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Frailty as a Predictor of Low-Energy Fractures in Older People with Osteoporosis: A Retrospective Study

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This study aims to elucidate the relationship between bone mineral density and frailty in older people with osteoporosis, as well as to assess the predictive value of frailty for low-energy fractures within this demographic. A retrospective analysis was conducted on clinical data from older people with osteoporosis admitted between January 2020 and January 2022. Frailty was evaluated using the Fried Frailty Phenotype, and data on demographics, medical history, lifestyle factors, and bone mineral density were collected. All patients were followed for three years post-enrollment to document the occurrence of low-energy fractures, thereby investigating the association between frailty status (frail, pre-frail, non-frail) according to the Fried Frailty Phenotype and fracture risk. A total of 129 patients were included in the study, with 115 completing the follow-up. The bone mineral density in frail patients was significantly lower than that in both pre-frail and non-frail participants, while pre-frail patients also exhibited significantly lower bone mineral density compared to non-frail individuals. The incidence of low-energy fractures was markedly higher in frail patients compared to their pre-frail and non-frail counterparts (72.4% vs. 40.4% vs. 20.5%). Multivariate logistic regression analysis identified frailty status (frail, pre-frail, non-frail) according to the Fried Frailty Phenotype and cardiovascular disease as independent risk factors for fractures. Frailty status (frail, pre-frail, non-frail) according to the Fried Frailty Phenotype is an independent predictor of low-energy fractures in older people with osteoporosis, indicating the need for its incorporation into comprehensive fracture risk management strategies.

Keywords: Frailty, Osteoporosis, Low-Energy Fractures.

INTRODUCTION

Global population aging represents a paramount public health challenge, with osteoporosis emerging as a critical determinant of morbidity and functional impairment in older adults[1]. This metabolic bone disease, characterized by compromised bone strength predisposing to fractures, manifests particularly through low-energy fragility fractures resulting from minimal trauma equivalent to a fall from standing height or less[2]. Such fractures incur substantial personal and societal burdens, including chronic pain, functional decline, diminished quality of life, and escalating healthcare expenditures[3,4]. Accurate prediction of fracture risk therefore constitutes a fundamental component of effective osteoporosis management and fracture prevention strategies[5].

Contemporary fracture risk assessment relies principally on bone mineral density (BMD) measurement alongside clinical risk factors integrated in algorithmic tools such as FRAX®[6]. While BMD provides valuable diagnostic information and

Ethics approval and consent to participate: The study was performed according to the Declaration of Helsinki (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/) and approval from the ethics committee of Affiliated Hospital of Zunyi Medical University (No. KLL-2024-575), and de-identified clinical data were used for secondary analysis, waiving the requirement for informed consent from patients.

remains the cornerstone of osteoporosis diagnosis, its limitations as a standalone predictor are well documented in longitudinal studies. Considerable fracture risk heterogeneity exists among individuals with comparable BMD values, underscoring the significant contribution of non-skeletal factors to fracture etiology, particularly those related to fall frequency and impact mechanics[7]. This recognition has stimulated investigation into multidimensional constructs that better reflect physiological resilience and integrated vulnerability in older adults, moving beyond purely bone-centric assessment paradigms[8].

The geriatric syndrome of frailty, operationalized through phenotypic criteria such as the Fried Frailty Phenotype, embodies precisely such multidimensional vulnerability. Characterized by diminished physiological reserve and impaired stress response capacity, frailty manifests through objectively measurable declines in strength, mobility, and energy metabolism[9]. Validated assessment tools capture this multisystem dysregulation, providing integrated measures of physiological integrity that transcend traditional disease-specific approaches[10]. Substantial epidemiological evidence establishes frailty as a robust predictor of diverse adverse health outcomes across clinical contexts, including hospitalization, disability, and mortality[11].

Within osteoporosis care, frailty's relationship to fracture risk presents a compelling yet incompletely characterized association. Multiple interconnected pathophysiological mechanisms including sarcopenia, chronic inflammation, endocrine dysregulation, and neuromuscular impairment potentially underlie both accelerated bone loss and increased fracture susceptibility in frail individuals. The convergence of these pathways creates a biological milieu where reduced bone strength coincides with elevated fall risk, substantially amplifying fracture probability. Nevertheless, the prognostic utility of frailty assessment specifically for low-energy fracture prediction in established osteoporosis populations remains inadequately defined, with existing studies yielding inconsistent conclusions due to methodological variations and population heterogeneity[12,13].

Notably, conventional fracture risk algorithms like FRAX, while incorporating multiple clinical variables, do not explicitly capture the integrated physiological vulnerability represented by frailty status[14-18]. This conceptual and methodological gap suggests potential complementarity between established risk assessment paradigms and direct evaluation of frailty as a distinct clinical entity.

To address this evidence gap, we conducted a retrospective cohort study examining the longitudinal association between baseline frailty phenotype and subsequent low-energy fracture incidence in older hospitalized patients with radiologically confirmed osteoporosis. We hypothesized that frailty status would independently predict fracture risk beyond conventional assessment parameters, potentially offering enhanced risk stratification and personalized management approaches in this vulnerable population.

METHODS

Study Design

This retrospective cohort study utilized clinical data from older adults with osteoporosis who were admitted to the Affiliated Hospital of Zunyi Medical University between January 2020 and January 2022. The study was designed to evaluate the association between baseline frailty status and the subsequent incidence of low-energy fractures. The study protocol was conducted in accordance with the ethical principles of the Declaration of Helsinki and received approval from the institutional ethics committee (Approval No. KLL-2024-575). As the analysis involved de-identified clinical data retrieved from hospital records, the requirement for individual informed consent was waived.

Participants

The study initially screened inpatient medical records of individuals aged 60 years or older who were diagnosed with osteoporosis during the enrollment period from January 2020 to January 2022. From this pool, participants were included if they met all of the following criteria: (1) aged 60 years or older; (2) diagnosis of primary osteoporosis confirmed by dual-energy X-ray absorptiometry (DXA) with a BMD T-score of $\leq$ -2.5 at the lumbar spine (L1-L4) or femoral neck, consistent with World Health Organization (WHO) diagnostic criteria; and (3) availability of complete medical records encompassing comprehensive demographic data, medical history, physical examination findings, laboratory results, and relevant imaging studies.

Patients were excluded from the analysis for any of the following reasons: (1) presence of secondary osteoporosis attributable to specific etiologies, including endocrine disorders, chronic rheumatic diseases, malignancies with bone involvement, or long-term use of medications known to affect bone metabolism; (2) documented history of fractures

resulting from high-energy trauma; (3) severe dysfunction of major organ systems that could confound frailty assessment or limit life expectancy; or (4) diagnosed psychiatric disorders or significant cognitive impairment that would preclude reliable participation in clinical assessments.

Assessment of Frailty

Frailty status was assessed using the Fried Frailty Phenotype (FFP), a validated instrument that evaluates five physical components: unintentional weight loss (>4.5 kg in the past year), self-reported exhaustion (based on two statements from the Center for Epidemiologic Studies Depression Scale), weakness (measured by dominant handgrip strength adjusted for sex and body mass index), slow walking speed (time to walk 4.57 meters, adjusted for sex and height), and low physical activity (kilocalories expended per week, derived from the Minnesota Leisure Time Activity Questionnaire)[19]. Participants were classified according to the number of criteria met: frail (≥3 criteria), pre-frail (1-2 criteria), or non-frail (0 criteria). The assessment was conducted at the time of hospital admission using standardized protocols to ensure consistent evaluation. Only baseline frailty status was determined for this study, with no longitudinal reassessment during the follow-up period. In all subsequent analyses, the main predictor variable was frailty status (frail, pre-frail, non-frail) according to the Fried Frailty Phenotype at baseline.

Definition of Low-Energy Fractures

Low-energy fractures were defined as fractures that occurred under minimal external forces during daily activities, such as standing, walking, or rising from a chair. Fracture diagnosis was based on clinical symptoms (e.g., new pain, swelling, limited mobility or loss of function) and physical examination findings (e.g., deformity, tenderness, crepitus), followed in all cases by confirmatory imaging (X-ray, CT, or MRI). Vertebral fractures were identified when patients presented with new back pain, height loss, or postural change (e.g., new kyphosis) and were confirmed on lateral spine radiographs or, when necessary, CT or MRI; systematic morphometric screening for asymptomatic vertebral deformities was not performed.

All suspected fracture cases underwent rigorous adjudication by at least two independent orthopedic surgeons with specialized experience in geriatric trauma. Diagnostic confirmation required both clinical evidence (documented symptoms including new-onset pain, functional impairment, or physical signs such as deformity and localized tenderness) and definitive radiographic evidence from X-ray, CT, or MRI. For vertebral fractures, identification was based on clinical presentation (acute back pain, documented height loss, or postural change) with subsequent radiographic confirmation; systematic morphometric screening for asymptomatic vertebral deformities was not performed. The fracture occurrence date was systematically recorded as the earlier of either the patient-reported symptom onset date or the initial imaging confirmation date, ensuring accurate temporal classification in subsequent analyses.

Data Collection

Baseline Data:

Data collected included patients' basic demographics, such as age, sex, height, and weight; medical history of chronic conditions like hypertension, diabetes, and cardiovascular diseases; lifestyle factors, including smoking and alcohol consumption; and bone density measurement results. For the purposes of this study, cardiovascular disease was defined as a documented history of coronary artery disease (including previous myocardial infarction or coronary revascularisation), heart failure or cardiomyopathy, atrial fibrillation or other chronic arrhythmias, or ischaemic or haemorrhagic stroke recorded in the medical record.

Follow-Up Data:

Patient enrollment occurred between January 2020 and January 2022, with all participants subsequently undergoing a standardized three-year prospective follow-up period. Follow-up assessments were conducted at predetermined intervals through structured outpatient clinic visits complemented by systematic telephone surveys. This dual-modality approach ensured comprehensive monitoring of fracture outcomes while maximizing data completeness and verification accuracy. All follow-up evaluations utilized standardized data collection instruments to maintain consistency in documentation across the study period.

Statistical Analysis

Data analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation or median (interquartile range), as appropriate, and were compared between groups using one-way analysis of variance or the Kruskal–Wallis H test. Categorical

variables are presented as counts (percentages) and were compared using the chi-squared test or Fisher's exact test, as appropriate.

For the analysis of fracture risk, univariable logistic regression models were first fitted with fracture (yes/no) as the dependent variable to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for each candidate predictor. BMD T-score was entered as a continuous variable, and the OR for BMD corresponds to the change in fracture odds per 1-unit decrease (worsening) in T-score.

Variables that showed an association with fractures at $p < 0.10$ in univariable analyses, together with clinically important factors identified a priori, were considered for inclusion in the multivariable logistic regression model. To reduce the risk of overfitting, the number of variables in the multivariable model was restricted so that the ratio of fracture events to the number of parameters was approximately in line with the commonly recommended rule of about 10 events per variable. A parsimonious final model was obtained by retaining variables with clear clinical relevance and/or statistical significance. BMD T-score was treated as a continuous variable, and the odds ratio corresponds to the change in fracture risk per 1-unit decrease in T-score.

All ORs are reported with two decimal places, and for very small ORs (e.g. < 0.01) three decimal places are used to avoid misleading rounding to 0.00. A two-sided p-value < 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

A total of 129 eligible participants were included in the final analysis and stratified into three groups according to their baseline Fried Frailty Phenotype classification: frail (n=32), pre-frail (n=53), and non-frail (n=44). Comparative analysis of demographic and clinical characteristics revealed significant intergroup differences. Participants in the frail group were significantly older and demonstrated substantially lower body mass index (BMI) values compared to both the pre-frail and non-frail groups. Furthermore, the prevalence of documented cardiovascular disease was significantly higher in the frail group relative to the non-frail group. No statistically significant differences were observed in gender distribution, hypertension prevalence, diabetes mellitus, smoking history, or alcohol consumption patterns across the three frailty categories. Detailed baseline characteristics are presented in Table I.

Bone Mineral Density

BMD profiles, expressed as T-scores, were systematically compared across the frailty spectrum. Initial assessment revealed a graded pattern of BMD reduction corresponding to worsening frailty status. Subsequent post-hoc pairwise analyses using the Tukey test confirmed statistically significant differences in BMD T-scores between the frail group and both the pre-frail group ($p < 0.001$) and the non-frail group ($p < 0.001$). However, no significant BMD difference was detected between the pre-frail and non-frail groups ($p = 0.214$). These findings demonstrate a pronounced association between frailty severity and bone mineral density, with significantly compromised BMD specifically characterizing the frail phenotype. Complete BMD comparisons are summarized in Table II.

Fracture Incidence

From the initial cohort of 129 patients, 115 (89.2%) completed the three-year follow-up protocol. Fourteen patients were excluded from the final analysis, including five who sustained high-energy fractures during follow-up and nine lost to contact. Among the 115 analyzed participants, 48 (41.7%) experienced at least one low-energy fracture during the observation period. The fracture distribution comprised 15 hip fractures (31.3%), 15 clinically diagnosed vertebral fractures (31.3%), and 13 fractures at other anatomical sites (27.1%). All vertebral fractures were identified through clinical presentation (new-onset back pain, documented height loss, or postural changes) with subsequent radiographic confirmation; no systematic morphometric screening for asymptomatic vertebral deformities was performed. Consistent with standard clinical practice, imaging examinations were initiated based on clinical suspicion rather than through protocol-mandated systematic screening.

Frailty status demonstrated a strong graded association with fracture incidence. The frail group exhibited substantially higher fracture rates (21/29, 72.4%) compared to both pre-frail (19/47, 40.4%) and non-frail groups (8/39, 20.5%). Statistical testing revealed significant differences across all group comparisons: frail versus pre-frail ($p < 0.01$), pre-frail versus non-frail ($p < 0.01$), and overall group difference ($\chi^2 = 18.48$, $p < 0.001$). This pattern indicates a progressive increase in fracture risk corresponding to advancing frailty severity (Table III).

Table I. — Baseline Information of Different Fried Frailty Phenotypes.

	Fried Frailty Phenotypes				
Characteristic	Frail, N = 32[1]	Pre-frail, N = 53[1]	Non-frail, N = 44[1]	Statistic	p-value
Age				26.18	<0.001[2]
Mean ± SD	76 ± 5	70 ± 7	70 ± 3		
Median (IQR)	78 (76, 79)	70 (64, 72)	69 (67, 73)		
Range	63, 84	62, 86	65, 74		
Gender				3.92	0.141[3]
Female	13 (40.6%)	31 (58.5%)	18 (40.9%)		
Male	19 (59.4%)	22 (41.5%)	26 (59.1%)		
BMI (kg/m²)				36.99	<0.001[2]
Mean ± SD	25.14 ± 3.28	24.49 ± 1.40	26.27± 0.60		
Median (IQR)	26.90 (21.90, 28.13)	24.60 (24.30, 25.10)	26.15 (25.70, 26.80)		
Range	20.50, 29.00	21.00, 28.50	25.50, 27.50		
Hypertension				0.07	0.964[3]
No	15 (46.9%)	26 (49.1%)	22 (50.0%)		
Yes	17 (53.1%)	27 (50.9%)	22 (50.0%)		
Diabetes				5.10	0.078[3]
No	13 (40.6%)	34 (64.2%)	21 (47.7%)		
Yes	19 (59.4%)	19 (35.8%)	23 (52.3%)		
Cardiovascular Disease				6.71	0.035[3]
No	14 (43.8%)	38 (71.7%)	25 (56.8%)		
Yes	18 (56.3%)	15 (28.3%)	19 (43.2%)		
Smoking History				2.86	0.240[3]
No	13 (40.6%)	31 (58.5%)	25 (56.8%)		
Yes	19 (59.4%)	22 (41.5%)	19 (43.2%)		
Alcohol History				3.47	0.177[3]
No	12 (37.5%)	27 (50.9%)	26 (59.1%)		
Yes	20 (62.5%)	26 (49.1%)	18 (40.9%)		

[1]n (%); [2]Kruskal-Wallis rank sum test; [3]Pearson's Chi-squared test.

Table II. — Comparison of Bone Density T-Values Among Different Frailty Phenotypes.

Characteristic	Frail, N = 32	Pre-frail, N = 53	Non-frail, N = 44	Statistic	p-value
T-scores				50.65	<0.001[1]
Mean ± SD	-2.97 ± 0.13	-2.68 ± 0.19	-2.70 ± 0.10		
Median (IQR)	-2.90 (-3.03, -2.90)	-2.70 (-2.70, -2.50)	-2.65 (-2.80, -2.60)		
Range	-3.20, -2.70	-3.10, -2.50	-2.90, -2.60		

[1]Kruskal-Wallis rank sum test

Table III. — Fracture Incidence Analysis.

Characteristic	Frail, N = 29[1]	Pre-frail, N = 47[1]	Non-frail, N = 39[1]	Statistic	p-value
Low-energy fractures				18.48	<0.001[2]
No	8 (27.6%)	28 (59.6%)	31 (79.5%)		
Yes	21 (72.4%)	19 (40.4%)	8 (20.5%)		

[1]n (%); [2]Pearson's Chi-squared test.

Fracture Risk Factors

Univariable logistic regression analyses were performed to evaluate potential determinants of low-energy fracture risk, with fracture occurrence designated as the dependent variable. Clinical characteristics, BMD T-scores, and frailty status were included as independent variables. Initial screening identified several variables significantly associated with fracture risk ($p < 0.10$), including age, hypertension, diabetes mellitus, smoking history, cardiovascular disease, BMD T-score, and frailty status.

These candidate variables were subsequently incorporated into a multivariable logistic regression model. After adjustment for confounding factors, cardiovascular disease (OR = 8.58, 95% CI: 2.62-

28.12, $p < 0.001$) and frailty status emerged as independent predictors of fracture occurrence. Using frail participants as the reference group, both pre-frail (OR = 0.61, 95% CI: 0.16-0.72, p = 0.005) and non-frail status (OR = 0.49, 95% CI: 0.10-0.82, p = 0.007) were associated with significantly reduced fracture risk, indicating their protective effect relative to frailty.

In the final adjusted model, BMD T-score was treated as a continuous variable, with the corresponding odds ratio representing the change in fracture risk per 1-unit decrease in T-score. Complete results of the regression analyses are presented in Table IV.

DISCUSSION

This hospital-based cohort study provides compelling evidence that frailty status, as defined by the FFP, serves as a powerful independent predictor of low-energy fractures among older inpatients with confirmed osteoporosis. Our findings demonstrate a clear gradient in fracture risk across frailty categories, with frail patients exhibiting substantially higher fracture incidence (72.4%) compared to pre-frail (40.4%) and non-frail (20.5%) individuals. Multivariable analysis identified both frailty status and cardiovascular disease as independent predictors of fracture occurrence, while pre-frailty and non-frailty demonstrated protective effects relative to the frail state.

The significant differences in BMD observed across frailty categories suggest an intimate relationship between frailty and accelerated bone loss. Our data reveal that frail patients presented with significantly lower BMD T-scores compared to both pre-frail and non-frail groups, supporting the concept that frailty and osteoporosis share common underlying pathophysiological mechanisms. This observation aligns with existing literature documenting the association between frailty and reduced BMD, potentially mediated through multiple interconnected pathways including sarcopenia, hormonal dysregulation, nutritional deficiencies, and chronic inflammation[20]. The progressive decline in BMD from non-frail to pre-frail to frail states reinforces the notion that frailty represents not merely a functional decline but also contributes substantially to skeletal vulnerability.

The substantially elevated fracture incidence among frail individuals (72.4% versus 20.5% in non-frail) underscores the multifactorial nature of fracture risk in this population. Frailty appears to create a perfect storm for fracture susceptibility through several complementary mechanisms. First, decreased muscle strength and reduced gait speed impair balance and mobility, thereby increasing fall frequency - the primary mechanism for most low-energy fractures[21,22]. Second, the chronic inflammatory state characteristic of frailty, marked by elevated cytokines such as TNF-α, IL-1, and IL-6, promotes accelerated bone resorption and compromises bone quality[24]. Third, the high burden of cardiovascular disease observed in our frail population (56.3% versus 28.3% in non-frail) contributes additional risk through activity limitation, vascular dysfunction, and medication effects. Finally, suboptimal nutritional status, particularly regarding calcium and vitamin D intake, further exacerbates bone loss in frail individuals[25].

Our findings are consistent with and substantially extend previous research in this field. The Global Longitudinal Study of Osteoporosis in Women (GLOW) previously demonstrated that frailty was associated with higher risks of fractures, disability, and falls among community-dwelling older women with low bone mass[12]. Similarly, multiple cohort studies and meta-analyses have reported that both frailty and pre-frailty confer substantially increased fracture risk compared to non-frailty in community settings, with effect sizes typically ranging from two- to threefold[26]. Recent large-scale cohort data further indicate that frailty is associated with long-term fracture-related hospitalizations and mortality, suggesting that frailty and osteoporotic fractures may act as mutual risk factors with shared pathophysiological mechanisms[27].

The novel aspect of our investigation lies in its specific focus on a hospitalized population with DXA-confirmed osteoporosis (T-score ≤ -2.5). While most previous frailty-fracture studies have been conducted in community-dwelling cohorts encompassing individuals with normal bone density or osteopenia[28], our restriction to hospitalized patients with established osteoporosis demonstrates that frailty status provides substantial additional prognostic information even within a population already considered at high baseline fracture risk. This finding highlights that functional capacity and comorbidity burden, as captured by frailty assessment, remain crucial determinants of fracture risk in this particularly vulnerable population.

Our results have important implications for fracture risk assessment in clinical practice. The finding that BMD T-score lost statistical significance in multivariable analysis after adjustment for frailty status and cardiovascular comorbidities, while frailty remained independently predictive, reinforces the concept that

Table IV. — Results of Univariate and Multivariate Logistic Regression Analysis of Fracture Risk Factors.

Variable	Category	Univariable OR[1]	95% CI[1]	p-value[2]	Multivariable OR[1]	95% CI[1]	p-value[2]
Age (years)	per 1-year ↑	1.18	1.09–1.27	<0.001***	1.03	0.92–1.17	0.589
Gender							
	Female	Reference	–	–	—	—	—
	Male	0.79	0.38–1.66	0.539	—	—	—
BMI (kg/m²)	per 1 kg/m² ↑	0.86	0.71–1.03	0.106	—	—	—
Hypertension							
	No	Reference	–	–	Reference	–	–
	Yes	2.96	1.37–6.42	0.006**	0.91	0.30–2.76	0.872
Diabetes							
	No	Reference	–	–	Reference	–	–
	Yes	2.68	1.25–5.75	0.011*	2.55	0.90–7.24	0.079
Smoking							
	No	Reference	–	–	Reference	–	–
	Yes	2.88	1.33–6.20	0.007**	1.98	0.66–5.97	0.223
Cardiovascular disease							
	No	Reference	–	–	Reference	–	–
	Yes	4.29	1.95–9.44	<0.001***	8.58	2.62–28.12	<0.001***
Alcohol consumption							
	No	Reference	–	–	—	—	—
	Yes	1.39	0.65–2.97	0.391	—	—	—
BMD T-score[3]	per 1-unit ↓	0	0.00–0.04	<0.001***	0.01	0.00–2.22	0.097
Frailty status (Fried type)							
	Frail	Reference	–	–	Reference	–	–
	Pre-frail	0.26	0.09–0.70	0.008**	0.61	0.16–0.72	0.005**
	Non-frail	0.1	0.03–0.30	<0.001***	0.49	0.10–0.82	0.007**

[1]OR, odds ratio; CI, confidence interval; [2]p < 0.05*, p < 0.01**, p< 0.001***; [3]BMD T-score was entered as a continuous predictor; the odds ratio represents the change in fracture risk per 1-unit decrease in T-score.

frailty captures multidimensional vulnerability not fully reflected by conventional assessment parameters. This pattern aligns with previous research comparing deficit-accumulation frailty indices with FRAX, which demonstrated that both measures predict fractures and that their combination improves risk discrimination[29,30]. Studies in community-dwelling older women have shown that adding frailty status to FRAX identifies additional high-risk individuals who would otherwise be missed by FRAX alone[15], while recent Framingham Heart Study analyses suggest that FRAX may underestimate fracture risk in frail individuals[18].

Rather than replacing established tools like FRAX, frailty assessment should be viewed as a complementary approach that provides a more comprehensive evaluation of fracture risk. The integration of frailty assessment into clinical practice could significantly enhance risk stratification and guide targeted intervention strategies.

The clinical implications of our findings are substantial. Older individuals with osteoporosis and high frailty scores warrant comprehensive management strategies that extend beyond conventional bone-targeted therapies. Essential components of such an approach should include structured fall prevention programs incorporating balance and strength training, home safety modifications, nutritional optimization with particular attention to protein, calcium, and vitamin D intake, and meticulous management of cardiovascular comorbidities. Implementation of routine frailty screening using practical tools like the FFP in geriatric and primary care settings could facilitate early identification of high-risk individuals and guide personalized intervention strategies.

Several limitations of this study warrant careful consideration when interpreting our findings. First, the single-center design and relatively limited sample size, particularly within the frail subgroup (n=32), may affect the generalizability of our results to broader populations. Although we employed statistical measures to maintain an appropriate events-per-variable ratio in our regression models, the modest number of fracture events (n=48) may still impact the stability and precision of the estimated odds ratios. Second, while our study featured a three-year follow-up period, the assessment of frailty was conducted only at baseline. Given the dynamic nature of frailty, this design limitation prevents examination of how transitions in frailty status over time might influence fracture risk. Third, our exclusive reliance on the Fried Frailty Phenotype means we cannot compare its performance against other established assessment tools, such as the Frailty Index based on Comprehensive Geriatric Assessment, which may capture different aspects of vulnerability. Finally, our study did not account for potential heterogeneity in frailty phenotypes, nor did it evaluate the effects of targeted interventions aimed at reducing either frailty or fracture risk. These limitations highlight important avenues for future investigation.

Future research should prioritize multicenter prospective studies with larger sample sizes to enhance statistical power and generalizability. Longitudinal designs incorporating repeated frailty assessments would elucidate how dynamic changes in frailty status affect fracture risk over time. Comparative effectiveness studies evaluating different frailty assessment tools in fracture prediction would help establish optimal measurement approaches. Furthermore, intervention studies examining whether frailty reduction strategies can subsequently lower fracture incidence represent a crucial next step in translating these findings into clinical practice. The development of integrated risk assessment models incorporating both traditional fracture risk factors and frailty metrics also merits investigation.

CONCLUSION

This study demonstrates that frailty status, as assessed by the Fried Frailty Phenotype, serves as a strong independent predictor of low-energy fracture risk in older adults with osteoporosis, while pre-frailty and non-frailty states exhibit protective effects. The findings support the integration of frailty assessment as a complementary component to established risk evaluation tools such as FRAX, enabling a more comprehensive approach to fracture risk stratification. Incorporating frailty evaluation into clinical practice could significantly enhance the identification of high-risk patients and inform the development of personalized prevention and treatment strategies for this vulnerable population.

Consent to Participate: Not applicable.

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REFERENCES

1. Grinin L, Grinin A, Korotayev A. Global Aging: An Integral Problem of the Future. How to Turn a Problem into a Development Driver? In: Sadovnichy V, Akaev A, Ilyin I, Malkov S, Grinin L, Korotayev A, eds. Reconsidering the Limits to Growth: A Report to the Russian Association of the Club of Rome. Cham: Springer International Publishing 2023:117-35.
2. Barnsley J, Buckland G, Chan PE, Ong A, Ramos AS, Baxter M, Laskou F, Dennison EM, Cooper C, Patel HP. Pathophysiology and treatment of osteoporosis: challenges for clinical practice in older people. Aging Clinical and Experimental Research 2021;33:759-73.

3. Zhu Y, Liu S, Chen W, Liu B, Zhang F, Lv H, Ji C, Zhang X, Zhang Y. Epidemiology of low-energy lower extremity fracture in Chinese populations aged 50 years and above. PLoS One 2019;14:e0209203.
4. de Joode S, Kalmet PHS, Fiddelers AAA, Poeze M, Blokhuis TJ. Long-term functional outcome after a low-energy hip fracture in elderly patients. J Orthop Traumatol 2019;20:20.
5. Fuggle NR, Curtis EM, Ward KA, Harvey NC, Dennison EM, Cooper C. Fracture prediction, imaging and screening in osteoporosis. Nature Reviews Endocrinology 2019;15:535-47.
6. Migliorini F, Giorgino R, Hildebrand F, Spiezia F, Peretti GM, Alessandri-Bonetti M, Eschweiler J, Maffulli N. Fragility Fractures: Risk Factors and Management in the Elderly. Medicina (Kaunas) 2021;57
7. Aibar-Almazán A, Voltes-Martínez A, Castellote-Caballero Y, Afanador-Restrepo DF, Carcelén-Fraile MDC, López-Ruiz E. Current Status of the Diagnosis and Management of Osteoporosis. Int J Mol Sci 2022;23
8. Li HL, Shen Y, Tan LH, Fu SB, Dai RC, Yuan LQ, Sheng ZF, Xie ZJ, Wu XP, Liao EY, Tang XL, Wu XY. Relationship between bone mineral density and fragility fracture risk: a case-control study in Changsha, China. BMC Musculoskelet Disord 2021;22:728.
9. Cohen CI, Benyaminov R, Rahman M, Ngu D, Reinhardt M. Frailty: A Multidimensional Biopsychosocial Syndrome. Med Clin North Am 2023;107:183-97.
10. Sapp DG, Cormier BM, Rockwood K, Howlett SE, Heinze SS. The frailty index based on laboratory test data as a tool to investigate the impact of frailty on health outcomes: a systematic review and meta-analysis. Age Ageing 2023;52
11. Ysea-Hill O, Gomez CJ, Mansour N, Wahab K, Hoang M, Labrada M, Ruiz JG. The association of a frailty index from laboratory tests and vital signs with clinical outcomes in hospitalized older adults. J Am Geriatr Soc 2022;70:3163-75.
12. Tom SE, Adachi JD, Anderson FA Jr, Boonen S, Chapurlat RD, Compston JE, Cooper C, Gehlbach SH, Greenspan SL, Hooven FH, Nieves JW, Pfeilschifter J, Roux C, Silverman S, Wyman A, LaCroix AZ; GLOW Investigators. Frailty and fracture, disability, and falls: a multiple-country study from the global longitudinal study of osteoporosis in women. J Am Geriatr Soc. 2013 Mar;61(3):327-34
13. Schini, M., Johansson, H., Harvey, N.C. et al. An overview of the use of the fracture risk assessment tool (FRAX) in osteoporosis. J Endocrinol Invest 47, 501–511 (2024).
14. Li G, Thabane L, Papaioannou A, Adachi JD. Comparison between frailty index of deficit accumulation and fracture risk assessment tool (FRAX) in prediction of risk of fractures. Bone. 2015 Aug;77:107-14.
15. Bartosch, P., Malmgren, L. Can frailty in conjunction with FRAX identify additional women at risk of fracture - a longitudinal cohort study of community dwelling older women. BMC Geriatr 22, 951 (2022).
16. Elsa Dent, Jack Dalla Via, Trent Bozanich, Emiel O Hoogendijk, Abadi K Gebre, Cassandra Smith, Kun Zhu, Richard L Prince, Joshua R Lewis, Marc Sim, Frailty increases the long-term risk for fall and fracture-related hospitalizations and all-cause mortality in community-dwelling older women, Journal of Bone and Mineral Research, Volume 39, Issue 3, March 2024, Pages 222–230.
17. Urano T, Kuroda T, Saito M, Shiraki M. Frailty and osteoporotic fractures represent mutual risks for each other with common physiological backgrounds. JBMR Plus. 2025 Jan 13;9(4):ziaf009. doi: 10.1093/jbmrpl/ziaf009.
18. Chattaris T, Yang L, Johansson H, Sahni S, Samelson EJ, Kiel DP, Berry SD. Performance of FRAX in older adults with frailty: the Framingham Heart Study. Osteoporos Int. 2024 Feb;35(2):265-275. doi: 10.1007/s00198-023-06950-0
19. Forssten, M.P.; Cao, Y.; Mohammad Ismail, A.; Tennakoon, L.; Spain, D.A.; Mohseni, S. Comparative Analysis of Frailty Scores for Predicting Adverse Outcomes in Hip Fracture Patients: Insights from the United States National Inpatient Sample. J. Pers. Med. 2024, 14, 621
20. Greco EA, Pietschmann P, Migliaccio S. Osteoporosis and Sarcopenia Increase Frailty Syndrome in the Elderly. Front Endocrinol (Lausanne) 2019;10:255.
21. Riviati N, Indra B. Relationship between muscle mass and muscle strength with physical performance in older adults: A systematic review. SAGE Open Med 2023;11:20503121231214650.
22. Abdelaziz H, Schröder M, Tien CS, Ibrahim K, Gehrke T, Salber J, Citak M. Resection of the proximal femur during one-stage revision for infected hip arthroplasty risk factors and effectiveness. Bone and Joint Journal 2021;103-B:1678-85.
23. Weiss CO. Frailty and chronic diseases in older adults. Clin Geriatr Med 2011;27:39-52.
24. Zhang L, Zeng X, He F, Huang X. Inflammatory biomarkers of frailty: A review. Experimental Gerontology 2023;179:112253.
25. Ni Lochlainn M, Cox NJ, Wilson T, Hayhoe RPG, Ramsay SE, Granic A, Isanejad M, Roberts HC, Wilson D, Welch C, Hurst C, Atkins JL, Mendonça N, Horner K, Tuttiett ER, Morgan Y, Heslop P, Williams EA, Steves CJ, Greig C, Draper J, Corish CA, Welch A, Witham MD, Sayer AA, Robinson S. Nutrition and Frailty: Opportunities for Prevention and Treatment. Nutrients 2021;13
26. Kojima G. Frailty as a predictor of fractures among community-dwelling older people: A systematic review and meta-analysis. Bone 2016;90:116-22.
27. Kojima G. Increased healthcare costs associated with frailty among community-dwelling older people: A systematic review and meta-analysis. Archives of Gerontology and Geriatrics 2019;84:103898.
28. Li X, Schöttker B, Holleczek B, Brenner H. Association of longitudinal repeated measurements of frailty index with mortality: Cohort study among community-dwelling older adults. EClinicalMedicine 2022; 53:101630.
29. Cunha AIL, Veronese N, de Melo Borges S, Ricci NA. Frailty as a predictor of adverse outcomes in hospitalized older adults: A systematic review and meta-analysis. Ageing Research Reviews 2019;56:100960.
30. Mathew SA, Gane E, Heesch KC, McPhail SM. Risk factors for hospital re-presentation among older adults following fragility fractures: a systematic review and meta-analysis. BMC Med 2016;14:136