Frailty: enhancing the known knowns

Every man desires to live long, but no man would be old.

Jonathan Swift, Thoughts on Various Subjects, 1711

Understanding frailty—the concept of vulnerability to adverse health outcomes of people of the same chronological age—continues to motivate research by geriatricians, epidemiologists, sociologists and laboratory-based scientists. While some clinicians have embraced frailty as the Holy Grail of geriatric medicine [1] or advocated it as another Geriatric Giant [2], others remain unconvinced about the feasibility of applying frailty measures in routine practice [3]. The potential to measure with precision the vulnerability of older people has been met with skepticism [4]. Some geriatricians suspect that objective frailty measures are meant to undermine clinical judgement, somehow reflecting an erosion of trust between patients and their doctors [5]. Moreover, efforts to underpin geriatric medicine with more scientific rigour have not been accompanied by reduced antipathy to our specialty [6].

The frailty index (FI), or deficit accumulation model, is one of the three main approaches to the measurement of frailty. It conceptualises frailty as a multidimensional risk state, which can be measured by the quantity rather than by the nature of health problems; individuals accumulate deficits throughout their lives and the more things individuals have wrong with them, the higher the likelihood they will be frail [7]. The FI employs a well-defined methodology (e.g. someone with 6 deficits out of 40 counted has a FI of 0.15). Alternative approaches are to identify frailty as a clinical syndrome or phenotype (such as that defined by Fried et al. [8] as the presence of ≥3 of 5 criteria: weight loss, exhaustion, weak grip strength, slow walking speed and low physical activity) or the measurement of frailty based on the clinician’s subjective opinion [9]. The former predicts adverse outcomes in large population samples [10]. The latter have strong face validity, but rely on judgement and depend on geriatric expertise (e.g. accurate assessment of functional status) limiting their generalisability.

Most FI studies have been conducted in North America; similar FI properties have been described in samples from Canada [11], the USA [12] and China [13]. Examining frailty across other populations would contribute to the ‘known knowns’ of frailty. The accompanying paper [14] is the most comprehensive investigation to date of the FI in Europe. The Survey of Health, Ageing and Retirement in Europe (SHARE) is a large cohort study of 29,905 community-dwelling participants aged over 50 years (mean 64 years) from 12 European countries (Austria, Germany, Sweden, Netherlands, Spain, Italy, France, Denmark, Greece, Switzerland, Belgium and Israel). An FI was determined for each participant as a proportion of accumulated deficits. In both sexes, there was a significant non-linear association between age and the FI. Higher FI scores were associated with higher mortality for participants of all ages. In the accompanying study, patients were followed up for different lengths of time, with a mean follow up of 2.4 years, the FI was a better predictor of death than chronological age.

One interesting finding from this study is the significant differences in mortality between sexes, with males having greater mortality rates despite having lower mean FI values. Our group has speculated on the mechanisms underpinning this male–female health-survival paradox [15]. A greater frailty burden in women might first represent a male ‘fitness–frailty pleiotropy’, resulting in men having lower physiological reserves in old age so that health deficits are more lethal. In short, the price of more optimal physiological functioning during youth is a lower threshold for system failure in old age. Conversely, a female ‘fertility–frailty pleiotropy’ might result in greater physiological reserves in women. Child birth and child rearing necessitate high levels of energetic and nutritional investment: women who have children live shorter lives. For the last 100 years or so, women have been limiting the number of children they bear and their life expectancies may be longer than predicted by evolutionary design. Furthermore, though the FI captures physical, cognitive and psychological vulnerability, it may not include all factors that impact life expectancy in older people; these factors may be present more in men than in women.

Though much has been done to advance our understanding of frailty, it is a paradigm still replete with ‘known unknowns’. For example, while the FI approach has been validated in tens of thousands of community-dwelling older people, studies with older inpatients are at a comparatively germinial stage. Recent work suggests that an FI derived from Comprehensive Geriatric Assessment may stratify patients’ risk of institutionalisation and death [7] and predict their rehabilitation potential [16]. Importantly, the FI is feasible for all older inpatients, even those unable to undertake performance-based tests. Whether an FI-CGA can be
incorporated into every day care on the wards and used to augment clinical decision making is a key focus of our translational research programmes.

The mechanisms leading to frailty and its precise pathophysiology are other current frailty ‘unknowns’. A growing body of evidence links frailty with inflammation—interestingly, frailty is the most strongly associated with a combination of immunological and physiological impairments, rather than a single biomarker [17]. This supports the conceptualisation of ageing as the progressive accumulation of damage to a complex system, resulting in aggregate loss of system redundancy. A critical mass of abnormalities across different systems seems to be a more important determinant of frailty than any individual pathway. The development of a mouse model of frailty [18] has the potential to underpin future investigations of frailty treatment and prevention.

Exercise, optimal nutrition and better education are of particular interest as therapeutic strategies for frailty since they are complex interventions which may modify the accumulation of deficits across many systems. These interventions should be flexible enough to accommodate the individual needs of the older adults. Exercise improves functional outcomes and reduces disability in frail older adults. Exercise improves fitness and frailty across the adult lifespan: evidence from the Canadian National Population Health Survey. CMAJ 2011; 183: E487–94.

And we have not even begun to consider the unknown unknowns…

RUTH E. HUBBARD1,*, OLGA THEOU2
1 Centre for Research in Geriatric Medicine, The University of Queensland, Brisbane, Australia
Tel: (+61) 7 3176 5330; Fax: (+61) 7 3176 6945.
E-mail: r.hubbard1@uq.edu.au
2 Geriatric Medicine Research Unit, Dalhousie University, Halifax, Canada
*To whom correspondence should be addressed

References