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Frailty and Comprehensive Geriatric Assessment

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ABSTRACT

Frailty is defined as a reduced physiologic reserve vulnerable to external stressors. For older individuals, frailty plays a decisive role in increasing adverse health outcomes in most clinical situations. Many tools or criteria have been introduced to define frailty in recent years, and the definition of frailty has gradually converged into several consensuses. Frail older adults often have multi-domain risk factors in terms of physical, psychological, and social health. Comprehensive geriatric assessment (CGA) is the process of identifying and quantifying frailty by examining various risky domains and body functions, which is the basis for geriatric medicine and research. CGA provides physicians with information on the reversible area of frailty and the leading cause of deterioration in frail older adults. Therefore frailty assessment based on understanding CGA and its relationship with frailty, can help establish treatment strategies and intervention in frail older adults. This review article summarizes the recent consensus and evidence of frailty and CGA.

Keywords: Comprehensive Geriatric Assessment; Frailty

INTRODUCTION

Frailty is defined as a condition of decreased physiologic reserve that leads to a vulnerable state and increase the risk of adverse health outcomes when exposed to a stressor in older adults.[1] Comprehensive geriatric assessment (CGA) is a multidisciplinary diagnostic process that evaluates medical, functional, psychological, and social capabilities, to eventually assess frailty status and various geriatric syndromes. Frailty assessment and CGA can be applied in risk stratifications such as mortality or morbidity, disease-specific treatment-related risk assessment, goal of care and advanced care planning, and frailty-targeted intervention.[2] However, a full CGA is rather time-consuming and its effectiveness is far limited without inter-department collaborative care and frailty-targeted optimized intervention programs.[3] In this review article, we summarize the clear benefits and limitations of frailty assessment and CGA in various clinical settings and decision making. We also review major successful

clinical intervention trials that showed significant evidence of beneficial effects to overcome the drawbacks of CGA. This article aims to help many medical institutions and policy makers to establish intervention programs based on frailty assessment and CGA services.

CURRENT CONSENSUS OF FRAILTY ASSESSMENT

Frailty is defined as a clinical syndrome driven by age-related biologic changes that drive physical characteristics of frailty and eventually, adverse outcomes. Frailty has been conceptualized as a pre-disability state, however it can also be described as co-existing with disability.[4]

There are many suggested models and definitions to operationalize frailty assessment in various settings. Frailty assessment has identified older adults at increased risk of adverse health outcomes, including mortality, disability, worsening mobility, falls, hospitalization and death.[5] The most well validated and widely-accepted tools to measure frailty are the phenotypic definition of frailty and the accumulation of deficits definition of frailty. An important difference between these two conceptualizations of frailty is in the interpretation of aging and the frailty mechanism.

Phenotypic frailty proposed by Fried and colleagues, views frailty as a biologic syndrome of decreased physiologic reserve. This results in the decrease of resiliency and adaptive capacity causing vulnerability to stressors, leading to the physical characteristics of frailty.[6] Intentionally measured five items, namely weakness assessed by grip strength, slowness from usual gait speed, exhaustion derived from self-reported fatigue questionnaire, and low activity by estimated energy expenditure calculated from physical activity questionnaire, and unintentional weight loss were validated based on the Cardiovascular Health Study (CHS). Frailty was considered when 3 out of 5 of the cut points were met. Phenotypic frailty validated by the CHS criteria is less time-consuming and is closely related to sarcopenia, neuroendocrine decline, immune dysfunction and adverse health outcomes.[7] However, because only limited items are evaluated, an accurate evaluation of the body function needs to be performed to reduce the bias of the test. Recently there is a call for more specific language that clarifies conceptual differences between frailty definitions. There are recommendations to term phenotypic frailty as "physical frailty."[8] Further research will help clarify the relationship between "physical frailty" and sarcopenia.

The accumulation of deficits definition of frailty, often termed as the frailty index (FI) is based on the cumulative effect of medical, functional and psychosocial age-related deficits. The greater the number of deficit one has, the higher the likelihood of adverse health outcomes. The FI developed by Rockwood and colleagues, is a count of 70 clinical deficits from the Canadian Study of Health and Aging. Each deficit is mapped to the interval 0–1 to represent the severity of the problem.[9] This approach has benefits as follows: 1) it can be generated by any healthcare data; 2) it contains self-reported items and measurement items; 3) it is expressed as a continuous scale and can be compared as a time series.[9] However, in constructing the FI caution must be taken: 1) at least 30–40 or more items need to be included in the measurements; 2) domain and items should be weighed equally; 3) it does not have to be a 70-item scale like Rockwood and Mitnitski[9] suggested.

In summary, frailty has no gold standard measure, however there are two commonly used frailty models. The frailty phenotype or "physical frailty" approach, views frailty as a syndrome

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whereas the FI approach views frailty as a spectrum of aging.[8,9] Frailty phenotype itself can detect high risk patients, however it is difficult to work out the causal relationship between the risk domains. The FI is known to predict death better than the frailty phenotype.[10,11] Nevertheless, the FI contains disability as an item, therefore it may not discriminate incidence of disability or future functional decline as well as the frailty phenotype.[12,13] Also, when constructing a FI, the domain composed of self-reported items does not necessarily have predictive power inferior to a physical performance-based measure.[14]

Frailty phenotype is more feasible for screening, whereas FI, derived from CGA, is better suited for management and follow-up. Therefore before establishing a frailty assessment it is important to apprehend the systemic pros and cons of each frailty assessment tool.

CGA AND ITS RELATIONSHIP WITH FRAILTY ASSESSMENT

CGA has been around for more than 3 decades and is one of the cornerstones of modern geriatric care and helps to develop a coordinated and integrated plan for treatment and long-term follow-up.[15] The core domains of CGA are functional status, cognition, emotional status, nutritional status, comorbidities, polypharmacy, and geriatric syndromes (fall risk, delirium, urinary incontinence, dentition, visual, or hearing impairments. In a new chapter of the recent edition of Harrison's Principles of Internal Medicine, CGA is introduced as the best way to evaluate health status and care need of older adults.[16] Nonetheless, CGA is resource intensive and is difficult to interpret and use for risk stratifications or frailty classifications.

Screening for frailty has been recommended to identify older adults who would most benefit from a CGA.[17] Frailty assessment using the frailty phenotype-5 items validated by the CHS criteria is less time-consuming in assessing frailty and its severity. However because only limited items are evaluated it lacks information to build strategy for frailty intervention.[6,7] Therefore it needs to be followed by a CGA to develop an interventional plan.

On the other hand, deficit accumulation model which calculates FI is more time-consuming. Nevertheless it provides a more quantitative value of frailty and can acquire information on the vulnerability domain and reversible cause which has substantial benefits.[9] FI can be calculated using items from the standard CGA and does not require a separate CGA process.[18,19] The FI-CGA was initiated by both using data from a standardized CGA and data derived from the clinical examination of a population study.[18,19] The FI-CGA correlated highly with an empirical FI and was associated with higher risk of death and institutionalization.

Fig. 1 shows the flow diagram of the frailty assessment process. As mentioned above, detailed frailty assessment is burdensome especially if applied to all older adults. Therefore frailty screening is more efficient in a large population as a first step of frailty assessment.[20] However in high risk older patients or patients undergoing interventions that have a high likelihood of treatment-related adverse outcomes, detailed frailty assessment from the beginning may be more effective.

CGA can be modified to fit a purpose. Operationalizing phenotypic frailty can be adapted and altered by measurements based on CGA.[11] We need to try and evaluate all physical domains in CGA, however it can differ due to clinical settings and subspecialty.[21]

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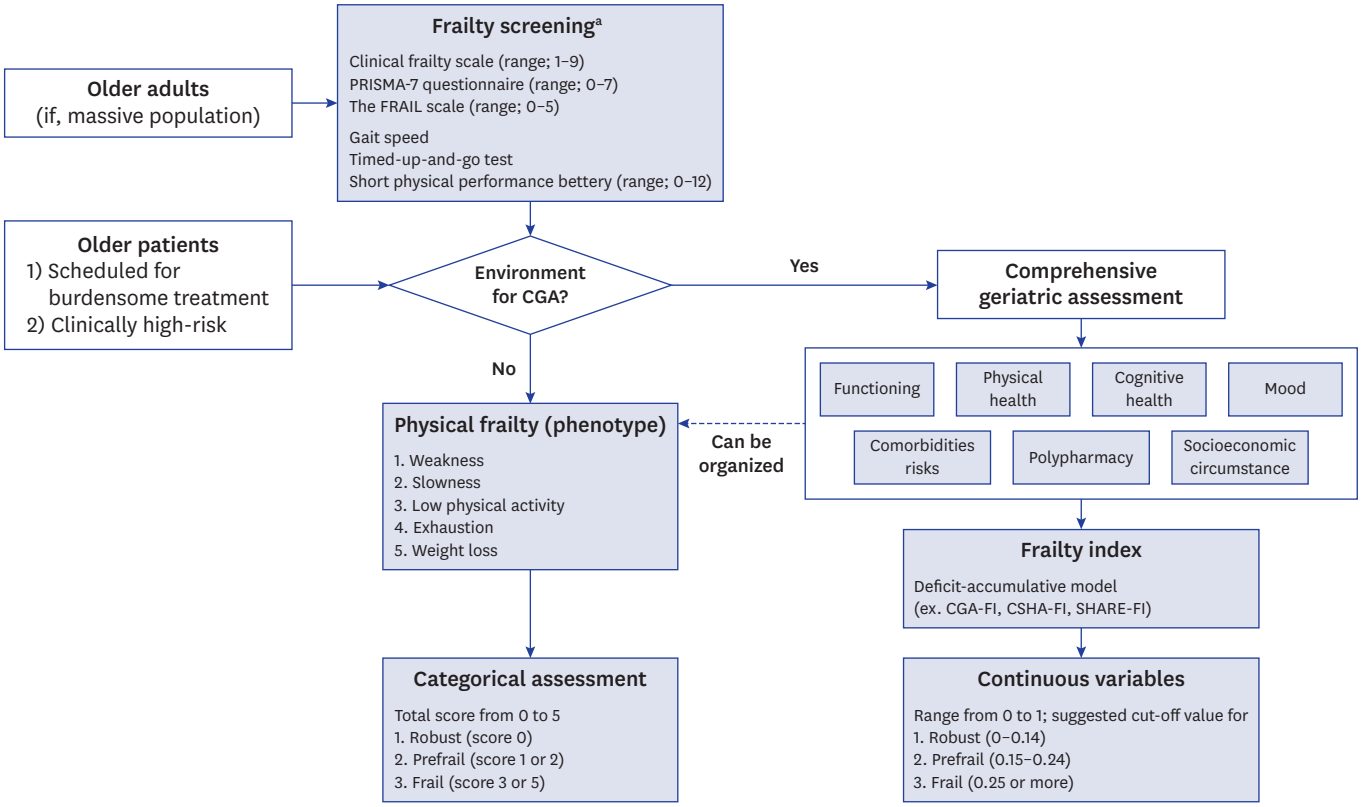

Fig. 1. Flow diagram of the frailty assessment process.
CGA = comprehensive geriatric assessment, FI = frailty index, CSHA = Canadian Study of Health and Aging, SHARE = Survey of Health, Aging and Retirement in Europe.
[a]Frailty screening can be omitted due to clinician's decision if comprehensive geriatric assessment is more necessary or available.

EXPANDING APPLICATION OF FRAILTY ASSESSMENT AND CGA ON VARIOUS CLINICAL SPECIALTIES

Various clinical specialties are beginning to adapt frailty assessment and CGA into their treatment plans. Primarily in disease entities with life-threatening burden, significant functional decline, or a large amount of treatment-related stress, frailty assessment and CGA has had impact in deciding their treatment strategies.

In the area of surgery, frailty is an independent risk factor for mortality, morbidity, length of stay, and postoperative complication.[4,22] Frailty assessment has been most widely used in orthogeriatrics for hip fracture surgery. FI calculated during routine CGA of post-operative hip fracture patients, was significantly associated with adverse outcome including mortality and length of hospital stay.[23] Also, frailty was associated with increased length of stay, complications after surgery and discharge to rehabilitation facilities in fracture patients.[24]

To establish treatment and discharge strategies for trauma elderly patients, the 15-item trauma-specific frailty index (TSFI) was validated from various centers. This TSFI, which consists of comorbidities, daily activities, health attitudes, sexual function, and nutrition domains can also be assessed by the caregiver. It is an independent predictor of unfavorable discharge if greater than 0.27.[25] Also, to determine frailty for geriatric patients undergoing

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emergency general surgery, the 15-variable Emergency general surgery specific frailty index (EGSFI) was validated in a prospective cohort.[26] The EGSFI-based frailty status significantly predicted postoperative complications (odd ratio, 7.3; 95% confidence interval, 1.7–19.8), but age was not a relevant factor. In patients undergoing kidney transplantation, the frailty phenotype showed significant ability to distinguish patients at high-risk of death or early readmission.[27] For older patients with end-stage liver disease waiting liver transplantation, researchers found that the frailty status determined the deterioration of quality of life rather than severity of liver disease.[28] Guidelines from American College of Surgeons for Surgery and National Institute for Health and Care Excellence also emphasized frailty assessment in acute care settings or preoperative period as a new screening criterion for fitness.[9,23]

Oncology is one of the areas where frailty is most widely integrated into clinical practice. Previous reports have consistently shown that frailty status increased the risk of all-cause mortality, postoperative complication, and chemotherapy-related adverse events. Therefore the US National Comprehensive Cancer Network, International Society of Geriatric Oncology and European Organization for Research and Treatment of Cancer recommend frailty assessment and CGA for older cancer patients to detect unrecognized health problems and treatment-related risks.[29]

The field of geriatric cardiology is also expanding to offer a CGA approach within a cardiology practice. A 2011 white paper from the Journal of the American College of Cardiology acknowledged that geriatricians provide skills that "augment quality and capacity of cardiac specialists to meet the needs of their older patients."[30] Particularly in treatment of aortic valve stenosis, the frailty concept is best implemented. The Placement of Aortic Transcatheter Valves (PARTNER) trial tried to assess the frailty status in various methods and revealed that TAVR was superior to SAVR at preventing death, stroke, or rehospitalization in low-risk patients ≥ 70 years with aortic stenosis.[31] In the same year, another research group conducted a prospective cohort study called The Frailty Assessment Before Cardiac Surgery and Transcatheter Interventions study, which implemented frailty screening and CGA method to patients receiving aortic valve replacement and showed frailty trajectories to predict functional outcomes.[32] Clinical trials on perioperative care and interventions to optimize functional outcomes are ongoing in the field of cardiology.[32]

Recently, frailty has been grafted into relatively younger patients. Rheumatologists constructed a FI based on the deficit-accumulation concept to patients with systemic lupus erythematosus and validated to differentiate patients vulnerable to adverse outcomes.[33]

In the UK, electronic frailty index (eFI) was recently developed and validated using routinely collected primary care electronic health record data. The eFI has robust predictive validity for outcomes of mortality, hospitalization and nursing home admission in older people with different frail trajectories.[34] Recently the use of eFI has been extended for utilization in community healthcare services.[35]

In summary, frailty assessment is useful for identification of those at highest risk for adverse outcomes and for risk stratifications to assist in clinical decision making. The value of CGA is greater in frail older adults as CGA identifies the impairments. Before establishing a frailty assessment and CGA in clinical settings, it is important to design an assessment system that reflects the clinical course of each disease.

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IMPORTANCE OF INTERVENTION AFTER FRAILTY ASSESSMENT AND CGA IMPLEMENTATION

Cautions have been raised against rushing to implement frailty assessment and CGA in general clinical settings. The most persuasive evidence of CGA comes from programs that rely on specialized inpatient units and long hospital stays. A striking, large-scaled, randomized controlled trial published in the New England Journal of Medicine revealed that a one-time frailty assessment by a consultative team cannot improve mortality and functional status for hospitalized patients.[36] They emphasized that hospitalized frail older patients only benefit from CGA when optimized management programs are accompanied continuously.

The benefits of CGA are conflicting in short-term consultation settings.[37,38] CGA by a consultation team with limited follow-up did not improve health or survival of hospitalized patients.[36,37] This is because results of the consultations and geriatric recommendations are not all accepted and implied causing limited effectiveness of frailty assessments.[36] Therefore continuous management system beyond simple one-time evaluation, frailty-targeted intervention programs, and a close inter-department communication system should be accompanied.

It is known that physical frailty is a manageable condition that can be targeted for intervention. There are 4 possible treatments that appeared to have some efficacy in the treatment of frailty; 1) exercise (resistance and aerobic), 2) caloric and protein support, 3) vitamin D, 4) reduction of polypharmacy.[39,40] Exercise in frail individuals increase functional performance, decrease hospitalizations and falls.[39] Protein-calorie supplementation is effective in the treatment of weight loss, increase in muscle mass and grip strength.[41] Vitamin D supplementation is also known to reduce falls, hip fractures and mortality.[42,43] Polypharmacy, a possible major contributor to the pathogenesis of frailty can be reduced to decrease costs and medication side effects in frail populations.[44,45]

Multifactorial interventions combining exercise, behavioral therapy, nutrition, and cognitive training are being developed. Individually tailored multifactorial interventions was found to improve frailty status and physical function.[40] Therefore, it is essential to develop and utilize interventional managements that can aim to reverse or provide support in areas of impairment identified on CGA.

FRAILTY-TARGETED INTERVENTION IN VARIOUS CLINICAL SETTINGS

Interventions in hospital settings

Some models of interventional frailty management based on CGA in hospital settings have shown benefits (**Table 1**).[46-49] One of the most successful and effective model to date is the orthogeriatric model.[46,47,50-54] Various studies reported that co-management with a geriatrician shows benefit for hip fracture patients in reducing hospital stay complications, mortality, readmissions, and delirium.[50-54] Programmed intervention by geriatricians is focused on the comorbidity management, review of drug regimens, pain, nutrition, osteoporosis, prevention of falls, management of delirium, depression, early mobilization and initiation of rehabilitation.[47,54,55] In Korea, there is a report from a single tertiary hospital that CGA and frailty-targeted intervention programs for hip fracture patients selected under orthopedic surgeons in the emergency room significantly reduced the length of stay.[56]

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Table 1. Previous studies and meta-analyses on frailty intervention in hospital settings

Clinical settings	Type of study	No. of trials	Type of intervention	Main findings of intervention		
				Mortality	Adm/readm (length of stay)	Functional status
Orthogeriatrics	Meta-analysis[46]	18 RCTs	Multidisciplinary	Decreased[a] in-hospital & long-term mortality	Length of stay: heterogenous	Decreased[a] post-op delirium
	Meta-analysis[47]	7 RCTs	Multidisciplinary	Decreased[a] in-hospital & long-term mortality	Decreased length of stay	Little or no difference of major post-op complication & delirium
Solid cancers	Systematic review[48]	3 RCTs	Multidisciplinary	Improved[a] survival	Decreased length of stay	Improved quality of life
Emergency hospital admission	Meta-analysis[49]	22 RCTs	Multidisciplinary	Decreased mortality	Decreased length of stay	Decreased functional decline Improved cognitive functioning

RCT = randomized controlled trials, Adm = admission, Readm = readmission.
[a]Statistically significant.

There are still only a few reports on randomized studies evaluating the effectiveness of CGA-linked interventions in geriatric oncology.[57,58] The examples of interventions involve changes in current chronic medication, nutritional care, memory evaluation, social support and psychological care. Further trials on CGA based geriatric interventions are ongoing.[48]

In older adults admitted to hospital as an emergency, they were significantly more likely to survive admission and return home, fewer will die or experience deterioration and more will have improved cognitive functioning if they undergo CGAs while they are inpatients.[49]

Interventions in community settings

The prevalence of frailty is estimated to be 10% in community dwelling older adults and increases up to 60% in those with advanced cardiovascular disease.[59] Several randomized controlled trials have tested the effect of interventions targeting mainly physical inactivity, nutritional status, depression or falls in community settings shown in **Table 2**.[60-64] The Lifestyle Interventions and Independence for Elders pilot study reported that a 12-month physical activity intervention was associated with 9% lower frailty prevalence.[61]

For a recent decade, there have been several frailty-targeted intervention trials in the community settings in Korea, most of which are targeted towards vulnerable older adults. A 24-week multicomponent program for socioeconomically vulnerable older adults that consisted of group exercise, nutritional supplementation, depression management, deprescribing medications, and home hazard reductions, sustained beneficial effects up to 1 year.[64] Therefore CGA based intervention programs can potentially promote healthy aging in community dwelling older adults.

Interventions in nursing home settings

Nursing home patients are shown to be very frail. A systemic review identified 9 studies with a total of 1,373 nursing home patients, and reported that the prevalence of frail and

Table 2. Previous studies on frailty intervention in community settings

Country	Type of study	No. of participants	Type of intervention	Functional status
USA	RCT[60]	188	Home-based physical therapy 6 mon	Prevent decline in ADL/IADL, mobility and physical performance
	RCT[61]	424	Moderate-intensity physical activity program for 1 yr	Improved SPPB score & 400 m walk test
Australia	RCT[62]	241	Individualized multidisciplinary intervention for 1 yr; exercise, nutrition, psychologic support	Improved CHS frailty score and SPPB score
Singapore	RCT[63]	246	4 intervention programs for 12–24 wk; physical, nutritional, cognitive, combined	Improved CHS frailty score
Korea	Designed-delay study[64]	187	24 wk multicomponent program; exercise, nutrition, depression, deprescribing, home hazard	Sustained benefit up to 1 year on physical function, frailty, sarcopenia, depressive symptoms and nutrition

RCT = randomized controlled trials, ADL = activities of daily living, IADL = instrumental activities of daily living, SPPB = short physical performance battery, CHS = cardiovascular health study.

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prefrail were 52.3% and 40.2%.[65] As the Korean society rapidly changes, nursing homes have increasingly become the site where many of the older adults spend their final years. According to the Korean Health Insurance Review and Assessment Service, in 2012 a total of 36,052 people died in nursing homes, a 60 percent increase compared to that in 2009.[66]

There have been task force discussions to promote early screening of frailty in nursing homes.[67] The FRAIL-NH scale has been developed to identify frail persons in nursing homes.[68] It is comprised of 7 items; energy, transferring, mobility, continence, weight loss, feeding and dressing. In Korea, there has been a study that measured frailty with the FRAIL-NH scale which used data obtained from the inpatient's data set in long-term care hospitals.[69]

Given a highly prevalence of frailty and disability in nursing homes, intervention trials to reverse frailty status or physical function are limited. Rather, most trials are mainly focused on preventing further functional decline or maintaining quality of life. **Table 3** shows previous interventions for frail older adults in nursing homes.[70-74] Also nutritional interventions such as protein supplement to prevent functional decline in nursing home patients are in progress.[75] However, intervention trials for nursing homes are still lacking and need more evidence and programs.

RECOMMENDATIONS

There are several simple screening tools available to recognize the frailty status. It is important to quickly apply simple frailty screening tools in consideration of the infra-structure, resources, and populations that are available. Well-validated simple screening tools include the Clinical Frailty Scale,[76] the FRAIL scale,[77] or the K-FRAIL scale.[78] If infrastructure is limited, it is useful to screen the frailty status by simply measuring the usual gait speed.[79,80] There are also brief frailty screening tools validated in special settings such as in the emergency department (ED).[81] Therefore it is encouraged for the development of frailty assessments to be carried out in ED settings.

For vulnerable older adults, routine frailty screening is important especially in clinical settings. In line with this, the consensus group, consisting of 6-major international, European, and US societies, recommended administering frailty screening in all older people aged 70 years or older.[39]

Based on the frailty assessment and CGA results, various co-care models should be activated for diseases with high-intensity treatments. In Korea, the most widely known ortho-geriatric co-care model for hip surgery has not been established yet. Tight inter-department collaborations can reduce the adverse outcomes due to frailty. It is also important to educate and nurture fellow clinicians who clearly understand the concept of frailty and geriatric syndromes.

Table 3. Previous studies and meta-analyses on frailty intervention in nursing homes

Type of study	No. of trials/participants	Type of intervention	Main findings of intervention
Meta-analyses[70]	22 RCTs	Functional targeting program	Improved movement, balance, ADL Improved mood, affect, behavioral problems
Meta-analyses[71]	6 RCTs	Exercise program	Improved motor performances
Meta-analyses[72]	17 RCTs	Fall prevention program	Uncertain of the effect of multifactorial interventions on the rate of falls
RCT[73]	70 Participants	Mood program	Improved depressive symptoms and cognitive status
Meta-analyses[74]	10 RCTs	Education intervention	Support residents in their growth and facilitate their self-determination

RCT = randomized controlled trials, ADL = activities of daily living.

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Finally, various intervention models that target frailty in various settings need to be developed. It is important to develop effective interventions especially both in hospitals and areas of resource-limited community settings. However, these interventional effects should be sustainable and not limited to the intervention period. To evaluate the effectiveness of the models, understanding the responsiveness of frailty measures and clinical meaningful changes is necessary. In depth understanding will help choose adequate frailty measures to track longitudinal changes of frailty in clinical settings and research.

CONCLUSION

Frailty assessment and CGA is capable of effectively exploring multiple domains in older ages in various clinical and community settings. Rushing to implement CGA is not ideal, if it is a one-time event with limited follow-up. An important aim in CGA is to develop and implement individually tailored geriatric interventions that can lead to continuous care. Further work should aim to develop CGA-based interventions that focus on improving clinical outcomes of older adults.

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