



Literature Review of Frailty and Multi-morbidity in Older Adults: Exploring the Complex Relationship

Author

Omar Sami Basubrain

Department of Medicine, Faculty of Medicine
Umm Al-Qura University, Makkah, Saudi Arabia

Abstract

In older adults, frailty and multi-morbidity are common conditions that lead to the increase vulnerability, healthcare outcomes and poor physical and mental health outcomes. This literature review contributes to the study of the complex and dynamic relationship of multi-morbidity and frailty. It also emphasizes various other factors that contribute to the frailty irrespective of presence of multi-morbidities. On dissecting existing literature, it is observed that high physical activity levels and functional independence play pivotal role on older adults in development of frailty. The presence of multiple morbidities and co-morbidity are indicators for development of risk of frailty. The targeted rehabilitation and treatment plan can help older adults to achieve good health outcomes in frail multi-morbid older adults. The frailty score is recognized tool for assessment of chronic stress and frailty known as Rockwood score system. The score system presents insights into frailty and multiple morbidity of older adults.

Keywords: Frailty, older adults, multi-morbidity, functionality, Rockwood Frailty Score, comorbidity.

1. Introduction

In older adults, multi-morbidity and frailty are two important aspects that greatly influence the health and well-being of individuals. Frailty is a state in which there is an increased risk of adverse health outcomes, hospitalization, and increased disability due to reduction in physiological reserves of body^[1]. On the other hand, multi-morbidity is defined as the occurrence of two or more health related chronic conditions in the same individual that contributes to the stress on individual, family, and community level hospital^[2]. In an ageing population, these phenomena are common and ultimately increasing functional decline, health

care utilization, dependency, and poor quality of life. It is important to understand dynamic relationship between frailty and multi-morbidity for developing strategies for optimizing patient care in older adults and promoting healthy ageing^[3].

It is commonly recognized that the existence of multi-morbidity in individuals leads to increased chances of frailty. There are some other factors that play a role in the development of frailty of individuals. It is seen that not all frail older adults have multi-morbidity and vice versa. The high activity levels, sedentary lifestyle and functional independence contribute to the increase or

decrease of frailty. It has been observed that there are lower chances for development of frailty who maintain their physical function by engaging in high activity levels. Functional independence through exercise, mobilization and increased daily activities contribute to good quality health and lower frailty^[4].

In addition to that, multi-morbidity is a higher risk factor for the cause of frailty. The co-existence of one or more chronic condition leads to increased hospitalization, polypharmacy, and difficulty in management of disease, leading to dependence, decrease activity levels and increased frailty. In management of morbidities of older individuals, increased risk of frailty should consider and promote more vigilant approach in their management^[5].

This literature review aims to establish complex relationship between frailty and multi-morbidity in older individuals. In the presence of current data, it is established that multi-morbidity is a warning sign for the development of increase frailty, but it is not only factor in development of the process. The importance of high physical activity levels and physical independence contributes to the decrease frailty. These interconnected factors are important for health professionals to develop preventive guidelines and clinical practice in preventing frailty and preserving overall health and function of older adults. The findings of this literature review will provide guidelines for optimal patient care, clinical guidelines in decision making and better health results in older individuals with multi-morbidity and frailty.

2. Complex relationship between frailty and multi-morbidity

2.1 Frailty

Frailty refers to physiological state in which there is decreased physiological reserve and increased vulnerability due to exogenous or endogenous stresses that put individual with risk of decline in good health^[6]. The manifestations of frailty can be in the form of sarcopenia, negative energy

balance, and decrease tolerance for exertion and disease. The increased frailty ultimately leads to poor aging, polypharmacy, dependency, and frequent hospitalizations^[7].

2.2 multi-morbidity

Multi morbidity is referred to presence of multiple chronic conditions simultaneously in an individual. The increased multi-morbidity means increased disability, increased hospitalization, polypharmacy, and poor health outcomes^[8].

2.3 Shared pathways and overlapping features of multi-morbidity and frailty

In older adults, multi-morbidity and frailty are two different phenomena but they often co-exist and play synergistic role in ailment of the individual. They both share several common pathways in their progression and development^[9]. Some overlapping pathways are listed below:

Oxidative Stress

It is the imbalance between antioxidants of immune system of body and free radicals. They play a role in the process of both chronic diseases and aging. The oxidative stress also plays role in cellular damage that led to both frailty and multi-morbidity^[10].

Inflammation and Immune Deregulation:

The presence of increased inflammatory markers such as C - reactive protein and interleukins contribute to aging and progression of chronic diseases. The deregulation of immune system is also contributed to vulnerability, increased physical dependence and progression of chronic diseases. They are key contributors in the development of both frailty and multi-morbidity.

Mitochondrial Dysfunction:

The key contributor to ageing is mitochondrial dysfunction and is linked with cellular damaging and dysfunction. Mitochondria play a role in cellular energy production and impairment leads to physical frailty. It is also significant in the development of pathogenesis of chronic disease.

Neuroendocrine Deregulation:

The optimal functioning of hypothalamic pituitary adrenal axis is important for normal body functioning. Any disturbance in this axis will lead

to increased cortisol levels. The altered cortisol is observed in chronic diseases. Cortisol levels will also disturb the stress response system and thus lead to adverse health outcomes.

Sarcopenia and muscle loss:

Sarcopenia is observed in adults who have multi-morbidity and frailty. Sarcopenia is a feature of muscle loss that is due to imbalance between protein breakdown and synthesis. In chronic disease there is muscle loss due to bed riddance and decrease physical inactivity^[11].

Lifestyle influences:

The unhealthy lifestyle and habits that includes sedentary behavior, alcohol consumption, smoking and poor nutrition contribute to vulnerability, dependency, multi-morbidity, and frailty. On the other hand, an active and healthy lifestyle with good dietary habits contributes to reduction in multi-morbidity and frailty^[12].

3. Factors Contributing to Frailty beyond Multi-morbidity

3.1 Functional Independence: A Key Determinant of Frailty

In older adults, frailty status is greatly influenced by individual functional independence. Frailty is not only influenced by the presence of morbidities, but it is also affected by physical as well as cognitive function. The overall health is greatly determined by the ADLs (activities of daily living) and IADLs (instrumental activities of daily living). They play an important role in declining the overall mortality and frailty^[13].

It is commonly observed that frail individuals have decline physical functions such as gait abnormality, reduced grip strength, and decreased mobility and bed riddance. These are attributed to increased chances of vulnerability to poor health conditions and reduced functional independence. Functional independence is also influenced by poor cognitive function, poor attention, and impaired memory and thus contributing to the development of frailty. The loss of functional independence is a vicious cycle making frail individuals vulnerable and further decline in

optimal physical and cognitive functioning. The decline in physical function led to dependency on others, minimal social interaction, and overall poor health outcomes of individual^[14].

It is essential to develop strategies to delay or prevent functional independence to reduce the risk of frailty in an individual. These strategies include physical rehabilitation, exercise, mobility, and increase physical activity that promotes balance and strength. Monitoring and assessment of older adult's functional ability should be in medical assessments. Early identification and intervention plans delay the development of frailty of the patient.

3.2 High Activity Levels: A Protective Factor against Frailty

Although multi-morbidity co-exists with higher frailty in older adults, it is noteworthy that not all individuals who have chronic stresses become frail. There are several other factors that are directly or inversely related to frailty. One of the factors is the activity levels of an individual. The activity levels are inversely related to the development of frailty. Studies have shown that engaging in regular physical activity means is protective against ailment and frailty. The increased physical activity has good outcomes on cognitive function, cardiovascular health and less hospitalizations and bed riddance^[15].

This protective mechanism is due to several good mechanisms. The high activity levels increase the muscle strength, functional independence, and minimal cardiovascular failures. These all mechanisms lead to better health outcomes, less dependency and decreased frailty. In conclusion, high level of activity leads to functional independence, less vulnerability and decreased frailty^[16].

3.3 Impact of Psychological and Social aspects on Frailty:

Frailty is not only influenced by physical health and well-being but also determined by social and psychological aspects of the individual. The frailty of an individual is also determined by cognitive function, social support, and psychological well-

being. Psychological well-being is determined by emotional resilience and mental health. The adverse psychological outcomes such as anxiety, depression, and addiction are associated with early development of frailty. The psychological outcomes disturb the cortisol levels and decelerate physical function and increase dependency leading to development of frailty. On the other hand, positive psychological health makes an individual self-sufficient and decreases the development of frailty^[17].

Studies have shown that cognitive function also plays a pivotal role in the development of frailty. Good memory, attention span, decision making keeps a person healthy. Rehabilitative activities that improve cognitive capacity mitigate the development of frailty.

Social engagement and connections also influence the development of frailty. The older adults who have social support and mobilization with good health have decreased frailty. The older adults who have self-isolating behavior are at increased risk of developing frailty. Social activities mitigate stress and lead to good health^[18].

3.4 Inflammatory Pathways and Frailty

There are many factors that influence frailty apart from activity level, physical and psychological wellbeing. Development of inflammatory mechanisms also contributes to the development of frailty in older adults. Studies have suggested that the oxidative stress or low-grade inflammatory mechanisms play an important role in the development of frailty irrespective of presence of chronic multi-morbidities. The presence of inflammation leads to the increased ageing process and decrease immunity and overall contributing to frailty. In frail older adults, it has been observed that pro-inflammatory substances are present^[19].

Numerous pathways are involved through which inflammation leads to frailty. The pro-inflammatory cytokines lead to muscle wasting, poor skeletal muscle functioning, less physical activity, and increased frailty.

4. Multi-morbidity as a Risk Factor and warning sign

4.1 The Role of Multi-morbidity in Frailty Risk

The presence of multiple chronic conditions simultaneously is a common phenomenon in older adults. The presence of chronic morbidities leads to functional decline of individual, economic utilization, hospitalization, and poor health outcomes. Multi-morbidity leads to frailty and physical dependency. Studies have shown that increased chronic stress will lead to progression of frailty^[20].

4.2 Early Intervention for Multi-morbid Frail older adults

The early intervention and tailored treatment plan can help older multi-morbid frail individuals. The targeted treatment regimens will help to achieve good quality life and prevent worse alimonies^[21]. The early interventions can be done in following ways:

- Comprehensive Geriatric Assessment
- Patient Education and Self-Management
- Physical Exercise and Rehabilitation
- Psychosocial Support
- Medication Review and Management
- Multidisciplinary Care Teams

4.3 Implications for Healthcare Providers:

The multi-morbidity and frailty in older adults have multiple implications for health care providers, some are listed below:

- Early Identification and Assessment
- Research and Innovation
- Person-Centered Care
- Education and Support
- Collaborative Care
- Comprehensive Management

5. The Rockwood Frailty Scale: Assessing Functionality and Morbidity

5.1 Overview of Rockwood Frailty Scale

The Rockwood frailty scale is widely used for assessment of frailty in older individuals. This tool is used to provide functionality of frailty of older adults. This scale dissects grades of frailty based on individual's frailty on dependency levels

and their functionality. The scale is graded from 1 to 9. Grade 9 represents terminal patients while grade 1 indicates healthy adults. The Rockwood Frailty Scale is procured from the frailty index. This index is a collection of various variables or deficits present in individual medical records that includes both laboratory measures and clinical functional. The deficits can count as cognitive decline, chronic diseases, psychological factors, and physical impairments^[22].

5.2 Description and Development of Frailty Index

1. Comprehensive Evaluation:

The Rockwood Frailty Index covers a wide range of frailty of individuals. It counts on different aspects that contribute to frailty. These aspects include cognitive, physical, chronic, and psychosocial elements. This wide range of score gives a more comprehensive approach in finding out frailty status of individual^[23].

2. Scoring system:

Each parameter of scale is measured based on its presence or absence. The higher the score is, the greater the frailty in an individual. The score is estimated to be between 0 to 1. The cut off value of the score is 0.7 that suggests an increase in mortality and morbidity of the individual.

3. Selection of Parameters:

The parameters or deficits are derived from medical records. The parameters would include cognitive decline such as memory problems or cognitive impairment, physical impairments such as muscle weakness or mobility impairment, chronic diseases such as heart disease or diabetes and psychosocial factors such as social isolation and depression^[24]. It should be a set of preselected common deficits based on the profile of the community or population being tested, as this differs from country to country.

3. Assessment of deficits:

The selected deficit would be assessed on its absence or presence in the individual. For example, if one of the parameters is heart failure, it would be evaluated whether an individual has been diagnosed with heart failure or not.

4. Counting the Deficits:

The deficits present in the individual will be counted. If deficit is present, it would be marked as 1 and if deficit is absent, it would be marked as 0.

5. Total Parameters:

The total number of parameters that are included in the index would be counted. It depicts the number of deficits that are comprehended in the assessment.

6. Calculation

The last step is calculation to find out the frailty index score. It is calculated as following:

Frailty Index score = Number of deficits present in individual / Total parameters included in study

It is important to point out that particular deficits included in the frailty index can be according to the settings and study.

7. Quick Screening Tool:

The Frailty Scale was developed to give us quick assessments for the screening of the frailty in individual. The scale is graded from 1 to 9. Grade 9 represents terminal patients while grade 1 indicates healthy adults. The frailty index needs more comprehensive data while Rockwood frailty scale is a more efficient and accessible method for identification of frailty.

5.3 Application and Benefits in Clinical Practice

The Rockwood Frailty Scores offers valuable clinical application. The clinical applications include early intervention, better informed treatment decisions, better patient outcome and better health outcome. The scale helps in following clinical applications:

1. Identification of high-risk adults:

The scale depicts adults who are at risk of developing poor health outcomes. The adults with higher scores indicate that these patients have greater morbidity and higher frailty. Higher scores mean these individuals have susceptibility to disability, hospitalization, mortality, and functional decline. The early detection means, early intervention and better outcome of health

^[28].

2. Treatment Approaches and guidance:

The Rockwood score indicates body vulnerability, tolerance, strength, and inflammatory response. These parameters will allow health professionals to tailor the treatment modalities, rehabilitation programs and surgical considerations according to an older adult's health condition. It will allow making informed choices and minimize the hazards.

3. Communication and informed Decision-Making:

The score system provides a blueprint for better communication about the condition of patients among health professionals. It makes a framework that is comprehensive and facilitates the evidence of prognosis, benefits, and risks of treatment modalities on health of the patients. The scale system also makes easy communication between health providers and the family of the patient.

4. Individualized Care Planning:

The score helps in the development of individual care planning as per individual needs. The needs of individuals will enable clinicians to advise care as per need. The customized plans can be made according to the functional independence and chronic stress of patient^[29].

Conclusion

Multi-morbidity and frailty are closely associated aspects of older adult's health. However, they both represent different elements of health for the individual. It is observed that multi-morbidity increases the occurrence of frailty. It cannot be implied that all multi-morbid older adults are frail, or all frail older adults are multi morbid. The frailty in older adults is also influenced by activity levels, functional independence, cognitive function, and psychological and social health. The existence of multi-morbidities is an early indicator of the development of frailty. Tailored medical treatment and rehabilitation can contribute to delaying the development of frailty. The Rockwood frailty score indicates the framework for assessment of both frailty and chronic stress.

These comprehensive evaluations will lead to better health assessments of older adults.

Conflict of Interest

The author declares no conflicts of interest.

References

1. Xue Q. L. (2011). The frailty syndrome: definition and natural history. *Clinics in geriatric medicine*, 27(1), 1–15. <https://doi.org/10.1016/j.cger.2010.08.009>
2. Skou, S. T., Mair, F. S., Fortin, M., Guthrie, B., Nunes, B. P., Miranda, J. J., Boyd, C. M., Pati, S., Mtenga, S., & Smith, S. M. (2022). Multimorbidity. *Nature reviews. Disease primers*, 8(1), 48. <https://doi.org/10.1038/s41572-022-00376-4>
3. Salisbury C. (2012). Multimorbidity: redesigning health care for people who use it. *Lancet (London, England)*, 380(9836), 7–9. [https://doi.org/10.1016/S0140-6736\(12\)60482-6](https://doi.org/10.1016/S0140-6736(12)60482-6)
4. Au Yong, P. S. A., Sim, E. Y. L., Ho, C. Y. X., He, Y., Kwa, C. X. W., Teo, L. M., & Abdullah, H. R. (2021). Association of Multimorbidity With Frailty in Older Adults for Elective Non-Cardiac Surgery. *Cureus*, 13(5), e15033. <https://doi.org/10.7759/cureus.15033>
5. Salive M. E. (2013). Multimorbidity in older adults. *Epidemiologic reviews*, 35, 75–83. <https://doi.org/10.1093/epirev/mxs009>
6. Proietti, M., & Cesari, M. (2020). Frailty: What Is It?. *Advances in experimental medicine and biology*, 1216, 1–7. https://doi.org/10.1007/978-3-030-33330-0_1
7. Dent, E., Martin, F. C., Bergman, H., Woo, J., Romero-Ortuno, R., & Walston, J. D. (2019). Management of frailty: opportunities, challenges, and future directions. *Lancet (London, England)*, 394(10206), 1376–1386.

- [https://doi.org/10.1016/S0140-6736\(19\)31785-4](https://doi.org/10.1016/S0140-6736(19)31785-4)
8. Pivetta, N. R. S., Marincolo, J. C. S., Neri, A. L., Aprahamian, I., Yassuda, M. S., & Borim, F. S. A. (2020). Multimorbidity, frailty and functional disability in octogenarians: A structural equation analysis of relationship. *Archives of gerontology and geriatrics*, 86, 103931. <https://doi.org/10.1016/j.archger.2019.103931>
 9. Espinoza, S. E., Quiben, M., & Hazuda, H. P. (2018). Distinguishing Comorbidity, Disability, and Frailty. *Current geriatrics reports*, 7(4), 201–209. <https://doi.org/10.1007/s13670-018-0254-0>
 10. Chen, S. Y., Wang, T. Y., Zhao, C., & Wang, H. J. (2022). Oxidative stress bridges the gut microbiota and the occurrence of frailty syndrome. *World journal of gastroenterology*, 28(38), 5547–5556. <https://doi.org/10.3748/wjg.v28.i38.5547>
 11. Tamura, Y., Ishikawa, J., Fujiwara, Y., Tanaka, M., Kanazawa, N., Chiba, Y., Iizuka, A., Kaito, S., Tanaka, J., Sugie, M., Nishimura, T., Kanemaru, A., Shimoji, K., Hirano, H., Furuta, K., Kitamura, A., Seino, S., Shinkai, S., Harada, K., Kyo, S., ... Araki, A. (2018). Prevalence of frailty, cognitive impairment, and sarcopenia in outpatients with cardiometabolic disease in a frailty clinic. *BMC geriatrics*, 18(1), 264. <https://doi.org/10.1186/s12877-018-0955-4>
 12. de Breij, S., Rijnhart, J. J. M., Schuster, N. A., Rietman, M. L., Peters, M. J. L., & Hoogendijk, E. O. (2021). Explaining the association between frailty and mortality in older adults: The mediating role of lifestyle, social, psychological, cognitive, and physical factors. *Preventive medicine reports*, 24, 101589. <https://doi.org/10.1016/j.pmedr.2021.101589>
 13. Wu, Y. H., Lee, H. N., Chang, Y. S., Wu, C. H., & Wang, C. J. (2020). Depressive symptoms were a common risk factor for pre-frailty and frailty in patients with Alzheimer's disease. *Archives of gerontology and geriatrics*, 89, 104067. <https://doi.org/10.1016/j.archger.2020.104067>
 14. de Breij, S., van Hout, H. P. J., de Bruin, S. R., Schuster, N. A., Deeg, D. J. H., Huisman, M., & Hoogendijk, E. O. (2021). Predictors of Frailty and Vitality in Older Adults Aged 75 years and Over: Results from the Longitudinal Aging Study Amsterdam. *Gerontology*, 67(1), 69–77. <https://doi.org/10.1159/000512049>
 15. Kehler, D. S., & Theou, O. (2019). The impact of physical activity and sedentary behaviors on frailty levels. *Mechanisms of ageing and development*, 180, 29–41. <https://doi.org/10.1016/j.mad.2019.03.004>
 16. Kehler D. S. (2018). The impact of sedentary and physical activity behaviour on frailty in middle-aged and older adults. *Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme*, 43(6), 638. <https://doi.org/10.1139/apnm-2018-0092>
 17. Pilotto, A., Custodero, C., Maggi, S., Polidori, M. C., Veronese, N., & Ferrucci, L. (2020). A multidimensional approach to frailty in older people. *Ageing research reviews*, 60, 101047. <https://doi.org/10.1016/j.arr.2020.101047>
 18. Fujiwara, Y., Kondo, K., Koyano, W., Murayama, H., Shinkai, S., Fujita, K., Arai, H., & Horiuchi, F. (2022). Social frailty as social aspects of frailty: Research, practical activities, and prospects. *Geriatrics & gerontology international*, 22(12), 991–996. <https://doi.org/10.1111/ggi.14492>

19. Michaud, M., Balardy, L., Moulis, G., Gaudin, C., Peyrot, C., Vellas, B., Cesari, M., & Nourhashemi, F. (2013). Proinflammatory cytokines, aging, and age-related diseases. *Journal of the American Medical Directors Association*, 14(12), 877–882. <https://doi.org/10.1016/j.jamda.2013.05.009>
20. Grippo, F., Désesquelles, A., Pappagallo, M., Frova, L., Egidi, V., & Meslé, F. (2020). Multi-morbidity and frailty at death: A new classification of death records for an ageing world. *Population studies*, 74(3), 437–449. <https://doi.org/10.1080/00324728.2020.1820558>
21. Berntsen, G. K. R., Dalbakk, M., Hurley, J. S., Bergmo, T., Solbakken, B., Spansvoll, L., Bellika, J. G., Skrøvseth, S. O., Brattland, T., & Rumpsfeld, M. (2019). Person-centred, integrated and pro-active care for multi-morbid elderly with advanced care needs: a propensity score-matched controlled trial. *BMC health services research*, 19(1), 682. <https://doi.org/10.1186/s12913-019-4397-2>
22. Rockwood, K., & Mitnitski, A. (2007). Frailty in relation to the accumulation of deficits. *The journals of gerontology. Series A, Biological sciences and medical sciences*, 62(7), 722–727. <https://doi.org/10.1093/gerona/62.7.722>
23. Martin, F. C., & O'Halloran, A. M. (2020). Tools for Assessing Frailty in Older People: General Concepts. *Advances in experimental medicine and biology*, 1216, 9–19. https://doi.org/10.1007/978-3-030-33330-0_2
24. Sun, J., Kong, X., Li, H., Chen, J., Yao, Q., Li, H., Zhou, F., & Hu, H. (2022). Does social participation decrease the risk of frailty? Impacts of diversity in frequency and types of social participation on frailty in middle-aged and older populations. *BMC geriatrics*, 22(1), 553. <https://doi.org/10.1186/s12877-022-03219-9>
25. Searle, S. D., Mitnitski, A., Gahbauer, E. A., Gill, T. M., & Rockwood, K. (2008). A standard procedure for creating a frailty index. *BMC geriatrics*, 8, 24. <https://doi.org/10.1186/1471-2318-8-24>
26. Martin, F. C., & O'Halloran, A. M. (2020). Tools for Assessing Frailty in Older People: General Concepts. *Advances in experimental medicine and biology*, 1216, 9–19. https://doi.org/10.1007/978-3-030-33330-0_2
27. Mitnitski, A. B., Mogilner, A. J., & Rockwood, K. (2001). Accumulation of deficits as a proxy measure of aging. *TheScientificWorldJournal*, 1, 323–336. <https://doi.org/10.1100/tsw.2001.58>
28. Church, S., Rogers, E., Rockwood, K., & Theou, O. (2020). A scoping review of the Clinical Frailty Scale. *BMC geriatrics*, 20(1), 393. <https://doi.org/10.1186/s12877-020-01801-7>
29. Shrier, W., Dewar, C., Parrella, P., Hunt, D., & Hodgson, L. E. (2021). Agreement and predictive value of the Rockwood Clinical Frailty Scale at emergency department triage. *Emergency medicine journal : EMJ*, 38(12), 868–873. <https://doi.org/10.1136/emermed-2019-208633>