Prevalence and factors associated with frailty in hospitalized older Patients

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Abstract

Background Frailty is a multidimensional syndrome that leads to an increase of an age-related disorder of several physiological systems, and cognitive abilities decline. The aim of this study was to evaluate the prevalence of frailty among older persons in Belgium and we examined the factors associated with frailty with a principal focus en cognitive, dietary status, and inflammatory parameters Methods A total of 124 participants (90 women, 34 men; age: mean ± SD: 85.9 ± 5.5 years) were studied, recruited from the Geriatrics department, Belgium. Nutritional, cognitive status and physical activity were assessed using MNA, MMSE, and Katz score, respectively. Frailty syndrome was evaluated using SEGA score. Medication and medical history were recorded. Analyzed biochemical parameters included C-reactive protein (CRP), complete blood count, blood creatinine, vitamin D level, and serum protein electrophoresis. According to SEGA score, participants were divided into non-frail (n=19), frail (n=25) and severely frail patients (n= 80). Results The SEGA score was inversely correlated with MMSE, MNA and Katz score. SEGA score was negatively correlated to albumin levels (r=-0.30; p<0.001) and positively correlated to CRP, polypharmacy and age. Logistic regression showed a strong association between frailty, Katz score, dementia, polypharmacy and living in nursing home. Conclusion Our results provide useful information for understanding mechanisms of frailty. This will help to develop preventive strategies for the elderly at the pre-frailty stage.

Introduction

Frailty is a geriatric syndrome, described as a clinical state of functional reserve decline associated with aging. Slowness, weakness, exhaustion and low activity are combined and affect the performance of functional tasks negatively *[1].* Disability, hospitalization, fragility fracture, institutionalization, and early mortality are the major frailty consequences *[2, 3].* Several physiological systems are dysregulated in frailty and lead eventually to function loss; such as musculoskeletal functioning, the inflammatory system, and the endocrine system *[4–6].* According to several studies, frailty is associated with cognitive impairment. In fact, severe cognitive decline accompanied by decreased physical function, poor muscle strength, slow gait speed, and weight loss; which lead in the affected elderly being entirely dependent on others *[7, 8].*In addition, associations between slower Timed up and go (TUG), poorer executive function and global cognitive impairment have been reported *[9].* Hence, a new term combining physical frailty with cognitive impairment was defined by the International Consensus Group as «cognitive frailty». Thus, a new possibility to characterize the relation between the two impairments and to detect elders at-risk with cognitive impairment caused by non-neurodegenerative conditions and then to develop interventions, improving their life quality, is now provided. In literature, certain markers of frailty have been shown as better predictors of cognitive decline than others. *Boyle et al. (2010)* suggested that grip strength and timed walk are important indicators of the Mild Cognitive Impairment (MCI) diagnosis *[10].* Previous studies reported poorer mobility in groups with poor cognitive function *[11, 12]* and associations between slower TUG and poorer executive function and memory *[13, 14].*

The aim of this study was to analyze the relationships between frailty and dementia in a sample of Belgian elderly. Furthermore, we intended to evaluate the causal link between biochemical measures and frailty, with a special focus on inflammation and nutrition.

Materials And Methods

Patients

This is a retrospective cohort study that used data from the department of geriatric, GHdC Belgium in the period between January and March 2018. Our analysis focused on 124 patients (90 women, 34 men; age: mean ± SD: 85.9 ± 5.5 years) who are selected according to a random sampling process. Protected health information was scrubbed from both structured and unstructured data prior to the analysis. All data were stored on a secured network approved by the institution.

Patients' information regarding age, gender, residency, medical history, number of drugs used and laboratory evaluation was recorded. All the patients underwent a comprehensive geriatric assessment. Depression was assessed using the Geriatric Depression Scale (GDS–15) and defined as having a score of > 4[*15].* Mini-Mental State Examination (MMSE) was used to evaluate the cognitive function, using the cutoff point <22[*16].* Mini Nutritional Assessment (MNA) was used to evaluate nutrition, using the cutoff of 17[*17].* The SEGA Frailty test was used, the maximum score is 26 points, representing the highest level of frailty. Individuals scoring from 0 to 8 points are considered "non-frail", 9 to 11 "frail" and 12 points or more "severe frail". Independence in Activities of Daily Living (ADL) was assessed using the Katz Score. The Katz score consists of six items (bathing, dressing, toileting, transferring, continence and feeding); each item was scored as dependent *vs* independent. The total sum score ranges from 0 (dependent) to 6 (independent). Dependency was defined as deterioration on at least one domain of ADL (score <6) [*18].* Polypharmacy is stated as concomitant five or more drug usage. Laboratory tests were conducted for all participants: a complete blood count, blood creatinine, C Reactive Protein (CRP), vitamins levels, and serum protein electrophoresis.

Statistical analyses

Results are expressed for continuous variables as the mean ± standard deviation and for qualitative variables as frequencies. Analyses were carried out by the Mann-Whitney U test or by the one-way analysis of variance (ANOVA) and Duncan's multiple range test with SPSS version 22 (Statistical Package for Social Science, SPSS Inc., Chicago, IL). The Spearman correlation test was also used to evaluate the relationships between various parameters. Data were considered statistically different at a p-value of 0.05 or less. Logistic regression was performed to assess the relationship between frailty status and predictor variables. The presence of severe frailty according to SEGA score was the dependent variable.

Results

The population includes 124 participants older than 65 years. The demographic features of the study population are summarized in *Table 1.* These participants were distributed, according to SEGA score, into non-frail (Score ≤ 8; n = 19), frail (8< Score ≤11; n = 25) and severely frail patients (11< Score ≤ 26; n = 80). Characteristics of the participants categorized by frail status are described in *Table 2.*

Of the total patients, 90 (72.6%) were women, yielding a male-female ratio of 0.37. A statistically significant age difference was observed ($p<0.05$). The mean age of the subjects was 85.9 ± 5.5 years, with a higher prevalence of subjects aged over 85 years old among severely frail patients compared to the other groups. The body mass index (BMI) of the studied population was in the normal weight range with a mean of 24.7 ± 5.7 kg/m². However, BMI was slightly higher than 25 for non-frail and frail groups. The percentages of residing in a nursing home or living with a spouse and /or children were higher for severely frail patients (29.0 % and 32.5 %, respectively) than the frail and non-frail patients. Almost all the subjects had gonarthrosis or osteoporosis (99.2%), and above half of the subjects reported their initial diagnosis as cardiac disorder and hypertension (54.0 and 59.7 % of total patients, respectively) with severely frail being the most represented (53.8 and 61.3 %, respectively). Dementia, confusion, and incontinence were all more common ($p<0.05$) in severely frail than frail and non-frail groups (*Table 2).* The majority of the studied patients (71.0 %) and in particular the severely frail group (78.8 %) consume more than 5 drugs per day (*Table 1 and 2).*

Cognitive and frailty screening was conducted using MMSE and SEGA tests. Severely frail patients had the significantly lowest MMSE score ($p<0.05$). The mean Katz score was 2.8 in all frail patients and 84.6 % had a Katz score less than 6, indicating an impairment in daily living autonomy in these patients. The highest prevalence of dependency was observed in severe frail patients (96.3 %). The Mini Nutritional Assessment (MNA) was performed in elderly patients and the mean score was of 16.2 ± 4.6 in total frail, indicating that most of these individuals are malnourished. Stratification of the study population according to the MNA score, showed that 50.4 % were malnourished and had an MNA score lower than 17. The highest prevalence of malnourished patients was observed in severely frail patients (62.3%) *(Table 2)* and in patients with dementia (28.3% of total demented patients) *(Data not shown).*

Biochemical parameters of frail subjects are summarized in *Table 3.* Compared to reference values, higher levels of CRP were observed in total frail patients. CRP and Vitamin D levels were significantly higher in severely frail patients than the other groups ($p<0.05$). Whereas, lower levels of albumin and prealbumin were observed (*Table 3).*

Among the frail population, the SEGA score was negatively correlated to MMSE, MNA and Katz scores ($r = -0.50$, $r = -0.39$ and $r = -0.67$; $p<0.01$). Furthermore, SEGA score was negatively correlated to albumin levels ($r = -0.30$; $p<0.01$) and positively correlated to CRP, polypharmacy, and age ($r = 0.28$, $r = 0.37$, and $r = 0.33$, respectively; $p<0.01$) *(Table 4).*

Using logistic regression, we found that dementia, polypharmacy ≥ 5, living in a nursing home, and decrease of functional capacity evaluated by Katz score were all associated with severe frailty as shown in (*Table 5).*

Discussion

The global interest in the study of aging processes and age-related diseases is due to the rise in the elder's proportion associated with an increased sanitary implication. Frailty constitutes a precise measurement of aging symptoms and it indicates a multidimensional syndrome of energy, physical ability, and cognition loss. The frailty has been considered as an avoidable syndrome and it was suggested that it could be reverted in its earlier stages. Thus, we conducted a cross-sectional study in Belgian elders (n = 124, aged 65 and over), classified according to their frailty status, in order to increase evidence related to frailty and to find parameters that could be used as early indicators.

The current study examined the relationship between frail status and cognitive function in Belgian elderly. We confirmed that physical frailty is correlated with a decline in cognitive functions, which support previous findings. Indeed, data from the Rush Memory and Aging study found that higher levels of frailty were associated with a faster rate of decline in all cognitive domains *[10].* Furthermore, the results of *Wu et al. (2015)* indicated that the appearance of memory impairment may indicate its association with higher frail status, suggesting that existing cognitive impairment is a risk factor for an additional frail decline *[19].* Also, it has been shown that cognitive function across all domains was significantly poorer in frail participants than non-frail. Poor cognition *was* also linked to weakness and walking speed *[20].* However, our findings contradict some studies suggesting the absence of an association between memory decline and frailty *[7, 21, 22].* This discrepancy could be explained by the size or the homogeneity of the samples in these studies *[7, 21; 22].*

Biological and psychological factors, including neuropathology, cardiovascular disease, inflammation, hormonal changes, nutrition, social vulnerability and isolation have been suggested to explain the link between frailty and cognition *[23].* In the present study, we tried to find an explanation for this association. Thus, several biochemical measures, frail status assessments and neuropsychiatric assessment, including the Mini-Mental State Examination has been performed in a population of Belgian elderly patients.

Some biochemical measures were associated with frailty. In fact, frailty was associated with CRP and albumin levels. It is well known that serum albumin is the most abundant blood protein in serum and is used as a marker of nutritional status. Hypoalbuminemia can reflect complications in different systems in elderly subjects. Since frailty is related to dysfunction in several organs, that could explain the observed inverse association between albumin and frailty index in the study population. These data are in accordance with other studies demonstrating that low albumin concentrations were associated with higher frailty scores *[24–26].* Recently, hypoalbuminemia was associated with chronic inflammation *[27].* Indeed, chronic low-grade inflammation has been found to be related to organ damage, muscle waste and chronic diseases, which are hallmarks of frailty *[6].* On the other hand, chronic inflammation appears as a consequence of chronic diseases such as Alzheimer dementia and atherosclerosis *[28].* This phenomenon has been linked to both cognitive function and frailty *[23].* Furthermore, several studies

support the direct association between serum CRP levels and frailty in elders *[29].* In accordance, we found that elevated levels of CRP were associated with higher frailty scores in the study population.

Furthermore, malnutrition has also been associated with hypoalbuminemia *[27].* Hence, the observed correlation between frailty and albumin deficiency could reflect a poor nutritional status in the studied population, suggesting that malnutrition is associated with higher frailty.

Nutritional deficiencies could reflect insufficient micronutrient intake. Knowledge about the relationship between micronutrient status and frailty could promote interventions to correct micronutrient deficiencies and thus could ameliorate frail people status. In fact, insufficient serum 25-hydroxyvitamin (25(OH) D) concentrations were associated with frailty status and measures of physical performance *[30].* Contrary to the literature, we could not find an inverse correlation between Vitamin D and frailty score *[5, 25, 31].* However, this is comparable to data of *Schoufour et al. (2015)* study, conducted on elderly people with intellectual disabilities *[26].* Furthermore, the Vitamin D levels were higher in frail and severely frail patients compared to non-frail. This could be explained by the supplementation since sufficient 25(OH) D was considered crucial for frailty prevention. Recently, it has been reported that among the hospitalized elders, deficiency of Vitamin D was prevalent suggesting a necessity to supplement this Vitamin in order to maintain the required levels *[32].*

In addition, our study confirms the existence of an association between the frequency of frailty and the number of drugs prescribed. Indeed, previous studies indicated that frail patients were likely to receive a more important number of drugs than non-frail ones *[33, 34].* Also, it was reported that each additional drug was associated with frailty with an odds ratio > 1*[33; 35–37].* The enhancement of the interactions and adverse reactions associated with each additional prescription could explain the effect of multiple drugs intake on frailty. *Herr et al. (2015)* suggested that polypharmacy may be utile to identify older patients, whose health is more susceptible to be deteriorated and then to carry out corrective actions with regard to physical activity, nutrition, and the control of chronic diseases *[36].*

The multivariable model using logistic regression identified dementia, polypharmacy ≥ 5, living in a nursing home, and decrease of ADL as significant ($P < 0.05$) predictors of frailty. Our findings are relevant to social and medical policy formulation. The knowledge of factors associated with frailty represents target conditions for programs and policies directed at reducing frailty in the elderly population.

Conclusion

Altogether, our data confirm the complicated pathophysiology behind frailty syndrome. Frailty associated parameters were given. We showed that dementia, polypharmacy, malnutrition, and decrease in physical activity are risk factors for frailty development in older persons. The results are useful for identifying older individuals at risk of developing frailty and a new need for, enabling implementation of preventive strategies.

List Of Abbreviations

BMI: The body mass index

CRP: C Reactive Protein

GDS–15: Geriatric Depression Scale

MMSE: Mini-Mental State Examination

MNA: Mini Nutritional Assessment

ADL: Activities of Daily Living

Declarations

Ethics approval and consent to participate

Protected health information was scrubbed from both structured and unstructured data prior to the analysis. All data was stored on a secured network approved by the institution.

We rigorously protect the confidentiality of health information in our study. The data are received by the eHealth service, we use anonymous electronic patient data to secure the privacy of information about individual patients, according to local guidelines

Consent for publication

Not applicable

Availability of data and materials

The authors can confirm that all relevant data are included in the article.

Competing interests:

The authors declare that they have no competing interests

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Authors' contributions

SH and AZ contributed equally to the design of the study and wrote the first draft of the manuscript. CP and IA, contributed equally to the design of the study and the direction of its implementation, NS and VL participated in the writing of the article. All authors read and approved the final manuscript

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References

1. Xue QL, The frailty syndrome: definition and natural history, Clin Geriatr Med, 2011; 27(1): 1–15. doi: 10.1016/j.cger.2010.08.009.
2. Cooper R, Kuh D, Cooper C, Gale CR, Lawlor D. A. Matthews F, Hardy R, FALCon and HALCyon Study Teams, Objective measures of physical capability and subsequent health: a systematic review, Age Ageing, 2011; 40(1): 14–23. doi: 10.1093/ageing/afq117.
3. Landi F, Cruz-Jentoft AJ, Liperoti R, Russo A, Giovannini S, Tosato M, Capoluongo E, Bernabei R, Onder G, Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from ilSIRENTE study, Age Ageing, 2013; 42 (2): 203–9. doi: 10.1093/ageing/afs194.
4. Gale CR, Baylis D, Cooper C, Sayer AA, Inflammatory markers and incident frailty in men and women: the English Longitudinal Study of Ageing, Age (Dordr), 2013; 35 (6): 2493–501. doi: 10.1007/s11357–013–9528–9.
5. Wong YY, McCaul KA, Yeap BB, Hankey GJ, Flicker L, Low vitamin D status is an independent predictor of increased frailty and all-cause mortality in older men: the Health in Men Study, J Clin Endocrinol Metab, 2013; 98 (9): 3821–8. doi:10.1210/jc.2013–1702.
6. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013; 381 (9868): 752–62. doi: 10.1016/S0140–6736(12)62167–9.
7. Yassuda MS, Lopes A, Cachioni M, Falcao DV, Batistoni SS, Guimaraes VV, Neri AL. Frailty criteria and cognitive performance are related: data from the FIBRA study in Ermelino Matarazzo, São Paulo, Brazil. J Nutr Health Aging. 2012; 16 (1): 55–61.
8. Buchman AS, Boyle PA, Yu L, Shah RC, Wilson RS, Bennett DA. Total daily physical activity and the risk of AD and cognitive decline in older adults. Neurology. 2012; 78(17):1323–9. doi: 10.1212/WNL.0b013e3182535d35.
9. Pondal M, del Ser T. Normative data and determinants for the Timed "Up and Go" test in a population-based sample of elderly individuals without gait disturbances. J Geriatr Phys Ther. 2008; 31: 57–63.

10. Boyle PA, Buchman AS, Wilson RS, Leurgans SE, Bennett DA. Physical frailty is associated with incident mild cognitive impairment in community-based older persons. J Am Geriatr Soc. 2010; 58(2): 248–55. doi: 10.1111/j.1532–5415.2009.02671.x.
11. Eggermont LH, Gavett BE, Volkers KM, Blankevoort CG, Scherder EJ, Jefferson AL, Steinberg E, Nair A, Green RC, Stern RA. Lower-extremity function in cognitively healthy aging, mild cognitive impairment, and Alzheimer's disease. Arch Phys Med Rehabil. 2010; 91(4):584–8. doi: 10.1016/j.apmr.2009.11.020.
12. Pettersson AF, Olsson E, Wahlund LO. Motor function in subjects with mild cognitive impairment and early Alzheimer's disease. Dement Geriatr Cogn Disord. 2005; 19(5–6):299–304.
13. Herman T, Giladi N, Hausdorff JM. Properties of the 'timed up and go' test: more than meets the eye. Gerontology. 2011; 57(3):203–10. doi: 10.1159/000314963.
14. Kimura N, Kazui H, Kubo Y, Yoshida T, Ishida Y, Miyoshi N, Ogino A, Doronbekov TK, Tokunaga H, Ikejiri Y, Takeda M. Memory and physical mobility in physically and cognitively-independent elderly people. Geriatr Gerontol Int. 2007; 7: 258–265. doi.org/10.1111/j.1447–0594.2007.00413.x
15. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. Clin Gerontol. 1986; 5: 165–173. doi.org/10.1300/J018v05n01_09
16. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J. Psychiatry Res. 1975; 12: 189–198.

*17.*Vellas B, Guigoz Y, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition. 1999; 15(2):116–22.

1. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The Index of ADL: a standardized measure of biological and psychosocial function. JAMA. 1963; 185(12):914–9. doi. 10.1001/jama.1963.03060120024016
2. Wu YH, Liu LK, Chen WT, Lee WJ, Peng LN, Wang PN, Chen LK. Cognitive Function in Individuals With Physical Frailty but Without Dementia or Cognitive Complaints: Results From the I-Lan Longitudinal Aging Study. J Am Med Dir Assoc. 2015; 16(10):899.e9–16. doi: 10.1016/j.jamda.2015.07.013.
3. Robertson DA, Savva GM, Coen RF, Kenny RA. Cognitive function in the prefrailty and frailty syndrome. J Am Geriatr Soc. 2014; 62(11):2118–24. doi: 10.1111/jgs.13111
4. Langlois F, Vu TT, Kergoat MJ et al. The multiple dimensions of frailty: Physical capacity, cognition, and quality of life. Int Psychogeriatr. 2012; 24:1429–1436. doi. 10.1017/S1041610212000634
5. Macuco CR, Batistoni SS, Lopes A et al. Mini-Mental State Examination performance in frail, pre-frail, and non-frail community dwelling older adults in Ermelino Matarazzo, Sao Paulo, Brazil. Int Psychogeriatr. 2012; 24:1725–1731. doi: 10.1017/S1041610212000907.
6. Robertson DA, Savva GM, Kenny RA. Frailty and cognitive impairment a review of the evidence and causal mechanisms. Ageing Res Rev.2013; 12: 840–851. doi. 10.1016/j.arr.2013.06.004

7. Collerton J, Martin-Ruiz C, Davies K et al. Frailty and the role of inflammation, immunosenescence and cellular ageing in the very old: cross-sectional findings from the Newcastle 85+ Study. Mech Ageing Dev. 2012; 133: 456–66. doi: 10.1016/j.mad.2012.05.005.
8. Fernandez-Garrido J, Ruiz-Ros V, Buigues C, Navarro Martinez R, Cauli O. Clinical features of prefrail older individuals and emerging peripheral biomarkers: a systematic review. Arch Gerontol Geriatr. 2014; 59: 7–17. doi: 10.1016/j.archger.2014.02.008.
9. Schoufour JD, Echteld MA, Boonstra A, Groothuismink ZM, Evenhuis HM. Biochemical measures and frailty in people with intellectual disabilities. Age Ageing. 2016; 45(1):142–8. doi: 10.1093/ageing/afv152.
10. Mirsaeidi M, Omar HR, Sweiss N. Hypoalbuminemia is related to inflammation rather than malnutrition in sarcoidosis. Eur J Intern Med. 2018; 53:e14-e16. doi: 10.1016/j.ejim.2018.04.016.
11. De Martinis M, Franceschi C, Monti D, Ginaldi L. Inflammation markers predicting frailty and mortality in the elderly. Exp Mol Pathol. 2006; 80: 219–27. doi: 10.1016/j.yexmp.2005.11.004

*29.*Velissaris D, Pantzaris N, Koniari I, Koutsogiannis N, Karamouzos V, Kotroni I, Skroumpelou A, Ellul J. C-Reactive Protein and Frailty in the Elderly: A Literature Review. J Clin Med Res. 2017; 9(6):461–465. doi: 10.14740/jocmr2959w.

*30.*Vaes AMM, Brouwer-Brolsma EM, Toussaint N, de Regt M, Tieland M, van Loon LJC, de Groot LCPGM. The association between 25-hydroxyvitamin D concentration, physical performance and frailty status in older adults. Eur J Nutr. 2019. 58(3):1173–1181. doi: 10.1007/s00394–018–1634–0.

1. Puts MT, Visser M, Twisk JW, Deeg DJ, Lips P. Endocrine and inflammatory markers as predictors of frailty. Clin Endocrinol (Oxf) 2005; 63: 403–11. doi: 10.1111/j.1365–2265.2005.02355.x
2. Pourhassan M, Wirth R. Seasonal Variation in Vitamin D Status among Frail Older Hospitalized Patients. J Frailty Aging. 2018; 7(2):95–99. doi: 10.14283/jfa.2018.10.
3. Ferrer A, Badia T, Formiga F, Sanz H, Megido MJ, Pujol R. Frailty in the oldest old: prevalence and associated factors. J Am Geriatr Soc. 2013; 61(2): 294–296. doi: 10.1111/jgs.12154.
4. Bennett A, Gnjidic D, Gillett M, et al. Prevalence and impact of fall-riskincreasing drugs, polypharmacy, and drug–drug interactions in robust versus frail hospitalised falls patients: a prospective cohort study. Drugs Aging. 2014; 31(3): 225–232. doi: 10.1007/s40266–013–0151–3.
5. Crentsil V, Ricks MO, Xue QL, Fried LP. A pharmacoepidemiologic study of community-dwelling, disabled older women: factors associated with medication use. Am J Geriatr Pharmacother. 2010; 8(3): 215–224. doi: 10.1016/j.amjopharm.2010.06.003.
6. Herr M, Robine JM, Pinot J, Arvieu JJ, Ankri J. Polypharmacy and frailty: prevalence, relationship, and impact on mortality in a French sample of 2350 old people. pharmacoepidemiol Drug Saf. 2015; 24: 637–646. doi: 10.1002/pds.3772.
7. Ding YY, Kuha J, Murphy M. Multidimensional predictors of physical frailty in older people: identifying how and for whom they exert their effects. Biogerontology. 2017; 18(2):237–252. doi:

10.1007/s10522–017–9677–9

Tables

Table 1: Baseline characteristics of the study population

	Total n= 124 (%)	
*Age (years),*Mean ± SD *Age≥85 years*		*85.9 ± 5.5* *78 (63)*
Gender (Female/Male)		*90/34*
BMI (Kg/m²),Mean ± SD		*24.7 ± 5.7*
Residency	*Live alone* *With spouse and/or children* *Nursing Home*	*46 (37.1)* *40 (32.3)* *38 (30.6)*
Medical history	*Diabetes* *HTA* *Dislipoproteinemia* *Dementia* *Depression* *confusion* *Cardiopathy* *Osteoarthritis/ osteoporosis* *Incontinence* *Falls*	*26 (21.0)* *74 (59.7)* *21 (16.9)* *49(39.5)* *26 (21* *59(48)* *67 (54.0)* *123 (99.2)* *39(31.7)* *60 (48.4)*
Professional medical frame	*90 (72.6)*	
Polypharmacy ≥ 5		*88 (71)*
Length of hospitalization (days)		*20.0 ± 15.1*
Comprehensive geriatric assessment	*MMSE Score*	*17.7± 6.8*
	Dependency for ADL *Katz score<6*	*104 (84.6)*
	Malnourished MNA <17	*60 (50.4)*
	SEGA score	*12.9 ± 3.9*
Disease progression	*Amelioration* *Stabilization* *Death*	*47 (38.2)* *55 (44.7)* *21 (17.1)*

SD : Standard deviation, BMI : Body Mass Index

Table 2: Differences regarding characteristics of frail and non-frail subjects

Characteristics		*Non frail n= 19(%)*	*Frail n= 25(%)*	*Severely frail n= 80(%)*
Age (years),Mean ± SD		*83.2 ± 7.2*	*85.4 ± 4.8*	*86.8 ± 5.1* *
Age≥85 years		*8(42)*	*16(64)*	*53 (67.5)**
Gender (Female/Male)		*12/7*	*21/4*	*57/23*
BMI (Kg/m²),Mean ± SD		*25.8 ± 4.8*	*25.3 ± 5.7*	*24.3 ± 5.9*
Residency	*Live alone*	*11 (57.9)*	*17 (68)*	*18 (22.5)*
	With spouse and/or children	*8 (42)*	*6 (24)*	*26 (32.5)*
	Nursing Home	*0*	*2 (8)*	*36 (29.0)*
Medical history	*Diabetes*	*4 (21)*	*7 (28)*	*15 (19)*
	HTA	*9 (47.4)*	*16 (64)*	*49 (61.3)*
	Dislipoproteinemia	*4 (21)*	*5 (20)*	*12(15)*
	Dementia	*4 (21)*	*5 (20)*	*40(50)**
	Depression	*4 (21)*	*6 (24)*	*16(20)*
	Confusion	*4(21)*	*10 (40)*	*45(57)**
	Cardiopathy	*7 (36.8)*	*17 (68)*	*43 (53.8)*
	osteoarthritis	*19 (100)*	*25 (100)*	*79 (98.8)*
	/osteoporosis	*6 (31.5)*		*41(51.2)*
	Falls	*1 (5.3)*	*13 (52)*	*32(40.5)**
	Incontinence		*6 (24)*	
Polypharmacy ≥ 5		*7 (36.8)*	*18 (72)*	*63 (78.8)**
Disease progression	*Amelioration*	*11 (57.9)*	*12 (48)*	*24 (30.4)*
	Stabilization	*4 (21)*	*10 (40)*	*41 (51.9)*
	Death	*4 (21)*	*3 (12)*	*14 (17.7)*
Length of hospitalization (days)		*18.8 ± 20.9*	*21.6 ± 10.8*	*19.7 ± 14.8*
Comprehensive geriatric assessment	*MMSE Score*	*23.2 ± 5.8*	*20.1 ± 6.1*	*15.6 ± 6.2* *
	Dependency for ADL Katz score <6	*2 (10.5)*	*15 (60)*	*77 (96.3)**
	Malnourished MNA <17	*5 (27.8)*	7(29.2)	*48 (62.3)**
	SEGA score	*6.7 ± 1.5*	*10.4 ± 0.8*	*15.2 ± 2.6* *
Professional medical frame		*3 (15.8)*	*16 (64)*	*71(88.8)*

* difference between values at p < 0.05 level BMI : Body mass index

Table 3: Biochemical characteristics and differences of frail and non-frail subjects

Population	Total n=124	Non frail n=19	Frail n=25	Severely frail n=80
Glycemia (mg/dL)	98.0 [32.0- 661.0]	89.0 [53.0- 241.0]	104.0 [60.0- 661.0]	97.0 [32.0-271.0]
HbA1c (%)	6.8 ± 12	6.3 ± 1.3	6.5 ± 1.5	7.0 ± 1.1
Cholesterol (mg/dL)	163.0 ± 41.8	182.5 ± 50.8	163.5 ± 34.8	157.9 ± 40.2
Leukocytes (10^3/µL)	9.0 ± 4.4	9.2 ± 3.2	8.2 ± 5.0	9.3 ± 4.5
Lymphocytes (%)	16.6 ± 9.6	15.2 ± 9.3 ^{b}	20.8 ± 11.3 ^{a}	15.6 ± 8.9 ^{b}
Hemoglobin (g/dL)	12.1 ± 2.7	12.5 ± 1.8	11.8 ± 1.8	12.2 ± 3.1
CRP (mg/L)	30.5 [3.0- 333.0]	19.0 [3.0- 315.0]	12.0 [3.0- 229.0]	44.5 [3.0-333.0] *
Albumin (g/L)	29.6 ± 5.1	31.6 ± 4.1	30.6 ± 6.3	28.8 ± 4.8
Prealbumin (mg/dL)	16.5 ± 6.8	19.1 ± 6.9	17.1 ± 6.7	15.7 ± 6.8
Creatinin (mg/dl)	1.1 ± 0.8	1.4 ± 1.0	1.0 ± 0.4	1.1 ± 0.8
Vit D (ng/ml)	21.6 ± 12.0	15.9 ± 9.7 ^{b}	20.3 ± 12.5 $^{a\,b}$	23.4 ± 12.0 ^{a}

* Correlation is significant at the 0.05 level (Mann-Whitney test) a, b : Different superscript letters in the same row indicate significant difference between values at p < 0.05 level (Duncan's multiple range test) and values are mean ± standard deviation or or median [minimum; maximum] (non-normal distribution)

Table 4: Correlation Coefficients according to SEGA score for selected items

Variables	*SEGA score*
Age	0 .33*
MNA score	-0.39*
MMSE score	*-0.50**
Katz score	*-0.67**
Polypharmacy (number)	0.37*
CRP	0.28*
Albumine	-0.30*

*Correlation is significant at the 0.01 level

Table 5 : Correlates of very frail among the study subjects (results of multiple logistic regression analysis)

Variable	β-Coefficient	Odds ratio	p
Dementia	1.39 (0.62)	4.04 *(1.1-4.7)*	**0.02**
Polypharmacy ≥ 5	1.18 (0.59)	3.2 *(1.01-6.7)*	**0.04**
Nursing home	1.23 (0.47)	3.42 *(1.5-4.9)*	**0.003**
Katz Score	3.09 (0.72)	4.7*(1.9-5.6)*	**0.000**

Age, sex, depression , MNA score, CRP, Albumin, confusion were not statistically significant
Figures in parenthesis are standard errors
Figures in italics are 95 % confidence intervals