ORIGINAL INVESTIGATION



Frailty at Risk Scale (FARS): development and application

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Abstract

The aim of this cross-sectional study was to develop a Frailty at Risk Scale (FARS) incorporating ten well-known determinants of frailty: age, sex, marital status, ethnicity, education, income, lifestyle, multimorbidity, life events, and home living environment. In addition, a second aim was to develop an online calculator that can easily support healthcare professionals in determining the risk of frailty among community-dwelling older people. The FARS was developed using data of 373 people aged \geq 75 years. The Tilburg Frailty Indicator (TFI) was used for assessing frailty. Multivariate logistic regression analysis showed that the determinants multimorbidity, unhealthy lifestyle, and ethnicity (ethnic minority) were the most important predictors. The area under the curve (AUC) of the model was 0.811 (optimism 0.019, 95% bootstrap CI = -0.029; 0.064). The FARS is offered on a Web site, so that it can be easily used by healthcare professionals, allowing quick intervention in promoting quality of life among community-dwelling older people.

Keywords Frailty · Determinants · Older people · At-risk · Multimorbidity · Online calculator

Introduction

Frailty may be defined as a dynamic state affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, and social), which is caused by the influence of a range of variables and increases the risk of adverse outcomes (Gobbens et al., 2010a). The influencing variables and adverse outcomes are presented in an integral conceptual model of frailty (Gobbens et al., 2010b). As the model shows, possible outcomes of frailty are disability (Liu et al., 2019), increased

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healthcare utilization (Fried et al., 2001; Rockwood et al., 2005), and mortality (Shamliyan et al., 2013; Vermeiren et al., 2016). Influencing factors (i.e., potential determinants of frailty) included in the model are: age, sex, marital status ethnicity, education, income, lifestyle, multimorbidity, life events, and home living environment (Gobbens et al., 2010b).

Many scales have been developed to assess multidimensional frailty, including physical, psychological, and social domains, among community-dwelling older people, such as the Frailty Index (FI) (Mitnitski et al., 2002), the Electronic Frailty Index (eFI) (Clegg et al., 2016), the Groningen Frailty Indicator (GFI) (Schuurmans et al., 2004), the SUNFRAIL tool (Gobbens et al., 2020), and the Tilburg Frailty Indicator (TFI) (Gobbens et al., 2010d). The last scale, the TFI, especially fits perfectly with the integral conceptual model of frailty. To prevent or postpone frailty, it is important to identify determinants of frailty. Numerous studies have been carried out on the associations between individual and combinations of determinants and frailty (Collard et al., 2012; Freer & Wallington, 2019; Gobbens et al., 2010c; Niederstrasser et al., 2019; Ocampo-Chaparro et al., 2019; van Assen et al., 2016; Yadav et al., 2019). For instance, a systematic review showed that the prevalence of frailty increased with age and was higher among women than men (Collard et al., 2012), and in a sample of 47,768 individuals aged \geq 65 years, similar findings were reached (van Assen et al., 2016). In addition, a study among community-dwelling older people aged 75 years or older observed that medium income, an unhealthy lifestyle, and multimorbidity were associated with frailty, after controlling for other determinants (age, sex, education, and life events) (Gobbens et al., 2010c). Another study stressed the importance of environmental factors in predicting frailty (Freer & Wallington, 2019).

It is important that healthcare professionals have at their disposal a scale with which determinants of frailty easily can be identified, since the findings of such an assessment tool can provide healthcare professionals with points of leverage for interventions to prevent or postpone frailty. As far as we know, such a scale does not yet exist. Therefore, the main aim of the present study was to develop a Frailty at Risk Scale (FARS) incorporating all determinants included in both the integral conceptual model of frailty and part A of the TFI. In addition, we aimed to develop an online calculator that can easily support primary care professionals in determining the risk of frailty among community-dwelling older people.

Methods

Study population and data collection

For the present cross-sectional study, we used a sample of 479 community-dwelling people aged \geq 75 years, referring to a 42% response rate, which has also been used in previous studies (Gobbens et al., 2010c, d). The participants were resident in (blinded for review) the Netherlands. In 2008, they received a self-report questionnaire by mail containing scales for determining frailty, quality of life, and disability.

Measures

Determinants

Part A of the TFI was used in order to collect data on the determinants of frailty: age, sex, marital status ethnicity, education, income, lifestyle, multimorbidity, life events, and home living environment (Gobbens et al., 2010d). Table 1 shows the questions and response categories referring to these ten determinants.

Frailty

We used part B of the TFI to assess frailty. This part contains 15 items referring to the physical (eight items), psychological (four items), and social (three items) domains of frailty (Gobbens et al., 2010d). The score ranges from 0 to 15, with

higher scores indicating greater frailty. The cut-off point for distinguishing non-frail and frail older people is 5 (Gobbens et al., 2010d). Previous studies have demonstrated that the TFI is a valid and reliable questionnaire for assessing frailty among community-dwelling older people (Dong et al., 2017; Gobbens et al., 2010d, 2012; Santiago et al., 2013; Uchmanowicz et al., 2016).

Statistical analysis

We used counts and percentages to describe the baseline characteristics of the participants. All variables were dichotomized for the modeling. The Chi-square test was used as a univariate technique to compare the dichotomous variables with respect to the dichotomized outcome variable. A *p*-value < 0.05 was considered as significant. Cramer's V, a statistic derived from the Chi-square value, was used as an association measure. Values toward 0 indicate weak association and values toward 1 indicate strong association. For the multivariate analysis, we used logistic regression with all ten dichotomized predictor variables and the dichotomized outcome (frail vs non-frail). The predictive performance of the model was measured using the area under the curve (AUC). An AUC > 0.700 was considered as an indication for good predictive performance (Steyerberg, 2009). Internal validation was done using bootstrapping (1000 repetitions) to gain insight in the optimism of the logistic regression model. External validation was performed using a dataset consisting of comparable participants in 2013. A nomogram was constructed based on the transformed coefficients (coefficients divided by the maximum of the coefficients and multiplied by 100) of the logistic regression model. Based on the nomogram, we designed a calculator that is accessible on the Web (blinded for review). For the analyses, we used R version 3.4.4. (R Core Team, 2018).

Results

Table 1 shows the participant characteristics. We dichotomized the variables that had more than two categories. Age was recoded into the categories < 85 and \geq 85 years, and frailty score was recoded into the categories < 5 (non-frail) and \geq 5 (frail), and we deleted the participants with missing values for one or more variables, leaving 373 participants. The percentage missing values for the variables varied from 0.0% to 8.6%. Table 1 also shows the *p*-values of the Chisquare test for each characteristic. Six out of ten characteristics had p-values < 0.05.

Figure 1 shows the univariate association of the variables measured by Cramer's V. The outcome variable (frail or non-frail) had the strongest association with diseases and/ or chronic disorders, followed by the variable lifestyle.

Table 1 Participant characteristics

	Distribution		Distribution after dichotomization			Non-frail		Frail		P value
	n	%	New category	n	%	n	%	n	%	
Which sex are you?										
Man	169	45.3	Man	169	45.3	109	53.7	60	35.3	< 0.001
Woman	204	54.7	Woman	204	54.7	94	46.3	110	64.7	
What is your age?										
75–76	73	19.6	<85	316	84.7	181	89.2	135	79.4	0.014
77–78	74	19.8	≥85	57	15.3	22	10.8	35	20.6	
79–80	69	18.5								
81-82	60	16.1								
83–84	40	10.7								
85–86	31	8.3								
87–88	19	5.1								
89–90	6	1.6								
91–92	1	0.3								
What is your marital status?	1	0.5								
Married or cohabiting	186	49.9	Married or cohabiting	186	49.9	119	58.6	67	39.4	< 0.001
Not married	35	9.4	Not married and not cohabiting	187	50.1	84	41.4	103	60.6	< 0.001
Divorced	13	3.5	Not married and not conducting	107	50.1	04	-11	105	00.0	
Widowed	139	37.3								
In which country were you bo		57.5								
The Netherlands	362	97.1	The Netherlands	362	97.1	200	98.5	162	95.3	0.126
Former Dutch East Indies	502 6	1.6	Other	502 11	2.9	3	98.5 1.5	8	95.5 4.7	0.120
Suriname	1	0.3	Other	11	2.9	5	1.5	0	4.7	
Netherlands Antilles	0	0.0								
	0	0.0								
Turkey Morocco	0	0.0								
Other	4	1.1								
			a amember a d							
What is the highest level of ed	142		-	216	047	170	83.7	140	85.9	0.669
None or primary		38.1 46.6	Primary or secondary	316 57	84.7 15.3	33	85.7 16.3	146		0.009
Secondary	174 57	46.6 15.3	Higher	57	15.5	33	10.5	24	14.1	
Higher										
Which category indicates your		-		100	20.2	75	26.0	24	20.0	10.001
600 or less	11	2.9	> 1800 euro	109	29.2	75	36.9	34	20.0	< 0.001
601–900	56	15.0	\leq 1800 euro	264	70.8	128	63.1	136	80.0	
901-1200	89	23.9								
1201-1500	51	13.7								
1501-1800	57	15.3								
1801–2100	41	11.0								
2101 or more	68	18.2								
Overall, how healthy would yo		-		200	·	1.55	07.0	102	(0)(0.001
Healthy	280	75.1	Healthy	280	75.1	177	87.2	103	60.6	< 0.001
Not healthy, not unhealthy	84	22.5	Not healthy	93	24.9	26	12.8	67	39.4	
Unhealthy	9	2.4								
Do you have two or more disea				10.	<i></i>		- 0 ·	10	6 0 -	
No	191	51.2	No	191	51.2	143	70.4	48	28.2	< 0.001
Yes	182	48.8	Yes	182	48.8	60	29.6	122	71.8	
Have you experienced the deat										
No	253	67.8	No life events	164	44.0	97	47.8	67	39.4	0.129
Yes	120	32.2	One or more life events	209	56.0	106	52.2	103	60.6	

Table 1 (continued)

	Distribution		Distribution after dichotomization			Non-frail		Frail		P value
	\overline{n}	%	New category	п	%	n	%	n	%	
Have you experienced a s	serious illness	yourself	?							
No	321	86.1								
Yes	52	13.9								
Have you experienced a s	serious illness	in a love	d one?							
No	263	70.5								
Yes	110	29.5								
Have you experienced a	divorce or end	ing of an	important intimate relationship?							
No	353	94.6								
Yes	20	5.4								
Have you experienced a t	traffic incident	?								
No	368	98.7								
Yes	5	1.3								
Have you experienced a	crime?									
No	372	99.7								
Yes	1	0.3								
Are you satisfied with yo	ur home living	g environ	ment?							
Satisfied	362	97.1	Satisfied	362	97.1	199	98.0	163	95.9	0.361
Not satisfied	11	2.9	Not satisfied	11	2.9	4	2.0	7	4.1	

Fig. 1 Association variables based on Cramer's V

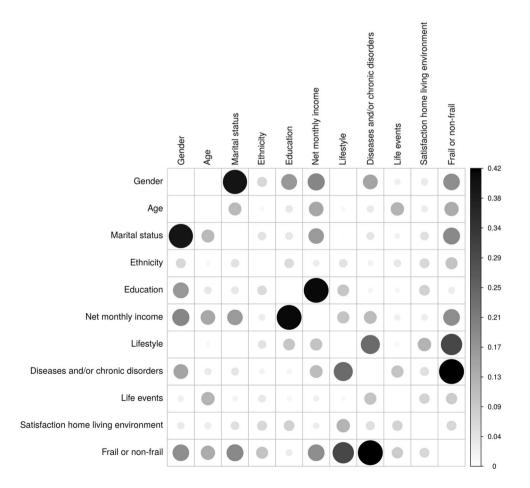


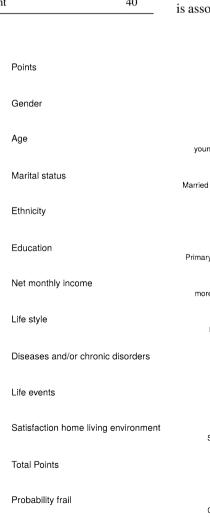
Table 2 shows the points for each variable based on multivariate analysis with the logistic regression technique. Table 2 also shows that variable diseases and/or chronic disorders had the highest influence on the outcome variable (frail vs non-frail), whereas variable education had the lowest influence.

Figure 2 is the nomogram derived from the logistic regression analysis with all ten predictors and frail/non-frail

Table 2 Points per variable

Variable	Points
Gender (woman)	27
Age (≥85)	47
Marital status (not married and not cohabitating)	40
Ethnicity (not Dutch)	73
Education (higher)	20
Net monthly income (≤ 1800)	39
Lifestyle (unhealthy)	81
Diseases and/or chronic disorders (yes)	100
Life events (one or more)	27
Satisfaction home living environment	40

Fig. 2 Nomogram dichotomous frailty

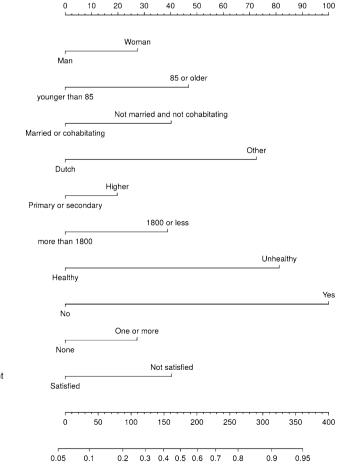


as outcome. An example of the use of this nomogram: Suppose the participant is a woman with an income ≤ 1800 euro. The total number of points for that participant is then 27 + 39 = 66, and the corresponding estimated probability for being frail is then approximately 0.15. Our online calculator (blinded for review), which automatically calculates the points and the probability for being frail for a participant, presents the same results. This calculator is prefilled for the most favorable situation, leading to a probability for being frail of 6%. By clicking on the radio buttons, the characteristics of a participant can be changed.

The AUC of model was 0.811 (optimism 0.019, 95% bootstrap CI = -0.029-0.064).

Discussion

Frail community-dwelling older people have a high risk of disability (Liu et al., 2019), increased healthcare utilization (e.g., hospitalization and institutionalization) (Fried et al., 2001; Rockwood et al., 2005), and premature death (Shamliyan et al., 2013; Vermeiren et al., 2016). Moreover, frailty is associated with lower quality of life (Kojima, Iliffe, Jivraj,



et al., 2016). It is therefore important to have insight into the determinants of frailty so that healthcare professionals can identify older people who are at increased risk of frailty, which allows the opportunity to carry out interventions to prevent or delay frailty. Currently, many studies have been conducted that provide evidence on individual determinants of frailty. In the present study, we expanded this viewpoint. We aimed to create a Frailty at Risk Scale (FARS) in which we included ten well-known determinants listed in the integral conceptual model of frailty and the TFI: age, gender, marital status, education, income, ethnicity, lifestyle, multimorbidity, life events, and home living environment (Gobbens et al., 2010b, 2010d).

In the model with all ten determinants, the AUC for predicting frailty (frail, non-frail) was 0.811, which can be considered an indication for a good predictive performance (Steyerberg, 2009). A nomogram derived from logistic regression analysis showed the points that must be given to the ten determinants used to predict frailty. These points range from 20 (education) up to and including 100 (diseases and/or chronic disorders). Not surprisingly, diseases and/or chronic disorders, referring to as multimorbidity, are the most important predictor of frailty. A systematic review and meta-analysis conducted by the Joint Action ADVAN-TAGE WP4 Group observed that multimorbidity was associated with frailty in pooled analyses (odds ratio = 2.27; 95% CI = 1.97 - 2.62, $1^2 = 47.7\%$) (Vetrano et al., 2019). Our logistic regression analysis also demonstrated that an unhealthy lifestyle and ethnicity were important predictors for frailty; in the FARS, 81 and 73 points were attributed to these two determinants, respectively. Previous studies also supported these findings. An unhealthy lifestyle is characterized by poor dietary habits, poor oral health, sedentary behavior, smoking, and excessive use of alcohol. For each of these factors, there is evidence that they are associated with frailty (Amiri & Behnezhad, 2019; Hakeem et al., 2019; Kojima, Iliffe, Liljas et al., 2017; Schoufour et al., 2019). However, it should be mentioned that a physical definition, the phenotype of frailty (Fried et al., 2001), was often used. With regard to the predictor ethnicity, ethnic minority migrants living in economically developed countries showed higher prevalence figures of frailty than white, indigenous older people (Majid et al., 2020). Moreover, in a sample of 47,768 Dutch people aged \geq 65 years, very large frailty differences, assessed with the TFI, existed between autochthonous people and people belonging to ethic groups (i.e., Surinamese, Turks, Moroccans) (van Assen et al., 2016).

Based on multivariate logistic regression analyses, nine determinants of frailty had the expected association with the dichotomized frailty score (frail, non-frail). The exception was education. Several studies provided evidence that a low educational level was associated with frailty (Etman et al., 2012; Hoogendijk et al., 2014). For instance, in a

sample of 1,205 Dutch people aged 65 years or older, it was observed that those with a low educational level had higher odds of being physically frail than those with a high educational level (relative index of inequality odds ratio, 2.94; 95% CI = 1.84-4.71) (Hoogendijk et al., 2014); however, this effect was reduced by 76% after adjustment for other predictors (e.g., income and number of chronic diseases) (Hoogendijk et al., 2014). In the present study, the coefficient of higher education in the univariate analysis with logistic regression was -0.166, indicating that higher education decreases the probability for being frail. In the multivariate analysis, the coefficient of higher education was 0.313, indicating that higher education increases the probability for being frail. Both coefficients, however, were not significant (p-values 0.568 and 0.422, respectively), so these effects can be considered as very small and an explanation for the low number of points allocated to education (only 20). Because previous studies used a physical definition of frailty, we recommend future studies to examine the association between education and multidimensional frailty, including physical, psychological, and social components.

Some limitations of our study should be mentioned. First, some variables have low frequencies in the categories. In particular, this applies to ethnicity, life events, and satisfaction with living environment. This may have influenced our findings. Secondly, our prediction model is based on one sample of community-dwelling older people. The generalizability of our findings can therefore be called into question. Because it is important to establish whether our model could also predict frailty in the future, we carried out an additional analysis using the same sample with a follow-up of five years (n = 140); the mean age was 83.8 (standard deviation = 3.1); the percentage of women was 49.3%. The AUC turned out to be 0.750, which can be regarded as good (Steyerberg, 2009). However, because our prediction model is only based on data of community-dwelling older people, validating in other populations (e.g., residents of assisted living facilities, hospitalized older people) is recommended. In addition, we recommend further validation of the FARS using other multidimensional frailty scales, e.g., the FI (Mitnitski et al., 2002), and more unidimensional frailty scales such as the Phenotype of Frailty (Fried et al., 2001), and the Clinical Frailty Scale (CFS) (Rockwood et al., 2005). Finally, the response rate was 42%. The consequence of non-response may be an underestimation of frailty among communitydwelling older people. This also reduces the generalizability of our findings.

The product in our study is a calculator that is accessible on the Web. This calculator allows healthcare professionals to easily enter data, on the basis of which risk of frailty is automatically calculated. If the risk of frailty is high, healthcare professionals may be able to deploy interventions to prevent frailty, e.g., lifestyle interventions, dealing with chronic diseases and life events, and contributing to greater satisfaction with one's living environment/home. Another option is to use part B of the TFI to determine the extent to which frailty already exists. The outcome of this assessment will support healthcare professionals in carrying out interventions focused on improving physical, psychological, and social frailty.

In conclusion, in the present study we developed a FARS, characterized by an excellent AUC for predicting frailty, containing ten questions referring to determinants of frailty that can be used to determine the risk level for an individual older person being frail. The determinants to which most weight has been assigned are: diseases and/or chronic disorders (present), lifestyle (unhealthy), and ethnicity (ethnic minority migrants). We offer the FARS on a Web site, so that the instrument can be used by healthcare professionals without a threshold, allowing timely intervention in promoting quality of life among community-dwelling older people.

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Author contributions RG was involved in study concept and design, acquisition of subjects and data, and preparation of manuscript (drafting, final approval). TP was involved in study concept and design, analysis and interpretation of data, and preparation of manuscript (drafting, final approval). Both authors agree to be accountable for all aspects of the work.

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Data availability and material All data were pseudonymized and stored in a central and secure server at (blinded for review). Furthermore, we have complied with the law with regard to personal data privacy information (Dutch Data Protection Authority.

Declarations

Conflict of interest The authors report no conflict of interest for this work.

Ethical approval For this study, medical ethics approval was not necessary as particular treatments or interventions were not offered or withheld from respondents. The integrity of the respondents was not encroached upon as a consequence of participating in this study, which is the main criterion in medical–ethical procedures in the Netherlands (Central Committee on Research Involving Human Subjects, 2010). This research was conducted according to the guidelines for good clinical practice. The researchers did not make the questionnaire long so the burden on participants would be limited; the average time for completing the questionnaire was 20 min. In addition, the questionnaire contained measures that have already been used in many previous studies among older people.

Consent to participate Informed consent related to detailing the study (e.g., information about the purpose of the study) and maintaining confidentiality was observed.

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