Frailty in Aging
Biological, Clinical and Social Implications

Volume Editors

Olga Theou  Halifax, N.S.
Kenneth Rockwood  Halifax, N.S.

22 figures and 6 tables, 2015
Contents

VII Introduction
Rockwood, K.; Theou, O. (Halifax, N.S.)

The Biology of Frailty

1 Frailty: Scaling from Cellular Deficit Accumulation?
Rockwood, K. (Halifax, N.S./Manchester); Mitnitski, A. (Halifax, N.S.); Howlett, S.E. (Halifax, N.S./Manchester)

15 Assessment of Frailty in Animal Models
Howlett, S.E. (Halifax, N.S./Manchester)

26 Frailty, Inflammation and Immunosenescence
Fulop, T. (Sherbrooke, Que.); McElhaney, J. (Sudbury, Ont.); Pawelec, G. (Tübingen); Cohen, A.A. (Sherbrooke, Que.); Morais, J.A. (Montreal, Que.); Dupuis, G.; Baehl, S. (Sherbrooke, Que.); Camous, X. (Singapore); Witkowski, J.M. (Gdansk); Larbi, A. (Singapore)

41 Sex Differences in Frailty
Hubbard, R.E. (Brisbane, Qld.)

54 Frailty and the Microbiome
Meehan, C.J.; Langille, M.G.I.; Beiko, R.G. (Halifax, N.S.)

Evaluation and Management of Frailty

66 Operationalizing Frailty Using the Frailty Phenotype and Deficit Accumulation Approaches
Theou, O. (Halifax, N.S.); Walston, J. (Baltimore, Md.); Rockwood, K. (Halifax, N.S.)

74 Comparison and Clinical Applications of the Frailty Phenotype and Frailty Index Approaches
Theou, O.; Rockwood, K. (Halifax, N.S.)

85 Frailty in Primary Care
Romero-Ortuno, R. (Cambridge)

95 Hospital Care for Frail Elderly Adults: From Specialized Geriatric Units to Hospital-Wide Interventions
Bakker, F.C.; Olde Rikkert, M.G.M. (Nijmegen)

107 Frailty and Mobility
Eeles, E. (Chermside, Qld.); Low Choy, N. (Chermside, Qld./Banyo, Qld.)
121  **Frailty and Interprofessional Collaboration**  
Briggs, M.C.E. (Sudbury, Ont./Toronto Ont.); McElhaney, J.E. (Sudbury, Ont.)

137  **Frailty and Rehabilitation**  
Cameron, I.D. (St Leonards, N.S.W.); Kurrle, S.E. (Hornsby, N.S.W.)

151  **End of Life Care in Frailty**  
Moorhouse, P.; Koller, K.; Mallery, L. (Halifax, N.S.)

---

**Social Aspects of Frailty**

161  **Frailty and Organization of Health and Social Care**  
Clegg, A.; Young, J. (Leeds)

174  **Frailty’s Place in Ethics and Law: Some Thoughts on Equality and Autonomy and on Limits and Possibilities for Aging Citizens**  
McNally, M.; Lahey, W. (Halifax, N.S.)

186  **Frailty and Social Vulnerability**  
Andrew, M.K. (Halifax, N.S.)

---

196  **Author Index**

197  **Subject Index**
Introduction

People today generally live longer and healthier lives than at any other point in history. This ‘demographic transition’ and its associated ‘epidemiological transition’ of changing disease patterns affect the global population. Due to low birth and mortality rates, national populations are aging at a rapidly increasing rate. Almost one in seven Canadians and one in every five Europeans is older than 65. Furthermore, the number of older adults is expected to double by 2036, and those older than 80 years are the fastest growing segment of the population. This is particularly important because it is amongst those aged 80+ years that health care use becomes especially disproportionate, with people aged 80+ composing little more than 2% of the population, but consuming 20% of adult, nonobstetrical hospital days.

To understand the impact of these well-known trends, we need to consider the achievements in medical technology and the increase in age-associated, noncommunicable diseases. As a consequence, many more people are able to tolerate more health deficits without dying. In Canada, 91% of older adults have at least one chronic condition, 50% have five or more, and 40% live with a disability. Canadian older adults account for 45% of all health care expenditures, and estimates from elsewhere show comparable results. This would be unproblematic if older adults received care that justified the expenditures, but that appears to not always be the case. Indeed, the growing number of adults with multiple, interacting medical and social problems is proving to be an important challenge in providing quality health care. Specifically, we need health systems that are appropriate to the needs of older adults, especially those who have more than one acute illness and who come from social environments that might not fully support their post-acute care needs.

Not every older adult has multiple problems, and in a haste to correct this perception, there can be a tendency to go too far in the other direction, as though no older adults have special needs. As one notorious health-planning paper put it, ‘the aging of the population matters less than you think’. However, variability in health status is an important phenomenon that becomes more important with age. Some older adults remain healthy even to a very old age, whereas other will experience multiple health problems from middle age [1, 2]. In geriatric medicine, the concept of frailty has been introduced to capture this variability in the rate of aging. This term is also used by
demographers and actuaries to denote a fixed factor that is associated with a shortened lifespan. In contrast, geriatricians see the frailty state as changing over the life course. The question of whether people have a lifelong predisposition to what geriatricians call frailty has not been resolved.

Frailty is noncontroversially understood as the concept of increased vulnerability to adverse outcomes among people of the same chronological age. Adverse outcomes associated with frailty include falls, cognitive impairment, disability, hospitalization, institutionalization, and death [3–7]. Frailty arises from a multisystem compromising the body’s ability to repair [8], which is essential in aging organisms that face a variety of potentially damaging insults. Much of the damage arises as the inevitable result of metabolism – for example in oxidative stress. The environment clearly impacts how much damage arises and how damage can be repaired over time. However, at present, we have only limited evidence about the association between cellular aging markers and frailty [9, 10].

Frailty represents an important challenge for aging populations. Pragmatically, at some point, the number of things that people have wrong with them becomes more important than the exact nature of what they have wrong with them, at least with respect to what they need and how their medical care is best administered. This is so even though, for individuals, it will always be important to know what exactly is wrong. Still, at some point, the complexity of needs in frail individuals means that knowing exactly what is wrong is best achieved in ways that allow complexity to be embraced. This approach of embracing complexity by looking at measures of whole-system function (cognition, mobility, balance, independence in daily activities) is in contrast to the problem list method, a long and widely used approach in medicine. Using the problem list approach, each problem present in an individual is enumerated and addressed, typically one problem at a time. However, when people are frail and have many things wrong with them, the better approach is to look for problems that indicate whole-system difficulty and to address those at the system level. For example, mobility impairment will always be important no matter what the cause; consequently, focusing on mobilizing patients will always be important. This holds true even in cases (such as tibial plateau fractures) in which early mobilization will need to be restricted. Likewise, being able to diagnose mobility impairment in the absence of focal neurological or musculoskeletal problems is essential. For example, weakness is commonly seen in hyponatremic patients, even if the causal chain between having low serum sodium and spending most time in bed is elaborate. Frailty seems to be a good lens through which to refract multimorbidity, dependence, disability and motor slowing (with or without impaired balance or frank disability). Assessing frailty can be done either at the screening level or by a comprehensive geriatric assessment. Given its pervasive impact on health and the outcomes of health care, it has been proposed that frailty should always be considered when treating the older patient [11]. To achieve this, we need tools with sound psychometric properties to assess frailty in clinical settings [12].
Even so, there is still heated debate over how to achieve consensus regarding the best definition of frailty for clinical uses [13].

Even though much has been done to advance our understanding of frailty, it is a concept full of ‘known unknowns’, such as the mechanisms leading to frailty and the management of frailty [14]. In order to examine these ‘known unknowns’ and to start considering the ‘unknown unknowns’, the new science of understanding and managing frailty requires an appropriate framing of the problem. This book aims to consider these and related questions. How can we recognize frailty? How does an understanding of frailty inform our understanding of the aging process? What are its more general implications for health care systems and society? To achieve these goals, we asked the authors to focus on the key points that are known in their area and then to put this information into the framework of frailty as a vulnerability state. We then asked for an arbitrary restriction of the number of references and for them to provide some key unanswered questions in their area. In this way, we hope that this book will be useful in summarizing what we now know and where we will go with these inquiries.

In the first section of the book, ‘The biology of frailty’, we begin by trying to understand the link between cellular deficit accumulation and the manifestation of microscopic/clinically visible deficits. We discuss how frailty might arise through the biological processes of metabolism, aging, and the accumulation of these subcellular deficits. In Chapter 2, we describe recent advances in animal models of deficit accumulation and the assessment of frailty in animals. In Chapter 3, we examine the role of faulty repair mechanisms that allow damage to accumulate, giving rise to frailty. These mechanisms include oxidative stress with metabolism, DNA repair, inflammation, and the aging of the immune system – ‘immunosenescence’. What is known regarding sex differences in frailty is laid out in Chapter 4. Concluding the first section, Chapter 5 considers the relationship between aging, frailty, and the microbiome.

In the second section, ‘Evaluation and management of frailty’, we begin by discussing how frailty is conceptualized and operationalized based on various approaches, including the two most common approaches – the frailty phenotype and the accumulation of deficits. In Chapter 8, we outline the importance and usefulness of identifying frailty early in primary care settings and further how frailty might be screened for and prevented. Chapter 9 describes how hospital-based care can be best organized to the benefit of frail older adults, who often present with multiple, interacting medical and social problems. Chapter 10 underscores how mobility can be an important marker of frailty and how frailty might be assessed by tracking mobility alone. Subsequently, we will describe the benefits of interprofessional collaborative practice for the care of frail older adults in Chapter 11, and we review the challenges and opportunities for rehabilitation in frail patients, who often experience rapid deconditioning, in Chapter 12. End-of-life care for frail older patients and how to best synthesize palliative and therapeutic care are each considered in Chapter 13.
The ‘Social aspects of frailty’ section begins by describing how the assessment of frailty can usefully inform the further organization of clinical care. Ethical and legal implications of frailty are discussed in Chapter 15, and the relationship between frailty, social vulnerability, and adverse outcomes is considered in Chapter 16.

Kenneth Rockwood, Halifax, N.S.
Olga Theou, Halifax, N.S.

References