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ORIGINAL ARTICLE

The Italian version of the "frailty index" based on deficits in health: a validation study

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Abstract

Background and Aim Several measurements were taken for frailty classification in geriatric population. "Frailty index" is based on "deficits in health," but it is still not available in Italian version. Thus, the aim of the present work was to validate a version of "frailty index" for the Italian geriatric community.

Methods The validation of Italian frailty index (IFi) is based on a cohort study that enrolled 1077 non-disabled outpatients aged 65 years or older (81.3 ± 6.5 years) in Naples (Italy). IFi has been expressed as a ratio of deficits present/deficits considered after a comprehensive geriatric assessment. IFi was stratified in light, moderate and severe frailty. Mortality, disability (considering an increase in ADL lost ≥1 from the baseline) and hospitalization were considered at 3, 6, 12, 18 and 24 months of follow-up. Area under curve (AUC) was evaluated for both Fried's and IFi frailty index.

Result At the end of follow-up, mortality increased from 1.0 to 30.3%, disability from 40.9 to 92.3% and hospitalization from 0.0 to 59.0% ($p < 0.001$ for trend). Multivariate analysis shows that the relative risk for unit increase in IFi is 1.09 (95% CI = 1.01–1.17, $p = 0.013$) for mortality, 1.04 (95% CI = 1.01–1.06, $p = 0.024$) for disability and 1.03 (95% CI = 1.01–1.07, $p = 0.041$) for hospitalization. AUC is higher in IFi with respect to Fried's frailty index when considering mortality (0.809 vs. 0.658, respectively), disability (0.800 vs. 0.729, respectively) and hospitalization (0.707 vs. 0.646, respectively).

Conclusions IFi is a valid measure of frailty after the comprehensive geriatric assessment in an Italian cohort of non-institutionalized patients.

Keywords Frailty · Frailty index · Deficits in health

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Introduction

There is strong evidence that frailty may become one of most relevant problems in public health. A global epidemiological transition is currently occurring, in which mortality is becoming more likely to be a consequence of age-related degenerative diseases with respect to infectious diseases [1]. In fact, age-related chronic diseases are largely prevalent in frailty leading to serious functional limitations and susceptibility to adverse outcomes. Since older people have been considerably raised in all countries, frailty prevalence is expected to dramatically increase [2].

Frailty does not yet have an established standard definition. However, frailty is considered as a geriatric dynamic condition characterized by an increased vulnerability to external stressors, by a multi-system dysfunction, by a complex etiology and by an intrinsic difficulty in

distinguishing from aging [3, 4]. Frailty is currently considered as "primary" or "preclinical" when the state is not associated directly with a specific disease, or when there is no substantial disability. Accordingly, the presence of three or more of the five Fried criteria is used for recognizing preclinical frailty (unintentional weight loss, exhaustion, low energy expenditure, slowness and weakness) [5]. In contrast, frailty is considered "secondary" or "clinical" when it is associated with known comorbidity and/or disability [6, 7]. The characteristics of clinical frailty include not only comorbidity and disability, but also polypharmacy and relative adverse drug reactions, hospitalization, health services utilization, age-associated sensory deficits and lack of social support [6, 7]. This condition is associated with higher long-term mortality alone and chronic disease as chronic heart failure [7–9].

How best to measure frailty is still controversial [10–12]. Several scores were computed for frailty classification and prognosis across a broad range of medical patients, including Fried's frailty phenotype and the "frailty index." "Frailty index" is based on "*deficits in health"* including symptoms, signs, diseases, disabilities or laboratory, radiographic or electrocardiographic abnormalities. Several groups have utilized the "frailty index" with different number of deficits, but the higher deficit count is always related to the larger number of adverse outcomes including death, disability and institutionalization [13–16].

To the best of our knowledge, the "frailty index" is still not available in Italian version. Thus, the aim of the present work was to prepare and validate a version of "frailty index" for the Italian geriatric community.

Methods

Study sample

The validation of Italian frailty index is based on a cohort study in Campania, a region of South Italy that enrolled individuals aged 65 years or older. Briefly, 1077 non-disabled outpatients, Italian speaking, with life expectancy and plans to stay in the area for more than 24 months were consecutively enrolled in the study. The enrollment started in September 2009.

Comprehensive geriatric assessment (CGA)

Elderly subjects underwent a comprehensive geriatric multidimensional assessment which included: cognitive function evaluation with Mini-Mental State Examination [17]; depressive symptoms with Geriatric Depression Scale [18]; comorbidity severity with a Cumulative Illness Rating Scale (CIRS-G) [19] and drug number; disability with Basic and Instrumental Activity of Daily Living [BADL and IADL] [20, 21]; nutritional assessment by Mini Nutritional Assessment (MNA) [22]; equilibrium and risk of fall with the Tinetti Scale [23]; physical performance with 4-m gait speed [m/s] [24]; physical activity with Physical Activity Scale for the Elderly (PASE) [25]; and social support evaluation with Social Support Assessment scored from 17 [subjects with the lowest support] to 0 (subjects with the highest support) (SSA) [26].

Italian frailty index (IFi)

The Italian frailty index (IFi) has been constructed by counting deficits in health, and it has been derived from a validated scale used in a cohort of New Haven (Connecticut, USA) in the Yale Precipitating Events Project study [27]. Briefly, these deficits were defined as symptoms, signs, disabilities and diseases. All health deficits include continuous, ordinal and binary variables. Disability in basic and instrumental activities of daily living including impaired grip strength and walking, comorbidity, self-rated health, and depression was evaluated. Frailty index includes information on 40 deficits that are measured in routine assessments of older adults. Grip strength and shoulder strength were evaluated using a handheld dynamometer (Mecmesin Advanced Force Gauge 500 N, GDM, Corsico (MI) Italy). The peak expiratory flow is measured with a peak flow meter for adults (Neupharma Imola, BO, Italy). All binary variables were coded, using the "0" to indicate the absence and "1" the presence of deficit. For intermediate response, we used "0.25," "0.5" and "0.75" (i.e., MMSE less than 10 = 1, 0.75 for scores $\geq$10 and $\leq$17, 0.5 for scores $\geq$18 and $\leq$20, 0.25 for scores >20 and <24, indicating a grading of cognitive impairment from 1 = severe dementia to 0.25 = mild cognitive impairment, and to 0 = no dementia). In order to better define "socioeconomic" and "nutritional" frailty, with respect to original "frailty index," the item #24 (feel lonely) and item #39 (usual pace) has been substituted in IFi by "social support score" (>13 = 1; 6–13 = 0.5 and 1–5 = 0) and by Mini Nutritional assessment (<17 = 1; 17–23.5 = 0.5 and 24 = 0). The index has been expressed as a ratio of deficits present to the total number of deficits considered: If 40 deficits were considered, and 20 were present in a given person, frailty index would be 20/40 = 0.50.

Only 12 participants reported 0.00 to IFi and are therefore excluded from the study. Then, IFi has been subdivided into tertiles (0.0/16.0, 16.1/27.0 and 27.1/40.0). Thus, 1065 participants were enrolled in the follow-up at 3, 6, 12 and 24 months from the baseline, and 907 patients completed the study (84.2%).

The Fried's frailty index was calculated by considering the following item of IFi: #9 (help lifting 10 lbs), #15

(lost more than 10 lbs in last year), #19 (cut down on usual activity in last month), #21 (feel everything is an effort) and #40 (4-m gait speed <10 s).

In Appendix 1 are reported the IFi, social support score and Mini Nutritional Assessment in Italian language.

Outcomes

Mortality, disability (considering an increase in ADL lost ≥1 from the baseline) and hospitalization were considered at 3, 6, 12, 18 and 24 months of follow-up.

Ethics

The study protocol was approved by the University of Naples Federico II (Comitato Etico per le attività Biomediche "Carlo Romano" prot. n.211/2013). All participants provided informed consent at baseline and at follow-up.

Statistics

Statistical analysis was performed using SPSS version 23. Continuous and categorical variables are presented as mean ± standard deviations (SD) or as percentages, respectively. ANOVA test with Bonferroni's post hoc correction was performed to compare continuous variables across groups, and Chi-square test was used for categorical variables. Logistic regression was used to examine receiver operating characteristics (ROC) curves in order to compare the performance of IFi Fried's frailty Index in predicting the outcomes. Area under curve (AUC) between 0.8 and 0.9 was considered good [28]. Sample size for two ROC curves method has been utilized; AUC for Fried's index = 0.75 and for IFi = 0.80, with a probability of type error $\alpha = 0.05$ and a power of the study $(1-\beta) = 0.90$, has been considered. Thus, 777 subjects are needed. To test inter-rater reliability of the IFi using the kappa coefficient (κ) and assuming that excellent agreement was indicated by a value of ≥0.80, we calculated a requirement of 25 subjects. Cronbach's value was employed to test internal reliability. Cox proportional hazards models were used to analyze the associations between frailty status as defined according to the IFi indexes and subsequent outcomes, including mortality, disability and hospitalization. The relative risk of each outcome, with 95% confidence intervals, was estimated for IFi and for each item adjusted for age and sex. Cumulative survival according to Cox regression analysis adjusted for age and sex of mortality, disability (considering the loss of 1 ADL vs. baseline) and hospitalization stratified in light, moderate and severe IFi was performed.

Results

The flowchart of the study with the final number of participants is shown in Fig. 1. The IFi showed a good inter-rater variability ($\kappa = 0.84$, $p < 0.001$; $n = 25$) and a good internal consistency (Cronbach's value = 0.83). Finally, in 25 participants, the time consumption of IFi was 40.2 ± 9.1 min. The time to administer IFi is relatively short if the administration is made after CGA (9.5 ± 3.1 min; $p < 0.001$).

Demographic characteristics and CGA of the cohort are described in Table 1. Mean age is 81.3 ± 6.5 years, and 997 subjects have completed the follow-up (82.4%). Female are 56.7% ($n = 611$) with a parallel increase with frailty severity degree increase (from 44.2 to 65.0%, $p < 0.001$). As expected, CIRS and total drugs increase with frailty (from 1.7 ± 0.4 to 2.0 ± 0.4 and 5.8 ± 3.0 to 6.7 ± 3.2, respectively; p for trend <0.001). ADL and IADL lost increase from 0.7 ± 1.4 to 3.5 ± 1.6 and from 1.9 ± 2.4 to 5.9 ± 2.2; p for trend <0.001). MMSE decreases, while GDS progressively increases with frailty

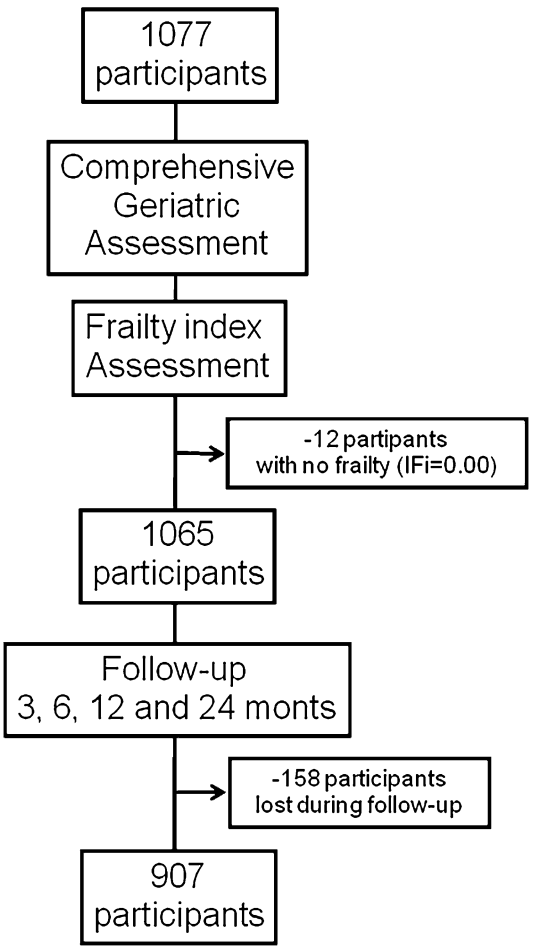


Fig. 1 Flowchart of the study with the final number of participants

Table 1 Demographic characteristics and comprehensive geriatric assessment of the sample

Variables	Frailty			*p* for trend
	Light ($n = 354$, 32.9%)	Moderate ($n = 350$, 32.5%)	Severe ($n = 373$, 34.6%)	
Age (years ± SD)	79.9 ± 6.6	81.8 ± 6.3	82.3 ± 6.3	0.001
Female sex (%)	44.2	62.0	65.0	0.001
Complete follow-up (%)	83.9	86.5	84.2	0.300
CIRS-G	1.7 ± 0.4	1.9 ± 0.4	2.0 ± 0.4	0.001
Total drugs	5.8 ± 3.0	5.9 ± 3.0	6.7 ± 3.2	0.025
MMSE	24.7 ± 4.7	22.2 ± 5.2	18.5 ± 6.8	0.001
GDS	4.5 ± 3.9	8.2 ± 3.9	9.8 ± 4.0	0.001
BADL lost	0.7 ± 1.4	1.8 ± 1.5	3.5 ± 1.6	0.001
IADL lost	1.9 ± 2.4	4.6 ± 2.1	5.9 ± 2.2	0.001
BMI	27.2 ± 4.9	27.7 ± 5.5	26.8 ± 8.1	0.160
MNA	23.5 ± 3.3	20.8 ± 3.5	18.0 ± 4.1	0.001
Tinetti score	23.1 ± 5.4	17.3 ± 5.8	11.2 ± 6.9	0.001
Social support score	6.1 ± 5.7	8.5 ± 4.4	10.1 ± 4.5	0.001
PASE	69.1 ± 58.4	32.2 ± 43.1	17.2 ± 38.4	0.001
Frailty index	10.3 ± 4.5	22.8 ± 2.9	30.4 ± 2.2	0.001
Fried's frailty index	2.1 ± 1.3	3.8 ± 1.1	4.7 ± 1.0	0.001

MNA Mini Nutritional Assessment (MNA), *MMSE* Mini-Mental State Examination, *CIRS-G* Cumulative Illness Rating Scale, *BADL* Basic Activity of Daily Living, *IADL* Instrumental Activity Daily Living, *GDS* Geriatric Depression Scale and *PASE* Physical Activity Scale for the Elderly

increase, reaching a value of 18.5 ± 6.8 and 9.8 ± 4.0, respectively (p for trend <0.001). Nutritional index as BMI and MNA as well as Tinetti, 4-m gait speed and PASE score, progressively decrease as frailty degree increases. Interestingly, low social support progressively decreases as frailty increases (from 6.1 ± 5.7 to 10.1 ± 4.5, p for trend <0.001). Accordingly, IFi reaches 30.4 ± 2.2, while Fried's frailty index 4.7 ± 1.0 in the highest frailty degree.

In Table 2 are reported the percentage of the 40 different items in the cohort. As expected, the higher percentage in all 40 items are reached in the highest degree of frailty. In particular, a percentage greater than 90% in the highest frailty degree were the item 8 (help up/down stairs = 96.3%), the item 21 (feel everything is an effort = 95.7%) and the item 2 (help dressing = 94.3%).

In Fig. 2 are reported the prevalence of mortality, disability (considering the loss of 1 ADL vs. baseline) and the hospitalization. At the end of follow-up (24 months), mortality was 13.0% in all subjects and progressively increases from 1.0 to 30.3% ($p < 0.001$ for trend). Disability was 68.2% in all subjects and progressively increases from 40.9 to 92.3% ($p < 0.001$ for trend). Hospitalization was 35.3% in all subjects and progressively increases from 18.2 to 59.0% ($p < 0.001$ for trend).

Multivariate analysis, adjusted for age and sex, shows that the relative risk for unit increase in IFi is 1.09 (95% confidence interval 1.01–1.17, $p = 0.013$) for mortality, 1.04 (95% confidence interval 1.01–1.06, $p = 0.024$) for disability and 1.03 (95% confidence interval 1.01–1.07, $p = 0.041$) for hospitalization (Fig. 3).

When IFi was separately analyzed for 40 items, different values of relative risk were found for the three outcomes and statistically significant items are reported in bold. For mortality, the most powerful value was the item 21 (feel everything is an effort = RR 4.83, CI 95% 1.32–17.5; $p = 0.02$), for disability was the item 29 (stroke = RR 2.29, CI 95% 1.24–4.23; $p < 0.01$) and for hospitalization was the item 22 (feel depressed = 2.77; CI 95% 1.46–5.26; $p < 0.01$) (Table 3).

In Fig. 4 are represented the ROC curves of IFi and Fried's frailty index. AUC is higher in IFi than Fried's frailty index on mortality, disability and hospitalization.

Discussion

Our results indicate that IFi is a valid measure of frailty after the comprehensive geriatric assessment in an Italian cohort of non-institutionalized patients. IFi has a good reliability, an acceptable internal consistency and a good validity including all concept of frailty (mental, physical, social and nutritional).

Table 2 Items description with their percentage in all participants and stratified for light, moderate and severe frailty

Items	Frailty			P for trend
	Light	Moderate	Severe	
1. Help bathing (yes = 1/no = 0, %)	3.9	61.4	98	0.001
2. Help dressing (yes = 1/no = 0, %)	5	49.6	94.3	0.001
3. Help getting in/out of chair (yes = 1/no = 0, %)	3.7	33.1	81.9	0.001
4. Help walking around house (yes = 1/no = 0, %)	1.8	23.6	74.5	0.001
5. Help eating (yes = 1/no = 0, %)	1.6	21.6	70.5	0.001
6. Help grooming (yes = 1/no = 0, %)	32.3	89.6	98.6	0.001
7. Help using toilet (yes = 1/no = 0, %)	1	31.4	83.4	0.001
8. Help up/down stairs (yes = 1/no = 0, %)	8.1	70	96.3	0.001
9. Help lifting 10 lbs (yes = 1/no = 0, %)	20.2	72.3	89.4	0.001
10. Help shopping (yes = 1/no = 0, %)	24.1	93.4	91.4	0.001
11. Help with housework (yes = 1/no = 0, %)	34.4	89.6	92.3	0.001
12. Help with meal preparations (yes = 1/no = 0, %)	19.4	73.8	96.6	0.001
13. Help taking medication (yes = 1/no = 0, %)	15.2	61.4	89.1	0.001
14. Help with finances (yes = 1/no = 0, %)	11	64	88.3	0.001
15. Lost more than 10 lbs in last year (yes = 1/no = 0, %)	18.1	38.3	59.3	0.001
16. Self-rating of health (poor = 1/fair = 0.75/good = 0.5/very good = 0.25/excellent = 0,%)	9.7	47.6	67.3	0.01
17. Health has changed in last year (yes = 1/no = 0, %)	48.3	76.7	91.7	0.001
18. Stayed in bed at least half the day due to health (in last month) (yes = 1/no = 0,%)	22	38	64.5	0.001
19. Cut down on usual activity (in last month) (yes = 1/no = 0, %)	31	50.4	77.4	0.001
20. Walk outside (yes = 1/no = 0, %)	26	75.2	92.6	0.001
21. Feel everything is an effort (most of time = 1/sometime = 0.5/rarely = 0, %)	42.3	82.4	95.7	0.001
22. Feel depressed (most of time = 1/sometime = 0.5/rarely = 0, %)	11.5	52.2	71.1	0.001
23. Feel happy (most of time = 1/sometime = 0.5/rarely = 0, %)	9.4	45.8	70.5	0.001
24. Social support (> 13 = 1/6–13 = 0.5/1–5 = 0)	5.8	15.9	31.5	0.001
25. Have trouble getting going (most of time = 1/sometime = 0.5/rarely = 0, %)	8.7	44.4	77.9	0.001
26. High blood pressure (yes = 1/suspected = 0.5/no = 0, %)	70.3	79.8	86.5	0.01
27. Heart attack (yes = 1/suspected = 0.5/no = 0, %)	21.5	18.7	25.8	0.001
28. CHF (yes = 1/suspected = 0.5/no = 0, %)	14.4	21.6	26.4	0.001
29. Stroke (yes = 1/suspected = 0.5/no = 0, %)	3.9	11.2	12.3	0.001
30. Cancer (yes = 1/suspected = 0.5/no = 0, %)	8.7	12.7	23.8	0.001
31. Diabetes (yes = 1/suspected = 0.5/no = 0, %)	21.5	32	34.4	0.01
32. Arthritis (yes = 1/suspected = 0.5/no = 0, %)	38.3	65.4	75.1	0.001
33. Chronic lung disease (yes = 1/suspected = 0.5/no = 0, %)	20.2	33.7	44.1	0.001
34. MMSE (< 10 = 1/11–17 = 0.75/18-20 = 0.5/20–24 = 0.25/> 24 = 0)	62.5	60.5	71.9	0.001
35. BMI (< 18.5, ≥ 30 = 1/25– < 30 = 0.5/18.5–24.9 = 0)	15.5	28.8	37	0.001
36. Peak Expiratory Flow (yes = 1/no = 0, %)	56.4	85.9	88.3	0.001
37. Shoulder strength (yes = 1/no = 0, %)	26.2	64.8	82.5	0.001
38. Grip strength (yes = 1/no = 0, %)	46.2	79.3	88.3	0.001
39. Mini Nutritional Assessment (< 17 = 1/17–23.5 = 0.5/24 = 0)	7.3	21.3	48.1	0.001
40. Rapid pace (> 10 = 1/≤ 10 = 0)	13.9	53.6	78.2	0.001

Frailty measurements: status of the art

Frailty measurements were utilized for frailty classification and prognosis across a large range of medical patients, including geriatric, oncology, and surgical, orthopedic, cardiovascular and renal patients. Among the most common frailty measurements, "Fried's frailty" and "frailty index" are the most common frailty scores [12].

"Fried's frailty" known as the Cardiovascular Health Study (CHS) Index [5] considers frailty by its physical characteristics, or "phenotype," defining the condition as the presence of three or more of shrinking [5]. It has been

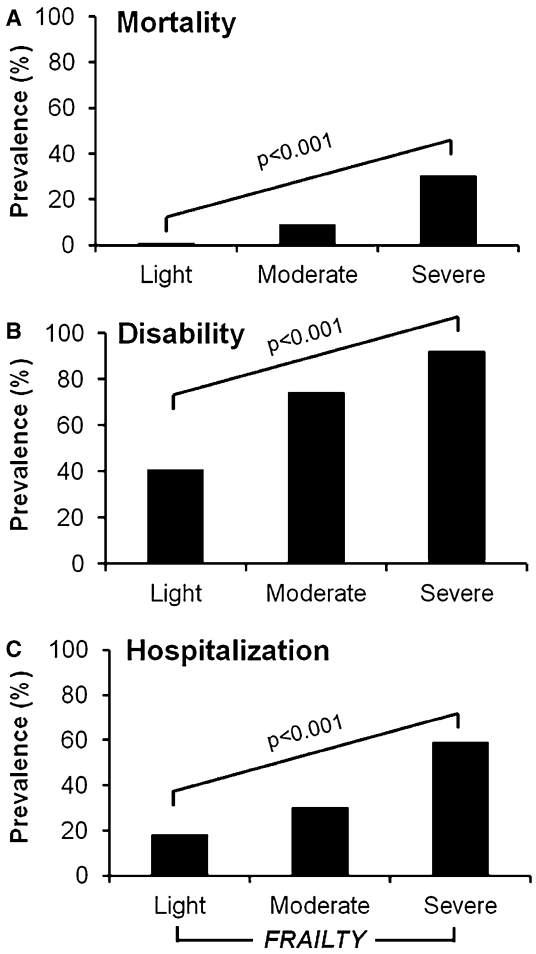


Fig. 2 Prevalence of mortality (**a**), disability (considering the loss of 1 ADL vs. baseline) (**b**) and hospitalization (**c**) at the end of follow-up (24 months) stratified in light, moderate and severe frailty index

applied to multiple epidemiological studies where it is predictive of adverse clinical outcomes, including mortality [5, 29, 30]. Moreover, the frailty phenotype often has been modified, and these modifications have important impact on its classification and predictive ability [31]. Modified criteria of the frailty phenotype were evaluated by estimating the prevalence and mortality by using the Survey of Health, Ageing and Retirement in Europe (SHARE). In this context, frailty prevalence ranged from 12.7 to 28.2%, agreement with the primary frailty phenotype ranged from 0.662 to 0.967, internal consistency ranged from 0.430 to 0.649, and AUC curves for discriminating five-year mortality ranged from 0.607 to 0.668 [31]. Unfortunately, "Fried's frailty" does not include psychosocial components of frailty.

The "frailty index" was based on accumulative deficits and firstly proposed by Rockwood and Mitnitski as a technique to include the multidimensional nature of frailty into an operational definition [27, 32]. It involves the accumulation of symptoms, diseases, disabilities or any deficit in health supposing that a greater number of health deficits define a higher frailty [33]. Importantly, health and not age "per se" is related to frailty [33]. The "frailty index" is well validated and applied to several study cohorts including the Survey of Health, Ageing and Retirement (SHARE). Moreover, several studies have demonstrated that the "frailty index" has a higher predictive ability of adverse clinical outcomes than other frailty measurements in both hospital and community settings [11, 33]. Interestingly, frailty index score rather than type of health deficits is most predictive of adverse events [6]. Despite its many positive characteristics. The "frailty index" has in the "time consuming" the greatest limitation [34, 35]. However, when derived from data already collected in a comprehensive geriatric assessment (CGA), the reliability becomes really consistent.

The Study of Osteoporotic Fractures (SOF) frailty index [36] defined frailty as the presence of ≥2 components out of list of three: weight loss, exhaustion and low mobility, and it is an independent predictor of adverse outcomes in community-dwelling older people [37]. Unfortunately, this tool is not easily applicable because patients with an acute medical condition often cannot perform a five-times-chair-rise (low mobility) [38].

The Edmonton Frail Scale (EFS) [39] contains nine components (cognition; general health status, self-reported health, functional independence, social support, polypharmacy, mood, continence and functional performance) in 17 items. The EFS has been used to identify frailty in specific clinical populations [40] and in acute care [41, 42].

Fatigue, Resistance, Ambulation, Illness and Loss of Weight (FRAIL) includes five components: fatigue (self-report), resistance, ambulation (slow walking speed), illness and loss of weight (5% or more in the past year) [43], and it has been found to be predictive of mortality in specific populations [44], but not in both hospitalized and community-dwelling older people.

Several other frailty instruments with different limitations have been validated including the "Clinical Frailty Scale" (CFS) [45], the "Multidimensional Prognostic Instrument" (MPI) [46], the "Tilburg Frailty Indicator" (TFI) [47], the "PRISMA-7 P" [48], the "Groningen Frailty Indicator" (GFI) [49], the "Sherbrooke Postal Questionnaire" (SPQ) [50], the "Gérontopôle Frailty Screening Tool" (GFST) [51] and the "Kihon Checklist" (KCL) [52].

In our study, "frailty index" was modified in terms of nutritional and socioeconomic state. In fact, IFi includes both MNA [22] and Social Support Assessment [26]. This may explain why in our cohort IFi was more predictive than "frailty index" on mortality (Relative risk for unit of increase = 1.09 in IFi and 1.03 for "frailty index") [27].

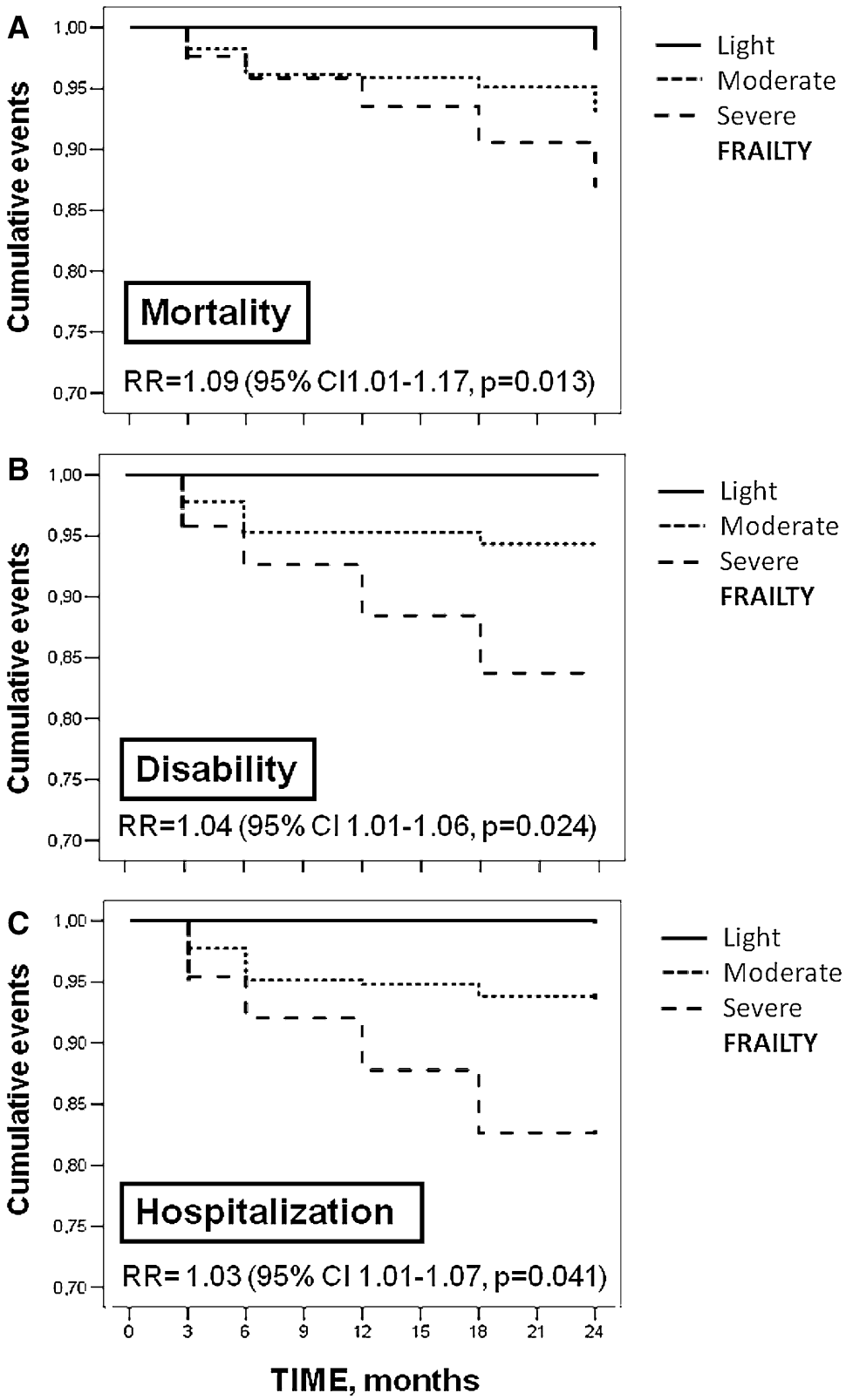


Fig. 3 Cumulative survival according to Cox regression analysis adjusted for age and sex of mortality (**a**), disability (considering the loss of 1 ADL vs. baseline) (**b**) and hospitalization (**c**) stratified in light, moderate and severe frailty index. *RR* Relative risk, *CI* confidence interval

Table 3 Relative risk and ranking weight of the 40 items of frailty index on mortality, disability (≥1 ADL lost) and hospitalization

Items	Mortality			Disability			Hospitalization		
	RR	CI 95%	*p*	RR	CI 95%	*p*	RR	CI 95%	*p*
1. Help bathing	0.98	0.32–1.14	0.08	**1.97**	**1.10–3.53**	**0.02**	0.84	0.48–1.46	0.53
2. Help dressing	2.69	0.73–9.88	0.14	**2.14**	**1.17–3.91**	**0.01**	0.86	0.50–1.48	0.59
3. Help getting in/out of chair	**2.82**	**1.20–6.62**	**0.02**	**2.05**	**1.17–3.61**	**0.01**	**1.53**	**0.99–.2.35**	**0.05**
4. Help walking around house	2.07	0.95–4.49	0.07	0.85	0.44–1.61	0.61	1.22	0.78–1.91	0.39
5. Help eating	**2.02**	**1.00–4.08**	**0.05**	0.66	0.35–1.22	0.18	1.24	0.82–1.88	0.32
6. Help grooming	0.97	0.31–2.97	0.95	0.77	0.45–1.32	0.34	1.63	0.96–2.77	0.07
7. Help using toilet	1.78	0.81–3.93	0.15	1.75	0.99–3.09	0.06	**1.63**	**1.06–2.49**	**0.03**
8. Help up/down stairs	**4.12**	**1.21–14.0**	**0.02**	1.00	0.62–1.62	0.99	1.46	0.92–2.31	0.11
9. Help lifting 10 lbs	1.83	0.85–3.94	0.12	1.11	0.74–1.66	0.61	1.01	0.69–1.48	0.96
10. Help shopping	0.71	0.23–2.21	0.55	1.32	0.79–2.20	0.30	0.96	0.56–1.63	0.87
11. Help with housework	0.66	0.29–1.50	0.33	0.93	0.55–1.57	0.78	0.95	0.59–1.52	0.82
12. Help with meal preparations	0.96	0.38–2.47	0.94	0.92	0.57–1.49	0.74	0.76	0.49–1.19	0.23
13. Help taking medication	0.69	0.32–1.52	0.36	0.94	0.60–1.47	0.78	0.78	0.52–1.17	0.23
14. Help with finances	0.89	0.41–1.93	0.76	1.21	0.74–1.96	0.45	1.10	0.71–1.69	0.68
15. Lost more than 10 lbs in last year	**2.28**	**1.31–3.94**	**0.00**	1.12	0.77–1.62	0.55	**1.36**	**1.00–1.86**	**0.05**
16. Self-rating of health	**0.12**	**0.03–0.56**	**0.01**	0.54	0.23–1.27	0.16	0.72	0.31–1.64	0.43
17. Health has changed in last year	1.39	0.60–3.21	0.44	0.96	0.63–1.45	0.83	1.19	0.80–1.77	0.40
18. Stayed in bed at least half the day due to health	**2.38**	**1.29–4.41**	**0.01**	1.26	0.85–1.87	0.25	**1.52**	**1.09–2.12**	**0.01**
19. Cut down on usual activity	1.85	0.89–3.85	0.10	1.05	0.72–1.55	0.79	1.38	0.98–1.95	0.06
20. Walk outside	0.92	0.42–2.01	0.84	1.08	0.72–1.62	0.71	0.95	0.64–1.41	0.79
21. Feel everything is an effort	**4.83**	**1.33–17.5**	**0.02**	1.02	0.63–1.65	0.93	1.22	0.73–2.03	0.45
22. Feel depressed	0.77	0.26–2.24	0.63	1.29	0.63–2.66	0.49	**2.77**	**1.46–5.26**	**0.01**
23. Feel unhappy	0.56	0.20–1.60	0.28	0.73	0.36–1.48	0.38	**0.43**	**0.23–0.80**	**0.01**
24. Social support	**2.30**	**1.00–5.31**	**0.05**	1.01	0.56–1.79	0.98	0.99	0.60–1.63	0.98
25. Have trouble getting going	**0.39**	**0.15–1.02**	**0.05**	0.97	0.56–1.70	0.93	1.01	0.60–1.68	0.98
26. High blood pressure	0.88	0.44–1.74	0.71	1.02	0.67–1.55	0.94	0.93	0.63–1.37	0.71
27. Heart attack	1.19	0.61–2.32	0.61	**0.58**	**0.38–0.90**	**0.02**	1.24	0.85–1.80	0.26
28. CHF	**2.25**	**1.17–4.33**	**0.02**	1.22	0.77–1.92	0.40	0.96	0.66–1.41	0.84
29. Stroke	0.97	0.45–2.13	0.95	**2.29**	**1.24–4.23**	**0.01**	1.17	0.74–1.84	0.51
30. Cancer	**2.93**	**1.61–5.35**	**0.00**	0.96	0.60–1.53	0.85	**1.91**	**1.30–2.81**	**0.00**
31. Diabetes	0.93	0.53–1.65	0.80	0.88	0.61–1.27	0.49	1.18	0.86–1.62	0.31
32. Arthritis	0.63	0.32–1.22	0.17	1.29	0.87–1.91	0.21	**0.65**	**0.45–0.95**	**0.02**
33. Chronic lung disease	1.18	0.65–2.13	0.58	1.42	0.97–2.08	0.07	1.16	0.83–1.60	0.38
34. MMSE	0.90	0.41–1.99	0.80	1.04	0.69–1.56	0.86	1.11	0.75–1.65	0.61
35. BMI	0.85	0.44–1.64	0.63	0.83	0.53–1.30	0.41	0.76	0.52–1.12	0.16
36. Peak Expiratory Flow	**2.42**	**1.10–5.21**	**0.03**	1.06	0.70–1.58	0.79	**1.51**	**1.01–2.27**	**0.05**
37. Shoulder strength	0.54	0.27–1.08	0.08	1.32	0.89–1.96	0.17	1.08	0.75–1.57	0.67
38. Grip strength	**2.56**	**1.13–5.82**	**0.02**	**1.56**	**1.04–2.35**	**0.03**	1.28	0.85–1.92	0.23
39. Mini Nutritional Assessment	0.72	0.33–1.57	0.41	**1.83**	**1.09–3.08**	**0.02**	0.84	0.53–1.32	0.45
40. Rapid pace	**2.00**	**1.06–3.80**	**0.03**	**1.59**	**1.08–2.34**	**0.02**	1.15	0.82–1.61	0.43

RR Relative risk; *CI* confidence interval

Comprehensive geriatric assessment before frailty measurements: is it the key point?

The frailty index derived from CGA is simply a frailty score deriving from a CGA. It is well known that CGA is the global standard clinical assessment for older people, and includes medical, nutritional, functional, mental and socioeconomic by a geriatric evaluation unit [53]. The CGA-frailty index was firstly performed in a ten-domain index, with 14 CGA components included [54, 55].

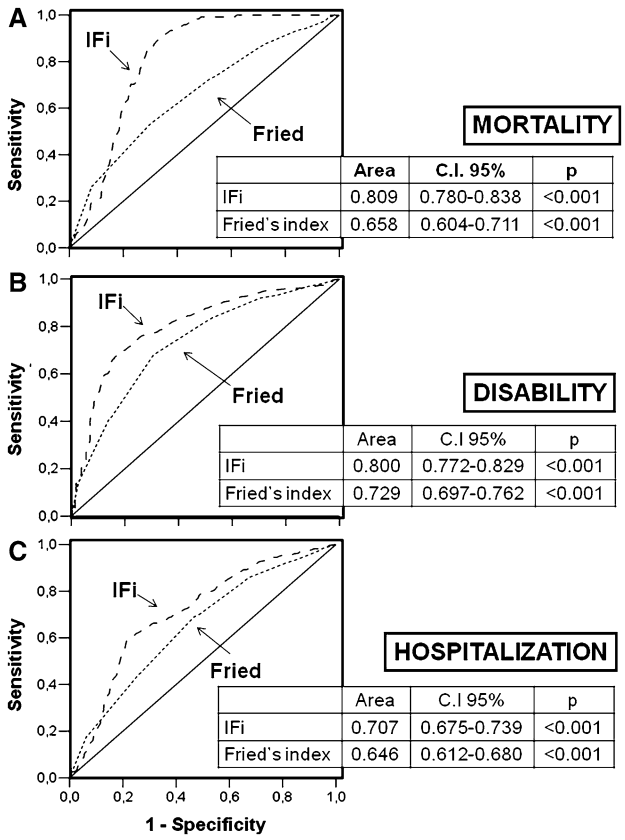


Fig. 4 Receiver operating characteristics (ROC) *curves* of frailty index based on deficit in health (IFi) and Fried's frailty index method on mortality (**a**), disability (considering the loss of 1 ADL vs. baseline) (**b**) and hospitalization (**c**)

Successively, Rockwood and colleagues include 52 CGA components [56]. The CGA is used as a clinical standard for geriatric assessment and has been found to predict negative outcome in several kinds of patients with different diseases [9, 57]. Thus, items from a standard routinely CGA may be combined with frailty score, and consequently, a risk stratification of future adverse outcomes may be routinely obtained. This approach is extremely positive when considering the "time consumption." In fact, if "frailty index" is performed without CGA, the administration time is excessively extended. In contrast, when "frailty index" is performed after CGA, the administration time is significantly comprised. In our protocol, IFi was performed after CGA takes less than 10 min.

Interestingly, CGA and frailty analysis are synergistic in predicting different outcomes. For mortality, the most powerful item was "feel everything is an effort," for disability was the history of stroke and for hospitalization was the presence of depression.

The integration of frailty measures in clinical practice

It is important that frailty is recognized in the clinical setting independently by the type of frailty measurement tool. Frailty is often included in the part of the normal aging process, and older patients are assessed on the basis of their medical conditions alone rather than accounting for their frailty status [58]. Thus, incorporating measurement of frailty into clinical practice may provide a tool for clinicians to identify and preventively manage this condition [59]. As underlined before, the time consumption seems to be the critical point of frailty measurements. In fact, some authors tried to reduce the time consumption by reducing the number of items used to assess frailty. Such approach often realizes shorter scales by reducing interpretability, generalizability or loss of useful information from the clinical point of view.

More importantly, the integration of frailty measures in clinical practice is essential for the improvement of interventions against age-related conditions, i.e., disability, in the elderly. Moreover, frailty is not only associated with increased disability and mortality, but also with higher risk of cardiovascular, neurological and metabolic diseases [60–62]. In "Progetto Veneto Anziani" (Pro.V.A.) study that involved older community dwellers, pre-frailty and frailty are associated with an increased risk of cardiovascular diseases [60] and of incident type 2 diabetes in the elderly [61]. Interestingly, among the physical domains of pre-frailty, low gait speed seems to be the best predictor of future cardiovascular diseases [61]. A recent meta-analysis indicates that frailty is a significant predictor of incident Alzheimer's disease, vascular dementia and all dementia [62]. Finally, long.-term mortality in chronic obstructive pulmonary disease has been associated to severe clinical frailty [63].

At this regard, it should be underlined that the two principal tools to evaluate the frailty, "Fried's frailty" and "frailty index," should be considered complementary and not alternative [64]. "Fried's frailty" exists even in the absence of nosographically classified conditions (i.e., disease) having as target older subjects in the absence of disability. In contrast, the frailty index is largely based on nosographically classified conditions having as target every any older subject also still experiencing disability. Thus, the Fried's frailty phenotype may be more appropriate for an immediate identification of non-disabled elders at risk of negative events, while the "frailty index" may summarize the results of a CGA providing a marker of deficits accumulation that are present and concur at depleting endogenous reserves. However, when considering the outcomes, mortality and disability AUC curves for IFi present a good discriminatory value with respect

to Fried's frailty (0.809 vs. 0.658 and 0.800 vs. 0.729, respectively).

Limitations of the study

The present study presents at least two limitations. First of all, the study is not a multicenter study, and therefore, it did not include participant from different geographic locations with the impossibility to compare results among centers with different demographic factors. Secondly, the participants are out- and not in-hospital patients with a possible selection bias of the disease's severity.

Conclusions

We conclude that IFi is a valid measure of frailty after CGA in an Italian cohort of non-institutionalized patients in predicting mortality, disability and hospitalization. IFi presents a good reliability, internal consistency and validity including all concepts of frailty (mental, physical, social and nutritional).

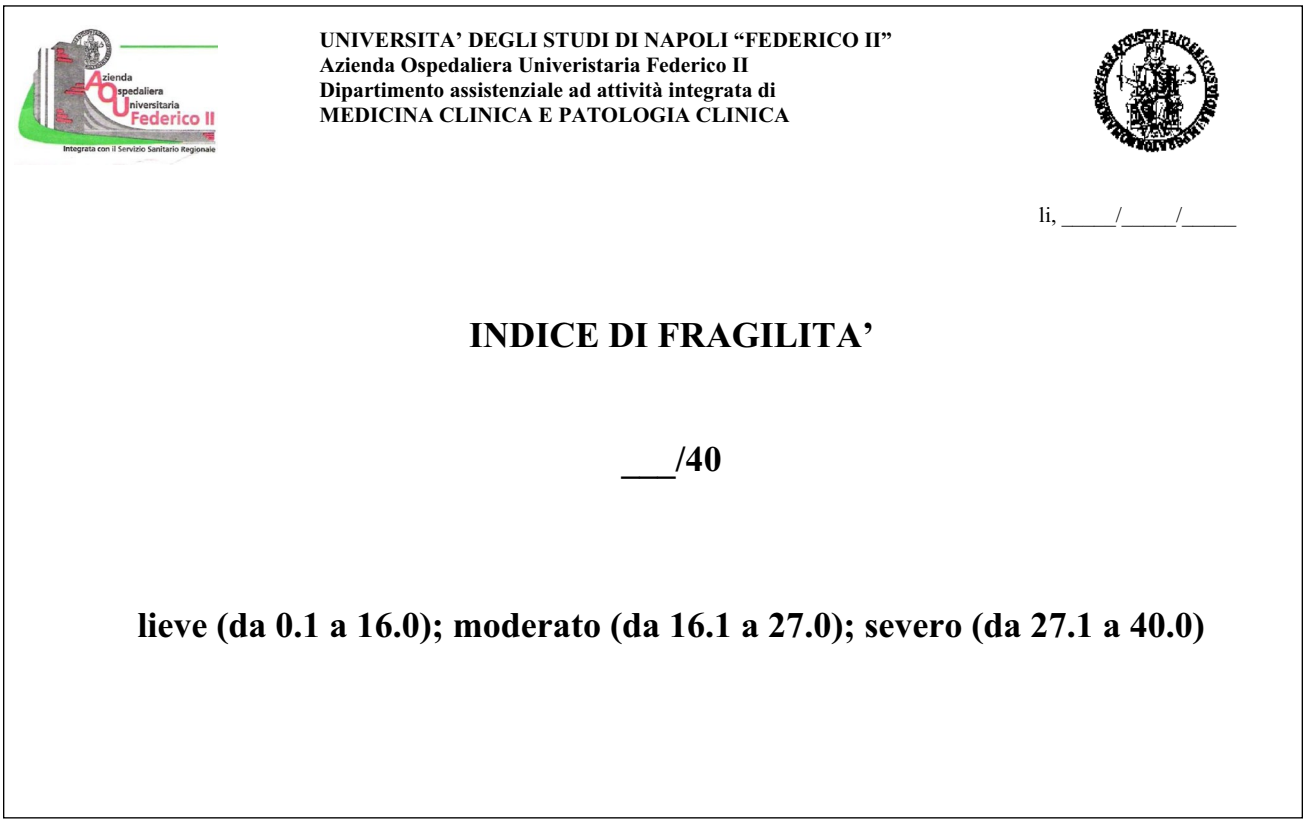
Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval The study protocol was approved by the University of Naples Federico II (Comitato Etico per le attività Biomediche "Carlo Romano" prot. n.211/2013).

Informed consent All participants provided informed consent at baseline and at follow-up.

Appendix 1



UNIVERSITA' DEGLI STUDI DI NAPOLI "FEDERICO II"
Azienda Ospedaliera Univeristaria Federico II
Dipartimento assistenziale ad attività integrata di
MEDICINA CLINICA E PATOLOGIA CLINICA

li, _____/_____/_____

INDICE DI FRAGILITA'

___/40

lieve (da 0.1 a 16.0); moderato (da 16.1 a 27.0); severo (da 27.1 a 40.0)

Paziente	Cart. cl.	Nato il__/__/__	Altezza = m	Peso = Kg	Tel.	*P*
1. Aiuto nel lavarsi	SI = 1	No = 0				
2. Aiuto nel vestirsi	SI = 1	No = 0				
3. Aiuto nel sedersi o alzarsi dalla sedia	SI = 1	No = 0				
4. Aiuto nel camminare in casa	SI = 1	No = 0				
5. Aiuto nel mangiare	SI = 1	No = 0				
6. Aiuto nella cura della casa	SI = 1	No = 0				
7. Aiuto nell'utilizzare il bagno	SI = 1	No = 0				
8. Aiuto nel salire o scendere le scale	SI = 1	No = 0				
9. Aiuto nell'alzare 4.5 kg	SI = 1	No = 0				
10. Aiuto nel fare la spesa	SI = 1	No = 0				
11. Aiuto nei lavori di casa	SI = 1	No = 0				
12. Aiuto nel preparare i pasti	SI = 1	No = 0				
13. Aiuto nell'assumere i farmaci	SI = 1	No = 0				
14. Aiuto nella gestione del denaro	SI = 1	No = 0				
15. Perdita di più di 4.5 kg di peso nell'ultimo anno	SI = 1	No = 0				
16. Giudizio sulla propria salute	Scarsa = 1	Discreta = 0.75	Buona = 0.5	Molto buona = 0.25	Eccellente = 0	
17. Come è cambiata la sua salute nell'ultimo anno?	Peggiorata = 1	Migliorata/stessa = 0				
18. Persistenza a letto almeno 1/2 giornata per motivi di salute, nell'ultimo mese?	SI = 1	No = 0				
19. Riduzione della solita attività nell'ultimo mese?	SI = 1	No = 0				
20. Uscire	<3 Giorni = 1	≥3 Giorni = 0				
21. Affaticarsi per qualsiasi cosa	Spesso = 1	Qualche volta = 0.5	Rara-mente = 0			
22. Sentirsi depresso	Spesso = 1	Qualche volta = 0.5	Rara-mente = 0			
23. Sentirsi infelice	Spesso = 1	Qualche volta = 0.5	Rara-mente = 0			
24. Social support score (vedi allegato 1)	>13 = 1	6–13 = 0.5	1–5 = 0			
25. Avere difficoltà a mettersi in moto	Spesso = 1	Qualche volta = 0.5	Rara-mente = 0			
26. Ipertensione	SI = 1	Sospetta = 0.5	No = 0			
27.Angina pectoris	SI = 1	Sospetta = 0.5	No = 0			
28. Insufficienza cardiaca cronica	SI = 1	Sospetta = 0.5	No = 0			
29. Ictus	SI = 1	Sospetta = 0.5	No = 0			
30. Cancro	SI = 1	Sospetta = 0.5,	No = 0			
31. Diabete	SI = 1	Sospetta = 0.5	No = 0			
32. Artrosi	SI = 1	Sospetta = 0.5	No = 0			
33. Broncopneumopatia cronica	SI = 1	Sospetta = 0.5	No = 0			
34. MMSE	<10 = 1	11–17 = 0.75	18–20 = 0.5	20–24 = 0.25	>24 = 0	

Paziente	Cart. cl.		Nato il__/__/__		Altezza = m	Peso = Kg	Tel.	*P*
35. BMI	<18.5, ≥30 = 1		25–<30 = 0.5		18.5–24.9 = 0			
36. Picco flusso espiratorio = _____L/min 1 = _____ 2 = _____ 3 = _____	≤340 (uomo), ≤310 (donna) = 1		>340 (uomo), >310 (donna) = 0					
37. Forza muscolare sollevamento = Kg 1 = _____ 2 = _____ 3 = _____	≤12 (uomo), ≤9 (donna) = 1		>12 (uomo), >9 (donna) = 0					
38. Forza muscolare presa = Kg 1 = _____ 2 = _____ 3 = _____	Uomo = 1		Uomo = 0					
	BMI ≤24,	Kg ≤29	BMI ≤24	Kg >29				
	BMI 24.1–28	Kg ≤30	BMI 24.1–28	Kg >30				
	BMI >28	Kg ≤32	BMI >28	Kg >32				
	Donna = 1		Donna = 0					
	BMI ≤23	Kg ≤17	BMI ≤23	Kg >17				
	BMI 23.1–26	Kg ≤ 17.3	BMI 23.1–26	Kg >17				
	BMI 26.1–29	Kg ≤18	BMI 26.1–29	Kg >18				
	BMI >29	Kg ≤21	BMI >29	Kg >21				
39. Mini nutritional Assessment (vedi allegato 2)	<17 = 1		17–23.5 = 0.5		24 = 0			
40. Tempo impiegato per percorrere 4 metri con passo rapido (sec)	>10 = 1		≤10 = 0					
Totale								

Scala supporto sociale

1. Stato civile	Vedovo o celibe = 1	Coniugato = 0
2. Figli viventi	No = 1	Sì = 0
3. Fratelli e sorelle viventi	No = 1	Sì = 0
4. Frequenza di rapporti familiari	Mai, raramente = 1	Spesso, di frequente = 0
5. Con chi abita	Solo = 1	In compagnia = 0
6. Aiuto finanziario da parte dei familiari	No = 1	Sì = 0
7. Rapporti stretti con parenti non familiari	No = 1	Sì = 0
8. Aiuto concreto da parte dei familiari	No = 1	Sì = 0
9. Con quante persone del vicinato si vede almeno una volta a settimana?	Nessuno = 1	Almeno una = 0
10. Ha amici intimi?	No = 1	Sì = 0
11. Frequenza rapporti?	Mai, raramente = 1	Spesso, di frequente = 0
12. Frequenta posti pubblici?	Mai, raramente = 1	Spesso, di frequente = 0
13. Frequenta cinema-teatri?	Mai, raramente = 1	Spesso, di frequente = 0
14. Frequenta associazioni di volontariato-ricreative?	Mai, raramente = 1	Spesso, di frequente = 0
15. Legge i giornali?	Mai, raramente = 1	Spesso, di frequente = 0
16. Ascolta radio e/o vede TV?	Mai, raramente = 1	Spesso, di frequente = 0
17. Si prende cura dei bambini?	Mai, raramente = 1	Spesso, di frequente = 0
Totale		

Dalla analisi della tabella si ottiene uno score in cui i punteggi più alti individuano i soggetti con un basso livello di supporto sociale: il più basso livello si individua con un punteggio di 17

Supporto sociale buono: 1–5

Supporto sociale discreto: 6–13

Supporto sociale scarso: 14–17

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