Original Article

Role of FIRE-MADE FI for diagnosing frailty in central rural India and its comparison with LASA FI

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Abstract

Background: An aging population ultimately has deprived physiological stores making them vulnerable for development of a syndrome called frailty, which presents with a cumulative decrease in tolerance, immunity, vision, balance, organ functions, health, and independent living. All these result in rising prevalence of frailty and its components, along with burden of disease, dependence, and health care cost. Thus, early estimation and assessment and interventions to correct it mark the mile stone in geriatric medicine. The present study was conducted with an aim to compare and correlate FIRE-MADE (Frailty Index in Rural Elderly – Mental status, Activities of daily living, Depression, and Events) FI (frailty index) with LASA (Longitudinal Aging Study Amsterdam) FI in central rural India's geriatric population. **Methodology:** A cross-sectional study for assessment of frailty in the geriatric population of central rural India, reporting to the medicine department of a tertiary hospital, situated at Wardha district, by using FIRE-MADE and LASA FI was undertaken. Their scores were compared. The efficiency of FIRE-MADE FI in comparison with LASA FI was calculated. A frailty threshold of ≥ 0.25 is considered for diagnosing frailty. Standard descriptive and inferential statistics were used to evaluate all parametric and non-parametric data. **Results:** Out of 250 geriatric people, 224 (89.6%) were frail according to LASA FI and 204 (81.6%) were frail according to FIRE-MADE FI. As compared to LASA FI, FIRE-MADE FI was 91.07% sensitive and 73.08% specific, with a positive predictive value of 96.68% and a diagnostic accuracy of 89.20%. **Conclusion:** The Indian rural population of central India has high prevalence of frailty. FIRE-MADE FI can be used as a potential, effective, and validated tool for early diagnosing and management of frailty. Among the parameters of FIRE-MADE FI, IHD was the most important contributing factor for development of frailty, followed by cognitive impairment, polypharmacy, and remaining factors mentioned in FIRE-MADE FI.

Keywords: Central rural India, elderly population, FIRE-MADE FI, frailty, geriatric, LASA FI

Introduction

People who aged 60 years or more are called geriatric people, as per the definition proposed by United Nations (UN) and World Health Organization (WHO). They are increasing with an extraordinary speed all over the world, and with them, diseases of old age are increasing.[1,2] These diseases are mostly the result of weaned off physiological stores and tolerance, resulting in a syndrome called "frailty", which is characterized by weight loss, and a decrease in muscular power, organ functions, immunity, balance, good health, and strength, leading to early fatigue, less physical activity, slow unbalanced gait, and increase dependence.[3] All these cause high disease burden on financial, political, medical, and social domains.[1,2]

Thus, early estimation and assessment and interventions to correct it become very essential not only to decrease disease burden but also for a healthy living of the geriatric population.

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Among the numerous indices available to measure the frailty,[4] we assessed and compared the frailty in the same population by two indices, FIRE-MADE FI and LASA FI.

FIRE-MADE FI is a recently proposed and internally validated tool.[5] We compared and correlated it with LASA FI in central rural India's geriatric population to predict frailty and to know its efficiency and thus to externally validate it.

Methodology

The present cross-sectional study was carried out at the medicine department of the tertiary care hospital of Wardha district from September 2019 to February 2020, following approval from the institutional ethical committee of the attached institute.

By considering the prevalence of 30% with 95% confidence interval and 6% of desired error of margin, we calculated the sample size.[6] A total of 256 subjects of central rural India, with an age more than 60 years, visiting the medicine department were included in the study. Of them, six chronically bedridden, completely dependent, and/or not willing to participate were kept out of the study.

The patient assessment forms were filled, which include the necessary details, like baseline characteristics, anthropometric data, visit reason, and co-morbidities [like diabetes mellitus (DM), hypertension (HTN), asthma, chronic obstructive pulmonary disease (COPD), cardiovascular diseases (CVDs) and cerebrovascular accidents (CVAs), medications, depression, and dependence].

The following figure [Figure 1] represents various components of FIRE-MADE FI and their scoring system.[5]

We also evaluated frailty in the same group using the LASA FI for comparison and validation. The LASA index, with 32 parameters, calculates frailty as the sum of deficits divided by the total number of areas considered, with a frailty cut-off of ≥0.25.

Sr. No.	Contributing factors	Result (0 to 10)
1	Mental status by Mini Mental State Examination (MMSE) score 27-30 = normal <27 = impaired cognitive function	Normal = 0 Impaired = 1
2	Activities of Daily Living (ADL) score (feeding, dressing, bathing, going to toilet, urinary continence, transferring).	No help = 0, Need help = 1, for any of the mentioned activity
3	Geriatric Depression Scale (GDS) (short version) score (>5 = probable depression)	No = 0 Yes = 1
4	Events like	
A	Polypharmacy,	No = 0, yes =1
B	DM	No = 0, yes =1
C	IHD	No = 0, yes =1
D	COPD/Asthma	No = 0, yes =1
E	Stroke	No = 0, yes =1
F	Cancer	No = 0, yes =1
G	Others	No = 0, yes =1
The index, calculated as the ratio of present deficits to total potential deficits (10 in this model), classifies scores: <0.25 as fit, 0.25-0.49 as mildly frail, 0.5-0.69 as moderately frail, and >0.7 as severely frail.		

Figure 1: Contributing factors/components of FIRE-MADE FI and their assigned scores

Results of the present study were analyzed by descriptive statistics using frequency, percentage, mean, and standard deviation and inferential statistics by using proportions Student's paired *t* test, Student's unpaired *t* test, and Chi-square test after recording, processing, and analyzing the entire data by Microsoft Excel 2010 and SPSS (16.0 version, IBM Analytics, New York) and GraphPad Prism 7.0 version.

All *P* values less than 0.05 were nomenclated as statistically significant.

Observations and Results

Table 1 shows baseline characteristics of 250 geriatric subjects, of which 58.4% were males and 41.6% were females. The average age was 68.08 ± 4.46, with no significant gender difference. The mean frailty scores of the total study population, assessed by FIRE-MADE FI and LASA FI, were 0.48 ± 0.23 and 0.57 ± 0.26, respectively. These scores showed no statistically significant differences ($P = 0.31$ and $P = 0.15$, respectively).

Table 2 shows age- and gender-wise distribution of the study population.

The male-to-female ratio was 1.4:1, with males (58.4%) outnumbering females (41.6%), but this was not statistically significant ($P = 0.245$). Most subjects (82.8%) were aged 61–70 years in both genders.

Figure 2 demonstrate contribution of various domains or factors of FIRE-MADE FI in development of frailty in our study.

In our study, of 97 cognitive impaired subjects, 49 were males and 48 were females, while 80 males and 70 females were dependent as per ADL score. GDS (short version) demonstrated that 100 males and 78 females were depressed.

Diabetes mellitus was found in 93 males and 54 females. Moreover, 61 males and 45 females suffered from IHD. In the study group, 57 males suffered from CVE, 14 with different types of cancer, and 54 with either asthma or COPD, whereas 33 females suffered from CVE, 11 with different types of cancer, and 56 with either asthma or COPD. Of 180 subjects taking polypharmacy, 104 were males 76 were females. All the components of FIRE-MADE FI had significantly contributed to development of frailty (309.91, $P < 0.0001$).

Table 3 shows distribution of total subjects according to FIRE-MADE FI.

Out of 250 geriatric subjects, 18.4% were fit, 31.6% mildly frail, 21.2% moderately frail, and 28.8% severely frail. The Chi-square test showed these results were statistically significant (48.95, $P < 0.00005$).

Table 1: Baseline characteristics of study population

Baseline characters	Male (*n*=146)	Female (*n*=104)	Total (*n*=250)	*p*
Average Age of study subjects in years±S.D	68.53±4.79	67.44±3.9	68.08±4.46	0.057
Average FIRE-MADE FI score of study subjects±S.D	0.47±0.24	0.5±0.21	0.48±0.23	0.31
Average LASA FI score of study subjects±S.D	0.55±0.28	0.6±0.25	0.57±0.26	0.15

Table 2: Age- and gender-wise distribution of study population

Age group	Male (*n*=146)	Female (*n*=104)	Total (*n*=250)	Chi Square Value
61-70 years	116 (79.45%)	91 (87.5%)	207 (82.8%)	
71-80 years	27 (18.49%)	12 (11.54%)	39 (15.6%)	2.812
81-90 years	3 (2.05%)	1 (0.96%)	4 (1.6%)	*p*=0.245 (NS)
Total	146	104	250	

Table 3: Distribution of total subjects according to FIRE-MADE FI

Frailty Category	Number	Percentage	⨀2
Fit (<0.25)	46	18.4%	
Mild Frailty (0.3-0.4)	79	31.6%	122.373
Moderate Frailty (0.5-0.6)	53	21.2%	*p*<0.0001 (S)
Severe Frailty (>0.7)	72	28.8%	
Total	250	100%	

Table 4 compares the efficiency of FIRE-MADE FI with LASA FI for diagnosing frailty.

Out of 224 frail patients according to LASA FI, 204 (91.07%) were also frail according to FIRE-MADE FI (true positive), while 20 (8.93%) were non-frail or fit (false negative). Out of 26 non-frail or fit subjects according to LASA index, 19 (73.08%) were also fit or non-frail by FIRE-MADE FI (true negative), while 7 (26.92%) were frail according to FIRE-MADE FI (false positive).

Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of FIRE-MADE FI were calculated as follows:

1. Sensitivity = TP/(TP + FN) ×100 = 204/224 = 91.07% (86.55% to 94.46%; 95% CI)
2. Specificity = TN/(TN + FP) ×100 = 19/26 = 73.08% (52.21% to 88.43%; 95% CI)
3. Positive likelihood ratio = sensitivity/(1 – specificity) =3.38 1.79 to 6.38; 95% CI)
4. Negative likelihood ratio = (1 – sensitivity)/specificity = 0.12 (0.08 to 0.20; 95% CI)
5. Positive predictive value = TP/(TP + FP) ×100 = 204/211 = 96.68% (93.92% to 98.21%; 95% CI)
6. Negative predictive value = TN/(TN + FN) ×100 = 19/39 = 48.72% (37.05% to 60.53%; 95% CI)
7. Diagnostic accuracy = (TP + TN)/TOTAL CASES × 100 = 223/250 = 89.20% (84.68% to 92.76%; 95% CI)

The internally validated tool, FIRE-MADE FI, demonstrated a sensitivity of 91.07%, a specificity of 73.08%, and a higher frailty prediction (positive predictive value) of 96.68% compared to the non-frailty prediction (negative predictive value) of 48.72% in our study.

Discussion

Frailty is the result of weaning of multiple physiological and biochemical reserves of the human body. Aging brings down hemoglobin, iron stores, albumin, immunoglobulin, macro- and micronutrients, insulin-like growth factor-1, and various other hormones or substances, causing a decrease in organ perfusion and functioning. Simultaneously, the process of aging enhances the inflammatory cascade by an increase in markers of inflammation (particularly interleukin-6 and tumor necrosis factor-α), hemoglobin A1c, arteriosclerosis, and atherosclerosis of vessels and increases susceptibility to various infectious or non-infectious insults.

However, recent studies demonstrated that frailty is the result of dysfunction of mostly multiple domains, rather than a single domain. More closer association of frailty is being found with physical, physiological, and immunological dysfunction.[7-9]

Some approaches for diagnosing frailty in the geriatric population were made in the past using a phenotypical approach, like FI – SOF (Study of Osteoporotic Fracture) and Fried Phenotype Approach (FPA); some used organ-specific definitions like Liver-Specific Frailty Index (LFI), but recent studies demonstrated that frailty is a multi-component failure, so multiple domains and multiple contributing factors were studied and different indices of frailty were proposed for diagnosis.[4] These multi-dimensional indices are FI-CD (Cumulative Deficits), FI- CGA (Comprehensive Geriatric Assessment), FI- MPI (Multidimensional Prognostic Index), LASA-FI, and FIRE-MADE FI.[4]

The present cross-sectional study was performed on 250 subjects of an age of 60 years or more with the mean age corresponding to the mean age of various developing countries' geriatric population. Increased life expectancy in the geriatric population will bring up the prevalence of the geriatric age group along with the diseases of geriatric age and ultimately will result in increased prevalence of frailty in near future.[5,10,11]

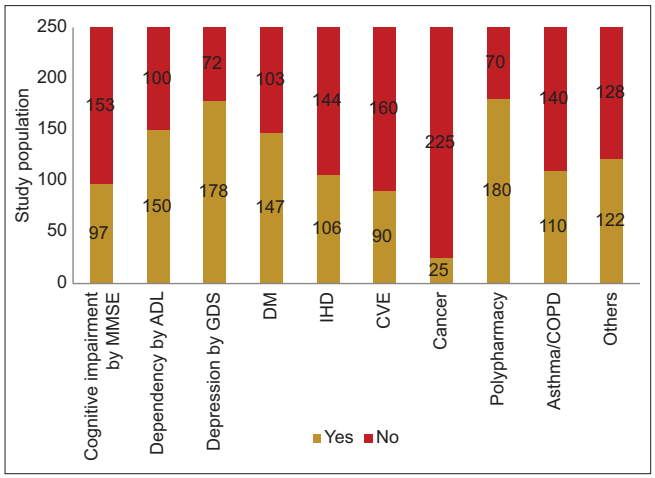

Figure 2: Different domains or factors contributing for FIRE-MADE FI

Table 4: Comparison of FIRE-MADE FI with LASA FI

Test	Frail according to LASA FI	Non frail (Fit) according to LASA FI	Total
Frail according to FIRE-MADE FI	204 (91.07%)	7 (26.92%)	211 (84.4%)
Non frail (Fit) according to FIRE-MADE FI	20 (8.93%)	19 (73.08%)	39 (15.6%)
Total	224 (100%)	26 (100%)	250 (100%)

Kendhapedi and Devasenapathy[12] found balance in gender distribution of their frail patients among 408 subjects. On applying Fried's FI and Tilburg FI tool, key components responsible for frailty were age, female sex, lower education, lower socio-economic status, minimum physical activity, and dependency. Kumar *et al.*[5] used FIRE-MADE FI on 1000 geriatric subjects and found no gender bias in frail subjects, and all the factors of FIRE-MADE FI were key determinants of frailty. These factors had adverse effects on outcome of patients.

Dasgupta *et al.*[11] found slight female dominance in frailty among 165 geriatric subjects. On applying Tilburg frailty indicator, he found that age, female gender, loss of spouse, illiteracy, economic dependency, no job/at home status, and ≥ 2 chronic diseases were the key elements in development of frailty. Choi *et al.*[13] and Slee *et al.*[10] found around 80% frailty prevalence in their studies on 503 and 73 subjects, respectively, concluding that females were more frail than males. Key determinants were loss of spouse, DM, HTN, sarcopenia, osteoporosis, low economic status, malnutrition, functional ability/disability, dependency, and decreased nutritional status markers.

The current study used FIRE-MADE FI and LASA FI in central rural India's geriatric population. The prevalence of frailty was 81.6% as per FIRE-MADE FI and 89.6% according to LASA FI. The prevalence of frailty was more or less similar in Kumar *et al.*,[5] Choi *et al.*,[13] Kendhapedi and Devasenapathy[12] and Dasgupta *et al.*[11] studies. Factors responsible for frailty and adverse outcome in the geriatric population were more or less similar in all studies.[5,10-13] In the present study, sarcopenia was the most important contributor of frailty, followed by IHD, cognitive impairment, polypharmacy, and rest others.

In the current study, according to FIRE-MADE FI, all the 97 (100%) patients who had cognitive impairment were having frailty. Similarly, all 106 (100%) patients who had IHD had frailty. 177 (99.44%) out of 178 patients with sarcopenia had frailty. 144 (97.96%) out of 147 patients who had diabetes had frailty. 176 (97.78%) out of 180 patients on polypharmacy had frailty. 87 (96.67%) out of 90 patients of CVE had frailty. 24 (96%) out of 25 cancer patients had frailty. 102 (92.73%) out of 110 patients of asthma or COPD had frailty. 138 (92%) out of 150 patients who had dependency had frailty. 152 (85.39%) out of 178 patients with depression had frailty.

FIRE-MADE FI was a recently developed and internally validated tool of diagnosing frailty. In the present study, we had compared the same tool with LASA FI and did external validation of FIRE-MADE FI. We found FIRE-MADE FI as 91.07% sensitive and 73.08% specific, with a positive predictive value of 96.68% and a diagnostic accuracy of 89.20%.

In their review, Puts *et al.*[14] analyzed 14 studies (12 RCTs, 2 cohort studies) on interventions to reduce frailty in a community-dwelling geriatric population. They examined various interventions like physical activity, combined physical activity and nutrition, memory training, home modifications, prehabilitation, and comprehensive geriatric assessment. They found that physical activity (in all forms and combinations) and prehabilitation significantly reduced frailty markers and prevalence. Due to limited time frames and resources, we were not able to follow up the patients. Furthermore, this was a hospital-based study, conducted at a tertiary center. More studies using geriatric registries or census data will give us generalized facts.

Conclusion

Based on results, we concluded that the Indian rural population of central India has high prevalence of frailty by both the frailty indices. External validation of FIRE-MADE FI gave us the efficiency of the tool as follows. In our study, it had the sensitivity of 91.07% and a specificity of 73.08%, with a positive predictive value of 96.68%, which was higher than the negative predictive value of the tool (48.72%).

Thus, it can be used as a valid tool to detect or predict frailty, and each component of FIRE-MADE FI had a significant effect on frailty. In our study, we found that IHD was the most important contributing factor for development of frailty, followed by cognitive impairment, polypharmacy, and remaining factors mentioned in FIRE-MADE FI.

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Conflicts of interest

There are no conflicts of interest.

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