Frailty Syndrome

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Frailty is defined by Fried et al. [1] as a phenotype according to the following criteria. The criteria are both subjective and objective.

- Weight loss: unintended weight loss of more than 5 kg or 5% of body weight in the last year
- Weakness: grip strength in the lowest 20% at baseline, adjusted for gender and body mass index
- Exhaustion or fatigue: as indicated by self-report exhaustion on maximal effort capacity
- Slowness: as measured in walking speed of 6 meters, being in the lowest quintile (in the original article by Fried et al. it was 15 feet walking speed)
- Low physical activity or mobility impairment: as calculated according to the patient's report of his or her weekly activities.

A diagnosis of frailty is reached when a patient meets three of these five criteria.

Although the phenotype definition is complicated and is based on clinical evaluation, it is of utmost importance for the management of elderly patients, especially for prevention of clinical deterioration and in decision making for choosing the optimal treatment. Therefore, using the definition of a medical syndrome, namely, a group of signs and symptoms that occur together and characterize a particular abnormality, Frailty is to be considered a multidimensional syndrome of decline in functional reserve, leading to impairment or dysregulation in multiple physiological systems with reduced ability to regain physiological homeostasis after stressful medical and surgical events.

Frailty can also be measured using frailty indices based on counting the accumulation of deficits in different systems [2]. The Vulnerable Elders Survey (VES) is another tool, which is easy to perform and highly recommended for identifying frailty in the elderly [3,4].

The diagnosis of frailty is based on the measurement of function and not on precise anatomic or physiologic damage. Medical practice in the 20th century used functional measurements in different fields: e.g., the NYHA (New York Heart Association) staging for heart diseases, and since Karnovski's functional scale (initiated in New York Memorial Sloan Kettering Cancer Center) several additional functional scales have been introduced into cancer program planning. Therefore, functional evaluation is considered an essential part of the medical evaluation of patients at any age.

Frailty syndrome is prevalent in the elderly. In a meta-analysis of 24 studies in the community, frailty was defined in 14% of elderly people over 65 years old and in 26% of those over 85 [5]. Frailty is an important if not the most important prognostic factor in the elderly. In all studies the rate of frailty increased with age. In the study by Fried and colleagues [1], frailty was associated with increased hazard ratio for functional decline as reflected by lower independence in activities of daily living (ADL), hospitalizations, falls, and mortality.

Frailty is explained by genetic as well as epigenetic influences on different physiological systems during the course of life. Chronic inflammation is likely the key underlying mechanism; it is associated with metabolic and endocrinological changes especially in DHEA, insulin growth factor-6, growth hormone, cortisol and vitamin D levels, as well as with sarcopenia. Sarcopenia is defined as an anatomic syndrome of decline in muscle mass of the body, while frailty is a syndrome of decline in function. In 2010 a European consensus combined function with the decrease in muscle mass [6] as the European consensus definition for sarcopenia. In a study performed in The Netherlands [7], sarcopenia (using the European criteria) did not explain all the cases of frailty, and frailty (using the Fried criteria) could not explain all the cases of sarcopenia. Increased counts of CD8+, CD28-T, CCR+T lymphocytes as well as positive immunoglobulin G titers for cytomegalovirus were shown to be associated with frailty [8,9]. Nevertheless, no factor was found to prevent frailty except for exercise [10].

In 2008 a national survey of the elderly was conducted in Israel using the Vulnerable Elders Survey questionnaire [11]. Bentur and co-authors [12] followed 281 patients of the Maccabi Healthcare Services 6 years later, in 2014, and their data are presented in this issue of *IMAJ*. These data show the rate of transition between different groups of frail and non-frail elderly in the community. The transition rate is similar and even lower than the known data from the United States [13]. It must be mentioned that the members of Maccabi Healthcare Services are considered to have the highest socioeconomic level in Israel compared to those of the three other health funds in Israel; consequently, the rate of frailty in the study

population is expected to be the lowest in the country, in view of the recognized effect of socioeconomic level on health and frailty. The study by Bentur et al. [12] is therefore important research as it defines the magnitude of transition to frailty in Israel's elderly population. The authors pay particular attention to the influence of frailty on the public health of the elderly population, by affecting morbidity and mortality in this weak population. Nevertheless, it is of benefit to use frailty in the clinical process of decision making for treatment of the elderly. Evaluation of frailty was found to benefit decisions regarding major surgery [14], cancer treatment, and management of congestive heart failure. It was even shown to predict lower benefit of Influenza vaccination [15].

In Great Britain every general practitioner has to define his/her 2% of patients at risk for recurrent hospitalizations. Since there is no treatment for frailty, the only way to manage it [16] is to use the holistic view of the Comprehensive Geriatric Assessment (CGA) in order to identify conditions leading to frailty and to treat those that may be reversible. This conclusion was adopted by the British Geriatrics Society and is featured in its guidelines [16].

The Israel National Cancer Council together with the National Council for Geriatrics last year declared an initiative for frailty evaluation in elderly cancer patients. This initiative led to certain programs for evaluating frailty in several medical centers. The question is who will perform the evaluation. Two strategies can be considered:

- Every elderly patient will be sent for another evaluation by the geriatric team in the process of planning the patient's oncologic treatment program
- The attending physician, irrespective of his/her specialty, will use a simple tool to identify frailty, like the VES, to evaluate the elderly patient for frailty

But, what are the optimal valid tools for evaluation of frailty, and must we use the same tools everywhere? These are some of the questions raised by the initiative. Some quantitative answers are given by Bentur et al. [12]. Given the capacities of the treating physician – whether oncologist, surgeon or internist – evaluating the frailty syndrome and understanding the meaning of this syndrome in their practice, as well as having experts coming from Geriatric Medicine to consult on questionable and severe cases, seems to be the optimal solution for management of elderly patients in aging societies, like in Israel.

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