Clinical Interventions in Aging

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REVIEW

Research Progress on Frailty in Elderly People

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Abstract: Global aging is rapidly accelerating, which significantly influences the health systems worldwide. Frailty emerges as the most conspicuous hallmark of aging, imposing novel global health challenges. Characterized by a multifaceted decline across physiological system, frailty diminishes an individual's capacity to maintain equilibrium in the presence of stressors, which leads to adverse outcomes such as falls, delirium, and disability. Several screening tools and interventions have been developed to mitigate the harm caused by frailty to human health, but research on frailty in mainland China commences belatedly with scant studies conducted. Therefore, it is imperative to explore screening methods and treatment modalities tailored to the Chinese context, thereby enhancing the older adults' quality of life and advancing social medicine. This review aims to elucidate the evolution, diagnosis, and management of frailty, alongside the challenges it poses, with the overarching goal of guiding future diagnostic and therapeutic endeavors. Specifically, we summarized the mechanisms of frailty and intervention strategies in elderly people, and meanwhile, we evaluated the advantages and disadvantages of different measurement tools.

Keywords: frailty, geriatrics, pathogenesis, assessment, intervention

Introduction

According to data from China's National Bureau of Statistics, the population aged 60 and above has already accounted for 21.1% at the end of 2023, indicating that China has officially entered a moderately aging society.[1] The United Nations projects that by 2050, the global population aged 60 and older will hit 2.1 billion, with 425 million people aged 80 or more.[2] It can be seen that older adults in China and even around the world is increasing rapidly. One of the most challenging issues of aging is the clinical syndrome of frailty. Frailty is a common clinical syndrome in geriatrics characterized by reduced physiological reserves and a diminished ability to maintain homeostasis, which is the result of age-related declines in a variety of physiological systems, making it more susceptible to a wide range of adverse outcomes such as falls, delirium, hospitalization and death.[3]

Substantial progress has been made in understanding the mechanisms underlying frailty, particularly in identifying biological risk factors. Chronic inflammation may be a critical pathophysiological process contributing to frailty, either directly or indirectly, through other intermediate physiological systems.[4,5] Other important factors contributing to frailty include nonbiological areas such as cognitive, social and psychological. Thus, managing frailty syndrome requires a comprehensive approach to assess its multifaceted causes.[6] In addition, if frailty can be identified at an early stage, followed by appropriate intervention, the burden on healthcare and society can be reduced, and the prefrail stage can be reversed to a healthy state.[7] Hence, risk grading of frailty can facilitate the efficient allocation of healthcare resources and facilitate the multidisciplinary team to implement treatment plans.

Currently, frailty screening and assessment tools are categorized into classical methods (eg Fried frailty phenotype, Frailty index) and derived scales (eg FRAIL scale, Tilburg Frailty Index, Groningen Frailty Index, Clinical Frailty Index, Comprehensive Geriatric Assessment, PRISMA-7, SHARE-FI) (Table 1). Since these scales are derived from developed countries and the heterogeneity of elderly people across countries is very large, whether they can be applied to the assessment of frailty in Chinese elderly people remains to be investigated. Therefore, it is important to find and validate

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Table 1 Instruments for Screening and Assessment of Frailty

Instrument	Components	Scoring	Classic Literature
Fried frailty phenotype (FFP)	Five criteria: weight loss; weakness; poor endurance; slowness; low activity	Score range 0 to 5. Frailty: ≥ 3 criteria present. Pre-frailty: 1 or 2 criteria present. No frailty: 0 criteria present.	Fried (2001)[10] Bandeen-Roche (2006)[11]
Frailty index (FI)	Sixty-eight indicators of possible deficits in 6 variables: demographic characteristics; physical health; somatic functioning; lifestyle behaviors; social functioning; psychological status; and cognitive functioning	Frailty: FI ≥ 0.25. Pre-frailty: 0.08<FI<0.25. No frailty: FI ≤ 0.08.	Mitnitski (2001)[12] Rockwood (2007)[13]
FRAIL scale	Five criteria: fatigue; decreased resistance; limited walking; coexistence of multiple diseases; weight loss	Frail: ≥ 3 criteria present. Pre-frailty: 1 or 2 criteria present. No frailty: 0 criteria present.	Dent (2016)[14] Hyde (2010)[15] Ravindrarajah (2013)[16]
Groningen frailty indicator (GFI)	Fifteen self-assessment items in four dimensions: somatic latitude; cognitive latitude; social latitude; and psychological latitude	Score range 0 to 15. Frailty: ≥ 4 points	Peters (2015)[17] Bielderman (2013)[18]
Tilburg frailty indicator (TFI)	Includes A, B two parts. Part A: ten items (No participation in scoring) Part B has fifteen items and includes three dimensions: somatic, psychological, social.	Score range 0 to 15. Frailty: ≥ 5 points.	Gobbens (2010)[19] Dong (2017)[20]
Edmonton frailty scale (EFS)	Nine dimensions, eleven items in total: cognitive ability; general health status; functional independence; social support; substance use; nutrition; mood; independence; and functional performance	Score range 0 to 17. Frailty: ≥ 6 points. Pre-frailty: 4~5 points. No frailty: 0~3 points.	Rolfson (2006)[21] Hilmer (2009)[22] Perna (2017)[23]
Comprehensive frailty assessment instrument (CFAI)	Four dimensions, eleven items in total: physical; psychological; social; environmental	Score range 20 to 97. Frailty:>20 points. No frailty: ≤20 points.	De Witte (2013)[24] Qiao (2018)[25]
PRISMA-7	Seven simple questions: over 85 years of age; male; limited mobility due to health problems; needs help from other people; cannot go out due to a health problem; needs social support; uses walking aid (cane, walker or wheelchair)	1 point for each question, score range 0 to 7. Frailty: ≥ 3 points.	Raiche (2008)[26] Hoffmann (2020)[27]
SHARE-FI	Five criteria: Poor mental health; loss of appetite; decreased mobility; labor frequency; poor grip strength	Automatically calculates frailty scores and determines the degree of frailty using an Internet model.	Romero-Ortuno (2010)[28] Romero-Ortuno (2013)[29] Dorner (2014)[30]

a sound, multidimensional frailty assessment tool for Chinese elderly people. The next step after frailty screening is intervention and treatment. The existing studies based on interventions for frailty in elderly people are inconsistent in recommending the best model for a single exercise or dietary program to intervene in frailty.[8] Nevertheless, some studies reported synergistic benefits of comprehensive intervention based on exercise and nutrition for frail older people.[9] Therefore, this review aims to summary the research progress on frailty with an aim to provide a theoretical basis for future diagnosis, intervention and policy formulation.

Definition of Frailty

Frailty encompasses both physical and psychological aspects, which can either improve or worsen over time. Despite numerous studies in the past attempting to define frailty, there is still no consensus on its definition. At present, the Fried Frailty Phenotype (FFP) and Frailty Index (FI) are the most commonly used methods for defining frailty. FFP defines a specific physical phenotype consisting of weight loss, slowness, weakness, self-reported exhaustion, and low level of

physical activity, which marks the potential physiological state of multisystem and energy loss.[10] The FI, on the other hand, aggregates the number of impairments and conditions to create a frailty index.[31] To date, many definitions of frailty are based on these two approaches.[32] Although there is no uniform definition, most of the concepts still share some common features, such as aging, decline in physiological reserve, multisystem decline, and diminished stress resistance. In 2013, international geriatricians defined physical frailty as a medical syndrome with multiple etiologies characterized by a decline in strength, endurance, and physiological function, increasing vulnerability to dependence or death.

Based on these characteristics, the World Health Organization has proposed a widely accepted definition of a clinically identifiable condition. In this state, the elderly experience reduced capacity to manage daily or acute stress because of age-associated deterioration in physiological reserves and the functioning of several organ systems which heightens their susceptibility.[33,34] In summary, the definition of frailty is constantly evolving, but a few of the points remain constant: (i) frailty is dynamic, its incidence increases with age; and (ii) frailty is preventable, and the development trend of frailty can be reversed through physical exercise and nutritional intervention.

Pathogenesis of Frailty

Frailty is a syndrome involving the interaction of multiple physiological systems. A significant aspect of frailty research is to explore how aging promotes the cumulative decline of multiple physiological systems.[35] Understanding the pathogenesis of frailty facilitates to formulate therapeutic measures to prevent and reverse frailty by strengthening physiological reserves and potential. Numerous studies have indicated that cellular and molecular aging processes could interact with the environment, genetic background and chronic diseases during the pathogenesis of frailty (Figure 1).[36–38] It has been well acknowledged that frailty is influenced by various risk factors, including clinical, social, biological, and lifestyle factors. Clinical factors comprise of disease, depression, and obesity. Social factors include economic conditions, education level, and family/marital status. Lifestyle factors consist of alcohol consumption, smoking, lack of exercise, and work schedule. Biological factors encompass endocrine disorders, impaired immune system, sarcopenia, impaired cognition, and vitamin deficiencies. Furthermore, several important multisystem pathophysiological processes, including the immune, skeletal muscle, and endocrine systems, have been reported to be involved with the pathogenesis of frailty (Figure 2).[39–41]

Musculoskeletal System

Musculoskeletal functioning is a key component in quantifying frailty.[39] Sarcopenia is a widespread musculoskeletal disorder marked by reduced muscle strength, mass, volume, and movement, which has been linked to negative outcomes in individuals with frailty.[42] Sarcopenia and frailty share many similar clinical manifestations, with aging being a common risk factor for both.[43,44] Therefore, sarcopenia is considered a key component of frailty. Indeed, there is a positive correlation between sarcopenia and frailty, which is featured by gradual increase of frailty in the presence of increased severity of sarcopenia.[45] Sarcopenia is influenced by chronic inflammation and aging. There might be increase in the inflammatory cytokines induced by chronic inflammation, which activates the ubiquitin-protease system, leading to protein degradation, muscle breakdown, and a decrease in muscle strength and mass.[46] A multitude of studies have explored the impact of inflammatory cytokines on sarcopenia. Studies have shown that these cytokines activate the NF-κB signaling pathway, leading to DNA breaks and

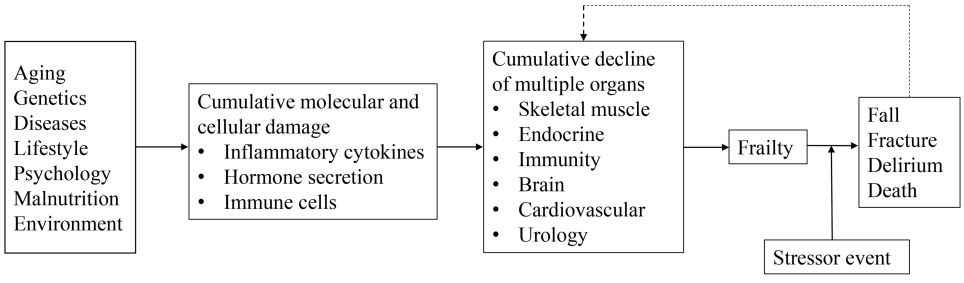

Figure 1 Schematic diagram of the pathophysiology of frailty.

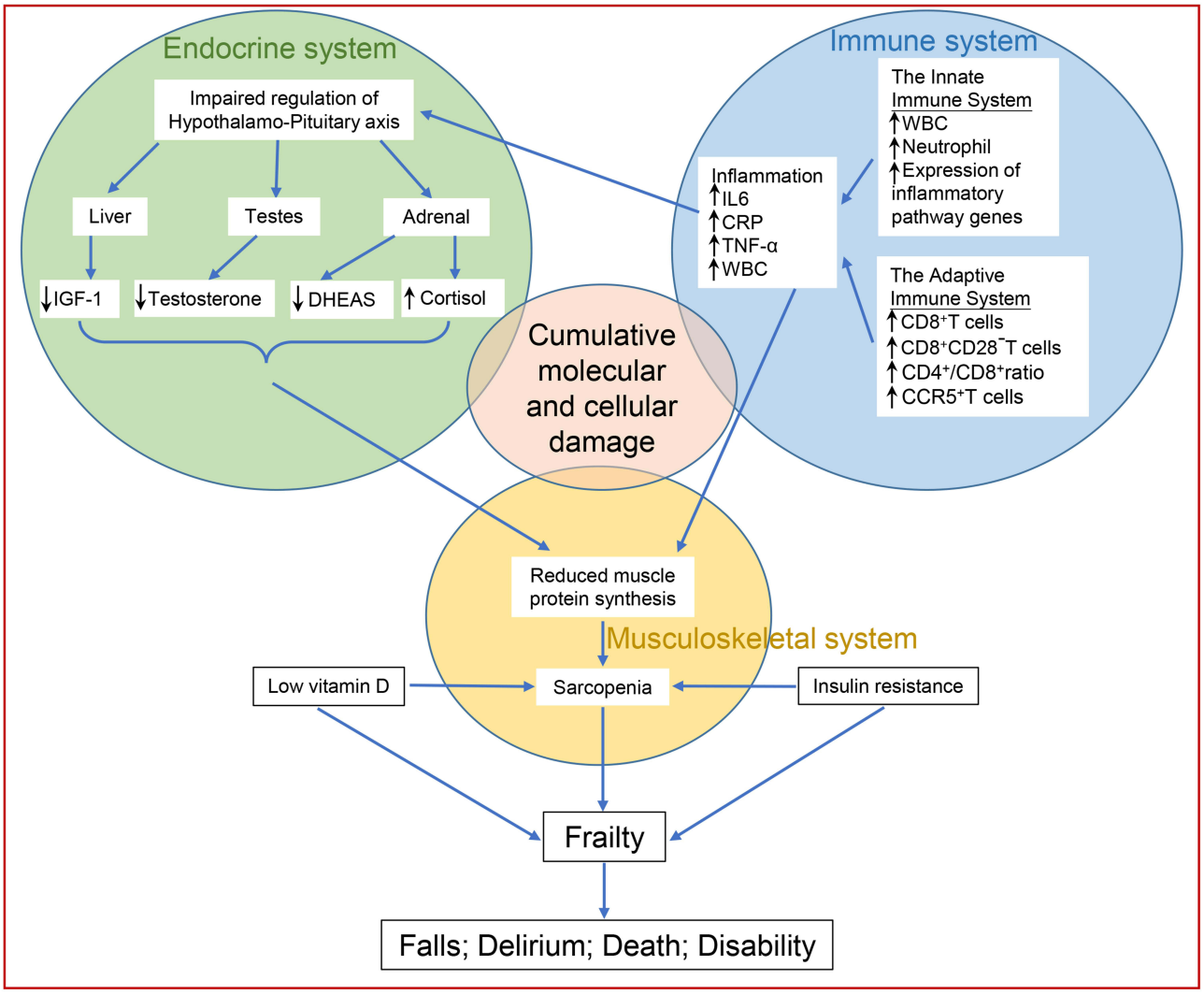

Figure 2 Alterations in the immune, endocrine, and musculoskeletal systems in frailty.
Abbreviations: CCR5, chemokine CC receptor 5; CRP, C-reactive protein; WBC, white blood cell.

apoptosis.[47] Additionally, tumor necrosis factor-α (TNF-α) promotes muscle catabolism by stimulating the Akt/mTOR pathway, resulting in a decrease in muscle mass.[48] Furthermore, the aging process can lead to a reduction in skeletal muscle mass, which progressively accelerates with age.[49] All these indicated that inflammatory responses and aging work together to facilitate the onset of sarcopenia, which is a crucial pathological factor in frailty.

Endocrine System

Endocrine system plays a crucial role in frailty due to its complex interrelationships with the brain, immune system, and skeletal muscle.[40] It involves in the regulation of metabolism by balancing hormone levels in the body through the hypothalamo-pituitary-adrenal axis.[50] In the individuals with frailty, there are significant changes of in the metabolic processes such as insulin-like growth factor-1 (IGF-1) signal transduction, concentration of sex hormones and the secretion of cortisol.[38]

Firstly, as a multifunctional factor, IGF-1 promotes cell proliferation and differentiation. With the aging process, the synthesis of growth hormone in pituitary decreases, resulting in down-regulation of IGF-1 secreted by the liver, while low IGF-1 may lead to diseases such as sarcopenia and osteoporosis.[51] Secondly, sex hormone levels in elderly people gradually decrease with age, which will lead to a decrease in muscle bulk and strength. Although a link between testosterone concentrations and frailty has been well established, testosterone is not a pathological factor, and instead, it

may serve as a sensitive biomarker.[52] Some studies have proposed the correlation between dehydroepiandrosterone sulfate (DHEAS) and frailty, but the effects of other mixed diseases cannot be excluded.[53] Thirdly, cortisol, a steroid hormone that maintains homeostasis, plays a crucial role in the frailty. The decrease in adrenocortical cell activity promotes cortisol release, leading to weakened anabolism and enhanced catabolism. Consequently, elevated cortisol is closely linked to muscle mass decrease and weight loss. Studies have found that aged female population with frailty show higher cortisol at night, and its 24-hr changes are positively correlated with the severity of frailty.[54] Afterwards, the activation of the stress response system would lead to adverse effects on human tissues and organs, which consequently brings in adverse consequences such as frailty and even death.

Immune System

The immune system has been likened to the leader of an aging long-distance running team by some scholars, as it weakens successively along with other organs and systems.[41] The body shows gradual decrease in the responses to pathogens and cancerous cells, together with increase in the unwanted stress responses, leading to inflammation and autoimmune diseases.[55] Immune system aging is marked by several features: clonal expansion of memory and effector T cells, reduction of naive T cells, and shrinkage of the T cell repertoire ($CD4^+$, $CD8^+$, $CD28^-$, $CCR5^+$T cells).[56] Studies have shown that changes in $CD4^+$ T cells can induce chronic inflammation and aggravate the frailty phenotype.[57,58]

T cell aging may play a major role in the process of immune aging and frailty. Hallmarks of T cell senescence include thymic degeneration, mitochondrial dysfunction, imbalance of memory and T cell. All these together explain immune deficiency and phenotypes of inflammation.[59] The aging immune system is usually fully functional under normal circumstances, but it can overreact to some abnormal inflammation and persist long after the removal of the inflammatory stimulus. The presence of inflammatory cytokines in the body for a long time will cause damage to the body. For example, advanced glycation end products (AGEs), produced by proteins, lipids, and nucleic acids, can cause extensive cellular injury by upregulating the inflammatory response, which is strongly linked with the frailty.[60] In summary, the immune system can eliminate harmful substances early or middle in life, but may be more harmful in late life. Therefore, reducing the antigen load in elderly people by using drugs or improving their diet can slow down the aging of the immune system and avoid the adverse consequences of frailty.

Screening and Assessment Methods for Geriatric Frailty

FFP

FFP is a standardized definition of frailty through long-term follow-up and testing of 5317 people aged 65 or more, which includes five diagnostic criteria: unexplained weight loss, self-reported fatigue, reduced grip strength, slower walking speed, and diminished physical activity (Table 2). A diagnosis of frailty is made when a person meets three or more of these criteria.[10] This provides a concise summary of frailty syndrome, which can predict falls, hospitalization, disability, and death, helping healthcare professionals take timely preventive measures to prevent adverse events. Although FFP is extensively utilized in clinical and scientific research, it does have limitations. It excludes conditions like stroke, depression, Parkinson's disease, and cognitive dysfunction, which focuses merely on physiological dimensions. Meanwhile, it does not take cognition, environment, and race into consideration, making its assessment dimensions

Table 2 The Fried Frailty Phenotype (FFP)

FFP diagnostic criteria	Measurement methods
Slowness	Walking time/15 feet: slowest 20% (by gender, height)
Weakness	Grip strength: lowest 20% (by gender, body mass index)
Unexplained weight loss	Weight loss of 10 lb or greater than 5% weight loss in the past year
Poor endurance and energy	Using the CES–D Depression Scale (self-reported)
Low physical activity level	Kcals/week: lowest 20% Males: 383 Kcals/week Females: 270 Kcals/week

less comprehensive. Additionally, assessing activities such as walking speed and grip strength requires professional tools and is time-consuming, which is less practical for large-scale use in the community.[61]

FI

FI was proposed by Canadian gerontologists in 2001, which is mainly based on the principle of cumulative deficits and established with health deficits as frailty variables.[12] These variables cover psychology, life, physiology, and past history. There is no uniform standard for the selection of specific variables, and user can choose them based on specific conditions. Therefore, the number and threshold values of variables are also different.[13] Each deficit is recorded as "1", while no deficit is recorded as "0". FI is the proportion of deficits items in the total number of deficits, and the index range is 0~1. The frailty threshold is generally 0.25. If it exceeds 0.25, it is considered as frailty.

FI has been considered to be effective to distinguish moderate and severe frailty than FFP.[62] A long-term study of 773 older adults living in the community demonstrated that FI was strongly associated with 5-year mortality and was a useful tool for predicting negative outcomes in elderly people.[63] FI has also been introduced into a number of studies in China. The Rugao Longevity and Aging Study (RuLAS) found a high degree of concordance between FI and FFP in their ability to screen for frail older people, and FI was more likely than FFP to identify those at high risk of falling or being hospitalized in the healthy population.[64] Based on the cumulative deficits model, Chinese scholars developed a frailty assessment scale suitable for local inpatients, with good internal consistency reliability (Cronbach's $\alpha = 0.93$), retest reliability ($r = 0.81$), content validity ($r = 0.96$), and structural validity (cumulative variance contribution rate of 75.90%), which provided a reliable diagnostic tool for clinical assessment of frailty.[65] In general, because the FI classifies the degree of frailty and evaluates it in a wide range of dimensions, it is more accurate in the clinical diagnosis of frailty and is also suitable for epidemiological studies. For community screening, it is too cumbersome and time-consuming to re-collect deficit indicators, and its feasibility can be increased by using information technology to extract from the archives of communities, hospitals or pension institutions, such as eFI technology.[66]

FFP and FI are two of the most classic methods for screening and assessing frailty, but the assessment steps are cumbersome. FFP requires specialized equipment to measure weight, grip strength, and step speed, while FI requires the collection of numerous indicators of deficits. Therefore, it is really difficult to use FFP and FI in primary health care settings. To simplify the process of assessing frailty, researchers have developed numerous frailty scales, the more commonly used of which are listed below. Table 1 provides a summary of selected tools that can be utilized for frailty screening.

FRAIL Scale

The FRAIL scale was proposed by the International Society for Nutrition and Aging based on FFP and FI, containing 5 items: fatigue, endurance (ability to climb stairs), free mobility (ability to walk a certain distance), disease, and weight loss.[67] If there are three or more, the person is considered frail, if there are 1 or 2, it indicates early frailty.

A large cohort study in Australia confirmed that FRAIL scale had good predictive validity for death ($HR > 1$) and daily activity disorder ($OR > 1$).[68] In a Chinese study, the Hong Kong male and female osteoporosis cohort showed that FRAIL had a better ability to predict repeated falls than FFP (AUC: 0.64 vs 0.63 for men and 0.61 vs 0.57 for women).[69] Chinese scholars applied the Chinese version of FARIL scale to 210 older patients and evaluated its reliability and validity. The results showed that the Cronbach's α coefficient of FRAIL scale was 0.705, indicating that the scale had good reliability; FRAIL scale had moderately positive correlation with each item, and the correlation was good (r=0.538~0.656), indicating that the scale has good structural validity. When the optimal critical value is 1.5 (AUC=0.779), the critical value is 1.5. The corresponding sensitivity is 58.8%, and the specificity is 90.5%.[70] The FRAIL scale has a good diagnostic value for older patients with frailty.

In summary, the FRAIL scale is similar to FFP in assessment content but can be assessed by clinicians via phone or self-assessment without specialized equipment or on-site physician assessment. This simplicity makes it easy to operate and highly predictive, aiding medical practitioners in quickly recognizing frail or pre-frail patients. However, being a self-reporting scale, older adults may not accurately assess their physical condition due to cognitive decline, reducing assessment credibility.

Groningen Frailty Indicator (GFI)

GFI is a self-reported, comprehensive frailty assessment scale proposed by Dutch researchers that contains 15 items in 3 dimensions: physical (shopping, toileting, dressing, walking, self-rated health, vision, hearing, polypharmacy, and weight loss), cognitive (memory), psychological (depression and calmness), and social (social participation, caring, and helping). The score ranges from 0 to 15, and ≥4 can be diagnosed as frailty.[71]

The GFI has been widely used all over the world, and it has high reliability and validity.[17,18] In China, more and more researchers have Sinicized GFI to study the reliability, validity and feasibility of its application in Chinese population.[72] A study found that the Chinese version of the GFI has good reliability and validity in Chinese pension institutions, with high internal consistency reliability (Cronbach's α = 0.712) and test-retest reliability (r = 0.939), good convergent, discriminant, and criterion validity (using FFP as the criterion, the area under the ROC curve is 0.823), which can be applied to the screening and evaluation of frailty in Chinese pension institutions.[73] Similarly, other studies have demonstrated acceptable internal consistency reliability (Cronbach's alpha = 0.64), good test-retest reliability within a 7~15 days interval (ICC = 0.87), and an AUC of 0.84 using the FI as the reference standard. The GFI has good diagnostic properties for screening frailty, with an optimal frailty cutoff of 3 points.[74]

It is important to note that the GFI utilizes a self-assessment method, involving fewer items than the FI. The Chinese version of the GFI is semantically equivalent to the original text, with good reliability and validity. Additionally, it is more suitable in Chinese pension institutions and communities. However, the grading system of the GFI, which defines ≥4 as frailty and 0–3 as non-frailty, lacks clarity and does not allow for differentiation between the boundaries of healthy and pre-frailty, moderate frailty, and severe frailty.

Tilburg Frailty Indicator (TFI)

The TFI, developed in the Netherlands in 2010, is a multidimensional screening tool for frailty encompassing physical, psychological, and social aspects.[20] The TFI assigns one point for the presence of each item and zero points for its absence, with a score of five or more indicating frailty.[19]

Currently, TFI has been widely used to assess frailty in older populations in Brazil, Denmark, and other countries due to its good reliability and validity.[75,76] In China, numerous researchers have Sinicized and validated the TFI for use in both community and hospital settings. A study conducted by Chinese scholars examined 917 community-dwelling individuals over the age of 60. The study found that the Chinese version of the TFI has good internal consistency reliability (Cronbach's α = 0.71), test-retest reliability (r = 0.88), and criterion validity (with FFP and FI as calibration standards, the AUC of TFI are 0.87 and 0.86 respectively).[20]

TFI is a self-reported comprehensive assessment scale that is similar in structure to the GFI, with the advantages of flexible testing and easy scoring. The above studies demonstrated that the TFI was highly reliable after being adapted for use in China, indicating its accuracy for screening early frailty in older individuals residing in both community and nursing home settings. Furthermore, the Chinese versions of the TFI and GFI exhibit lower frailty thresholds when applied to the Chinese community compared to older adults in other countries.[74,77] This may be due to the fact that Chinese older people have different perceptions of the extent to which their health problems affect their lives than those of other countries. The Sinicized frailty scale's optimal cut-off values should be adjusted to suit the perceptions of Chinese. Therefore, it is necessary to test the reliability of the TFI in different countries and populations.

Edmonton Frailty Scale (EFS)

EFS developed by Rolfson et al consists of 11 items across 9 dimensions including substance use, social support, cognitive ability, self-reported performance, underlying health status, independence, nutrition, incontinence, and mood. The scale is evaluated using a hierarchical scoring system with a maximum of 17 points. A score of 3 or less indicates a healthy state, 4~5 indicates mild frailty, 6~8 indicates moderate frailty, and 9 or more indicates severe frailty.[21] It is simple and operable compared to the FFP and FI as it did not involve the specialized equipment or personnel, or the utilization of data from the comprehensive geriatric assessment.

The EFS has been extensively used worldwide, and its reliability and validity has been validated through cross-sectional or longitudinal studies. Consistently, EFS has good reliability, structural validity, and acceptable internal consistency.[21] In China, research on the EFS is increasing. Scholars compared the consistency and applicability of the FFP, FRAIL scale, and EFS in screening for frailty among older adults in Chinese communities. Results indicated that the EFS had a higher area under the ROC curve (0.787) in predicting the ability to perform activities of daily living (ADLs) and a higher cross-validated accuracy in predicting the decline in ADLs (75.70%) than the other two scales, which suggests that the EFS, as a multidimensional frailty assessment tool, has better predictive ability for daily living ability than the other two.[78] A cross-cultural study was conducted to debug the EFS. The results showed that the Chinese version of the EFS has good internal consistency reliability (Cronbach's $\alpha = 0.73$), ideal structural validity (the Spearman correlation coefficients of the items and dimensions with the total score of the scale ranged from 0.338~0.718), and ideal predictive validity (a negative correlation between the total scores of the EFS and the total scores of the SF-36, $r = -0.622$, $p<0.01$).[79]

Furthermore, the EFS was used to assess the frailty of older patients with diabetes and cancer after Sinicization.[80,81] The above results indicate that the Chinese version of the EFS has good reliability and validity when applied to the Chinese community. However, some studies have used convenience sampling with small sample sizes, which limits their generalizability, and in the future, further validation in large-sample studies is necessary.

Comprehensive Frailty Assessment Instrument (CFAI)

CFAI is a self-reported screening tool developed by De Witte et al. It is based on an integrative model and is the first scale to incorporate environmental factors into the assessment of frailty. It includes physical, psychological, social, and environmental dimensions, and is consists of 23 items with a total score of 20~97 points.[24]

Large-sample studies have confirmed that the CFAI is an effective instrument for detecting frailty in aged community members.[24] Chinese scholars have Sinicized the CFAI, which has confirmed that the scale has good internal consistency reliability (Cronbach's $\alpha = 0.837$), test-retest reliability ($r = 0.789$), criterion validity (using WHOQOL-BREF as the criterion, $r = -0.764$), and structural validity (with a cumulative variance contribution of 64.05%).[82] Another study found that CFAI can predict the occurrence of falls to some extent. This may provide a reference point for healthcare professionals to identify high-risk groups in advance and prevent adverse outcomes of falls.[83]

In summary, the Chinese version of CFAI achieves equivalence with the original scale in terms of content and format semantics with good reliability and validity. However, the scale has more assessment items, which require a lot of manpower, energy and time. Additionally, there are really differences in the social support part of the Chinese version of the CFAI in domestic and international studies, which may be due to the differences in the concepts of seeking social support for older adults in the domestic and international communities. Further studies are needed to explore whether it is applicable to older adults in China.

Interventions

Attention has been paid to the nursing and hospice care for older people with incapacity and dementia, while health interventions during their frailty period are usually neglected. This period is longer than the disability and terminal periods, making it the most valuable stage for intervention. Effective interventions during this period could potentially compress the disability and terminal periods. Thus, early intervention offers the greatest potential benefit. The prevention and treatment of frailty are still in the initial stages of exploration, and there are fewer clinical trials of specific treatments for frailty. However, some studies have found that older people in the early and middle stages of frailty respond well to interventions (eg physical activity and nutritional management), while those with severe frailty benefit less.[84] Effective interventions, both domestically and internationally, include physical activity and nutritional interventions.

Physical activity, such as resistance training and aerobic exercise, is widely considered the most investigated intervention to prevent frailty.[85] Exercise helps to maintain muscle morphology, strength, and function, as well as improving aerobic metabolism and balance. Additionally, regular exercise contributes to maintenance of the organelles ultrastructure and downregulates the expression of genes involved in autophagy and detoxification of reactive oxygen species.[86] Older people who engage in regular physical activity have a significantly lower risk of developing frailty compared to those who lead a sedentary lifestyle.[87] In China, traditional exercises like Yi Jin Jing, Tai Chi, Ba Duan Jin,

and Wuqinxi (Five-animal Exercises), as the essence of traditional Chinese culture, are highly regarded by older adults population and are effective in improving explosive strength, flexibility, and balance. For instance, in a randomized group trial of 60 frail older patients was conducted, which indicated that Tai Chi combined with resistance training could improve the patients' frailty conditions, quality of life, and physical activity.[88] Another study randomly divided 60 aged patients with pre-frailty into Ba Duan Jin group and control group, individuals practicing Ba Duan Jin for a period of 2 weeks showed a lower TFI score and a higher compliance rate than the control group.[89]

Furthermore, there is a close relationship between malnutrition and frailty, with aged individuals in the frailty stage often experiencing poorer nutritional status due to inadequate nutrient intake.[90] In addition, malnutrition severity was associated with the increased risks of frailty.[91] Nutritional interventions may improve weight loss and reduce mortality in aged people with frailty who are malnourished. However, there is insufficient evidence to support this in non-malnourished counterparts. For instance, consuming too much protein is associated with an increased risk of frailty in older people, but adding protein to the diet may be effective in preventing frailty.[92] Recent studies have linked 25 hydroxyvitamin D [25(OH)D] deficiency to disability and frailty. Vitamin D improves muscle strength through highly specific nuclear receptors in muscle tissue, reduces the incidence of fractures in older people, and facilitates the prediction of physical activity disorders and the treatment of autoimmune deficiency diseases.[93] According to the Third US Health and Nutrition Examination Survey, 25(OH)D deficiency was associated with a 3.7-fold increased risk of developing frailty.[94] In addition, a meta-analysis showed a 27% increased risk of frailty in older adults when comparing the lowest and highest recorded levels of 25(OH)D.[95] Therefore, strength training combined with protein supplementation is the most effective intervention for treating frailty.[96]

Impacts and Challenges of Frailty on Health Systems

The rapid population ageing has become a major challenge for most countries. Older people represent a significant demographic in healthcare, with frail patients often requiring long-term and complex medical attention. This can consume up to six times the healthcare resources of younger patients, which has a significant negative impact on the sustainability of health care systems globally.[97] Furthermore, the conventional medical service model priorities emergency care and disease treatment, whereas older people require more long-term care and health management. However, In numerous countries, health-care systems lack sufficiently developed services tailored to the needs of older adults.[98] Therefore, it is crucial to establish a system of public health policies and socio-economic security at the national level.

Currently, studies on frailty in elderly people have been gradually increasing worldwide. Screening and intervention on frailty has begun to take shape in developed countries, while it is still in its infancy in developing countries. In recent years, Chinese geriatricians have conducted extensive research on geriatric frailty. However, there is still a lack of large-scale epidemiological data, a lack of rapid and uniform screening tools for geriatric frailty and clear biomarkers suitable for older adults population in China, and a lack of simple, effective, accessible and comprehensive intervention techniques.[99]

Summary

Currently, China's research on frailty in the older adults is still in its infancy and has not yet been translated into clinical practice, remaining in the theoretical research stage. Although classic frailty assessment tools such as the FFP and FI play important roles in clinical diagnosis, their complexity limits their use in primary healthcare. Simplified scales like the FRAIL, GFI, and TFI, particularly the Chinese versions, have demonstrated high practicality and reliability in community and nursing home settings. Future research should focus on optimizing the applicability of these tools, especially to meet the specific needs of the older population in China. Moving forward, we must concentrate on basic research into mechanisms, target drug development, as well as multidisciplinary interventions including traditional Chinese medicine. It is necessary to establish an integrated care system that promotes healthy aging and enhances the resilience of frail older individuals in coping with stress.

Data Sharing Statement

All data generated or analysed during this study are included in this published article.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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