

**Clinical Vignette**

An 81-year-old female falls at home, sustaining three rib fractures and a humerus fracture. She is awake and neurologically intact but having pain and dyspnea. Her family reports two falls in the recent past, neither requiring hospitalization. She has hypertension and diabetes and has had a prior hip replacement. She uses a beta blocker, long- and short-acting insulin, and a diuretic. Her family reports forgetfulness, anorexia, and 10-pound weight loss in the last 6 months and less interest in traveling outside the home. She's admitted to the ICU where her oxygenation and urine output are marginal. She is assessed by physical and occupational therapy and found to have a Barthel index of 35/100 (indicating 65 % impairment of activities of daily living (ADLs) performance) and a trauma-specific frailty index of .48 (indicating high risk for discharge to a sub-acute nursing facility). A family meeting is held within 1 day of ICU admission to establish goals of care.

**Key Points**

1. Frailty is a syndrome of fatigue, loss of strength and weight, decreased physical activity, and exhaustion and is increasing in prevalence.
2. Frailty can and should be measured.
3. Objective frailty measures can be used to predict outcome and guide therapy.
4. Frailty may be modifiable.

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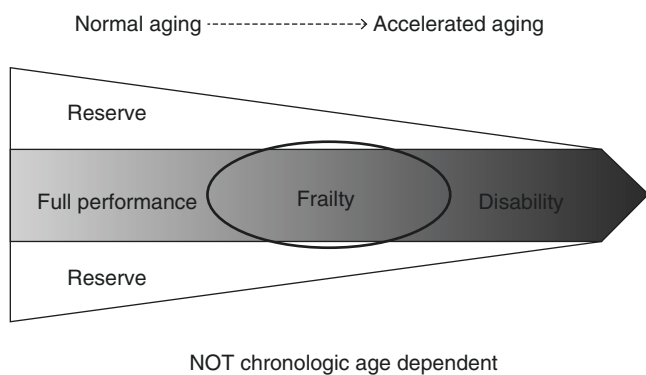
**Introduction**

Debilitation is a functional impairment that can contribute to or result from acute and/or critical illness. Debilitation is sometimes used interchangeably with frailty, which is a progressive decline in performance that often coincides with aging plus chronic disease, ultimately placing individuals at greater vulnerability to acute illness, injury, disease, and disability.

Frailty is increasing in prevalence as the world population ages. Various tools can measure frailty and debilitation and be used in triage, risk stratification, goal setting, resource allocation, targeting interventions, and predicting recovery and survival [1]. Frailty assessment is recommended routinely in geriatric patients because frailty is more specific than chronologic age in predicting complications and resource utilization [2]. Frailty assessment should also be a component of routine health maintenance and part of any preoperative assessment in older patients [3]. Trauma and critical care providers are faced with the challenge of assessing frailty after a patient is admitted for an acute injury or illness when they are not at their functional baseline.

**Definition**

A 2013 consensus conference concluded that there are four fundamental principles of physical frailty [4]: (1) frailty is a syndrome; (2) frailty can be prevented and treated; (3) simple screening tools exist; and (4) all persons age 70 years and older should be screened. Frailty is not a moment in time or a threshold that patients cross but rather a gradual progression that increasingly limits physiologic reserve. Frailty is not related to aging alone but rather results from biologic aging influenced by environmental factors including nutrition, exercise, social support, and healthcare, all placed in the context of acute and chronic illness and overlaid by psychological and emotional health and even personality [5] (see Fig. 10.1).



**Fig. 10.1** The aging continuum and development of frailty [5]

## Diagnosing and Measuring Frailty

Frailty may be measured in many ways. Not every measure of frailty is appropriate for every patient because all variables are not attainable in every patient. At least a dozen frailty measures are relevant to trauma or ICU patients and hold some validity at present (Table 10.1).

Dr. Linda Fried first described frailty as a unique phenotype in 2001 [6]. Fried's frailty phenotype is distinct from either comorbidity or disability and is characterized by three of the following five findings: fatigue, diminution of strength, weight loss (>10 pounds in last year), decreased physical activity, and exhaustion. This definition is now widely accepted, and tallying the components constitutes one of the longest-standing and simplest frailty measures: not frail (score 0 components), pre-frail (1–2 components), and frail (3–5 components) [7]. Fried's criteria correlate with social, psychological, and physical function [8]. Fried score and other tools have been used to predict death and disability in comorbid outpatients and also major adverse cardiac and cardiovascular events in older patients undergoing transcatheter or open cardiovascular procedures [9]. Predictive value of Fried criteria in ICU patients has not been established [10].

Frailty index (FI) is the most studied of all frailty measures. Described in 2001 by Minitski et al., from Montreal, FI was developed using 92 items from the Canadian Study of Health and Aging [11] and remains an important frailty assessment and a validation benchmark for novel frailty measurement tools. FI uses a list of dichotomous and ordinal values expressed over a denominator. If only the dichotomous variables of FI are used (excluding the ordinal variables which grade debilitation on a scale), FI is easier to calculate and maintains high predictive value for mortality, as proven in several large population-based databases [12]. FI and Fried criteria are used frequently in clinical practice and have been expanded upon and modified by many with the resulting tools often being referred to as “modified frailty index” and “modified Fried criteria.”

Necessity for easily reproducible, reliable predictors of specific outcomes in specific populations has led to the development of novel frailty assessment tools. Joseph et al. have modified the FI to a shorter, 15-variable trauma-specific FI (TSFI) that reliably predicts unfavorable discharge (discharge to a subacute nursing facility) [13]. The Trauma Quality Improvement Program (TQIP) Geriatric Trauma Management Guidelines recommend a simple test such as the Short Simple Screening Test for Functional Assessment, which, if positive, can then be followed by a more detailed evaluation for functional impairment [14].

Long before Linda Fried's description of the frailty phenotype, the timed “get up and go” test was described by Mathias et al. as an assessment of balance [15]. Also called the “timed up and go” test or TUG, this test is performed by recording the time in seconds required to rise from an arm chair, walk to a line 3 m away, return, and sit again. TUG correlates well with the Berg Balance Scale which measures fall risk and the Barthel index which measures ADL [16, 17]. The TUG has been modified (m-TUG) and expanded (ETUG) and the novel versions evaluated systematically, but these modifications may not significantly change the original TUG's utility for the geriatric ICU/trauma population [18].

The Berg Balance Scale (BBS) is a well-studied and reliable assessment of functional status that focuses on standing from a sitting position, stationary standing, and transfers. BBS cannot be easily applied in patients with limited lower-extremity weight bearing and is therefore most valuable in monitoring progress during rehabilitation [19].

Gait speed can be assessed at a health maintenance visit, preoperatively, or in ambulatory hospitalized patients, in which case it can be used in planning transition of care. Pamoukdjian performed a systematic review of gait speed, both by itself and as a component of the TUG, and found a gait speed of less than 1 m/s over a 4-m distance to be a predictor of early death, disability, falls, and institutionalization [20].

The British Geriatric Society (BGS) has recommended that frailty be assessed in older patients whenever they encounter community health or social service providers and that simple tools like gait speed (<0.8 m/s) and the TUG test (>10 s) be used as indicators [21]. In its recommendations, the BGS suggests that if signs of frailty are identified, they should prompt discussion with patients and families about frailty, direct attention to medical illnesses that could be treated, and suggest those frailty signs serve as a basis for physical conditioning. Such an approach would be ideal prior to major elective surgery, especially in patients who are likely to require admission to the ICU postoperatively.

The Short Physical Performance Battery (SPPB) can be used in community and in acute settings. SPPB assesses

**Table 10.1** Current frailty measures relevant to trauma

Test [Reference]	Measured end-point	Key aspects
Fried score [8, 10]	Death and disability	Range 1–5, robust/pre-frail/frail
Frailty index (FI) [11, 76]	Mortality, disposition	Range 0–1, 40 possible variables
Trauma-specific frailty index (TSFI) [13]	Discharge disposition	Range 0–1, 15 possible variables
Short simple screening test for functional assessment [14]	Risk for functional limitation of activities of daily living (ADL)	4 questions regarding ADL
Timed “Up & Go” (TUG) [15–17]	Balance; falls risk; correlates with ADL	3-m walk, sitting to sitting
Berg Balance Scale [19]	Balance, standing, transfers	Range 0–56, balance and imbalance
Barthel index [60]	ADL	0–100 scale, ADL
Gait speed [20]	Early death, disability, falls, hospitalization	5 m, $\geq 6$ s indicates frailty
Short Physical Performance Battery (SPPB) [22]	Falls, functional dependence, Fried criteria, FI	Range 0–12, functional performance, primary lower extremities
Vulnerable Elders Survey [24]	Complications and death after trauma	Range 1–10, self-report
Grip strength [26]	Physical function, sarcopenia	Continual, performance test
Functional independence measure (FIM) [27]	Functional outcome	7-point scale, functional independence
Score Hospitalier d’Evaluation du Risque de Perte d’Autonomie (SHERPA) [29]	Post-discharge functional status	5 variables: age, ADL performance, prior falls, self-rated health, and cognitive impairment
Assessing Dementia 8 Screening Interview (AD8) [31]	Driving errors	Range 0–8, cognition, screen for Alzheimer’s disease
Katz activity of daily living survey/ Katz-6/Katz-15 [32]	Unfavorable health outcomes	Range 0–6, ADL
Short Form 36 (SF-36) [34]	Postoperative complications	36-item, self-report health survey
Life Space Assessment [25]	Community mobility, decreased score coincides with falls	Range 0–120, life space mobility, independence, and frequency
Charlson index [36, 37]	Functional recovery at 1 year; mortality	17 categories of comorbidity
Albumin [39, 40]	Intubation, pneumonia, institutionalization	Serum
Sarcopenia [41, 77]	ICU length of stay, mortality, ventilator days	Multiple methods: imaging, bio-impedance, anthropometrics, physical function

three parameters of physical function: (1) static balance, (2) gait speed, and (3) standing from a chair. Each category scores 0–4 with a composite score of 12. SPPB is a valid, reliable predictor of falls and functional dependence and has been correlated with frailty index and the modified Fried criteria [22, 23].

The Vulnerable Elders Survey-13 (VES-13) predicts complications and death in geriatric trauma patients [24]. The Life Space Assessment (LSA) developed at the University of Alabama at Birmingham assesses mobility over the preceding 4 weeks including mobility away from home, frequency of mobility, and level of independence from assistance or assistive devices. Decreasing LSA coincides with falls, but the LSA’s predictive value in hospitalized patients has not been validated [25].

Handgrip strength is commonly used to assess weakness, which is an important adverse effect of hospitalization and one of the Fried criteria for frailty. Grip strength alone predicts ICU paresis and also correlates with Physical Function Intensive Care Test (PFIT) and 6-min walk test (6MWT), though the exact clinical utility of PFIT and 6MWT themselves is uncertain [26]. PFIT, grip strength, and 6MWT can, however, identify trends and thus may be

used to measure effect of interventions in the ICU targeted at reducing the harmful effects of ICU stay on functional status.

Functional independence measure (FIM) is a well-validated measure of overall physical function, social and psychological function, and ADL. FIM predicts post-discharge functional status, is worse at discharge in patients with a lower admission FIM score, and correlates with frailty index [27]. The Chelsea Critical Care Assessment Tool has also been assessed in the ICU population and been found to be valid in measuring changes in performance among ICU patients, but its relevance specifically in geriatric and frail ICU patients has yet to be established [28].

The Score Hospitalier d’Evaluation du Risque de Perte d’Autonomie (SHERPA) uses five variables: age, ADL performance, prior falls, self-rated health, and cognitive impairment, to predict functional status after hospital discharge. The SHERPA’s utility above other scoring systems remains unproven [29]. Contrary to what one might think, dementia alone may not be a reliable predictor of outcome among ICU patients [30]. However, the Assessing Dementia 8 (AD8), a commonly used screening tool for Alzheimer’s disease, correlates with driving errors so therefore is perhaps

relevant to injury prevention measures on discharge among older drivers [31].

Several assessment tools have been used in the primary care, community health, and preoperative settings but because of complexity may not be applicable to the ICU or acute care environments. The Katz Activity of Daily Living Survey measures ADLs, mobility, and instrumental ADL and has been widely validated for a number of outcome measures. Originally known as the Katz-6, it has now been modified to the Katz-15 which predicts unfavorable overall health outcome [32]. Green et al. combined the Katz activity of daily living survey with serum albumin, grip strength, and gait speed to derive a novel score predicting outcome after transcatheter aortic valve replacement (TAVR) [33]. The SF-36 correlates with frailty index and postoperative complications [34]. The cognitive mini exam (Mini-Cog) has also been used to predict outcome [35].

Some assessment tools for frailty can be performed without physically evaluating the patient. The Charlson comorbidity score was first reported by Charlson et al. in 1987 and uses diagnosis data from 19 categories to predict long-term outcome, including functional recovery at 1 year in elderly ICU patients [36, 37]. Kim et al. developed a predictive model of poor functional status using claims data. The model offers a high level of discrimination and could be used in epidemiologic studies and in understanding resource use across a healthcare system or population [38]. Laboratory and radiology tests can also be used to assess frailty, guide resource use, and predict prognosis. In one recent study, albumin was used as one component, along with COPD, assisted status, tube thoracostomy, injury severity score, number of rib fractures, and CHF, to comprise a frailty score to predict intubation and pneumonia in elderly patients with rib fractures [39]. Albumin has long been used as a predictor of outcome in surgical patients and can predict institutionalization at discharge after surgery among geriatric patients though not as reliably as TUG and overall functional dependence [40]. CRP, IL-6, TNF- $\alpha$ , D-dimer, albumin, IL-1, 25(OH)D, and low cholesterol have all been correlated with frailty and functional decline, but their clinical application is not yet clear [5].

A rapidly expanding body of evidence supports sarcopenia as an ideal objective measure for frailty that can be determined by diagnostic testing. Critical illness and muscle disuse are associated with altered protein synthesis and cell signaling that exacerbates skeletal muscle loss in the acutely and critically ill. The Nutrition and Rehabilitation Investigators Consortium reported sarcopenia to be a reliable indicator of ventilation, ICU stay, and death [41]. Future studies must elucidate the differential roles of preadmission sarcopenia versus sarcopenia as a result of critical illness [42].

## Using Debility in Management

Frailty assessment should help guide treatment. Surrogate responses must sometimes be used to assess physical function and frailty because the patient cannot participate completely or at all [43]. Maxwell et al. reported good agreement between patient and proxy on the VES-13, the modified Barthel index, and the Life Space Assessment [43]. Providers should assure that the frailty assessment tool they are using has been validated in the population to which it is being applied and should consider whether surrogate responses are valid.

Frailty assessment may require incorporating providers with geriatric training and experience into the trauma team, but this is not a requirement. Composition of the geriatric trauma and critical care team is a matter of great interest among providers and these compositions are changing. More than half of survey respondents who were members of the American Association for the Surgery of Trauma (AAST) reported that geriatric-specific personnel and resources are rarely or never used at their institution [44]. However, almost half of these respondents felt that further research regarding the “use of gerontologist, geriatric teams, or geriatric centers in the management of trauma patients” should be a high priority.

The American College of Surgeons Trauma Quality Improvement Program Geriatric Management Guidelines and many authors recommend proactive geriatric consultation. Seventy percent of the respondents in the AAST survey report that skilled nursing facilities (SNFs) have become the most common discharge destination, but few agree that SNFs are the best disposition. Geriatric consultation can reduce the risk of discharge to a long-term acute care facility and can also reduce the number of episodes of delirium, decrease in-hospital falls, shorten length of stay, and improve functional recovery [45].

Geriatric Rehabilitation Units staffed by a multidisciplinary team, usually led by a physiatrist, can coordinate care of the elderly patient’s chronic health issues as well as their environmental factors. Regardless of whether the trauma/ICU team includes a geriatrician, multidisciplinary care is essential in geriatric trauma. The British Geriatric Society recommends a holistic medical review such as a comprehensive geriatric assessment (CGA) for the management of frailty that will diagnose medical illnesses, optimize treatment, apply evidence-based medication review checklists, include discussion with older people and caregivers to include defining the impact of illness, and then create an individualized care and support plan [21]. TQIP guidelines also recommend such CGAs for geriatric trauma patients with certain risk factors. The CGA, which should include a frailty assessment, may then serve as a basis for patient/

family meeting regarding care plans and prognoses. Interventions should be targeted at optimizing physiology, minimizing complications, maintaining functional status, and returning the geriatric patient to their preadmission functional level and environment as often and as quickly as possible. For example, early physical therapy/occupational therapy in the ICU conveys better functional outcome when discharged, shorter periods of delirium, and more ventilator-free days [46].

Frailty assessment can be used to influence end-of-life care and palliative care decisions. Frailty index has been used to predict survival past 30 days in a specialized geriatric ICU. Every 1 % increase in FI correlates with an 11 % increase in mortality. In that study, no patient with FI > 0.46 survived past 90 days [47].

## Outpatient Care

Frailty assessment and the CGA can guide the transition of care. The “Continuum of Care for Frail Older People” intervention study by Eklund et al. showed that after hospitalization, nurses with geriatric training who followed frail patients from the emergency room to their home with a multi-professional team were able to double the odds of improved ADL independence [48]. Watkins reported a social worker transitional care model for at-risk elderly patients that performed a home visit within 74 h of discharge to assess the home environment, aided in medical management, and made referrals for other services with follow-up phone calls and visits [49]. This model decreased hospital readmissions by 61 % and showed significantly improved quality-of-life scores [49].

Returning patients to the community after discharge requires that multidisciplinary care continue even as an outpatient. Beland et al. assessed all integrated systems of care for the frail elderly and found that essential to each model is coordination of resources across care providers to ensure continuity of care [50]. Unfortunately, interventions and care models with solid evidence of efficacy are lacking. De Stampa showed that the Coordinating Care for Older People (COPA) model, which integrated primary care and intensive community case management for very frail elderly patients, was able to reduce unplanned hospitalizations, but though the group experienced less depression and dyspnea, planned hospital readmissions increased, so the total hospital admissions did not change [51]. Metzeltin studied the interdisciplinary primary care approach and its effect on disability reduction in the community-dwelling frail elderly patients [52]. Twelve general practices were randomized and delivered a multidimensional assessment of its patients and then a tailor-made treatment plan with regular evaluation and follow-up.

Unfortunately, there was no evidence of effectiveness as measured by disability at 24 months [52]. The optimal transition and outpatient care model for frail injured elderly remains to be determined.

## Preoperative Optimization

Preoperative comprehensive geriatric assessment optimizes functional status and improves outcome by better management of comorbidity and reducing frailty [53]. Treatment of depression and alcohol abuse and dependence has also been shown to improve outcomes. Preoperative physical activity may positively impact several components associated with frailty syndrome including sarcopenia, functional impairment, cognitive performance, and depression [54].

In order to reduce frailty in an elderly patient, multiple facets of physical function should be assessed including strength, range of motion, mobility, endurance, and flexibility. A physical therapy program should include an exercise plan, necessary assistive devices, and environmental modifications. Innovative interventions show promise including improving physical health of frail elderly patients prior to elective hip surgery through a preoperative home-based physical therapy program [55]. Hoogeboom reported that a preoperative home exercise program was well tolerated and demonstrated improved preoperative functional status but that the improvements were not sustained post-operatively [56]. Home exercise programs have also increased walking speed and scores on the Activity Measure for Post Acute Care tool over a 12-month intervention among 241 community-dwelling older people in Australia [57]. Tai Chi exercises may be even more effective than conventional physical therapy. Tousignant et al. randomized community-dwelling frail elderly to 15 weeks of either therapy, and while both reduced fall incidence, Tai Chi was more protective [58].

Functional circuit training programs including functional balance and lower-body strength-based exercises over 12 weeks improved self-reported fear of falling and physical function and the effects were sustained at 36-week follow-up [59]. In a prior study by this group, functional circuit training in a randomized controlled trial was also associated with significant improvements in function and reduced physical frailty among frail older adults [60]. In 2014, this group performed a meta-analysis of physical exercise intervention studies and found improved normal gait speed, fast gait speed, and the Short Physical Performance Battery when compared to control groups without exercise intervention. However, other parameters were not affected, such as balance, endurance, or ADL functional mobility [61]. Chou et al. performed a meta-analysis in 2012 which demonstrated

that exercise groups increased their gait speed and Berg Balance Scale (BBS) score and improved ADL performance compared to control groups, but that exercise had no effect on timed up and go test and quality of life [62]. So it appears that the answer to whether exercise improves functional status depends very much on the type of exercise and the parameter being tested.

Sarcopenia undoubtedly contributes to frailty, but protein supplementation can improve muscle mass and physical performance [63]. Sixty-five frail elderly subjects were randomized to daily protein or placebo supplements. Skeletal muscle mass did not change in either group, but muscle strength increased in both. Physical performance was significantly increased in the protein supplementation group [63]. In a second study from the same group, protein supplementation combined with a progressive resistance-type exercise training program increased lean body mass but did not increase strength or physical performance compared to the randomized control group of exercise training alone, so the precise role of protein supplementation is still under investigation [64].

Decreased testosterone in aging men may contribute to loss of muscle mass and strength leading to the development of frailty. Testosterone replacement is a potential treatment of frailty proposed by O'Connell et al. in 2011 [65]. This group found that traditional androgen therapy and selective androgen receptor modulators (SARMs) may have similar potent anabolic effects on skeletal muscle mass and function [66]. Marzetti et al. demonstrated that muscle integrity and improved physical performance in late life can be achieved by downregulating myocyte apoptosis through a combination of calorie restriction, exercise training, hormonal supplementation, drugs (angiotensin-converting enzyme inhibitors, acetaminophen, antimyostatin antibodies), nutraceuticals, or genetic interventions (PGC-1 $\alpha$  overexpression) [67]. Optimal medical therapy for frailty remains unclear. For example, though the majority of elderly patients with heart failure have frailty and management of comorbidity like hypertension may help prevent frailty, aggressive management may have negative consequences for those already frail [68, 69].

## Future Research

Research in geriatric trauma and critical care is highly relevant given the world's aging population, but enrollment and retention in frailty research can be difficult. Lack of perceived benefit, difficulty with subject retention, distrust of investigators, and poor mobility to and from research interventions are just some of the barriers to geriatric trauma research [70]. Fundamentally, a consensus definition is needed for frailty in ICU care [71]. A standard definition for sarcopenia is also needed, including differential effects of preexisting sarcopenia and iatrogenic sarcopenia and their respective treatments

[72]. Improved triage of patients to appropriate centers or care areas would logically follow from these improved definitions of the geriatric trauma population [47].

Members of the AAST identified indicators of frailty as a research need along with optimal post-discharge rehabilitation, fall prevention, and the use of gerontologists or geriatric teams/centers in the management of trauma patients [73]. Predictors of mortality exist, like the frailty index which may reliably predict survival among geriatric ICU patients, and other frailty scoring systems may be similarly or more effective at predicting outcome [47].

Assessment and measurement of frailty at baseline, changes in frailty during the care continuum, and the use of frailty scoring in transition of care will remain important as will the use of frailty scoring as a threshold for palliative care consultation. Frailty education does appear effective at improving discrimination, and further research into frailty assessment education is warranted as centers train teams to better care for geriatric trauma patients [74]. Whether frailty can be modified by physical training among hospitalized patients is not known. Mobility programs and other interventions must be studied, like the SOMS study, which was conducted in Germany and Italy with results expected soon [75].

## References

1. Milte R, Crotty M. Musculoskeletal health, frailty and functional decline. *Best Pract Res Clin Rheumatol.* 2014;28(3):395–410. doi:10.1016/j.berh.2014.07.005.
2. Joseph B. Superiority of frailty over age in predicting outcomes among geriatric trauma patients: a prospective analysis. *JAMA Surg.* 2014;149(8):766–72. doi:10.1001/jamasurg.2014.296.
3. Amrock LG, Deiner S. The implication of frailty on preoperative risk assessment. *Curr Opin Anaesthesiol.* 2014;27(3):330–5. doi:10.1097/ACO.000000000000065.
4. Morley JE. Dementia with Lewy bodies: a common condition in nursing homes? *J Am Med Dir Assoc.* 2013;14(10):713–4. doi:10.1016/j.jamda.2013.07.009.
5. Hubbard JM, Jatoi A. Incorporating biomarkers of frailty and senescence in cancer therapeutic trials. *J Gerontol A Biol Sci Med Sci.* 2015;70(6):722–8. doi:10.1093/gerona/glu046.
6. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001;56(1):M146–56. doi:10.1093/gerona/56.3.M146.
7. Theou O, Cann L, Blodgett J, Wallace LM, Brothers TD, Rockwood K. Modifications to the frailty phenotype criteria: systematic review of the current literature and investigation of 262 frailty phenotypes in the Survey of Health, Ageing, and Retirement in Europe. *Ageing Res Rev.* 2015;21:78–94. doi:10.1016/j.arr.2015.04.001.
8. Op het Veld LP, van Rossum E, Kempen GI, de Vet HC, Hajema K, Beurskens AJ. Fried phenotype of frailty: cross-sectional comparison of three frailty stages on various health domains. *BMC Geriatr.* 2015;15:77. doi:10.1186/s12877-015-0078-0.
9. Sepehri A, Beggs T, Hassan A, Rigatto C, Shaw-Daigle C, Tangri N, et al. The impact of frailty on outcomes after cardiac surgery: a systematic review. *J Thorac Cardiovasc Surg.* 2014;148(6):3110–7. doi:10.1016/j.jtcvs.2014.07.087.

10. Frisoli Jr A, Ingham SJ, Paes AT, Tinoco E, Greco A, Zanata N, et al. Frailty predictors and outcomes among older patients with cardiovascular disease: data from Fragicor. *Arch Gerontol Geriatr*. 2015;61(1):1–7. doi:[10.1016/j.archger.2015.03.001](https://doi.org/10.1016/j.archger.2015.03.001).
11. Minitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *Scientific World Journal*. 2001;1:323–36. doi:[10.1100/tsw.2001.58](https://doi.org/10.1100/tsw.2001.58).
12. Peña FG, Theou O, Wallace L, Brothers TD, Gill TM, Gahbauer EA, et al. Comparison of alternate scoring variables on the performance of the frailty index. *BMC Geriatr*. 2014;14:25. doi:[10.1186/1471-2318-14-25](https://doi.org/10.1186/1471-2318-14-25).
13. Joseph B, Aziz H, Pandit V, Kulvatunyou N, Hashmi A, Tang A, et al. A three-year prospective study of repeat head computed tomography in patients with traumatic brain injury. *J Am Coll Surg*. 2014;219(1):45–51. doi:[10.1016/j.jamcollsurg.2013.12.062](https://doi.org/10.1016/j.jamcollsurg.2013.12.062).
14. Lachs MS, Feinstein AR, Cooney Jr LM, Drickamer MA, Marottoli RA, Pannill FC, et al. A simple procedure for general screening for functional disability in elderly patients. *Ann Intern Med*. 1990;112(9):699–706. doi:[10.7326/0003-4819-112-9-699](https://doi.org/10.7326/0003-4819-112-9-699).
15. Mathias S, Navak US, Isaacs B. Balance in elderly patients: the “get-up and go” test. *Arch Phys Med Rehabil*. 1986;67(6):387–9.
16. Posiadlo D, Richardson S. The timed “Up & Go”: a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc*. 1991;39(2):142–8. doi:[10.1111/j.1532-5415.1991.tb01616.x](https://doi.org/10.1111/j.1532-5415.1991.tb01616.x).
17. Salgado R, Lord SR, Packer J, Ehrlich F. Factors associated with falling in elderly hospital patients. *Gerontology*. 1994;40(6):325–31.
18. Faria CD, Teixeira-Salmela LF, Nadeau S. Predicting levels of basic functional mobility, as assessed by the Timed “Up and Go” test, for individuals with stroke: discriminant analyses. *Disabil Rehabil*. 2013;35(2):146–52. doi:[10.3109/09638288.2012.690497](https://doi.org/10.3109/09638288.2012.690497).
19. Lee J, Geller AI, Strasser DC. Analytical review: focus on fall screening assessments. *PM R*. 2013;5(7):609–21. doi:[10.1016/j.pmrj.2013.04.001](https://doi.org/10.1016/j.pmrj.2013.04.001).
20. Pamoukdjian F, Paillaud E, Zelek L, Laurent M, Lévy V, Landre T, et al. Measurement of gait speed in older adults to identify complications associated with frailty: a systematic review. *J Geriatr Oncol*. 2015;6(6):484–96. doi:[10.1016/j.jgo.2015.08.006](https://doi.org/10.1016/j.jgo.2015.08.006).
21. Turner G, Clegg A, British Geriatrics Society, Age UK, Royal College of General Practitioners. Best practice guidelines for the management of frailty: a British Geriatrics Society, Age UK and Royal College of General Practitioners report. *Age Ageing*. 2014;43(6):744–7. doi:[10.1093/ageing/afu138](https://doi.org/10.1093/ageing/afu138).
22. Quadri P, Tettamanti M, Bernasconi S, Trento F, Loew F. Lower limb function as predictor of falls and loss of mobility with social repercussions one year after discharge among elderly inpatients. *Aging Clin Exp Res*. 2005;17(2):82–9. doi:[10.1007/BF03324578](https://doi.org/10.1007/BF03324578).
23. Jung P, Pereira MA, Hiebert B, Song X, Rockwood K, Tangri N, et al. The impact of frailty on postoperative delirium in cardiac surgery patients. *J Thorac Cardiovasc Surg*. 2015;149(3):869–75. doi:[10.1016/j.jtcvs.2014.10.118](https://doi.org/10.1016/j.jtcvs.2014.10.118).
24. Min L, Ubhayakar N, Saliba D, Kelley-Quon L, Morley E, Hiatt J, et al. The vulnerable elders survey-13 predicts hospital complications and mortality in older adults with traumatic injury: a pilot study. *J Am Geriatr Soc*. 2011;59(8):1471–6. doi:[10.1111/j.1532-5415.2011.03493.x](https://doi.org/10.1111/j.1532-5415.2011.03493.x).
25. Lo AX, Brown CJ, Sawyer P, Kennedy RE, Allman RM. Life-space mobility declines associated with incident falls and fractures. *J Am Geriatr Soc*. 2014;62(5):919–23. doi:[10.1111/jgs.12787](https://doi.org/10.1111/jgs.12787).
26. Nordon-Craft A, Schenkman M, Edbrooke L, Malone DJ, Moss M, Denehy L. The physical function intensive care test: implementation in survivors of critical illness. *Phys Ther*. 2014;94(10):1499–507. doi:[10.2522/ptj.20130451](https://doi.org/10.2522/ptj.20130451).
27. Kawryshanker S, Raymond W, Ingram K, Inderjeeth CA. Effect of frailty on functional gain, resource utilisation, and discharge destination: an observational prospective study in a GEM Ward. *Curr Gerontol Geriatr Res*. 2014;2014:357857. doi:[10.1155/2014/357857](https://doi.org/10.1155/2014/357857).
28. Corner EJ, Wood H, Englebretsen C, Thomas A, Grant RL, Nikolettou D, et al. The Chelsea critical care physical assessment tool (CPAx): validation of an innovative new tool to measure physical morbidity in the general adult critical care population; an observational proof-of-concept pilot study. *Physiotherapy*. 2013;99(1):33–41. doi:[10.1016/j.physio.2012.01.003](https://doi.org/10.1016/j.physio.2012.01.003).
29. Cornette P, Swine C, Malhomme B, Gillet JB, Meert P, D’Hoore W. Early evaluation of the risk of functional decline following hospitalization of older patients: development of a predictive tool. *Eur J Public Health*. 2006;16(2):203–8. doi:<http://dx.doi.org/10.1093/eurpub/cki054>.
30. Pisani MA, Redlich CA, McNicoll L, Ely EW, Friedkin RJ, Inoué SK. Short-term outcomes in older intensive care unit patients with dementia. *Crit Care Med*. 2005;33(6):1371–6. doi:[10.1097/01.CCM.0000165558.83676.48](https://doi.org/10.1097/01.CCM.0000165558.83676.48).
31. Barco PP, Baum CM, Ott BR, Ice S, Johnson A, Wallendorf M, et al. Driving errors in patients with dementia. *J Am Geriatr Soc*. 2015;63(6):1251–4. doi:[10.1111/jgs.13499](https://doi.org/10.1111/jgs.13499).
32. Laan W, Zuithoff NP, Drubbel I, Bleijenberg N, Numans ME, de Wit NJ, Schuurmans MJ. Validity and reliability of the Katz-15 scale to measure unfavorable health outcomes in community-dwelling older people. *J Nutr Health Aging*. 2014;18(9):848–54. doi:[10.1007/s12603-014-0479-3](https://doi.org/10.1007/s12603-014-0479-3).
33. Green P, Arnold SV, Cohen DJ, Kirtane AJ, Kodali SK, Brown DL, et al. Relation of frailty to outcomes after transcatheter aortic valve replacement (from the PARTNER trial). *Am J Cardiol*. 2015;116(2):264–9. doi:[10.1016/j.amjcard.2015.03.061](https://doi.org/10.1016/j.amjcard.2015.03.061).
34. Saxton A, Velanovich V. Preoperative frailty and quality of life as predictors of postoperative complications. *Ann Surg*. 2011;253(6):1223–9. doi:[10.1097/SLA.0b013e318214bce7](https://doi.org/10.1097/SLA.0b013e318214bce7).
35. Romera L, Orfila F, Segura JM, Ramirez A, Möller M, Fabra ML, et al. Effectiveness of a primary care based multifactorial intervention to improve frailty parameters in the elderly: a randomised clinical trial: rationale and study design. *BMC Geriatr*. 2014;14:125. doi:[10.1186/1471-2318-14-125](https://doi.org/10.1186/1471-2318-14-125).
36. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–83.
37. Heyland DK, Garland A, Bagshaw SM, Cook D, Rockwood K, Stelfox HT, et al. Recovery after critical illness in patients aged 80 years or older: a multi-center prospective observational cohort study. *Intensive Care Med*. 2015;41(11):1911–20. doi:[10.1007/s00134-015-4028-2](https://doi.org/10.1007/s00134-015-4028-2).
38. Kim DH, Schneeweiss S. Measuring frailty using claims data for pharmacoepidemiologic studies of mortality in older adults: evidence and recommendations. *Pharmacoepidemiol Drug Saf*. 2014;23(9):891–901. doi:[10.1002/pds.3674](https://doi.org/10.1002/pds.3674).
39. Gonzalez KW, Ghneim MH, Kang F, Jupiter DC, Davis ML, Regner JL. A pilot single-institution predictive model to guide rib fracture management in elderly patients. *J Trauma Acute Care Surg*. 2015;78(5):970–5. doi:[10.1097/TA.0000000000000619](https://doi.org/10.1097/TA.0000000000000619).
40. Robinson TN, Wallace JI, Wu DS, Wiktor A, Pointer LF, Pfister SM, et al. Accumulated frailty characteristics predict postoperative discharge institutionalization in the geriatric patient. *J Am Coll Surg*. 2011 Jul;213(1):37–42. doi:[10.1016/j.jamcollsurg.2011.01.056](https://doi.org/10.1016/j.jamcollsurg.2011.01.056).
41. Moisey LL, Mourtzakis M, Cotton BA, Premji T, Heyland DK, Wade CE, et al. Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. *Crit Care*. 2013;17(5):R206. doi:[10.1186/cc12901](https://doi.org/10.1186/cc12901).
42. Gordon BS, Kelleher AR, Kimball SR. Regulation of muscle protein synthesis and the effects of catabolic states. *Int J Biochem Cell Biol*. 2013;45(10):2147–57. doi:[10.1016/j.biocel.2013.05.039](https://doi.org/10.1016/j.biocel.2013.05.039).
43. Maxwell CA, Dietrich MS, Minnick AF, Mion LC. Preinjury physical function and frailty in injured older adults: self- versus proxy responses. *J Am Geriatr Soc*. 2015;63(7):1443–7. doi:[10.1111/jgs.13486](https://doi.org/10.1111/jgs.13486).

44. Kozar RA, Arbabi S, Stein DM, Shackford SR, Barraco RD, Biff WL, et al. Injury in the aged: Geriatric trauma care at the crossroads. *J Trauma Acute Care Surg.* 2015;78(6):1197–209. doi:[10.1097/TA.0000000000000656](https://doi.org/10.1097/TA.0000000000000656).
45. Tillou A, Kelley-Quon L, Burruss S, Morley E, Cryer H, Cohen M, Min L. Long-term postinjury functional recovery: outcomes of geriatric consultation. *JAMA Surg.* 2014;149(1):83–9. doi:[10.1001/jamasurg.2013.4244](https://doi.org/10.1001/jamasurg.2013.4244).
46. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, Spears L, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet.* 2009;373(9678):1874–82. doi:[10.1016/S0140-6736\(09\)60658-9](https://doi.org/10.1016/S0140-6736(09)60658-9).
47. Zeng A, Song X, Dong J, Mitnitski A, Liu J, Guo Z, et al. Mortality in relation to frailty in patients admitted to a specialized geriatric intensive care unit. *J Gerontol A Biol Sci Med Sci.* 2015;70(12):1586–94. doi:[10.1093/gerona/glv084](https://doi.org/10.1093/gerona/glv084).
48. Eklund K, Wilhelmson K, Gustafsson H, Landahl S, Dahlin-Ivanoff S. One-year outcome of frailty indicators and activities of daily living following the randomised controlled trial: “Continuum of care for frail older people”. *BMC Geriatr.* 2013;13:76. doi:[10.1186/1471-2318-13-76](https://doi.org/10.1186/1471-2318-13-76).
49. Watkins L, Hall C, Kring D. Hospital to home: a transition program for frail older adults. *Prof Case Manag.* 2012;17(3):117–23. doi:[10.1097/NCM.0b013e318243d6a7](https://doi.org/10.1097/NCM.0b013e318243d6a7).
50. Béland F, Hollander MJ. Integrated models of care delivery for the frail elderly: international perspectives. *Gac Sanit.* 2011;25(Suppl 2):138–46. doi:[10.1016/j.gaceta.2011.09.003](https://doi.org/10.1016/j.gaceta.2011.09.003).
51. de Stampa M, Vedel I, Buyck JF, Lapointe L, Bergman H, Beland F, et al. Impact on hospital admissions of an integrated primary care model for very frail elderly patients. *Arch Gerontol Geriatr.* 2014;58(3):350–5. doi:[10.1016/j.archger.2014.01.005](https://doi.org/10.1016/j.archger.2014.01.005).
52. Metzeltin SF, van Rossum E, de Witte LP, Ambergen AW, Hobma SO, Sipers W, et al. Effectiveness of interdisciplinary primary care approach to reduce disability in community dwelling frail older people: cluster randomised controlled trial. *BMJ.* 2013;347:f5264. doi:[10.1136/bmj.f5264](https://doi.org/10.1136/bmj.f5264).
53. Bettelli G. Preoperative evaluation in geriatric surgery: comorbidity, functional status and pharmacological history. *Minerva Anesthesiol.* 2011;77(6):637–46.
54. Landi F, Abbatecola AM, Provinciali M, Corsonello A, Bustacchini S, Manigrasso L, et al. Moving against frailty: does physical activity matter? *Biogerontology.* 2010;11(5):537–45. doi:[10.1007/s10522-010-9296-1](https://doi.org/10.1007/s10522-010-9296-1).
55. Oosting E, Jans MP, Dronkers JJ, Naber RH, Dronkers-Landman CM, Appelman-de Vries SM, et al. Preoperative home-based physical therapy versus usual care to improve functional health of frail older adults scheduled for elective total hip arthroplasty: a pilot randomized controlled trial. *Arch Phys Med Rehabil.* 2012;93(4):610–6. doi:[10.1016/j.apmr.2011.11.006](https://doi.org/10.1016/j.apmr.2011.11.006).
56. Hoozeboom TJ, Dronkers JJ, Hulzebos EH, van Meeteren NL. Merits of exercise therapy before and after major surgery. *Curr Opin Anaesthesiol.* 2014;27(2):161–6. doi:[10.1097/ACO.0000000000000062](https://doi.org/10.1097/ACO.0000000000000062).
57. Fairhall N, Sherrington C, Kurrle SE, Lord SR, Lockwood K, Cameron ID. Effect of a multifactorial interdisciplinary intervention on mobility-related disability in frail older people: randomised controlled trial. *BMC Med.* 2012;10:120. doi:[10.1186/1741-7015-10-120](https://doi.org/10.1186/1741-7015-10-120).
58. Tousignant M, Corriveau H, Roy PM, Desrosiers J, Dubuc N, Hébert R. Efficacy of supervised Tai Chi exercises versus conventional physical therapy exercises in fall prevention for frail older adults: a randomized controlled trial. *Disabil Rehabil.* 2013;35(17):1429–35. doi:[10.3109/09638288.2012.737084](https://doi.org/10.3109/09638288.2012.737084).
59. Giné-Garriga M, Guerra M, Unnithan VB. The effect of functional circuit training on self-reported fear of falling and health status in a group of physically frail older individuals: a randomized controlled trial. *Aging Clin Exp Res.* 2013;25(3):329–36. doi:[10.1007/s40520-013-0048-3](https://doi.org/10.1007/s40520-013-0048-3).
60. Giné-Garriga M, Guerra M, Pagès E, Manini TM, Jiménez R, Unnithan VB. The effect of functional circuit training on physical frailty in frail older adults: a randomized controlled trial. *J Aging Phys Act.* 2010;18(4):401–24.
61. Giné-Garriga M, Roqué-Fíguls M, Coll-Planas L, Sitjà-Rabert M, Salvà A. Physical exercise interventions for improving performance-based measures of physical function in community-dwelling, frail older adults: a systematic review and meta-analysis. *Arch Phys Med Rehabil.* 2014;95(4):753–769.e3. doi:[10.1016/j.apmr.2013.11.007](https://doi.org/10.1016/j.apmr.2013.11.007).
62. Chou CH, Hwang CL, Wu YT. Effect of exercise on physical function, daily living activities, and quality of life in the frail older adults: a meta-analysis. *Arch Phys Med Rehabil.* 2012;93(2):237–44. doi:[10.1016/j.apmr.2011.08.042](https://doi.org/10.1016/j.apmr.2011.08.042).
63. Tieland M, van de Rest O, Dirks ML, van der Zwaluw N, Mensink M, van Loon LJ, de Groot LC. Protein supplementation improves physical performance in frail elderly people: a randomized, double-blind, placebo-controlled trial. *J Am Med Dir Assoc.* 2012;13(8):720–6. doi:[10.1016/j.jamda.2012.07.005](https://doi.org/10.1016/j.jamda.2012.07.005).
64. Tieland M, Dirks ML, van der Zwaluw N, Verdijk LB, van de Rest O, de Groot LC, van Loon LJ. Protein supplementation increases muscle mass gain during prolonged resistance-type exercise training in frail elderly people: a randomized, double-blind, placebo-controlled trial. *J Am Med Dir Assoc.* 2012;13(8):713–9. doi:[10.1016/j.jamda.2012.05.020](https://doi.org/10.1016/j.jamda.2012.05.020).
65. O’Connell MD, Ravindrarajah R, Tajar A, Wu FC. Low testosterone in ageing men: a modifiable risk factor for frailty? *Trends Endocrinol Metab.* 2011;22(12):491–8. doi:[10.1016/j.tem.2011.08.003](https://doi.org/10.1016/j.tem.2011.08.003).
66. O’Connell MD, Wu FC. Androgen effects on skeletal muscle: implications for the development and management of frailty. *Asian J Androl.* 2014;16(2):203–12. doi:[10.4103/1008-682X.122581](https://doi.org/10.4103/1008-682X.122581).
67. Marzetti E, Calvani R, Bernabei R, Leeuwenburgh C. Apoptosis in skeletal myocytes: a potential target for interventions against sarcopenia and physical frailty - a mini-review. *Gerontology.* 2012;58(2):99–106. doi:[10.1159/000330064](https://doi.org/10.1159/000330064).
68. Murad K, Kitzman DW. Frailty and multiple comorbidities in the elderly patient with heart failure: implications for management. *Heart Fail Rev.* 2012;17(4-5):581–8. doi:[10.1007/s10741-011-9258-y](https://doi.org/10.1007/s10741-011-9258-y).
69. Jeffery CA, Shum DW, Hubbard RE. Emerging drug therapies for frailty. *Maturitas.* 2013;74(1):21–5. doi:[10.1016/j.maturitas.2012.10.010](https://doi.org/10.1016/j.maturitas.2012.10.010).
70. Provencher V, Mortenson WB, Tanguay-Garneau L, Bélanger K, Dagenais M. Challenges and strategies pertaining to recruitment and retention of frail elderly in research studies: a systematic review. *Arch Gerontol Geriatr.* 2014;59(1):18–24. doi:[10.1016/j.archger.2014.03.006](https://doi.org/10.1016/j.archger.2014.03.006).
71. Rothman MD, Leo-Summers L, Gill TM. Prognostic significance of potential frailty criteria. *J Am Geriatr Soc.* 2008;56(12):2211–6. doi:[10.1111/j.1532-5415.2008.02008.x](https://doi.org/10.1111/j.1532-5415.2008.02008.x).
72. Edwards MH, Buehring B. Novel approaches to the diagnosis of sarcopenia. *J Clin Densitom.* 2015;18(4):472–7. doi:[10.1016/j.jocd.2015.04.010](https://doi.org/10.1016/j.jocd.2015.04.010).
73. Davis JW, Sise MJ, Albrecht R, Kuhls DA. American Association for the Surgery of Trauma Prevention Committee topical updates: getting started, fall prevention, domestic violence, and suicide. *J Trauma.* 2011;70(4):996–1001. doi:[10.1097/TA.0b013e318210894e](https://doi.org/10.1097/TA.0b013e318210894e).
74. Ferguson MK, Thompson K, Huisingh-Scheetz M, Farnan J, Hemmerich J, Acevedo J, et al. The impact of a frailty education module on surgical resident estimates of lobectomy risk. *Ann Thorac Surg.* 2015;100(1):235–41. doi:[10.1016/j.athoracsur.2015.03.016](https://doi.org/10.1016/j.athoracsur.2015.03.016).
75. Meyer MJ, Stanislaus AB, Lee J, Waak K, Ryan C, Saxena R, et al. Surgical Intensive Care Unit Optimal Mobilisation Score (SOMS) trial: a protocol for an international, multicentre, randomised controlled trial focused on goal-directed early mobilisation of surgical



- ICU patients. *BMJ Open*. 2013;3(8):e003262. doi:[10.1136/bmjopen-2013-003262](https://doi.org/10.1136/bmjopen-2013-003262).
76. Joseph B, Pandit V, Zangbar B, Kulvatunyou N, Tang A, O'Keeffe T, et al. Validating trauma-specific frailty index for geriatric trauma patients: a prospective analysis. *J Am Coll Surg*. 2014;219(1):10–17.e1. doi:[10.1016/j.jamcollsurg.2014.03.020](https://doi.org/10.1016/j.jamcollsurg.2014.03.020).
77. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010;39(4):412–23. doi:[10.1093/ageing/afq034](https://doi.org/10.1093/ageing/afq034).