Frailty: from clinical syndrome to epidemiological construct?

Published Online
June 13, 2018
http://dx.doi.org/10.1016/S2468-2667(18)30112-9

See Articles page e313 and e323

More people now live to advanced ages. The health and social care needs of the growing population with age-related frailty are becoming important public health and health policy concerns. Frailty has been described as "a distinctive health state related to the ageing process in which multiple body systems gradually lose their in-built reserves,"[1] rendering frail individuals susceptible to adverse outcomes such as falls, fractures, hospital admissions, and mortality. The notion of frailty has potential for risk stratification, but how can it be defined and recognised and what are the causes of frailty?

A qualitative study,[2] published earlier this year, found that physicians can generally recognise frailty when they see it in their patients but clinicians acknowledge uncertainty and lack of reliability in classifying their patients' frailty status in the absence of clear definitions and diagnostic criteria. Many researchers have tried to operationalise definitions of frailty, of which the most widely accepted is the frailty phenotype proposed by Fried and colleagues.[3] This model is based on the co-occurrence of at least three of five apparently non-specific features including unintentional weight loss, self-reported exhaustion, weakness (low grip strength), slow walking speed, and low physical activity.[3] Another approach to the classification of frailty draws on the cumulative deficit model leading to the calculation of a quantitative frailty index. The Frailty Index developed by Rockwood and colleagues.[4] considers the number of possible deficits in an individual. Recent exemplars of this approach include the e-Frailty Index[5] and the Hospital Frailty Risk Score.[6] The construction of these indices shows considerable overlap with the concept of multiple morbidity.[7] Frailty indices are generally strongly associated with mortality[5] and this finding suggests that some patients with frailty might be approaching a stage of terminal decline.[8]

Two papers, one by Eric Brunner and colleagues[9] and the other by Peter Hanlon and colleagues,[10] in this issue of *The Lancet Public Health,* explore the epidemiology of frailty in the context of two well-known UK cohort studies, the Whitehall II and UK Biobank studies, respectively. Both reports assessed relatively young populations. The Whitehall II study assessed participants at a mean age of 69 years, with a minority of women, whereas the analysis of UK Biobank study included participants aged 37–73 years. Both reports used Fried's phenotype to assess frailty, classifying participants as pre-frail if they showed one or two features, and frail if they showed three or more. In the Whitehall II study,[9] fewer than 2% showed evidence of frailty under the age of 65, increasing to more than 10% at 75 years or older. There were substantial inequalities in the occurrence of frailty, which was more frequent in women, ethnic minority groups and those with low employment grade. Low employment grade at age 50 years was associated with 2·60 times higher odds of later frailty (95% CI 1·89–3·58). Participants who had long-term conditions or lifestyle risk factors for long-term conditions at the age of 50 years were more likely to develop frailty in later life, and these characteristics largely accounted for inequalities in frailty. These findings are consistent with those of a recent international study,[11] which explored inequalities in walking speed in old age and support the view that social inequality has a major negative effect on healthy ageing.[12]

In the UK Biobank study,[10] 16 538 (3%) of 493 737 participants met the criteria for frailty, with more than a third of the sample (185 360 [38%] of 493 737) meeting the criteria for pre-frailty. Multiple morbidity was strongly associated with frailty in the UK Biobank data with participants with four or more long term conditions having 27 times higher odds of frailty than those with no long-term conditions (OR 27·1, 95% CI 25·3–29·1). Of all individual long-term conditions, frailty was most frequently observed in patients with multiple sclerosis and chronic fatigue syndrome. Obesity at midlife was associated with frailty in both studies, suggesting that targeting modifiable risk factors at midlife might reduce the occurrence of frailty at later ages.

These new analyses advance our understanding of the association between long-term conditions, multiple morbidity, and frailty. These studies show that long-term conditions and their risk factors are often antecedents of frailty; multiple morbidity and frailty often co-exist. The data also raise questions concerning our present epidemiological definitions of frailty. The high proportion of participants classified as pre-frail in the UK Biobank study could suggest that the definition lacks specificity; however, pre-frailty was associated with mortality in the UK Biobank data with hazard ratios for

mortality at age 65–73 years compared with the non-frail group of 1·45 in men (95% CI 1·34–1·57) and 1·50 in women (1·34–1·68). Other recent studies have assessed the associations of low walking speed[11] or low grip strength[13] with mortality without invoking the concept of frailty. There is a lack of consensus on the definition of frailty; the classification of individuals as frail depends on the theoretical construct incorporated in the frailty model,[14] raising a possibility that there might be more than one kind of frailty. At present, the term frailty might be viewed as describing one phase of an ageing continuum and this continuum is perhaps not readily dichotomised.

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We declare no competing interests.

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