



Review article

Frailty and multimorbidity: Two related yet different concepts



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ABSTRACT

The extension of life expectancy is a global phenomenon. The growth in the ageing population has created a new health scenario in which there is a higher prevalence of frailty and multimorbidity. The attention received by both conditions derives from their strong association with disability, hospitalization, and death. The aim of the present paper is to conceptualize and differentiate these terms and to discuss their interrelations. We conclude that, yet related, they represent two different clinical conditions. Frailty identifies the increased vulnerability to stressors due to a dynamic, non-linear, and multidimensional depletion of physiological reserve and redundancy, whereas multimorbidity refers to the coexistence of two or more clinically manifest chronic diseases.

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1. Introduction

Lifespan is increasing as a consequence of both the improvement in socio-sanitary conditions and the progress of medicine and technology. Nevertheless, living longer is not a synonym of good health. In fact, as the World Health Organization (WHO) states at its Statis-

tics Report [1], the global median life expectancy at birth for both sexes is 71,4 years whereas the median healthy life expectancy (HALE) is 63,1 years. This discrepancy is reproduced at the European Region, where the median life expectancy at birth is 76,8 years whereas the median HALE is 68 years. Such difference should not be considered harmless, as it translates into life years deprived of full health due to disease and/or deficits, including disability. Increased expenditure, both from governmental and private health organizations, as well as decreased quality of life (QoL) at the individual level, are the consequences.

Hence, it is not surprising the increasing interest of policy-makers in the promotion of healthy ageing, as it is for example

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the Horizon 2020 program of the European Union [2]. In this way, prevention of deleterious outcomes and management of geriatric syndromes have become important issues. Advances in knowledge have incorporated new concepts, as for example, the categorization of different states of health. In this sense, frailty has increasingly become a crucial condition [3–6], as it defines vulnerability in otherwise healthy people.

Frailty is interrelated with multimorbidity and disability, so that the three conditions have been used interchangeably [7]. However, although overlapping in some people, they represent three distinct clinical concepts [8]. Even so, the recognizable difference between frailty and disability translates into a more difficult task when trying to disentangle that of frailty and multimorbidity [9].

2. Method

An electronic search at the PubMed database was conducted to identify reviews and empirical articles published between January 2000 and August 2016. The following Boolean query was employed: (frailty[All Fields] AND concept[All Fields]) OR (“comorbidity”[MeSH Terms] OR “comorbidity”[All Fields] OR “multimorbidity”[All Fields] AND concept[All Fields]) OR (“comorbidity”[MeSH Terms] OR “comorbidity”[All Fields] AND concept[All Fields] AND (“2000/01/01”[PDAT]: “2016/07/31”[PDAT])). No language restrictions were applied. This search yielded 1694 papers, and another 21 papers were then identified through a manual search of the reference lists of pertinent original articles and selected review papers. After removing duplicates, one team member (PV-F) screened the titles and excluded 1476 articles that were clearly not related to the topic, reducing the number of potentially relevant papers to 237. Two authors (PV-F and EN-P) independently appraised the abstracts to exclude further articles that were not eligible. Discrepancies between the two authors were resolved with the consensus of a third author (AC). Attention was then focused on scrutinizing the full text of the remaining 88 articles. When articles led to similar conclusions, priority was given to those more relevant according to quality and impact factors. Forty-one articles were finally included in the qualitative synthesis, although the reference list in the present review includes 5 additional sources that have been used to support the discussion. The flow chart of the search strategy [10] is displayed in Fig. 1.

3. Frailty

The term frailty refers to a dynamic and multidimensional clinical condition of increased vulnerability to poor resolution of homeostasis when facing a stressor event. This situation leads to an increased risk of adverse health outcomes. There is not a clear understanding of the pathways converging into frailty, but it seems that the losses imposed by ageing, the impact of acute or chronic disease, and the own genetic endowment of the individual may be at play [11,12]. A complete and definitive operational definition of frailty remains yet to be agreed among the experts [9,13]. Two approaches are the most popular and dominate the field: the Frailty Phenotype (FP) [8] and the Frailty Index (FI) [14], and each of them has generated a different assessment tool.

The FP recognizes frailty as a clinical syndrome identified by the presence of three or more of the following components: shrinking-weight loss-, weakness-grip strength-, poor endurance and energy-exhaustion-, slowness-gait speed-, and low physical activity [8]. This operationalization considers as intermediate, or prefrail, people with one or two of those characteristics present, and as robust all those free of any of those features. The most consistent critic to this conceptualization is the omission of important dimensions, like cognitive and other psychosocial components [3,13–16].

The FI is a mathematical model that identifies frailty as an accumulation of deficits [14]. It is based on the Comprehensive Geriatric Assessment (CGA) and the principle is to count health deficits in a whole range of areas from purely physical to more psychosocial. These health deficits should be age-related yet not too early saturated, and can be symptoms, signs, diseases, disabilities or laboratory, radiographic or electrocardiographic abnormalities [17]. Frailty, then, is operationalized as the ratio between the number of deficits present in an individual and the total number of deficits counted [14,17–20]. It is important to note that, although the theoretical maximum of the FI by definition is 1, the 99% upper limit has consistently been proven to be less than 0.722 [21].

Both operationalizations provide predictive power for mortality and incident physical limitation [22] and have their strengths and weaknesses. The phenotypical operationalization has attracted most of the attention so far [13,16]. Much of its acceptance resides in his qualitative and categorical nature [23], as it makes the assessment outcome more intuitive and easily interpretable by clinicians and general practitioners. However, the quantitative and continuum nature of the FI makes it more sensitive and a better predictor of the adverse outcomes related to frailty [13,16]. Despite the proposing investigators named them differently -cycle of frailty [8] vs. model of fitness and frailty [14]-, both lines converge in their theoretical rational. The two paradigms consider frailty as an age-related, dynamic, stochastic, non-linear, and multidimensional depletion of systems that leads to a loss of physiological reserve and redundancy where even minor stressors can lead to adverse health outcomes and complications due to the inability of the system to recover homeostasis [8,14,17–19,24]. Clegg et al. [11] identified the nervous, endocrine, immune, and musculoskeletal as the main systems in which the development of frailty has been best investigated, and provided a very illustrative description of the role each systems plays in the so called spiral of physiological decline.

4. Multimorbidity

A disease is classified as chronic if it is permanent, caused by non-reversible pathological alteration, or requires rehabilitation or a long period of care. Although not totally overlapping, the more recent denomination of “non-communicable disease” (NCD) has gained popularity and has integrated much of what has been traditionally assigned to the concept of chronic diseases [25]. NCDs are the leading causes of disability and death worldwide, according to the WHO [26].

The cluster of cardiovascular diseases ranks first in the list of deaths related to NCD, followed by cancer, chronic obstructive pulmonary disease (COPD) and diabetes; other diseases that also tend to be present are painful condition, depression, anxiety, heart failure, stroke/transient ischemic attack, atrial fibrillation, and dementia [27]. To reduce the burden, the WHO and the United Nations have adopted the slogan “25 by 25” [28]. The objective is a 25% reduction by 2025 in mortality from NCDs among individuals of age 30–70 years, in comparison with mortality in 2010.

The term multimorbidity refers to the co-occurrence of several diseases in the same individual, i.e. the presence of two or more chronic diseases in the same person [27,29,30]. Important to notice, multimorbidity has emerged as an entity in itself, and not just the sum of single diseases [31]. Indeed, multimorbidity is conceived as a synergy of the different individual diseases associated with worse health outcomes and a more complex clinical management [32]. Some authors have proposed a distinction between comorbidity and multimorbidity [32–35], but this conceptual differentiation goes beyond the scope of the present paper.

The prevalence rates of multimorbidity increase substantially with ageing, ranging from 55% to 98% in people aged 65 or older

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