has been defined as progressive loss of skeletal muscle mass, strength and function [3].

Over the last two decades, multiple operational definitions of frailty and sarcopenia have been proposed but wide consensus has not been reached. At present, although there is no gold standard definition for frailty, two operational frailty concepts are commonly used: phenotypic and frailty index of accumulated deficits [4,5]. Sarcopenia is also regarded as a key component of frailty [6]. Some have considered it to be both the biological substrate for the development of frailty and the pathophysiological pathway, through which adverse health outcomes of frailty ensue [6]. Similar to frailty definition, six consensus were put forward to define sarcopenia [7]. The most

prevailing definition used to date is the European Working Group on Sarcopenia in Older People (EWGSOP) [3]. Frailty and sarcopenia are both characterized by a similar condition: impairment of physical function, which is usually measured objectively by gait speed and muscle strength. Such impairment can be responsible for the development of disability. In general, both frailty and sarcopenia are treatable conditions if recognized and intervened early.

It is clear from the last three decades of research that both frailty and sarcopenia leads to significant adverse clinical outcome. There is no doubt that both conditions, when untreated will lead to increased risk of falls, fracture, worsening disability, functional decline, hospitalization and mortality (Table 1) [8-14]. Furthermore, in the year 2000, it was estimated that sarcopenia will cost the healthcare system of US\$1 billion US dollars [15].

The epidemiological data on frailty and sarcopenia sends an ominous warning of an impending “tsunami” that will affect a significant proportion of the older population. The prevalence of frailty varies substantially depending on the operational definitions and differences in inclusion or exclusion criteria between studies. In one systematic review of 21 community-based cohort studies of 6,500 older people, prevalence rates of frailty was between 4.0% and 59.1% [16].

	Year	Country	Participants [n]	Length of follow-up [years]	Falls, HR/OR [95%CI]	Worsening disability, HR/OR [95% CI]	Hospitalisation, HR/OR [95%CI]	Mortality, HR/OR [95%CI]
Cardiovascular Health Study [4]	2001	USA	5317	7	1.23* [1.50-2.21]	1.79* [1.47-2.17]	1.27* [1.11-1.46]	1.63* [1.27-2.08]
Canadian Study of Health and Aging [8]	2004	Canada	9008	5	NA	NA	NA	3.69† [2.26-6.02]
Women’s Health and Aging Study [9]	2006	USA	1438	3	1.18* [0.63-2.19]	NA	0.67* [0.33-1.35]	6.03* [3.00-12.08]
Study of Osteoporotic Fractures [10]	2008	USA	6701	4.5	2.44† [1.95-3.04]	2.79† [2.31-3.37]	NA	2.75† [2.46-3.07]

*HR: Hazard ratio, NA: Not available, †OR: Odds ratio
The comparator for hazard ratios and odds ratios is people who are not frail.

Table 1: Covariate-adjusted associations between severe frailty and adverse outcomes from four large prospective studies.

When the analysis was restricted to studies that used the phenotype model, the weighted average prevalence rate was 9.9% (95% CI 9.6-10.2) for frailty and 44.2% (44.2-44.7) for pre-frailty. The

prevalence of frailty in nursing home residents has been studied in three studies and was found to range from 34.9% to 85% using different operational definitions [17-19]. The prevalence of sarcopenia

varies depending on the definitions or cut-offs used, settings [community-dwelling, hospital or nursing home] and age group [7]. In the community, the prevalence of sarcopenia has ranged between 5 and 13% [20-24]. In another study of nursing home residents aged ≥ 70 years in Italy, the prevalence of sarcopenia was 33% [11].

Despite this, there remain significant barriers in translating frailty and sarcopenia into clinical practice. Areas where these remained a challenge include the lack of standardized practical screening tools that could be used to identify and monitor the progress and a consistent approach to prevention and treatment of frailty and sarcopenia. Therefore effective tools to identify older people with frailty and sarcopenia at an early stage are important. In addition, effective interventions to treat these conditions are also needed so that adverse health-related outcomes can be prevented.

The comprehensive geriatric assessment (CGA) remains the gold standard for identifying frailty. However, CGA is time and resource-intensive to implement. Useful screening tests for frailty need to be quick and easy to administer, ideally utilizing data that are readily available to clinicians. The sensitivity should be high enough to make the exercise worthwhile while retaining the specificity to prevent indiscriminate use of resources. An effective population-based screening program has the potential to be a "warning system" for the impending "tsunami".

A large study from the Toulouse Gerontopole Frailty Clinic has demonstrated positive results that general practitioners can use the Gerontopole Frailty Screening Tool to screen older people for frailty and those who are positive will be referred for a CGA [2,25]. In 200, Fried et al. created and validated a physical frailty phenotype [4]. Their definition included weight loss, exhaustion, weakness (grip strength), walking speed, and low physical activity. Based on this, a simple 5-point questionnaire (FRAIL scale – fatigue, resistance, aerobic, illness and loss of weight) was developed [26]. This scale has been validated by several studies and performed as well as the other more complex scales [27-29]. Of the five components of the FRAIL scale, both resistance (climbing a flight of stairs) and aerobic [walking one block] are also components of sarcopenia as defined by multiple groups [30,31]. This tool has been validated as a "rule in" test for frailty among community-dwelling older people in Hong Kong [32]. Recently, the FRAIL-NH scale has been proposed for use among nursing home residents but this scale has yet to be validated [33].

Another approach to frailty screening known as "frailty index" was developed by Rockwood et al. [5]. This consists of adding together all the deficits a person has and then mathematically designated a frailty score. While this is highly predictive of outcomes, some have argued that it is more of a comorbid score [34].

Single measurement such as gait speed and handgrip strength measured by a dynamometer has the potential to identify frailty in older people. A systematic review of nine prospective studies [3,485 participants] found that slow gait speed was associated with adverse outcomes in older people and had similar accuracy to complex multivariate models of assessment [35]. In a UK study of people aged between 64 and 74 years, grip strength was associated with more markers of frailty than chronological age [36]. Therefore, grip strength may prove a more useful single marker of frailty for older people of similar age than chronological age alone. Its validity in a clinical setting needs to be tested.

Five possible screening methods have been proposed for sarcopenia. The EWGSOP have used an algorithm to aid screening and diagnosis

of sarcopenia [3]. Malmstrom and Morley have developed the SARC-F (Slowness, Assistance walking, Rising from chair, Climbing stairs and Falls) questionnaire as a rapid screening tool for sarcopenia [37]. This has been validated in several studies [38,39]. Others have developed prediction models for sarcopenia [40-42]. There is currently no consensus on a single screening tool.

Treatment interventions should be initiated as early as possible before the loss of skeletal muscle mass, strength and function lead to frailty. Strategies for treating frailty include physical exercise, nutrition (particularly protein supplementation), vitamin D, optimization of medical illness and reduction of polypharmacy. Exercise, including both aerobic and resistance has shown positive impact on both physical and functional abilities on patients with sarcopenia [43]. However the challenge lies in how exercises for older people can be individualized and maintained over a period of time because benefits were evident when therapy is structured, of longer duration (≥ 5 months) and performed regularly (3 times per week) for 30-45 minutes [44].

Nutrition plays an important role in preventing and reversing frailty. Increasing age is associated with reduced appetite and early satiety resulting in many older people failing to meet the recommended daily dietary allowance (RDA) for protein that has important implications for skeletal muscles [45]. Evidence has shown that increased protein requirement is required for enhancement of muscle mass and quality [46]. Vitamin D supplementation has been found to improve muscle strength and balance [47]. Ensuring adequate replacement of vitamin D to minimize these outcomes is important.

A large multi-centre trial known as the Sarcopenia and Physical frailty in older people: A multi-component treatment strategy (SPRINT-T) is currently underway in Europe [48]. This trial involves multicomponent treatment strategies that combine exercise, nutritional advice and innovative technologies to prevent frail older people from becoming disabled and losing their mobility.

However, to what extent frailty can be influenced is unclear because instruments designed to assess frailty have not been validated as evaluative outcome instruments in clinical practice. Monitoring outcomes of interventions in sarcopenia and frail people need methods that are sensitive to change [49]. A 50-item evaluative frailty index for physical activity (EFIP) has been developed and found to be a reliable and valid instrument to evaluate the effect of physical activity on frailty in research and in clinical practice [50]. However, its use still needs to be tested in a larger population and the need to obtain data for 50 items may be cumbersome in a clinical setting.

One of the pressing needs in the research of frailty and sarcopenia is the standardization of method to screen, diagnose and grade the severity of these conditions. Standardization of measurement will enable studies to be compared and outcomes to be reassessed at different time points in longitudinal research. Then the long-term efficacy of multicomponent interventions to treat frailty and sarcopenia can also be examined. Parallel with the research into diagnostic and therapeutic aspects of frailty and sarcopenia, there is a need for translation of these findings into a community-based service to identify and manage older people with these conditions. Further work is required to determine the most effective way to introduce such services.

In conclusion, the clinical picture of frailty overlaps substantially with that of sarcopenia and both these conditions are reversible.

Sarcopenia may be considered the central element of frailty, which indicates that interventions specifically targeting the skeletal muscle may offer preventive and therapeutic benefits against these conditions [6]. The high prevalence of frailty and sarcopenia in the community can be viewed as an approaching "tsunami". Therefore there is a need for reliable instruments to screen for these conditions in the general older population as well as effective preventive strategies. Further research is required to better define the appropriate multicomponent interventions that are effective in treating frailty and sarcopenia.

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