EDITORIAL

FRAILTY: DIAGNOSIS AND MANAGEMENT

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Frailty is a common condition occurring in approximately 1 in 20 persons over 60 years of age (1). Frailty is a condition in which a functional older person is at increased risk of developing either disability or dying when exposed to physical or psychological stressors (2-5). A frail person has decreased reserve and diminished resistance due to an accumulation of multiple deficits which can be social, psychological or physiological (6-9). The attempt of operationalizing this definition has led to a number of variable definitions of frailty. For a definition to be meaningful it should correlate at baseline with self-rated health, be more common in females than males and tend to increase with advancing age. The criterion for a successful definition needs to be that it predicts an adverse outcome such as mortality, hospitalization, institutionalization, loss of basic activities of daily living, and decline in social interaction or injurious falls (10, 11). The definition should not have to rely on the presence in the population of a subpopulation who can be identified by already having a deficit in basic activities of daily living. Finally while a person may be frail because of a single disease, eg, end stage heart failure or chronic obstructive pulmonary disease, the definition should not be disease driven (Figure 1).

At present, three different domains have been used to construct frailty models. These are functional, deficit accumulation (burden) and biological/physiological models. The functional domain model used deficiencies in four areas of functioning (physical, nutrition, cognition and sensory) and was developed in the Alameda County Study (12). Rockwood and colleagues (13, 14) developed a frailty index that measures the cumulative burden of deficits including symptoms, diseases, conditions and disability. It was developed in the Canadian Study of Health and Aging (15). Fried et al (16) developed the biological model based on five criteria namely weight loss, exhaustion, low energy expenditure, slowness (walking time) and weakness (grip strength). The Study of Osteoporotic Fractures developed a biological model based on weight loss, fatigue and power (arising from a chair 5 times) (17). The SHARE-Frailty Index is similar to the Fried model and includes grip strength (18). The individual models show poor identification of the same groups of people being frail with the concordance ranging from 25 to 40% (19). Psychosocial models of frailty (eg, dementia, depression, poverty, problematic environment) will not be considered in this editorial (20, 21).

None of the above models are currently suitable for widespread clinical application. For this reason, the International Association of Nutrition and Aging (IANA) developed the FRAIL scale (22, 23). F is for fatigue, R is for resistance (climbing one flight of stairs), A is for aerobic (walk one block), I is for illnesses (5 or more) and L is for loss of weight (>5% in last year). One or two positive is prefrail and 3 or more is frail. This scale has been validated with and without the inclusion of ADLs (24 and Morley, Malmstrom and Miller unpublished). The scale overlaps with the biological, the burden and the functional scales. Its advantage is it can be very quickly administered as it is a set of simple questions. It would appear that the FRAIL Index is the clinical instrument of choice.

Pathophysiology

A key in the development of frailty is the anorexia of aging and the associated weight loss, particularly when illness is superimposed (25, 26). The prevalence of protein energy malnutrition in older persons is common (27-33). Both gait speed and functional status have been associated with malnutrition (34, 35). This has led to the question of whether the Mini Nutritional assessment could be an appropriate tool to measure frailty in older persons (36). Most persons with

Figure 1
The Frailty Cascade

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cachexia will also have associated frailty (37, 38). This may be associated not only with the increase in malnutrition, but also with the cytokine excess seen in persons with cachexia (39, 40).

The loss of muscle mass, strength and power classically seen in frailty is closely associated with the development of sarcopenia (41-46). Sarcopenia leads to mobility loss and a decrease in gait speed. The development of sarcopenia closely parallels the decline in testosterone that occurs in age (47, 48). Frailty is correlated with declining testosterone levels in some but not all studies (24, 49-51). In frail older women multiple anabolic hormonal deficiencies are present in frail older women (52). Other major factors include poor protein intake (53, 54), cytokine excess (55) and decreased motor endplates (56).

Other factors associated with frailty include anemia (57), depression (58, 59) and cognitive decline (60-62). All of these can lead to fatigue, decreased food intake and decreased physical activity. Vitamin B12 deficiency has also been associated with frailty (63, 64).

Management

The FRAIL index should be given to all persons over 60 years of age being seen by a physician. Clearly the first step in managing frailty is exercise. Fiatarone et al (65) originally demonstrated the utility of resistance exercise in managing frailty. A meta-analysis has demonstrated that exercise improves outcomes in frail older persons (66). Exercise has been shown to also be beneficial in delaying functional deterioration in nursing homes (67).

An adequate caloric and protein intake represents a cornerstone of managing frailty (68). A high leucine balanced amino acid supplement is recommended for optimal outcomes (69, 70). Supplements should be given between meals (71). Between 1.2 to 1.5g of protein per kilogram body mass is the recommended daily protein intake. Low 25(OH) vitamin D is commonly associated with frailty and sarcopenia (72-76). Vitamin D at 1000 IU daily is a minimal replacement dose (77-81). If 25(OH) vitamin D levels are obtained, the replacement dose should aim at circulating levels of 70nmol.

Three studies in frail elderly have shown that testosterone tends to increase muscle mass and power (82-84). More impressive effects have been seen in persons with end stage cardiac failure (85-87). While one study suggested testosterone increased cardiovascular disease this was predominantly due to increased pedal edema. Edema is common in frail older persons and associated with heart disease. In frail persons, the increase in water retention would be expected to increase edema. In these studies there have been more deaths in the placebo compared to the treatment group. A single study in assisted living found that testosterone with a caloric supplement decreased hospitalizations (88).

Dehydroepiandrosterone (DHEA) levels decrease with aging and have, in cross-sectional studies, been associated with declining function (89). Most studies of DHEA in humans have produced minimal positive results. Kenny et al (90) did find that DHEA combined with exercise improved muscle strength

and physical function in frail older females.

A number of selective androgen receptor molecules (SARMs) are under development. These may be particularly useful in the management of frailty. Whether or not this is the case awaits the outcome of appropriately designed and powered clinical trials (91).

Frailty and falls are strongly related to anemia (91-93). However, there are no studies showing that correction of anemia improves outcomes in frail persons. Certainly all frail persons should have the causes of the anemia carefully assessed for treatable causes. The use of erythropoietin to treat anemia of chronic disease is problematic but most probably reasonable when the hemoglobin is less than 10 g/dl (94, 95). Development of therapeutic antibodies to hepcidin are enthusiastically awaited. Meanwhile a small study in Castleman syndrome showed improvement in anemia with the use of an interleukin-6 antibody (96).

Geriatric evaluation and management programs have been shown to be successful in improving outcomes in persons with poor function (97). However, a study aimed specifically at using comprehensive geriatric assessment in 310 pre-frail and frail older persons failed to improve the Barthel Index though the changes were in the expected direction (98). Three other studies did show positive interventions of comprehensive geriatric assessment programs (99-101). A focus on correcting orthostasis where present appears to be a clear area for improvement (102, 103). Care should also be undertaken to reduce polypharmacy where possible (104-106). Aggressive referral for physical therapy including for limitations in dual tasking (107, 108).

Table 1 lists the appropriate treatments whose need should be evaluated and carried out where indicated.

Table 1
Appropriate Management for Frailty

A.	Administer FRAIL Index:
	Fatigue
	Resistance (walk up on flight of stairs)
	Aerobic (walk one block)
	Illness (5 or greater)
	Loss of weight (>5% in one year)
	(1 or 2 = prefrail; 3 or more = frail)
B.	Treatments for all frail
1.	Exercise therapy including:
a.	Aerobic
b.	Resistance
c.	Balance
d.	Dual-tasking
2.	High protein diet (1.2-1.5g/kg)
3.	Leucine enriched essential amino acids supplement between meals
4.	Vitamin D 1000 IU daily
C.	Focused treatment
1.	Testosterone in males with low testosterone levels
2.	Treat anemia – treatable causes and erythropoietin if Hb< 10g/dl
3.	Treat Depression
4.	Reduce polypharmacy

JNHA: FRAILITY AND COGNITIVE DECLINE

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