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Editorial

Broadening the Horizon for Frailty Assessment

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EDITORIAL

Frailty has become a topic of controversy among healthcare professionals in the pursuit of tailoring patient management. Caregivers, however, have yet to settle on a standardized definition for frailty and, subsequently, a universally agreed upon clinical tool designed to identify 'frail' patients. Although the Comprehensive Geriatric Assessment (CGA) remains the cornerstone of geriatric practice owing to its multifaceted, patient-centered approach, it is also time-consuming and easily disregarded by caregivers – particularly in an acute setting [1]. As a result, physicians are more likely to "eyeball" patients from the foot end of the bed, as opposed to employing an actual frailty measuring tool [2]. The diagnostic process is, more often than not, a very subjective one. This lends to an amplified risk of patient-care hindrance and possible mortality.

A careful literature review illuminates upon a potential for investigating certain molecular biomarkers and exploring genetic sequencing for a more accurate measurement of frailty [3,4]. Identification of related biological markers could support early diagnosis of frailty-susceptible populations. International guidelines concerning frailty agree upon its reversibility and potential for prevention [5]. The 'Spanish Society of Cardiology for the Assessment of Frailty in Elderly Patients with Heart Disease (2019) accentuates that "frailty in patients with no severe disability can potentially be prevented or even reversed to some degree through the control of specific diseases" [5]. Similarly, the '2016 European Society of Cardiology guidelines for the diagnosis and treatment of acute and chronic failure' encourages "monitoring frailty and seeking and addressing reversible causes (cardiovascular and non-cardiovascular) of deterioration in frailty score" [5].

Biological markers could be used as a confirmatory test for frail patients following initial diagnosis. Examples of molecular biomarkers that have been associated with frailty include, but are not limited to, increased β-2 microglobulin, dimethylarginine and TNFα levels [3]. While these individual biomarkers may not be sufficient indicators of frailty, they could substantiate diagnosis in a patient that has already been methodically evaluated for frailty with another diagnostic instrument.

Nonetheless, determination of biomarkers will not always be practical in the long run as their use during a general checkup, for example, is time-consuming and costly in nature. A review article on 'Frailty in Heart Failure' highlights paramount overlap of international guidelines on the management of frail patients and that emphasizes upon the significance of "certain prerequisites" being met "before validating a frailty assessment tool, including practicality and a user-friendly interface." [5]. Therefore, the authors recommend that biomarkers be identified to investigate prefrail patients as well as a confirmatory test in patients who have antecedently undergone and completed a primary assessment tool, such as the Edmonton Frail Scale (EFS) or The Tilburg Frailty Indicator (TFI) [1].

Genetic biomarkers have also been associated with frailty. According to Pansarasa et al., at least five single nucleotide polymorphisms (SNPs) have been significantly correlated with frailty [4]. These SNPs contribute towards the loss of physiological homeostasis and inflammatory processes that are highly characteristic of frailty [4]. Thus, it opens a gateway for discerning frail-susceptible populations through genetic sequencing and encouraging them to take preventative measures. The authors suggest that a thorough investigation of SNPs be undertaken to facilitate application of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas9 technology in the future for targeted gene correction, thereby reducing the progression of frailty to incapacity.

Moreover, the relationship between frailty and comorbidity is a bidirectional one [1]. In other words, pathology may affect, or be affected by, a frail status. Delving into a search for genetic biomarkers will enable healthcare professionals to more accurately differentiate between the effects of frailty, and the effects of the primary diagnosis or its treatment – as in cancer therapy-related cardiotoxicity, for instance. Hence, confirmatory molecular and genetic biomarkers support caregivers in providing targeted management plans.

The support of biomarkers will increase accuracy of frailty diagnosis and, as a result, aid the selection and participation of appropriate subjects for relevant frailty-related studies. The significance of this lies in the fact that cohort selection is a crucial determinant and may lead to unsuccessful clinical trials, if not done meticulously. Establishing a quantifiable confirmatory tool with set cut-off values will enhance the application of artificial intelligence, which can

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use deep learning to objectively select the most suitable candidates [6]. Recognition and adequate evaluation of frailty among patients involved in a clinical trial, for example, may improve relevance and coherence of results. That is, it may help explain whether a specific outcome is frailty-related, treatment-related, or a combination of both.

Ultimately, frailty lacks a quintessential definition that will help propel the medical community's search for an all-encompassing frailty measuring tool that can be utilized in both the inpatient and outpatient settings. Caregivers are, regrettably, accustomed to making subjective diagnoses that do not reliably foresee patients that fall in frailty's "gray zone".

Insufficient research has been done concerning the potential for using molecular and genetic biomarkers in identifying prefrail patients or confirming frail status among suspected cases. We recommend that, because of the time and cost required to assess biomarkers and genetic sequences, that this tool be used as a confirmatory test following administration of a simple, yet efficient, preliminary frailty assessment. The systematization of diagnosing frailty will help reduce the socioeconomic burden of caring for frail patients and tailoring high-quality patient care. It would also support inclusivity of frail patients in clinical trials, and the consistency of future research.

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