Frailty and Potential Biomarkers in Aging

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Received date: July 20, 2016, Accepted date: July 22, 2016, published date: July 29, 2016

Abstract

Frailty is an age-related syndrome that has been well-described in the last ten years. It can be characterized by diminished strength, endurance, and reduced physiologic function. With multiple causes and contributors, frailty is highly correlated with functional decline and chronic diseases. Currently, there are no standardized tests or biomarkers that can be used to identify frail patients, though there have been a number of assessments used in research such as the Fried Frailty Phenotype or the Rockwood Frailty Index. Identification of biomarkers for frailty is a major consideration for future studies of this syndrome.

Keywords: Frailty; Biomarkers; Aging; Muscle mass

Introduction

Frailty is an age-related syndrome that is highly correlated with functional decline and chronic disease, leading to loss of independence and increased mortality [1,2]. There are multiple causes and contributors to frailty, which can be characterized by diminished strength, endurance, and reduced physiologic function [3]. Theoretically, frailty has also been defined as a state of increased vulnerability due to aging-associated decline in reserve and function across multiple physiologic systems, leading to an inability to cope with chronic or acute stressors [4].

Although a number of biomarkers have been tested in relation to frailty, experts have agreed that no single biomarker by itself is adequate for the assessment of frailty [5]. There are some indications that a combination of biomarkers may be more useful, however there has been no consensus on which combination would be best. Therefore for clinical purposes, laboratory testing for frailty is not indicated. For research purposes, however, there are some more common biomarkers that have been shown to be associated with physical frailty [6,7].

Inflammatory Markers

Interleukin-6 (IL-6) is a pro-inflammatory cytokine that has been studied as part of the theory that chronic inflammation leads to physical function decline and thereby increases frailty (Figure 1). One study in older adults has shown a significant association between elevated IL-6 blood concentrations and frailty as defined by the Fried Frailty Phenotype (low grip strength, slow walking speed, exhaustion, decreased physical activity, and weight loss) [8]. In addition, significant correlations have been found between high serum IL-6 levels and other physical measures such as decreased hand grip strength [9-11], decreased muscle mass [11], decreased lower extremity strength [11], slower gait speed [12], and difficulty walking or climbing steps [13].

Figure 1: Potential Biomarkers (modified from Rockwood’s Pathophysiology of Frailty [18])

Elevations in another common inflammatory cytokine, tumor necrosis factor-alpha (TNF-α), has been associated with decreased hand grip strength [11], decreased muscle mass [11], decreased lower extremity strength [11], and difficulty walking or climbing steps [12].

C-reactive protein (CRP) is an acute phase reactant that is released by the liver during inflammation. High levels of CRP have been significantly associated with decreased hand grip strength [9,10], and difficulty walking or climbing steps [13]. In a large group of community-dwelling older adults, a cross-sectional analysis showed that phenotypically frail participants had increased levels of CRP [14].

Clinical Markers

Since inflammatory markers are not commonly used in clinical practice, other markers such as hemoglobin have been studied to determine if they can be used for clinical diagnosis of frailty. Anemia
as defined by a hemoglobin (Hgb) concentration below 12 g/dL in women and below 13 g/dL in men was associated with disability in basic and instrumental activities of daily living, poorer performance on the Short Physical Performance Battery (walking, balance, standing), decreased lower extremity strength and decreased hand grip strength [15].

**Nutritional Markers**

There has also been research into whether using nutrition or exercise can help reverse the effects of frailty. Vitamin D insufficiency is common in older adults and low levels of 25-hydroxyvitamin-D (25-OHD) have been associated with decreased gait speed, poor balance, more difficulty standing, and decreased lower extremity strength [16]. A study of older adult participants in the National Health and Nutrition Examination survey found inverse associations between frailty and blood 25-OHD levels [17].

**References**

1. Fried LP, Tangen CM, Walston J (2001) Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 56: 146-156.
2. Boyd CM, Xue Q-L, Simpson CF, Guralnik JM, Fried LP (2005) Frailty, hospitalization, and progression of disability in a cohort of disabled older women. Am J Med 118: 1225-1231.
3. Morley JE, Vellas B, Abellan van Kan G (2013) Frailty consensus: a call to action. JAMDA 14: 392-397.
4. Xue Q-L (2011) The frailty syndrome: definition and natural history. Clin Geriatr Med 27: 1-15.
5. Rodriguez-Manas L, Feart C, Mann G (2013) Searching for an operational definition of frailty: a Delphi method based consensus statement. The frailty operative definition-consensus conference project. J Gerontol A Biol Sci Med Sci 68: 62-67.
6. Calvani R, Marinò F, Cesari M (2015) Biomarkers for physical frailty and sarcopenia: state of the science and future developments. J Cachexia Sarcopenia Muscle 6: 278-286.
7. Fernandez-Garrido I, Ruiz-Roz V, Buigues C, Navarro-Martinez R, Cauli O (2014) Clinical features of prefrail older individuals and emerging peripheral biomarkers: a systematic review. Arch Gerontol Geriatr 59: 7-17.
8. Leng ZX, Cappola AR, Andersen RE (2004) Serum levels of insulin-like growth factor-1 (IGF-1) and dehydroepiandrosterone sulfate (DHEA-S), and their relationships with serum interleukin-6, in the geriatric syndrome of frailty. Aging Clin Exp Res 16:153-157.
9. Cesari M, Penninx BW, Pahor M (2004) Inflammatory markers and physical performance in older persons: the InCHIANTI study. J Gerontol A Biol Sci Med Sci 59: 242-248.
10. Tainen K, Hurme M, Hervonen A, Luukkaala T, Jylha M (2010) Inflammatory markers and physical performance among nonagenarians. J Gerontol A Biol Sci Med Sci 65: 658-663.
11. Visser M, Pahor M, Taaffe DR (2002) Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: the Health ABC Study. J Gerontol A Biol Sci Med Sci 57: 326-332.
12. Vergheese J, Holtzer R, O-Park M, Derby CA, Lipton RB, et al. (2011) Inflammatory markers and gait speed decline in older adults. J Gerontol A Biol Sci Med Sci 66: 1083-1089.
13. Penninx BW, Kritchevsky SB, Newman AB (2004) Inflammatory markers and incident mobility limitation in the elderly. J Am Geriatr Soc 52: 1105-1113.
14. Walston J, McBurnie MA, Newman A (2002) Frailty and activation of the inflammation and coagulation systems with and without clinical comorbidities: results from the Cardiovascular Health Study. Arch Intern Med 162: 2333-2341.
15. Penninx BW, Pahor M, Cesari M (2004) Anemia is associated with disability and decreased physical performance and muscle strength in the elderly. J Am Geriatr Soc 52: 719-724.
16. Mastaglia SR, Seijo M, Muzio D, Sommoza J, Nunez M, et al. (2011) Effect of vitamin D nutritional status on muscle function and strength in healthy women aged over sixty-five years. J Nutr Health Aging 15: 349-354.
17. Smit E, Winters-Stone KM, Loprinzi PD, Tang AM, Crespo CJ (2013) Lower nutritional status and higher food insufficiency in frail older US adults. Br J Nut 110: 172-178.
18. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K (2013) Frailty in elderly people. Lancet 381: 752-762.