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Frailty Indices and Their Importance in Elderly Patients: A Perspective Review

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Abstract

The aging demographic landscape of the United States highlights a concomitant rise in chronic conditions and infectious diseases. Older adults face a heightened susceptibility to infections, particularly pneumonia and urinary tract infections, and comorbidities such as cancer, cardiovascular disease, and dementia. Frailty, defined by a set of phenotypic criteria, emerges as a crucial predictor of adverse outcomes in infections, affecting hospitalization and post-care interventions. In the context of cancer, various frailty indices demonstrate their utility in predicting complications, mortality, and long-term outcomes. Cardiovascular diseases, including acute coronary syndrome and myocardial infarctions, exhibit varied associations with frailty, influencing both short-term and long-term prognosis. Frailty's impact extends to valvular heart disease, necessitating risk assessment and tailored care. In dementia patients, frailty is linked to cognitive decline, mortality, depression, and reduced daily living activities, emphasizing the need for holistic assessment and intervention. This review explores the role of frailty indices in predicting outcomes across diverse health conditions, with a focus on infections, cancer, cardiovascular disease, and dementia. Future interventions should address the role of frailty in predicting poor prognostic outcomes, including mortality, readmission rates, and complications across diverse health conditions.

Keywords: Frailty, Infection, Dementia, Cancer, Cardiovascular disease

1. Introduction

Estimates from the 2022 census of the US reveal that about 17.3% of the total population was older than 65 years of age.[1] Previous surveys have revealed that chronic conditions were relatively more common in older US adults.[2] Infectious diseases are responsible for about one-third of the deaths in older people according to a 2001 study.[3] The most common infections include urinary tract infections and pneumonia.[4] Another comorbid condition includes cancer. Estimates from 2019 revealed that 1,944,280 adults ages 85 and older were alive with a history of cancer, representing one-third of all men and one-fourth of all women in the age group in the United States.[5] Similar estimates have been noted for cardiovascular disease and dementia. Dramatic changes are anticipated in the US population. Anticipated estimations reveal that individuals ≥85 years of age will account for 4.3% of the population in 2050, representing a more than two-fold increase from 2010.[6] These future projections will lead to a significant burden in terms of morbidity, mortality, and costs related to diseases in the frail population. In estimating mortality and morbidity, one of the scoring systems that has been extensively studied is frailty index.[7] Frailty phenotype is defined as a distinct clinical syndrome meeting three or more of five phenotypic criteria: weakness, slowness, low level of physical activity, self-reported exhaustion, and unintentional weight loss. The presence of three or more phenotypic criteria is termed as frailty.[8] The Frailty Index (FI) was created by Rockwood and colleagues through an extensive evaluation of older adults, encompassing various deficits such as diseases, physical

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limitations, cognitive impairments, psychosocial risks, and common geriatric issues, excluding frailty itself.[7] To qualify as a deficit, a variable must be acquired with age, linked to adverse outcomes, and not peak too early.[7] Frailty index is deemed as a more sensitive indicator of outcomes because it overcomes age-associated factors and therefore, the importance of chronological age is decreased. The final criterion of the frailty index ensures that deficits included in the calculation are informative by avoiding those prevalent in nearly all older adults, as they lose their discriminatory value.[8] For instance, while nocturia disrupts sleep and is age-associated, it is too widespread (seen in over 90% of men aged 75 or older) to contribute to the index. Typically, the index incorporates between 30 and 70 deficits out of a potential total of 80, maintaining a balance between comprehensiveness and practicality.[8] It is important to note that different frailty indices have different parameters and therefore, their utilization and interpretation might vary. For example, the Clinical Frailty Scale (CFS) is a 9-point assessment tool that provides an overview of an older adult's overall fitness or frailty level. A CFS score of 5 or higher is generally considered frail.[9] The Frail Index of Cumulative Deficits (FI-CD) involves tallying 30 or more health-related issues such as comorbidities, symptoms, disabilities, or any health deficiencies, with the premise that a greater number of health deficits indicates higher frailty; frailty was defined as a ratio of more than 0.25, indicating over 8 out of 32 deficits.[9] The Short Physical Performance Battery (SPPB) calculates a score based on three timed tasks and each task is scored from 0 (poor performance) to 4 (excellent performance), with a total score ranging from 0 to 12. A score of 6 or lower indicates frailty.[9]

2. Infections

The most common types of infections in the frail population include pneumonia, urinary tract infection and abdominal infections. In a study conducted in Korea using a deficit-accumulation frailty index (FI), patients with FI > 0.25, defined as moderately to severely frail, were more likely to meet CURB-65 criteria. The same cohort was likely to have a prolonged hospitalization with discharge disposition being a long-term care facility.[10] Another study utilizing the same scale revealed that more post-care acute interventions were needed in patients with higher frailty scores.[11] Further indexing systems, for example the FI-LAB, was useful in determining rate of complications and mortality in frail patients with community acquired pneumonia.[12]

Urinary tract infections have also been studied using the modified Frailty Index (mFI) and patients with higher scores were more likely to have post-operative urinary retention as compared to patients with lower scores.[13] Older patients with inflammatory bowel disease were also evaluated for serious infections using frailty indices, however, frailty was not associated with an increased risk of serious infection.[14] However, the utility of such indices was relatively limited in patients with orthopaedic infections.[15]

Viral infections and their outcomes in older patients were also evaluated. In a study with older patients and herpesvirus infections, frailty indices were not associated with adverse or favourable outcomes.[16] In fact, paradoxical results were seen in a patient cohort with cytomegalovirus infection as a positive serology was inversely related to frailty.[17]

HIV disease has also been extensively studied, particularly in quantifying vulnerability in older patients with HIV.[18] Certain markers suggestive of a weakened immune system in HIV patients have been correlated with frailty. Frailty was associated with elevated expression of glucose-transporter 1, expression of total monocytes, increased levels of immune activation markers suggesting that increased immune activation was not only present in frail patients but suggestive of abnormal lipid profile in frail patients with HIV.[18] Long-term outcomes, specifically, worsening of cognitive function was related to higher levels of frailty.[19]

Table 1 illustrates the aforementioned frailty indices.

3. Cancer

Identification of patients at risk of frailty is perhaps the first step towards optimizing and predicting outcomes in such a cohort. Carolina Frailty Index (CFI) based on geriatric assessment was also studied. The tool emerged as a significantly valid aid in not only identifying frailty but predicting all-cause mortality in older adults with cancer.[20]

Frailty indices have been widely studied in older patients with cancer. Gastric cancer in octogenarians was studied using a modified frailty index based on albumin <3.4 g/dl, hematocrit <35% and creatinine levels >2 mg/dL.[21] Patients with higher modified frailty indices had increased risk of post-operative complications and decreased cancer-free survival.[21]

Kim et al. also evaluated another validated index, Laboratory Frailty Index, based on hemodynamic and clinical parameters.[22] Increased scores had less associations with preoperative optimization but were associated with prolonged length of stay,

Table 1. Frailty indices in infections.

Author	Frailty Index	Parameters	Categories	Healthcare System	Outcomes
Park et al.[10]	50-item deficit-accumulation frailty index (FI)	26 comorbidities, polypharmacy (≥5 prescription drugs), self-reported ability to perform 21 listed activities, weight loss >5 kg in past year, body mass index <21 kg/m2, and serum albumin <3.5 g/L	Robust (<0.15), pre-frail (0.15−0.24), mild-to-moderately frail (0.25−0.44), and severely frail (≥0.45) categories	University Hospital	Primary outcome: death or functional decline Secondary outcomes: intensive care unit admission, psychoactive drug use, nasogastric tube feeding, length of stay >15 days, and discharge to a long-term care institution.
Park et al.[11]	50-item deficit-accumulation frailty index (FI)	26 comorbidities, polypharmacy (≥5 prescription drugs), self-reported ability to perform 21 listed activities, weight loss >5 kg in past year, body mass index <21 kg/m^2, and serum albumin <3.5 g/L	Robust (<0.15), pre-frail (0.15−0.24), mild-to-moderately frail (0.25−0.44), and severely frail (≥0.45) categories	University Hospital	Study outcomes were (1) death and (2) a composite outcome of death or functional decline
Huang et al.[12]	FI-LAB	Parameters were 44 and included counts from complete blood profile, hepatic function panel, coagulation profile, random blood glucose testing, electrolytes	Robust/non-frail (<0.2), pre-frail (0.2−0.35), and frail (≥0.35)	Teaching Hospital	Outcomes were complications and mortality
Tuddenham et al.[13]	Modified Frailty Index-5	Preoperative functional status and the presence or absence of four medical conditions: diabetes, chronic obstructive pulmonary disease, congestive heart failure, and hypertension.	"not frail" (0−1) versus "frail" (>2). A score of >2 corresponds to a "high" score on the original mFI-11 (≥4 of 11 frailty traits)	Teaching Hospital	Comparison between patients with and without urinary tract infections
Singh et al.[14]	Hospital Frailty Risk Score	Parameters included specific ICD-10 codes	Nonfrail" (frailty risk score <5) or "frail" (frailty risk score 5 or higher)	NIS analysis	Primary outcome was time to serious and/or opportunistic infections, defined as infection requiring hospitalization.
Erne et al.[15]	Modified Frailty Index-5	Preoperative functional status and the presence or absence of four medical conditions: diabetes, chronic obstructive pulmonary disease, congestive heart failure, and hypertension.	Used as a continuous variable	Level 1 Trauma Center	Outcomes: revision, re-admission or mortality rates, length of hospital stay and forecast power of other useful screening tools

(*continued on next page*)

Table 1. (continued)

Author	Frailty Index	Parameters	Categories	Healthcare System	Outcomes
Wang et al.[16]	Frailty Index	Weight loss, exhaustion, low energy expenditure, slowness, and weakness.	3 or more of these criteria were classified as frail, 1 or 2 as prefrail, and 0 as nonfrail.	Community	Outcomes: association with baseline serum antibody levels against four human herpesviruses, VZV, EBV, HSV-1, and HSV-2, and the risk of three-year incident frailty and five-year mortality.
Guaraldi et al.[18]	Frailty Index	Used 37 variables detailed in the study using both comorbid conditions and biochemical measures	Continuous variable with higher scores indicating frailty	University Hospital	Outcomes: multimorbidity

higher rates of re-admission and increased mortality.[22]

The Memorial Sloan Kettering-Frailty Index (MSK-FI) was also evaluated for older surgical patients with cancer.[23] However, this tool was found to be useful for both perioperative and postoperative outcomes in surgical oncology based on older patients.[23] Similar results were also observed in oncological older patients with COVID-19.[24]

Long-term outcomes after oncological interventions have also been assessed using frailty indices. A deficit accumulation frailty index (DAFI) was used to evaluate breast cancer survivors who were diagnosed at 60 years of age and about 5–15 years free of disease. More patients scored poorly on language and memory.[25] Additionally, frailty syndrome was more commonly observed in the same cohort.[25] Cognitive decline was linearly proportional to increased DAFI scores.[25] Patients with gynecological cancer were also evaluated using the Frailty Index (FI).[26] The results of the study revealed that FI was one of the strongest predictors of 1-year mortality.[26]

In one of the large-scale studies, the International Myeloma Working Group (IMWG) frailty index was utilized to investigate outcomes in older patients with multiple myeloma.[27] Frail patients had a complicated progression-free interval.[27] Interestingly, prognostic assessment could be performed by using both frailty index and the staging system.[27]

Older patients with lymphomas with incurable tumors were assessed for frailty using a Deficit Accumulation Index (DAI).[28] Frail patients have an increased risk of depression and distress.[28]

Hospital Frailty Risk Score (HFRS) was evaluated in older patients with head and neck cancer. Higher rates of readmissions at 30-days, increased cost of resource utilization, and longer length of stay were associated with higher scores.

Evaluation of patients with pancreatic cancer reveal slightly different results. The modified frailty index (mFI) was used to assess response to therapy and long-term outcomes.[29] Patients with lower scores were more likely to receive 5-fluorouracil, irinotecan and oxaliplatin.[29] However, toxicity, readmission rates and complications were not related to the index at all.[29] Interestingly, the same mFI was associated with higher rate of 30-day adverse outcomes in neurosurgical patients who were frail.[30] The mFI was also studied in older patients receiving PD-1 inhibitors for lung cancer.[31] There was no significant difference in the occurrence of adverse events in frail patients.[31] However, the cohort was at higher odds of multiple adverse events and chemotherapy-induced pneumonitis.[31]

Table 2 presents a summary of these indices.

Table 2. Frailty indices in cancer.

Author	Frailty Index	Parameters	Categories	Healthcare System	Outcomes
Guerard et al.[20]	Carolina Frailty Index	36 variables reported single-item questions concerning IADLs, physical function, comorbidities, number of daily medications, vision, hearing, nutrition, mental health, and social activity.	Robust (0−0.2), pre-frail (0.2−0.35), and frail (>0.35).	County level analysis	Primary outcome: all-cause mortality
Kim et al.[22]	Laboratory Frailty Index (FI-Lab)	Based on previous reports from the Canadian Study of Health (CSHA)18 and the European Male Aging Study	Frailty scores were categorized as follows: < 0.25, 0.25−0.4, and >0.4	Tertiary Hospital	Outcomes were postoperative length of stay (LOS), readmission within 30 days, intensive care unit (ICU) admission within 30 days, and mortality
Shahrokni et al.[23]	MSK-FI	Parameters were (1) chronic obstructive pulmonary disease or pneumonia within 30 days before surgery, (2) diabetes, (3) congestive heart failure, (4) myocardial infarction, (5) coronary artery disease, (6) hypertension, (7) peripheral vascular disease, (8) impaired sensorium, (9) cerebrovascular accident, and (10) transient ischemic attack	Continuous variable with higher scores indicating frailty	Tertiary Hospital	Outcomes were established geriatric assessment and surgical outcomes (ie, frequency of complications, length of stay, 30-day surgical complications, 30-day intensive care unit admissions, and 30-day readmissions) and 1-year survival.
Ahles et al.[25]	Deficit Accumulation Frailty Index (DAFI score)	Score ranging between zero and one based on up to 44 possible frailty indicators, as described by Cohen et al.	Robust (DAFI < 0.2), pre-frail (0.2 ≤ DAFI < 0.35), or frail (DAFI ≥ 0.35)	Teaching Hospital	Cognitive function
Gilmore et al.[28]	Deficit Accumulation Frailty Index (DAI)	Self-reported and objective measures from the geriatric assessment, without the inclusion of emotional health variables.	Robust (0 to <0.2), prefrail (0.2 to <0.35), and frail (≥0.35) categories	National Data	Emotional Health

4. Frailty and cardiovascular disease

4.1. Frailty and ACS

Different results have been observed with frailty in elderly patients with acute coronary syndrome. In one study, a frailty index based on 5 components of the Fried score and albumin concentration, as malnutrition index, was assessed with respect to postdischarge all-cause mortality.[32] The results concluded that the index could be used as a marker for long-term prognosis. However, in another study, frailty was termed as an indicator for short-term outcomes and prognosis.[33]

4.2. Frailty and myocardial infarction

Frailty has been explored intensively in patients with cardiovascular disease. The rate of 30-day readmissions increased with frailty in patients with frailty ($p < 0.001$).[34] Percutaneous coronary intervention was needed in 86.40% of low-risk, 66.03% of intermediate-risk, and 58.90% of high-risk patients ($p < 0.001$).[34] Intermediate and high-risk frailty had longer length of stay, higher total cost, and were more likely to be discharged to a skilled facility ($p < 0.001$).[34] Further studies discussed the similar indices with respect to increased Charlson comorbidity index.[35]

Intensive cardiac care is less common in patients with frailty and with increased all-cause mortality postdischarge.[36] However, mortality rates were not cardiac specific.[36] Apart from frailty index, MELD-XI score has also been evaluated for prognosis with higher MELD-XI scores correlating with a poor prognosis.[37]

4.3. Frailty and valvular heart disease

Valvular heart disease (VHD) poses a significant health challenge, particularly among the aging population. Frailty, characterized by diminished physiological reserves and increased vulnerability to stressors, has garnered attention due to its association with adverse outcomes in various medical conditions, including cardiovascular disease.[38–40]

Assessing frailty in VHD patients becomes paramount for risk evaluation and tailored care. Studies have shown that frail individuals undergoing cardiac interventions, such as aortic valve replacement, face increased adverse outcomes.[41,42] The utilization of tools like the FRAIL Scale has been deemed useful in evaluating the frailty status of heart valve disease patients.[43] These assessments aid in identifying patients who might benefit from targeted interventions to improve their overall resilience.

The potential benefits of exercise training in mitigating frailty and enhancing recovery among elderly VHD patients have gained attention.[44] The postoperative period following cardiac surgery or interventions presents a critical juncture for implementing exercise programs.[44] Tailored exercise regimens can help improve cardiovascular fitness, muscle strength, and overall functional capacity, thereby contributing to better postoperative outcomes.[44] Integrating exercise training into the care continuum for elderly VHD patients can potentially enhance their quality of life and reduce the impact of frailty-related challenges.

Frailty has been observed to influence disease-specific health status among cardiovascular disease patients.[45] The integration of frailty assessment into the evaluation of VHD patients can provide insights into their overall well-being and prognosis, enabling healthcare providers to design personalized interventions that address both the cardiac condition and frailty-related issues.

Table 3 discusses the frailty indices mentioned.

5. Dementia

Frailty has been a cause of major complications in patients with dementia. It has been proposed that patients with physical frailty are at higher risk of cognitive decline resulting in higher rates of mortality.[46] This is partly related to neuropsychology as assessed by a study focusing on frailty scales; the higher the rate of neuropsychological decline, higher the rate of frailty and associated mortality.[46,47] Additionally, the syndrome has been associated with depression and reduced activities of daily living.[48] Further studies have discussed that prefrailty is associated with a decreased disability free interval in older adults.[49] Interestingly, genetics has been described to play a limited role in this regard. In a study examining the Rockwood frailty index (FI) based on 44 health deficits, a 10% increase in FI was associated with an increased risk of dementia (hazard ratio [HR] 1.17 (95% confidence interval [CI] 1.07, 1.18)).[49] However, higher hazard ratios were not observed when APOE ε4 carrier status was considered.[50] Furthermore, some frailty indices also have a relationship with increased caregiver burden in patients with dementia.[51]

A Dutch study constructed a frailty index to measure comorbidity burden in patients with dementia.[52] It was concluded in the study that short-term predictive value of frailty is higher in patients with dementia as these characteristics are likely to change over time.[52] The type of scale used has been

Table 3. Frailty indices in cardiovascular disease.

Author	Frailty Index	Parameters	Categories	Healthcare System	Outcomes
Alonso Salinas et al.[33]	SHARE-FI	Self-perceived fatigue, appetite, lack of energy or slowness, physical activity and handgrip strength measurement	'frail', 'pre-frail' and 'non-frail'.	Four tertiary care Hospitals	Primary endpoint: combination of in-hospital death or non-fatal myocardial (re)infarction. Secondary endpoints included the assessment of individual rates of (re)infarction, mortality, stroke, major bleeding and the combination of in-hospital death, (re)infarction and mortality.
Heaton et al.[34]	Gilbert's Hospital Score	ICD-10 codes and weights used in calculating the frailty score	Low (<5), intermediate (5–15), and high (>15)	NRD analysis	Readmission rates, PCI implementation, healthcare utilization.
Sohn et al.[41]	FI-L	Proportion of 32 variables based on blood and urine tests and the blood pressure and pulse rate	Continuous variable; high score indicated more frailty	Single institution	Outcomes were mortality, aortic valve-related events (AVREs).
Duchnowski et al.[43]	FRAIL scale	Fatigue, resistance, aerobics, illness or loss of weight indicated the presence of a frailty.	Presence of 3/5 indicated frailty	Single institution	Short-term prognosis, post-operative mortality

debated widely given the many scales that have been used globally, for example, the FI scale or CFI scale.[50,53–55]

6. Frailty and COVID-19 pandemic

Frailty was also associated with negative outcomes in COVID-19 patients. In a study based in Sweden, frailty was assessed using a 48-item electronic Frailty Index (eFI), the Clinical Frailty Scale, and the Hospital Frailty Risk Score, while comorbidity was measured with the Charlson Comorbidity Index.[56] The eFI was significantly associated with higher risks of in-hospital mortality, 30-day mortality, 6-month mortality, and longer hospital stays, independent of age and sex.[56] In another study based in the UK, frailty was assessed by specialist COVID-19 teams using the Clinical Frailty Scale (CFS), categorizing patients based on their scores: fit (CFS 1–2), vulnerable (CFS 3–4), showing initial signs of frailty (CFS 5–6), and severe or very severe frailty (CFS 7–9).[57] Compared to those with a CFS score of 1–2, patients with higher CFS scores had increased hazard ratios for time from hospital admission to death and increased odds ratios for day-7 mortality, indicating a stronger association with frailty severity.[57]

7. Future interventions

It is important to determine the utility of these indices in both short and long-term using similar measures. While frailty indices are widely used and applicable in concomitant syndromes of dementia and infections, the role of such indices in cardiovascular disease and cancer has not been extensively studied. Specific measures for each of these conditions should be assessed taking into account confounding factors in order to better assess poor prognostic outcomes including mortality, readmission rates and complications. As discussed above, these frailty indices can also be used to screen population into a high and low-risk cohort so that targeted approaches can be used. Frailty indices have been used on multiple levels. However, the common use is in tertiary care centers and university-associated healthcare institutions suggesting that most of the resource allocation for frail patients is primarily in these centers and a more homogeneous resource allocation is warranted.

8. Conclusions

In conclusion, this comprehensive review underscores the pivotal role of frailty indices in predicting outcomes across a spectrum of health conditions, including infections, cancer,

cardiovascular disease, and dementia. The evidence presented highlights the versatility of frailty assessments in anticipating complications, mortality, and long-term consequences in various patient populations. As the aging population grows and healthcare systems face increasing challenges, understanding and leveraging frailty indices become crucial for tailored interventions and optimized care. However, the review also emphasizes the need for future research to delve deeper into the specific nuances of frailty in cardiovascular diseases and cancer, ensuring a better understanding of its impact and applicability. Overall, this research about frailty indices contributes valuable insights for healthcare professionals, guiding them in enhancing patient care and outcomes across diverse health conditions.

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