International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 15-11-2020; Accepted: 29-11-2020; Published: 15-12-2020
www.medicalsciencejournal.com
Volume 6; Issue 12; 2020; Page No. 70-74

Symptoms of frailty and health-related quality of life: The use of physical inactivity as a frailty indicator

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Abstract
Background: Health-related quality of life (HRQOL) is an important outcome measure in older adults as it focuses on the impact that health status has on quality of life.
Objectives: The aim of this study was to examine the relationship between frailty symptoms and HRQOL in older adults while using a measure of physical inactivity (PIA) as a frailty indicator.
Design: This was a cross-sectional study that included interview and examination data collected during the 2013 to 2018 National Health and Nutrition Examination Survey (NHANES) periods.
Setting: Non-institutionalized community dwelling adults 65+ years of age.
Participants: Data were used from 3,536 adults with mean age of 72.7 years, majority female (55%), and majority non-Hispanic White (79%).
Measurements: Frailty symptoms were assessed using a modified Fried index including exhaustion, weakness, low body weight, and low activity replaced by a measure of PIA. PIA was assessed using five questions asking participants if they engage in (for at least 10 minutes) work, recreational, and transportation-related activity. Those responding "no" to all five questions were considered physically inactive. Demographic and health status covariates included sex, age, race, income, depression, IADL, frequency of healthcare use, BMI, smoking status, and sedentary time.
Results: Approximately 19.9% (95% CI: 17.2-22.5) of older adults reported poor HRQOL. After adjusting for demographic and health status covariates, odds of poor HRQOLwere significantly greater stepwise for each additional frailty symptom (OR=1.65, 95% CI: 1.37-2.00).
Conclusion: Results from this study show that using PIA as an indicator of frailty is useful in predicting HRQOL independent of covariates in older adults.

Keywords: Frailty, health-related quality of life (HRQOL), depression, aging and health

Introduction
Health-related quality of life (HRQOL) is a multidimensional construct that typically includes, at minimum, domains of physical, mental, and social well-being [1]. HRQOL can be defined as the subjective rating of the quality of one's life specifically affected by their health status [2]. HRQOL is a clinically relevant outcome measure due to its demonstrated ability to predict mortality in generally healthy and diseased populations [3, 4]. Due to the growing evidence supporting HRQOL as a health indicator, the U.S. *Healthy People* report recently added two national objectives to improve self-reported physical and self-reported mental health in adults [5]. Both objectives concern increasing the proportion of adults who self-report good, very good, or excellent health status.
Frailty is a clinical state where an individual has an increased risk of adverse health after experiencing a stressor [6]. One diagnostic definition of frailty is the presence of three or more of the following physical characteristics: exhaustion, weakness, low activity, slowness, and weight loss [7]. Frailty is a major public health concern because it has strong links to HRQOL. Specifically, after considering related morbidities, it has been shown that frailty independently predicts lower levels of both physical and mental health components of HRQOL [8]. One problem with this type of frailty research is that many population-based studies have used single item questions to assess "low activity" of participants. Moreover, some of these single item activity questions ask participants to rate their level of activity relative to their peers – disregarding the obvious potential for misclassification. Therefore, the purpose of this study was to examine the relationship between frailty symptoms and HRQOL in older adults while using a measure of physical inactivity (PIA) as a frailty indicator.

Materials and Methods
Study procedures
Data were used from adults 65+ years of age participating in the 2013-2018 National Health and Nutrition Examination Survey (NHANES). The NHANES design includes a multistage stratified sample from the non-institutionalized population [9]. The purpose of NHANES is to assess health behavior, health status, and nutrition of civilian residents. The NHANES data come from personal interviews, standardized physical examinations, and laboratory tests. The current study used data only from personal interviews (demographic data and questionnaire data) and physical examinations (body measures data).

Frailty variables
A modified Fried phenotype was used to create a frailty symptoms index [10]. The modifications were in part due to limitations in NHANES items and in part due to the interest in using a measure of PIA as a frailty indicator. The frailty

symptom index therefore included four measures: 1) exhaustion, 2) weakness, 3) low body weight, and low activity replaced by a measure of 4) PIA. Exhaustion was determined by a response of "some" or greater difficulty when asked how much difficulty they have walking from one room to another on the same level. Weakness was determined by a response of "some" or greater difficulty when asked how much difficulty they have lifting or carrying something as heavy as 10 pounds. Low body weight was determined by a body mass index (BMI) less than or equal to 18.5 kg/m^2. PIA was assessed using five questions asking participants if they engage in (for at least 10 minutes) work, recreational, and transportation-related activity. Both recreational and work activity components included separate questions regarding vigorous-intensity (large increases in breathing or heart rate) and moderate-intensity (small increases in breathing or heart rate) activities. Transportation activity included distinct activities specifically conducted to get to and from places. Those responding "no" to all five questions were considered physically inactive. The final frailty symptom index was formed as the sum of the four frailty indicators, among those with complete data, ranging from 0 to 4.

HRQOL and health status variables

HRQOL was the outcome variable in this study and assessed from participant responses to a question asking them how they rate their general health. Those responding with "excellent", "very good", or "good" and those responding with "fair" or "poor" were considered to have good and poor HRQOL, respectively. A total of six health status variables were used in this study to describe the sample and/or to control for their confounding effects. The Patient Health Questionnaire (PHQ9) was used to define depression with an overall score ranging from 0 (not depressed) to 27 (more depressed) and a PHQ9 score ≥ 10 indicating "being depressed". Healthcare use was assessed as a proxy for comorbidities and evaluated from responses to a question asking how many times they had seen a doctor or similar professional during the past month. The Instrumental Activities of Daily Living (IADL) scale was assessed from responses to three questions regarding the ability to 1) manage money, 2) do house chores, and 3) prepare meals. Those indicating "some" or greater difficulty in either question were considered to have difficulty in that IADL task. A final IADL score was formed as the sum of the three IADL indicators, among those with complete data, ranging from 0 to 3.

Current smoking status was assessed from two questions with a current smoker defined as having reported smoked more than 100 cigarettes in their entire life and currently smokes at least some days. A measure of obesity was used for description and defined as a BMI ≥ 30 kg/m^2. Finally, sedentary time (hr/day) was assessed from a question asking about the time spent sitting on a typical day excluding sleeping.

Demographic variables

In order to control for possible demographic confounding, sex, age, race, and income were used in this study. Sex was a categorical variable represented by two groups: males and females. Age was a numeric variable ranging from 65 to 80+ years.

Race was a categorical variable and comprised the following four groups: 1) Non-Hispanic White, 2) Non-Hispanic Black, 3) Mexican/Hispanic, and 4) Other Races / Multi-racial. Finally, income was a numeric variable, collected as family income, and comprised twelve different income brackets ranging from 1 = $0 to $4,999 to 12 = $100,000 and over.

Statistical analyses

The statistical analysis plan included computing prevalence estimates (%) with standard errors (SE) and 95% confidence intervals (CI) for HRQOL status across demographic and health status variables along with associated chi-square tests of independence. Additionally, logistic regression was used to estimate the frailty symptom-related odds of poor health status in three different models including a crude model (Model 1), a model controlling for demographic variables (Model 2), and a model controlling for demographic and health status variables (Model 3). Regression model statistics included odds ratios (OR) and 95% CIs. Since three different NHANES survey periods were used (2013-2014, 2015-2016, and 2017-2018) in this study, interview and examination weights were corrected to produce generalizations representative of the larger noninstitutionalized population of adults aged 65+ years. SAS version 9.4 was used for all analyses [11, 12].

Results

A total of N = 3,536 (N_{male} = 1,761, N_{female} = 1,775) participants had complete HRQOL and frailty symptom data with mean age of 72.7 (SE = 0.18) years, 55.0% (SE = 0.85) female, and 78.7% (SE = 1.77) non-Hispanic White. Table 1 contains prevalence estimates of HRQOL status overall and across demographic and health status characteristics. Approximately 19.9% (95% CI: 17.21-22.54, p <.001) of adults 65+ years of age reported poor HRQOL, with no significant difference seen across sex (p =.172) or age group (p =.407). However, participants who are Hispanic (p <.001) and have lower family income (p <.001) reported significantly lower HRQOL, as compared to their counterparts. Additionally, all health status variables showed significant (ps <.001) differences in HRQOL, with participants reporting less healthy status more likely reporting poor HRQOL.

Table 2 contains results from the three logistic regression analyses, each modeling the odds of poor HRQOL with respect to the number of frailty symptoms. The crude model 1 indicated the odds of reporting poor HRQOL was 2.5 times greater (OR=2.51, 95% CI: 2.21-2.85) for each additional frailty symptom suffered by participants. Interestingly, similar odds of poor HRQOL for each frailty symptom suffered (OR=2.45, 95% CI: 2.11-2.83) was noted in model 2, after controlling for demographic variables. These results indicate that frailty symptoms are related to HRQOL in this population, independent of their demographic characteristics. In model 3, after controlling for demographics and relevant health status variables, the odds of reporting poor HRQOL remained significantly greater, with approximately 65% greater odds (OR=1.65, 95% CI: 1.37-2.00) for each additional frailty symptom suffered. Model 3 also displays the independent effects that each health status variable has on HRQOL in light of frailty symptoms, with the exception of sedentary time (p =. 338).

Table 1: Prevalence of HRQOL status by demographic characteristics and health status variables in adults 65+ years of age, 2013-2018 NHANES.

	Poor HRQOL				Good HRQOL				χ^2
Variable	**%**	**SE**	**LL**	**UL**	**%**	**SE**	**LL**	**UL**	**p**
Overall (*N*=3,536)	19.9	1.33	17.21	22.54	80.1	1.33	77.46	82.79	<.001
Sex									.172
Male	18.8	1.36	16.08	21.55	81.2	1.36	78.45	83.92	
Female	20.7	1.61	17.50	23.98	79.3	1.61	76.02	82.50	
Age (yr)									.407
65-69	18.0	2.05	13.85	22.12	82.0	2.05	77.88	86.15	
70-74	21.6	2.07	17.40	25.72	78.4	2.07	74.28	82.61	
75-79	20.4	2.10	16.14	24.61	79.6	2.10	75.39	83.86	
80+	20.7	1.73	17.17	24.14	79.3	1.73	75.86	82.83	
Race									<.001
White	15.6	1.28	13.06	18.21	84.4	1.28	81.79	86.95	
Black	34.3	2.24	29.82	38.86	65.7	2.24	61.14	70.18	
Hispanic	45.2	2.53	40.06	50.26	54.8	2.53	49.74	59.94	
Other	25.2	3.32	18.53	31.91	74.8	3.32	68.09	81.47	
Income (US $)									<.001
0-24,999	31.1	2.23	26.57	35.54	68.9	2.23	64.46	73.43	
25,000-74,999	19.2	1.52	16.11	22.24	80.8	1.52	77.76	83.89	
75,000+	10.0	1.98	5.98	13.96	90.0	1.98	86.04	94.02	
Frailty symptoms (#)									<.001
0	9.8	1.16	7.51	12.18	90.2	1.16	87.82	92.49	
1	22.6	2.07	18.43	26.76	77.4	2.07	73.24	81.57	
2	44.0	3.42	37.05	50.85	56.0	3.42	49.15	62.95	
3+	59.7	4.35	50.98	68.50	40.3	4.35	31.50	49.02	
Depressed									<.001
No	16.3	1.24	13.81	18.79	83.7	1.24	81.21	86.19	
Yes	59.3	3.89	51.46	67.14	40.7	3.89	32.86	48.54	
Healthcare use									<.001
0-2 times past month	11.4	1.16	9.05	13.71	88.6	1.16	86.29	90.95	
3+ times past month	26.8	1.83	23.08	30.44	73.2	1.83	69.56	76.92	
IADL (#)									<.001
0	11.1	0.98	9.15	13.08	88.9	0.98	86.92	90.85	
1-3	39.7	2.68	34.34	45.11	60.3	2.68	54.89	65.66	
Current smoker									<.001
No	18.9	1.38	16.14	21.71	81.1	1.38	78.29	83.86	
Yes	29.9	3.47	22.92	36.90	70.1	3.47	63.10	77.08	
Obese									<.001
No	16.4	1.24	13.92	18.90	83.6	1.24	81.10	86.08	
Yes	25.5	2.03	21.45	29.62	74.5	2.03	70.38	78.55	
Sedentary time (hr/day)									.006
0-4.99	17.0	1.48	14.02	19.97	83.0	1.48	80.03	85.99	
5+	20.9	1.41	18.07	23.73	79.1	1.41	76.27	81.93	

Note: HRQOL is health-related quality of life. Good HRQOL defined as self-rated general health of "excellent", "very good", or "good". Poor HRQOL defined as self-rated general health of "fair" or "poor". Frailty symptoms include low body weight, exhaustion, weakness, and physically inactive. Depressed status assessed as having a Patient Health Questionnaire-9 (PHQ9) score ≥ 10. Healthcare use measured as # of times in past year. IADL is Instrumental Activities of Daily Living scale ranging from 0 to 3 difficulties. Current smoker status defined as having smoked more than 100 cigarettes in entire life and currently smokes at least some days. Obesity defined as a BMI ≥ 30. Sedentary time assessed as sitting time per day excluding sleeping. % is weighted prevalence estimate. SE is standard error. LL is lower limit of the 95% CI. UL is upper limit of the 95% CI. χ^2 is the Rao-Scott chi-square test of independence statistic.

Table 2: Odds of poor HRQOL in relation to frailty symptoms, demographics, and health covariates in adults 65+ years of age, 2013-2018 NHANES.

	Model 1 (*N*=3,536)			Model 2 *N*=3,293)			Model 3 *N*=2,850)		
Variables	**OR**	**LL**	**UL**	**OR**	**LL**	**UL**	**OR**	**LL**	**UL**
Frailty symptoms (#)	2.51	2.21	2.85	2.45	2.11	2.83	1.65	1.37	2.00
Sex									
Male				1.31	1.05	1.63	1.38	1.03	1.84
Female				1.00			1.00		
Age (yr)				0.98	0.96	1.00	1.00	0.97	1.03
Race									
White				1.00			1.00		
Black				2.11	1.62	2.75	2.59	1.95	3.44
Hispanic				2.95	2.12	4.10	3.95	2.81	5.55
Other				1.54	0.94	2.52	2.18	1.14	4.17

Income ($)				0.89	0.85	0.94	0.89	0.85	0.94
Depressed									
No							1.00		
Yes							4.06	2.31	7.16
IADLs (#)							1.73	1.39	2.14
Healthcare use (#)							1.27	1.19	1.35
BMI (kg/m^2)							1.02	1.00	1.04
Current smoker									
No							1.00		
Yes							1.63	1.08	2.47
Sedentary time (min/day)							1.00	1.00	1.00

Note: Frailty symptoms range from 0 to 4. Income ranges from 1 to 12. IADL score ranges from 0 to 3. OR is odds ratio estimate. LL is lower limit of the 95% CI. UL is upper limit of the 95% CI. Model 1 includes frailty symptoms only. Model 2 additionally controls for age, sex, race, and income. Model 3 additionally includes BMI, IADL, healthcare use, smoking status, and sedentary time.

Discussion

The purpose of this study was to examine the relationship between frailty symptoms and HRQOL in older adults while using a measure of physical inactivity (PIA) as a frailty indicator. Results clearly showed that each additional frailty symptom increased stepwise the likelihood of reporting poor HRQOL. Moreover, the number of frailty symptoms and HRQOL relationship remained after controlling for both demographic and health status variables. These results highlight the utility of using a frailty phenotype in detecting poor HRQOL. As well, these results underscore the effectiveness of using a measure of PIA in lieu of a low activity measure assessed by subjective comparison to peers. Albeit, this study did not compare the difference between the use of PIA versus a relative activity question, it is known that multi-item measures yield scores 1) with less measurement error, 2) that cover the trait with greater trait variability, and 3) that provide more information to categorize individuals [13].

One strength of this study is the NHANES study protocol such as its complex survey design that ensures inferences represent the larger population of noninstitutionalized older adults. Additionally, the frailty indicator of low body weight (BMI $\leq$ 18.5 kg/m^2) used in this study was objectively assessed by trained health practitioners. Finally, this study used three different NHANES survey periods, allowing for greater statistical power while analyzing the relatively smaller subgroup of older adults. There are also limitations worth mentioning. The main independent variable in this study, namely the frailty symptoms of exhaustion, weakness, and PIA, were assessed subjectively via questionnaire and may include measurement error not accounted for. Therefore, future research should focus on studying the relationship between frailty symptoms and HRQOL while using objective measures of frailty. Since HRQOL was also assessed via questionnaire in this study, future research should focus on validating the use of PIA as a frailty indicator against objective HRQOL proxy measures such as illness, disability, and mortality. Finally, this study is cross-sectional in nature and therefore findings do not reflect cause-and-effect relationships between frailty and HRQOL in older adults.

Conclusions

Findings from this study show that using PIA as an indicator of frailty is useful in predicting HRQOL in older adults. Furthermore, this relationship is independent of demographic and health status covariates. Health professionals should consider using PIA as a frailty phenotype variable.

Author contributions

Peter D. Hart solely contributed to all aspects of this research, including its design, data management, analysis, and manuscript writing.

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