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Determinants of Quality of Life in Pre-Frail Older Adults According to Phenotypic Criteria: the VERISAUDE Study

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Abstract
Frailty is a dynamic clinical syndrome considered as part of an age-associated continuum of severity, including pre-frailty as an intermediate frailty status with potential reversibility to robustness. The main purpose of this study was to analyse the relationship between the different domains of quality of life, functional dependence and depressive symptomatology in older adults diagnosed as pre-frail, before progression to frailty occurs. Logistic regression analyses were conducted to examine whether sex, age, level of education and scores in the Geriatric Depression Scale 15-item Short Form (GDS-SF) and the Instrumental Activities of Daily Living Lawton scale determine the worst score in the WHOQOL-BREF (World Health Organization Quality of Life) in older adults meeting one or two frailty phenotypic criteria. Depressive symptomatology (GDS-SF score) was the main determinant of poor quality of life in both groups, and in all areas of WHOQOL-BREF. Age was only associated with poor satisfaction with own health. Female sex and low educational level were linked to low physical QOL and poor self-rated health, respectively, but only in older adults meeting one frailty criterion. Association between functional status and WHOQOL-BREF scores was only found in the univariate analysis. These results underline the importance of identifying multiple aspects, but mainly the presence of depressive symptomatology, as risk factors for all dimensions of quality of life in the pre-frailty process, where interventions might be targeted to reduce the progression of pre-frailty and frailty in older adults.

Keywords
Depressive symptomatology; Frailty; Functional status; Older adults; Quality of life

Introduction

Frailty is defined as 'a clinical state in which there is an increase in an individual's vulnerability for developing increased dependency and/or mortality when exposed to a stressor' (Morley et al. 2013), increasing the risk of negative consequences (disability, falls, hospitalization) and illness (Gobbens et al. 2010; Hogan et al. 2003; Levers et al. 2006), or death (Fried et al. 2004).

Several definitions of frailty have been published (Levers et al. 2006; Morley et al. 2013). Nevertheless, two main definitions of frailty are mostly used (Collard et al. 2012): Fried Frailty Index (FFI) defining a physical phenotype (Fried et al. 2001) and another broader characterization, including social and psychological aspects (Rockwood et al. 1999)—accumulated deficit model.

A physical phenotype of frailty coming from the FFI definition (Fried et al. 2001) attracted the attention of clinical researchers, identifying frail people by the presence of three or more of the following five physical criteria: unintentional weight loss (4.5 kg in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed and low physical activity. The absence of these signs defines a person as robust, and the presence of one or two of these phenotypic criteria defines pre-frailty, an intermediate frailty status identifying a subset at high risk of progressing to frailty (Fried et al. 2001). Thus, frailty is a dynamic process that can be described along a continuum of severity, with different stages of the frailty process: robustness, pre-frailty meeting one criterion, pre-frailty meeting two criteria, and frailty (meeting three out of the five criteria). Further exploring pre-frailty status is critical because a high percentage of community-dwelling older adults are pre-frail (being the most common criteria, a low grip strength (95.0% in Lorenzo-López et al. 2016; about 45% in Drey et al. 2011) or self-reported exhaustion (70.2%, Chang et al. 2012)), showing an increased risk of progressing to frailty in the next years. It has been previously reported that an increased number of phenotypic frailty criteria increases risk of mortality (Kulminski et al. 2008), to have medical conditions and to require assistance in activities of daily living (Camicioli et al. 2015). Older populations in the transition from a robust to a frail status have been investigated to a lesser extent than frail populations (see Fernández-Garrido et al. 2014, for a recent review).

Given that the FFI includes a self-reported exhaustion criterion, it is not surprising the demonstrated association between frailty or pre-frailty and depressive symptomatology (Buttery et al. 2015; Chen et al. 2010; Vaughan et al. 2015), with a prevalence of depressive symptoms higher than 10% of adults aged 55 years or older, ranging from 20.7 to 53.8% (Vaughan et al. 2015), while depressive symptoms yield an average prevalence of 13.5% in older adults living independently in the community, with rates varying from 2.8 to 35% among the studies (Beekman et al. 1999). A relationship between pre-frail and frail status and an increased risk of functional dependence has also been demonstrated (Bandeen-Roche et al. 2015; Snih et al. 2009; Wong et al. 2010). Functional dependence in basic (ADL) and instrumental activities of daily living (IADL) has been associated with age, female gender, comorbidity and mortality (Millán-Calenti et al. 2010). Since frailty has an important health impact, its early identification is crucial to prevent all these overlapping aspects.

Another aspect to be taken into account is that frailty is also associated with poor quality of life (QOL) in older people (Bilotta et al. 2010, 2011; Chang et al. 2015; Ferrer et al. 2010; Gobbens and van Assen, 2014; Masel et al. 2009). The World Health Organization (WHO, WHOQOL Group 1995) defines QOL as 'an individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns'.

When the association betweenQOL and frailty is studied, researches highlight the need to consider the complex relationships between frailty condition and certain multidimensional factors (Bilotta et al. 2010; Gobbens et al. 2013; Reis et al. 2014). In this regard, it has been shown that both functional status (Giebel et al. 2015; Lin et al. 2011) and depressive symptomatology affect the QOL in older adults (Ponte et al. 2014; Renaud and Bédard 2013). IADL/ADL disability and depressive symptomatology have a reciprocal effect across time (Ormel et al. 2002). Research to reduce both symptoms, implying an increasing QOL in frail older people, constitutes an important health care demand. In fact, the effect of geriatric case management on quality of life has been demonstrated in frail older adults (Hsieh 2009). Moreover, community-dwelling elderly have better QOL than institutionalized older adults (de Almeida Moreira et al. 2016).

Based on this background, the aim of our study was twofold: (1) to evaluate the relationship between socio-demographic variables, WHOQOL-BREF scores (overall QOL, general health and four domains: physical health, psychological, social relationships and environment), functional dependence in IADL and depressive symptomatology among pre-frail older adults and (2) to determine the association of socio-demographic aspects, IADL dependence and depressive symptomatology on WHOQOL-BREF scores among pre-frail older adults meeting one or two frailty criteria. To our knowledge, no previous studies have explored QOL in older adults meeting one or two criteria separately, before progression to frailty occurs. In our opinion, further exploring frailty natural progression (robustness/frailty continuum) is critical for identifying specific risk factors and new areas for frailty treatment at preclinical stages, when preventive interventions and potential reversal from states of greater frailty to states of less frailty could be most possible.

Methods

Participants and Procedure

Information was gathered from a large longitudinal study (the present paper is using cross-sectional data, collected from October 2013 to March 2014) called VERISAÚDE (Effectiveness of the Comprehensive Gerontological Assessment (CGA) and longitudinal follow-up in the healthy ageing promotion). It included a representative sample of 749 community-dwelling older adults in Galicia (NW of Spain), who were over 65 years and older, and living at their home and frequenting senior centres. With a level of confidence of 95%, accuracy ±4% and estimation for data follow-up losses 20% (refuse to participate, drop out before the study ends, dataset with incomplete information…), the distribution of the sample by age and sex was similar to that of the entire Galician older population, according to data from the Official Spanish Bureau of Statistics (Instituto Nacional de Estadística 2011). Older adults were recruited from 43 local senior centres. They were invited to participate in the project in different ways and through multiple sources. Associations for the elderly in Galicia were asked to issue an announcement of the study in their centres, by using flyers and word of mouth, so that people who were interested in participating could register. The participants were involved on a voluntary basis and were recruited by representatives of the associations involved in the project.

Inclusion criteria were the following: (a) being aged 65 years of older, (b) be actively enrolled in a Galician association or senior centre, (c) willingness to sign the informed consent form and (d) meet one or two frailty criteria proposed by Fried et al. (2001). Exclusion criterion was the inability to perform the CGA. After applying the inclusion/exclusion criteria, 538 (71.8%) older participants were diagnosed as pre-frail and eligible, 24.4% as robust and 3.7% as frail older adults, as reported in a previous article (Maseda et al., 2016). The manuscript was written according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement (Vandenbroucke et al. 2014; von Elm et al. 2014).

Measures

A multidisciplinary team of professionals with wide experience in CGA administered the instruments. Information on age, sex and education was self-reported. Education was categorized into levels according to years of formal education (≤8 years, 9–17 years, ≥18 years). All of the participants were assessed using standardized tests validated for the Spanish language in the following aspects:

a. Frailty

The frailty status was measured by FFI (Fried et al. 2001). It includes five criteria: (a) unintentional weight loss (i.e. not due to dieting or exercise): at least 4.5 kg in the past year. (b) Self-reported exhaustion: identified by two questions from the modified ten-item Center for Epidemiological Studies-Depression (CES-D) scale (Radloff 1977) in its Spanish version (Ruiz-Grosso et al. 2012). (c) Weakness: grip strength in the lowest 20% at baseline, adjusted for sex and BMI. (d) Slow walking speed: the slowest 20% at baseline, based on time to walk 4.57 m (15 ft), adjusting for sex and standing height. (e) Low physical activity: the lowest 20% at baseline, based on a weighted score of kilocalories expended per

week, calculated according to the Spanish validation of the Minnesota Leisure Time Activity (MLTA) questionnaire (Ruiz Comellas et al. 2012), according to each participant's report, and adjusting for sex. Subjects assessed with three or more positive criteria are defined as frail, with one or two positive criteria are considered to be pre-frail, and those who do not meet any of the criteria as robust or non-frail.

b. Quality of Life

QOL was measured by the World Health Organization's Quality of Life measure-brief version (WHOQOL-BREF) instrument (WHOQOL Group 1998), adapted to the Spanish population (Lucas Carrasco 1998). This is a scale consisting of 2 items from the overall QOL and general health and 24 items, categorized into 4 major domains: physical health (7 items), psychological (6 items), social relationships (3 items) and environment (8 items). Each item is answered on a five-point response scale, with higher scores indicating a higher self-rated QOL.

c. IADL Performance

Spanish version of the Lawton and Brody's Scale (Lawton and Brody 1969; Vergara et al. 2012) was used to assess the level of independence in IADL performance. Responses to each of the eight items included in the scale are coded as zero (unable or partially able) or one (able) and the responses are summed. The total score ranges from zero (low function, dependence) to 8 (high function, independence).

d. Depressive Symptoms

Depressive symptomatology was assessed using the Short Form of the GDS (GDS-SF, Sheikh and Yesavage 1986), a 15-item scale extensively used in the older population (Wall et al. 1999). We specifically administered a Spanish-validated version recommending a cut-off score of 5 or above to consider the existence of probable clinically depressive symptoms (Martínez de la Iglesia et al. 2002); scores of 10 or more indicate the presence of a severe depressive episode (Almeida and Almeida, 1999).

Statistical Analysis

Descriptive statistics (means, standard deviations and percentages) were used to characterize the sample. The differences in the distribution of the characteristics between one or two criteria pre-frailty groups were examined using chi-squared tests for categorical variables and *t* test for continuous variables. For multiresponse variables, column proportions were compared using custom tables (*Z* test). Pearson or Spearman correlation coefficients were used to testing the association between the analyzed variables and the IADL Lawton and GDS-SF scores according to the number of frailty criteria. Correlation coefficients were interpreted as very weak ($r = 0.00–0.19$), weak ($r = 0.20–0.39$), moderate ($r = 0.40–0.59$), strong ($r = 0.60–0.79$) and very strong ($r = 0.80–1.00$) (Swinscow 1997). We estimated the Cohen's q value to compare the effect size of the correlations, using the benchmarks for 'small ES' ($q = 0.10$), 'medium ES' ($q = 0.30$) and 'large ES' ($q = 0.50$) proposed by Cohen (1988).

Multiple forward stepwise logistic regression analysis (Wald method, inclusion or retention of a variable was made dependent on a F value with $p < 0.05$) was performed to determine the best combination of independent (determinant) variables that would modify the dependent (determined) variable (two general items and four domains of the WHOQOL-BREF) in pre-frail older adults meeting one or two frailty criteria. Dependent variables with more than two values were dichotomized (1: very poor/poor/neither poor nor good overall QOL and 0: good/very good overall QOL; and 1: very dissatisfied/dissatisfied/neither satisfied nor dissatisfied general health facet and 0: satisfied/very satisfied general health facet of the WHOQOL-BREF) and continuous variables (four domains of the WHOQOL-BREF) by dividing them into two categories at the median value. Statistical significance was set at $p < 0.05$. The data analysis was conducted using the statistical software package IBM SPSS Statistics v.23.0 (IBM Corporation, Armonk, New York, USA).

Results

Descriptive Statistics

The characteristics of the pre-frail older adults included in the analysis are reported in Table 1. The mean age was 76.64 years (SD = 7.34), 65.6% were women and 62.6% had ≤8 years of education. Significant differences were found according to the number of frailty criteria in age ($p < 0.001$), sex ($p = 0.041$) and health-related variables as the general health facet ($p < 0.001$) and three domains of the WHOQOL-BREF (physical health, $p < 0.001$; psychological, $p < 0.001$; and environment, $p = 0.010$; with lower scores in those older adults meeting two frailty criteria). *Z* test of proportions revealed statistical differences in the general health facet (higher values of 'neither satisfied nor dissatisfied' in older adults meeting two frailty criteria vs. higher values of 'very satisfied' in those meeting only one frailty criterion). We also found significant differences between groups in IADL and GDS-SF scores ($p = 0.004$ and $p = 0.025$, respectively), with a higher IADL dependence and presence of depressive symptoms in older adults presenting two frailty criteria.

Table 1 Characteristics of the pre-frail older adults included in the analysis

	Total (n = 538)	One frailty criterion (n = 424)	Two frailty criteria (n = 114)	p value
Age (years), mean ± SD[a]	76.64 ± 7.34	75.98 ± 7.09	79.11 ± 7.76	<0.001**
Sex, n (%)[b]				
Female	353 (65.6)	269 (63.4)	84 (73.7)	
Male	185 (34.4)	155 (36.7)	30 (26.3)	
Education (years), n (%)[b]				
≤8	337 (62.6)	258 (60.9)	79 (69.3)	
9–17	118 (21.9)	98 (23.1)	20 (17.5)	
≥18	83 (15.4)	68 (16.0)	15 (13.2)	
WHOQOL-BREF				
How would you rate your quality of life?, n (%)[b]				0.122
Very poor	3 (0.6)	2 (0.5)	1 (0.9)	
Poor	11 (2.0)	6 (1.4)	5 (4.4)	
Neither poor nor good	169 (31.4)	128 (30.2)	41 (36.0)	
Good	274 (50.9)	219 (51.7)	55 (48.2)	
Very good	81 (15.1)	69 (16.3)	12 (10.5)	
How satisfied are you with your health?, n (%)[b]				<0.001**
Very poor	3 (0.6)	2 (0.5)	1 (0.9)	
Poor	11 (2.0)	6 (1.4)	5 (4.4)	
Neither poor nor good	169 (31.4)	128 (30.2)	41 (36.0)	
Good	274 (50.9)	219 (51.7)	55 (48.2)	
Very good	81 (15.1)	69 (16.3)	12 (10.5)	
How satisfied are you with your health?, n (%)[b]				<0.001**
Very dissatisfied	5 (0.9)	4 (0.9)	1 (0.9)	
Dissatisfied	26 (4.8)	17 (4.0)	9 (7.9)	
Neither satisfied nor dissatisfied	101 (18.8)	67 (15.8)	34 (29.8)	
Satisfied	298 (55.4)	237 (55.9)	61 (53.5)	
Very satisfied	108 (20.1)	99 (23.4)	9 (7.9)	
Physical health WHOQOL-BREF score, mean ± SD[a]	14.00 ± 2.05	14.28 ± 1.93	12.92 ± 2.14	<0.001**
Psychological WHOQOL-BREF score, mean ± SD[a]	14.27 ± 1.95	14.42 ± 1.93	13.69 ± 1.93	<0.001**
Social relationships WHOQOL-BREF score, mean ± SD[a]	13.89 ± 2.54	13.96 ± 2.54	13.65 ± 2.52	0.245
Environment WHOQOL-BREF score, mean ± SD[a]	13.67 ± 1.82	13.77 ± 1.83	13.28 ± 1.77	0.010*
IADL Lawton scores, mean ± SD[a]	7.78 ± 0.71	7.85 ± 0.52	7.54 ± 1.13	0.004*
GDS-SF scores, mean ± SD[a]	1.57 ± 2.10	1.45 ± 1.95	2.03 ± 2.54	0.025*

WHOQOL-BREF World Health Organization Quality of Life-Brief Form, *IADL* instrumental activities of daily living, *GDS-SF* Global Deterioration Scale-Short Form
*Significant (p value) < 0.05; **significant (p value) < 0.01
[a] t test
[b]Chi-squared test

Correlation of WHOQOL-BREF Scores, IADL Lawton and GDS-SF Scores According to the Number of Pre-Frailty Criteria

Table 2 presents the relationship between age, educational level and WHOQOL-BREF, IADL Lawton and GDS-SF scores according to the number of frailty criteria. As shown in the table, in older adults meeting one frailty criterion, very weak correlations between IADL Lawton scores and age ($r = -0.162$, $p = 0.001$) or physical health ($r = 0.113$, $p = 0.020$) were observed. In older adults meeting two frailty criteria, IADL Lawton scores showed a very weak association with education ($r = 0.199$, $p = 0.034$) and weak associations with age ($r = -0.364$, $p < 0.001$), physical health ($r = 0.284$, $p = 0.002$) and psychological domain ($r = 0.222$, $p = 0.017$). IADL Lawton scores also correlated weakly and negatively with GDS-SF scores ($r = -0.243$, $p = 0.009$). The number of variables associated with IADL Lawton scores was higher in participants meeting two frailty criteria. In terms of difference between amounts of relationship according to the number of frailty criteria, small-medium Cohen's q effect sizes were observed in the significant correlation values.

Table 2. Associations between variables of interest and the IADL Lawton and GDS-SF scores according to the number of frailty criteria

	IADL Lawton scores		Effect size (Cohen's q)	GDS-SF scores		Effect size (Cohen's q)
	One frailty criterion	Two frailty criteria		One frailty criterion	Two frailty criteria	
Age (years)[a]	−0.162**	−0.364**	0.218	−0.023	−0.147	0.125
Education (years)[a]	0.089	0.199*	−0.112	−0.086	−0.016	−0.070
How would you rate your quality of life?[b]	0.007	−0.039	0.046	−0.265**	−0.383**	0.132
How satisfied are you with your health?[b]	0.052	0.050	0.002	−0.295**	−0.424**	0.149
Physical health WHOQOL-BREF score[a]	0.113*	0.284**	−0.179	−0.327**	−0.492**	0.199
Psychological WHOQOL-BREF score[a]	0.057	0.222*	−0.169	−0.566**	−0.565**	−0.001
Social relationships WHOQOL-BREF score[a]	−0.049	0.180	−0.231	−0.331**	−0.353**	0.025
Environment WHOQOL-BREF score[a]	−0.057	−0.127	0.071	−0.222**	−0.128	−0.097
GDS-SF scores[a]	−0.089	−0.243**	0.159	–	–	

IADL instrumental activities of daily living, *GDS-SF* Global Deterioration Scale-Short Form, *WHOQOL-BREF* World Health Organization Quality of Life-Brief Form
*Significant (p value) < 0.05; **significant (p value) < 0.01
[a]Pearson's correlation coefficient
[b]Spearman's correlation coefficient

In the group meeting one frailty criterion, GDS-SF scores correlated with the two general items and four domains of WHOQOL-BREF. All the associations were weak, except for the relation between GDS-SF scores and the psychological domain (moderate, $r = -0.566$, $p < 0.001$). In those participants presenting two frailty criteria, similar results were found although with a higher association (moderate) for general health ($r = -0.424$, $p < 0.001$), physical health ($r = -0.492$, $p < 0.001$) and psychological domain ($r = -0.565$, $p < 0.001$), and a lack of association with environment. As observed (Cohen's q values), the significant associations between QOL and GDS-SF scores were higher in overall quality of life, general health and physical health in those patients fulfilling two frailty criteria but no effect was observed in other QOL domains.

The age-adjusted partial correlation coefficients (Table 3) were very similar and the significant relationships previously found remained. In addition, two new significant associations were observed, between IADL Lawton scores and overall QOL ($r = 0.231$, $p = 0.014$) and social relationships ($r = 0.229$, $p = 0.014$) in pre-frail older adults meeting two frailty criteria. Results revealed little or no effect of age, except on associations with IADL Lawton scores in the presence of two frailty criteria, with higher partial correlation coefficients and a marked age effect.

Table 3. Correlation coefficients between WHOQOL-BREF domains, IADL Lawton and GDS-SF scores according to the number of frailty criteria (partial correlations controlling for age)

	IADL Lawton scores			GDS-SF scores		
	One frailty criterion	Two frailty criteria	Effect size (Cohen's *q*)	One frailty criterion	Two frailty criteria	Effect size (Cohen's *q*)
How would you rate your quality of life?[a]	0.011	0.049	−0.038	−0.266**	−0.369**	0.115
How satisfied are you with your health?[a]	0.086	0.231*	−0.149	−0.302**	−0.411**	0.125
Physical health- WHOQOL-BREF scores[b]	0.107*	0.412**	−0.331	−0.329**	−0.475**	0.175
Psychological WHOQOL-BREF scores[b]	0.048	0.293*	−0.254	−0.569**	−0.556**	−0.019
Social relationships WHOQOL-BREF scores[b]	−0.053	0.229*	−0.286	−0.332**	−0.345**	0.015
Environment WHOQOL-BREF scores[b]	−0.074	−0.123	0.049	−0.226**	−0.124	−0.105
GDS-SF scores[b]	−0.094	−0.321**	0.238			

WHOQOL-BREF World Health Organization Quality of Life-Brief Form, *IADL* Instrumental Activities of Daily Living, *GDS-SF* Global Deterioration Scale-Short Form
* Significant (p value) < 0.05; **significant (p value) < 0.01
[a] Spearman's partial correlation coefficient
[b] Pearson's partial correlation coefficient

Multiple Regression Models According to the Number of Pre-Frailty Criteria

Multiple logistic regression analysis according to the number of frailty criteria are shown in Tables 4 and 5. In participants meeting 1 frailty criterion (Table 4), the most robust model to explain the determinants of poor self-rated QOL, correctly classifying 70.5% of subjects, included GDS-SF scores ($\beta = 0.307$) and education ≤8 years ($\beta = -0.648$). Therefore, subjects showing higher scores in GDS-SF and lower educational level reported poor self-rated QOL. According to satisfaction with their health, younger participants ($\beta = -0.047$) with higher scores in GDS-SF ($\beta = 0.294$) had a poor satisfaction with their health, with an overall correct classification rate of 80.0%. The model to explain the determinants of physical health was able to correctly classify 70% of the subjects, showing that higher scores in GDS-SF ($\beta = 0.319$) and being a woman ($\beta = -0.455$) had a fewer score in this domain of QOL. The model to explain the determinants of psychological health (72.4% of subjects correctly classified; $\beta = 0.525$), social relationship (59.1% of subjects correctly classified; $\beta = 0.259$) and environment (62.3% of subjects correctly classified; $\beta = 0.199$) only included GDS-SF scores. Again, subjects with one frailty criterion and highest scores in GDS-SF reported poor QOL in their psychological, social relationship and environment domains.

Table 4 . Regression analyses (Odds ratio, 95% confidence interval) of variables predicting WHOQOL-BREF measures in subjects with 1 frailty criterion

	Poor self-rated QOL	Poor satisfaction with their health	Physical health <13.7143	Psychological health <14.00	Social relationship <14.6667	Environment <13.50
Sex (female)			0.634* (0.405–0.994)			
Age		0.954* (0.920–0.989)				
GDS-SF scores	1.360** (1.208–1.530)	1.342** (1.191–1.513)	1.376** (1.221–1.550)	1.690** (1.463–1.953)	1.295** (1.149–1.460)	1.220** (1.094–1.360)
Education (≤8 years)	0.523* (0.332–0.825)					
-2LL	492.413	400.264	505.377	480.979	564.587	560.578
Cox and Snell R^2	0.089	0.074	0.086	0.155	0.050	0.033
Nagelkerke R^2	0.125	0.116	0.119	0.212	0.066	0.044
% Correct	70.5	80.0	70.0	72.4	59.1	62.3

-2 LL -2 log Likelihood of full model, *% Correct* proportion of correctly classified events, *QOL* quality of life, *WHOQOL-BREF* World Health Organization Quality of Life-Brief Form *GDS-SF* Global Deterioration Scale-Short Form
Significance at *p value < 0.05 and **p value < 0.01

Table 5. Regression analyses (Odds ratio, 95% confidence interval) of variables predicting WHOQOL-BREF measures in subjects with 2 frailty criteria

	Poor self-rated QOL	Poor satisfaction with their health	Physical health <13.7143	Psychological health <14.00	Social relationship <14.6667	Environment <13.50
Age		0.905* (0.851–0.962)				
GDS-SF scores	1.370* (1.133–1.657)	1.562** (1.242–1.965)	1.326* (1.071–1.641)	1.759** (1.346–2.300)	1.326* (1.097–1.604)	1.177* (1.001–1.384)
-2LL	140.803	118.100	143.099	129.842	146.983	153.572
Cox and Snell R^2	0.113	0.258	0.076	0.219	0.091	0.037
Nagelkerke R^2	0.153	0.350	0.103	0.292	0.122	0.050
% Correct	65.8	76.3	63.2	71.9	58.8	58.8

-2 LL -2 log Likelihood of full model, *% Correct* proportion of correctly classified events, *QOL* quality of life, *WHOQOL-BREF* World Health Organization Quality of Life-Brief Form, *GDS-SF* Global Deterioration Scale-Short Form
Significance at *p value < 0.05 and **p value < 0.01

In participants meeting two frailty criteria (Table 5), GDS-SF scores were the only variable included in the most robust models, except to classify poor satisfaction with own health, where the younger subjects ($\beta = -0.100$) with higher GDS-SF scores ($\beta = 0.446$) ranked worst their satisfaction level. Therefore, high scores in GDS-SF explained the model to determine poor self-rated QOL (65.8% correctly classified; $\beta = 0.315$), poor satisfaction with own health (76,3% correctly classified; $\beta = 0.446$), and worst scores in the 4 domains of the WHOQOL-BREF: physical health (63.2% correctly classified; $\beta = 0.282$) psychological (71.9% correctly classified; $\beta = 0.565$), social relationship (58.8% correctly classified; $\beta = 0.283$) and environment (58.8% correctly classified; $\beta = 0.163$). The highest proportion of correctly classified events corresponds with the largest pseudo-R^2 measures (−2 log Likelihood, Cox and Snell R^2 an adjusted Nagelkerke R^2, with the range of possible values extended to 1).

In the univariate analysis, IADL Lawton scores were found to be significantly correlated with physical health in individuals meeting one frailty criterion and also with the psychological domain in those meeting two frailty criteria. Nevertheless, when considering along with other variables in logistic regression models for the different domains and according to the number of frailty criteria, IADL dependence was not relevant.

Discussion

The relationship between the domains of QOL measured by WHOQOL-BREF, socio-demographic aspects, functional status and depressive symptomatology, measured by IADL Lawton scores and GDS-SF scores, among pre-frail older adults fulfilling one or two frailty criteria was investigated to further understand the robustness/frailty continuum of severity. In addition, the best determinants of poor QOL according to the number of frailty criteria were identified. Part of our objectives was met by the data and poor QOL in pre-frail older subjects was associated with socio-demographic and psychological determinants. However, no association between QOL and IADL dependence was observed. Importantly, the determinants were different depending on the severity of pre-frailty.

First, with respect to socio-demographic variables, age was a significant determinant of poor satisfaction with health, independently of the number of frailty criteria. Age had already been associated with the presence of frailty (Bandeen-Roche et al. 2015; Buttery et al. 2015; Chen et al. 2010). In this study, younger adults reported a worst satisfaction level, and no association was observed with other QOL domains. Consistent with these observations, Ferrer et al. (2010), support the idea that the QOL seems not to worsen in the oldest old people (older than 89 years). Younger age was also associated with worse health-related quality of life (Lewis et al. 2007). This is in contrast to the findings of another study where age has been identified as a significant variable in the gerontological literature, showing worse overall QOL in the old-old elderly, persons older than 80 years (Azpiazu Garrido et al. 2003). In other studies (Aghamolaei et al. 2010; Gobbens et al. 2013; Zaninotto et al. 2009), age was also associated with QOL, with lower QOL scores in aged individuals. Lower QOL in older individuals was mediated by limitations in functional ability (Hirve et al. 2014). Nevertheless, other authors (Gobbens et al. 2013) found this association on all four quality of life domains.

Besides, a relationship was found between being female and low scores in the physical health domain, but only in the group meeting two frailty criteria. Frailty severity is more prevalent in the female gender (Bandeen-Roche et al. 2015; Chen et al. 2010) and in this line, worse perceived health status and quality of life in women than men have been reported (Azpiazu Garrido et al. 2003; Hirve et al. 2014). Female gender was also found to be associated with lower physical health, but also with psychological QOL (Gobbens et al. 2013). On the other hand, women reported higher scores in social relationships and environment domains (Trentini et al. 2011).

Educational level was the only determinant of poor self-rated QOL in pre-frail older adults meeting one frailty criterion but not in those fulfilling two criteria. The prevalence of frailty is associated with less education (Chen et al. 2010). Also, a high level of education, usually linked to a higher level of social networking and a regular income, has been related to a better QOL (Hirve et al. 2014). In another research (Gobbens et al. 2013), educational level was found to be a determinant of three quality of life domains, except with social relationships, as observed by other authors (Aghamolaei et al. 2010) demonstrating that elderly unable to read and write are more likely to report low QOL scores than literate ones, especially in the physical domain. Other findings (Trentini et al. 2011) are not able to establish if education determines low QOL or if lower level of formal education is linked to other aspects (more tiresome jobs, had less

access to health care, more difficulty with understanding medical prescriptions, including lower levels of opportunity and lower socioeconomical level) that would be affecting QOL.

The results on socio-demographic aspects show that the number of fulfilled frailty items is relevant when analyzing poor self-rated QOL and low scores in the physical health domain, where variables as female gender or low educational level are determining these low QOL indicators. This relationship is not observed in subjects meeting two frailty criteria. Therefore, these different contexts should be considered when the continuum of the frailty process is assessed, affecting only in the first stages of the pre-frailty status. In this line, other authors (Masel et al. 2009) emphasize the need for considering that lower scores in physical QOL (presence of physical problems, lack of energy and/or worse self-rated health, measured with the physical component of the SF-36) are more frequent in subjects identified as frail and pre-frail than in those being non-frail.

Contrary to our hypothesis, no relationship was found between QOL and IADL dependence, regardless of the number of frailty criteria. IADL Lawton score was not a predictor of QOL in the present study. This fact could be due to the low proportion of subjects with IADL functional dependence in our sample (13.4%). It is expected that, although the ageing process per se is associated with the risk of functional limitations, some accelerating factors, as exposure to lifetime adversity and a high level of depressive symptoms, are affecting (Shrira and Litwin 2014). Lower functional status is an independent predicting factor of poor QOL (Ferrer et al. 2010). Pre-frailty status was associated with an increased risk of ADL disability over a 10-year period among non-disabled subjects (Snih et al. 2009). Over the years, people are more susceptible to present difficulties in ADL and IADL, and those with a disability on at least one IADL item implies a higher prevalence of frailty because of the presence of associated disorders, cognitive impairment or falls (Nourhashémi et al. 2001). Higher QOL mitigates the age-related decline in functional status (Palgi et al. 2015). Besides, ADL performance has been associated with QOL in different stages of dementia (Giebel et al. 2015) and we must consider that the presence of cognitive impairment was very low in our sample (8.0%).

Lastly, GDS-SF scores contributed in all predictive models independently of the number of frailty criteria met by the subject. Depressive symptoms have been identified as determinants of frailty (Buttery et al. 2015; Chen et al. 2010). Different studies (Chachamovich et al. 2008; Chang et al. 2015; Trentini et al. 2011) established a relationship between the presence of this symptomatology and the worst perception in domains of QOL. These results were consistent with our study since the GDS-SF score was the strongest variable to determine a poor QOL both in self-rated QOL and satisfaction with health and all the four domains of WHOQOL-BREF, in both pre-frail groups. Nevertheless, more studies regarding depressive symptomatology in frail population are needed to validate the positive effect of this association since in other's researches the presence of depressive symptomatology in the older people did not seem to affect more psychological QOL than the other domains (Chang et al. 2015; Trentini et al. 2011), as observed in our data. Other research (Bilotta et al. 2010) also showed that GDS-SF scores affected all domains of QOL regardless of the degree of frailty but, when this syndrome evolved, other factors such as age could determine the satisfaction with health. This effect was mentioned by other authors (Fillit and Butler 2009) and called the 'frailty Identity Crisis', representing 'a psychological syndrome that may accompany the transition from independence to frailty', affecting health and QOL of frail older adults. A recent systematic review on the topic has reported that the prospective relationship between depressive symptomatology and increased risk of frailty is robust, while the opposite relationship is less conclusive (Vaughan et al. 2015). Another study (Chang et al. 2015) identified the mediator role of depressive symptoms in the association between ADL dependence and QOL scores.

Strengths and Limitations

The strengths of this research include the large sample size and the fact that these findings are pioneering in scientific literature since it represents an initial attempt to explore QOL in the robustness/frailty continuum of the severity in the elderly, considering others aspects relevant for the older people fulfilling one or two frailty criteria: social characteristics (age, gender and educational level), IADL dependence and depressive symptomatology (GDS-SF scores). However, our study has also limitations. We classified pre-frailty elderly subjects based on physical criteria (Fried et al. 2001), without considering psychological or social factors, predictive factors of QOL (Gobbens and van Assen 2014) and so, limiting the findings in relation to the QOL. The VERISAÚDE study did not have an enough number of individuals meeting three or more criteria for frailty to be able to compare the factors affecting QOL

with the pre-frail ones. Besides, our results could be limited by the selection of the sample study, from senior centres. It has been demonstrated that senior centres users are more socially involved (Miner et al. 1993), had more social contacts, better mental health and fewer ADL dependence (Calsyn and Winter 1999) than non-attendees. Although QOL correlated with several of the studied variables, some associations were weak and should be interpreted with caution, also due to the fact of dichotomizing continuous data using sample median splits in the multivariate analysis that can reduce the predictive power and information. The cross-sectional nature of the study did not allow us to know the direction of the association pre-frailty and QOL or to establish its longitudinal evolution. Hence, longitudinal studies are needed to consider the importance of other social, functional and psychological factors when characterizing pre-frailty.

Conclusions

Given the robustness/frailty continuum, the potential reversibility of frailty status and the high prevalence of pre-frailty in the older adults, it is necessary to identify specific determinants of QOL in pre-frail older adults meeting one or two frailty criteria. This is relevant to further understand the natural progression of frailty development. In the present study, the main determinant of poor QOL was the presence of depressive symptomatology in both pre-frail groups, as a risk factor for all dimensions of QOL in the pre-frailty process. Socio-demographic aspects are mostly relevant in older adults meeting only one frailty criterion. It is important to identify pre-frailty patients at greater risk for poor QOL to implement intervention measures in previous states of frailty with the objective, among others, to reverse from an intermediate frailty to robustness and minimize the socio-economic impact of this geriatric syndrome on public health. Poor QOL as an indicator of risk of the presence of multiple co-occurring diseases and geriatric syndromes is relevant for planning and implementing health promotion and preventive programs for older adults, especially to direct efforts at preventing or delaying frailty status among community-dwelling older people. Considering pre-frailty as a preceding status of frailty, the prevalence and types of depressive symptoms continuously worsen with increasing severity of frailty, increasing lower positive feelings (Nascimiento et al. 2016). In this regard, we demonstrate the need for a comprehensive and multidisciplinary approach aimed at preventing frailty and also the impact of depressive symptoms and, consequently, improving the QOL in older people. This approach, undoubtedly, should take into account the definitional elements of frailty, the occurrence of depressive symptoms as psychological marker of frailty-attenuating adverse outcomes (Lohman et al. 2015) and the different dimensions of QOL.

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Compliance with Ethical Standards
The study protocol was drafted according to the principles embodied in the Declaration of Helsinki and was approved by the Ethics Committee of the University of A Coruña. Informed consent was obtained from all individual participants included in the study.

Conflict of Interest
The authors declare that they have no conflict of interest.

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