Journal of Forensic and Legal Medicine 30 (2015) 34–38

Contents lists available at ScienceDirect

Journal of Forensic and Legal Medicine

journal homepage: www.elsevier.com/locate/jflm

Review

Frailty syndrome – Medicolegal considerations☆

Roger W. Byard*

School of Medical Sciences, The University of Adelaide, Frome Road, Adelaide, SA, 5005, Australia

ARTICLE INFO

Article history:
Received 12 November 2014
Accepted 29 December 2014
Available online 7 January 2015

Keywords:
Frailty syndrome
Sarcopenia
BMI
Weakness
Exhaustion
Hypothermia

ABSTRACT

The frailty syndrome refers to the concurrence of a number of specific clinical manifestations that include unintentional weight loss, decreased muscle mass (sarcopenia), exhaustion, reduced physical strength and activity, and slow ambulation. It involves multiple systems, is an increasing problem in elderly populations, and is strongly associated with increases in both morbidity and mortality. Despite its recognition clinically, the frailty syndrome is not often identified in forensic situations and is only infrequently mentioned in the associated literature. As there is a direct relationship between the frailty syndrome and significant adverse health outcomes the syndrome has clear medicolegal significance.

1. Introduction

Significant unintentional weight loss, decreased muscle mass (sarcopenia), exhaustion, reduced physical strength, declining activity, and slow ambulation characterize the frailty syndrome. Multiple systems are affected with a strong association with increased morbidity and mortality in the elderly. Features include cardiovascular and renal disease, immunological dysfunction, diabetes mellitus, malignancy, osteoporosis and fractures, and neurological conditions (including dementia).[1–7]

2. History

The possibility of the above features being components of a syndrome were first discussed in the mid 1990's, which led to the subsequent development of the Frailty Index and a tool for screening individuals known as FRAIL.[5,8] The latter looked specifically for **F**atigue, **R**esistance (inability to walk up a flight of stairs), **A**mbulation (inability to walk a short distance), **I**llness (>five comorbid conditions), and **L**oss of body mass (>5% of total body weight). The frailty index is a clinical guide which measures the range of deficits and enables prediction of outcome. For example, once age, sex and educational level were controlled for, a one degree change per year in the frailty index was associated with a five times increased risk of death, and an 85% increased risk of disability.[5] The term "pre-fail" has been used for individuals with only one or two of the above characteristics.[9]

There have, however been a variety of other definitions proposed for the syndrome with no clear consensus in the literature[2,10,11] which may make evaluation of cases and correlation with other conditions difficult for the forensic pathologist at the time of autopsy. This is particularly so given that the clinical criteria need to have been identified ante-mortem. For example, another earlier proposal for the diagnosis required two or more impairments in the following areas: nutrition, physical activity, sensory ability and cognition.[12] Although frailty predisposes to disability it is distinguished from the latter as it results from a complex interaction of a variety of processes that lead to frank disability only once there has been the additive effect of a particular event or stressor. The significance of frailty is that it increases an individual's susceptibility to stressors, something that has been referred to as "a domino effect that increases mortality".[5]

3. Epidemiology

The data for frailty syndrome are difficult to extract for different communities as there may not be effective monitoring and recording of cases. It has been estimated that 22 million individuals

☆ This review is dedicated to the memory of my parents, Bill and Mary Byard, both of whom suffered from the frailty syndrome for many years.

* Discipline of Anatomy & Pathology, Level 3 Medical School North Building, The University of Adelaide, Frome Road, Adelaide 5005, Australia. Tel.: +618 8313 5441; fax: +618 8313 4408.
E-mail address: roger.byard@sa.gov.au.

http://dx.doi.org/10.1016/j.jflm.2014.12.016
1752-928X/

in the United States over 65 years have problems with basic physical activities such as walking, with frailty syndrome affecting approximately six to 25% in that age group. Higher rates have been reported in females and in minority groups.[5,13–15] In a study of 420 aged women living in the community in the United States, 9% developed frailty syndrome, of whom 76% had reported weakness at the start of the study.[16] Other predictors of frailty are poor appetite and low food intake, with a risk of disability over two years more than double that of those with better appetites.[17] The likelihood of dying in frail individuals is three to five times the non- or prefrail.[18]

4. Pathophysiology

The range of definitions and diagnostic parameters that have been suggested all focus on the underlying problem of accumulating deficits that lead to generalized progressive physiological deterioration in multiple organ systems. Affected individuals have a limited capacity to respond to stressful situations and are much less able to maintain normal homeostatic functions.[3]

Frailty syndrome therefore involves the inter-relation of the normal physiological changes of aging with comorbid diseases, inadequate nutrition, and genetic and environmental factors. Problems with dysregulation of neuromuscular, immune and endocrine systems occur which predispose to a number of conditions ranging from diabetes mellitus to falls with hip fractures. Although the precise etiology of the syndrome has not been determined, hormonal changes, low grade inflammation and activation of coagulation pathways with cellular senescence and apoptosis have all been identified.[4,5] Increases in cytokine production with elevated levels of proinflammatory factors such as interleukin-6, tumour necrosis factor-alpha (TNF-α), and C-reactive protein occur, with decreases in the levels of anti-inflammatory cytokines such as interleukin-10.[19,20] Reduction in serum cholesterol due to malnutrition and pro-inflammatory cytokine overload may be a marker for the syndrome.[7] In addition, there may be alteration in factor VIII and fibrin D-dimer levels, and elevated levels of white cells including neutrophils, monocytes and T-lymphocytes. It is not clear however, whether these changes represent a cause of frailty syndrome, a response to stress or infection, or are simply markers for some other underlying disturbance in homeostasis.[5,13]

5. Manifestations

A variety of features may be present at autopsy that may point to a diagnosis of frailty syndrome.

5.1. Sarcopenia

Loss of lean body/muscle tissue is a normal part of the aging process, however in frailty syndrome it is exaggerated and further contributed to by the resultant immobility. Sarcopenia is defined as a lean body mass two standard deviations or more below the mean and is associated not only with reduced muscle bulk but with fatty infiltration which further compromises strength. This may be identified histologically. Somewhat paradoxically the effect may actually be worse in obese individuals (see below). Reduction in muscle bulk may be related to the actions of pro-inflammatory factors interleukin-6, tumour necrosis factor-alpha, C-reactive protein and fibrin D-dimer which decrease muscle repair and increase catabolism by inhibiting insulin like growth factor-1. Tumour necrosis factor-alpha also triggers apoptosis.[5]

5.2. Malnutrition

Inadequate nutrition is an ongoing problem in the elderly associated with a variety of factors that include altered gastrointestinal function, reduced metabolic rate, chronic disease, polypharmacy, cognitive impairment, economic factors and social isolation. The term “nutritional frailty” has been used to describe this phenomenon to distinguish it from sarcopenia.[5]

It is not uncommon to see an elderly individual at the time of forensic autopsy with a BMI well below 18.5. A variety of factors contribute to this end point involving anorexia, muscle break down, insulin resistance with abnormal levels of appetite control peptides such as neuropeptide Y and leptin. Hormonal changes involving reduction in testosterone also occur and these may also be associated with increases in leptin levels contributing to anorexia. Lowered blood ghrelin levels may also enhance the anorectic effects of certain pro-inflammatory cytokines.[21–23]

5.3. Comorbidities

More than 70% of individuals with frailty syndrome have an average of two significant chronic diseases, with hypertension and osteoarthritis being the most prevalent.[5] Given the association of frailty syndrome with the following diseases and conditions, evidence of these should be specifically sought at the time of autopsy examination.

5.3.1. Endocrine disease

Hyperglycemia is a feature of frailty syndrome associated with insulin resistance and established diabetes mellitus. The effects are again synergistic with frail diabetics having a significantly increased risk of falling (1.6 times) and of sustaining a fracture from the fall (1.7 times).[5] Many of the complications of diabetes and frailty are shared.[24] Urine stick testing at the time of autopsy and vitreous glucose and β-hydroxy butyrate levels are useful in frail elderly individuals, particularly if there is renal cortical pallor noted at the time of dissection.[25]

5.3.2. Renal disease

Frailty syndrome is related to chronic renal failure possibly due to underlying thyroid hormone abnormalities.[5] Protein-energy wasting may complicate both entities.[26]

5.3.3. Cardiovascular disease

Hypertension is the most common underlying condition in those with frailty syndrome being found in up to 60% of cases.[27,28] There is also a strong correlation of severe coronary artery disease and cardiac failure with frailty in the elderly, possibly related to activation of proinflammatory factors and coagulation pathways. The prevalence of frailty syndrome in patients with cardiac failure has ranged from 15 to 74%[29] with the increased morbidity and mortality also relating to cardiovascular surgical and transcatheter interventions.[30,31]

5.3.4. Hematological disease

Anemia is a common finding in frail individuals due to iron deficiency and chronic disease, or from an unknown etiology.[5]

5.3.5. Bone disease

Osteoarthritis is found in around 80% of elderly women with frailty syndrome,[27] with decreases in bone mineral density leading to significant osteoporosis. The risk of hip fracture is 25 times greater in elderly women with frailty and a history of falls[5,32–34] and fractures with a fear of falling accelerating the onset of disability.[35] The mortality rate from hip fracture in the first 12