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Original Study

A New Functional Classification Based on Frailty and Disability Stratifies the Risk for Mortality Among Older Adults: The FRADEA Study

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A B S T R A C T

Objectives: The aim of the current study was to investigate whether a new functional classification, based on basic (BADL) and instrumental (IADL) activities of daily living and frailty, is associated with mortality in older adults during 10 years of follow-up.
Design: Cohort study, with a follow-up of 10 years.
Setting and participants: A total of 924 participants aged 70 and older from the Frailty and Dependence in Albacete (FRADEA) study, a population-based sample of Spanish older adults.
Measures: At baseline, a new functional classification of 8 categories was constructed with limitations in BADL using the Barthel Index, limitations in IADL using the Lawton IADL Index, and the criteria of the frailty phenotype. Associations with 10-year mortality were assessed using Kaplan-Meier curves and Cox proportional hazard models.
Results: The risk of mortality gradually increased toward the less functionally independent end of the classification. The presence of mild, moderate, or severe BADL impairment was associated with mortality, in models adjusted for age, sex, comorbidity and institutionalization. The analyses also revealed that those who were BADL independent, IADL dependent and prefrail [hazard ratio (HR) = 2.27, 95% confidence interval (CI) = 1.22-4.20], and those who were BADL independent and frail (HR = 3.74, 95% CI = 1.88-7.42) had an increased risk of mortality.
Conclusions/implications: A new functional classification composed of BADL, IADL, and frailty representing the functional continuum is effective in stratifying the risk for mortality in older adults. Frailty is a high-mortality-risk state close to subjects with mild disability in BADL, needing an intensive specialized approach. Prefrailty with any impairment in IADL has an intermediate mortality risk and should be offered primary care interventions.

Maintaining functional independence is of major importance for older adults in order to enable well-being in later life and to delay or prevent adverse outcomes, as highlighted in the recent *World Report on Ageing and Health* of the World Health Organization (WHO).[1] Therefore, assessing the level of functioning in older adults has become a crucial part of clinical care.[2] It is also of major interest to health policy makers for developing public health responses to population aging.[1]

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The diverse needs of older people are best viewed as a continuum of functioning, ranging from high to low functional independence.[3] Based on the level of functioning, specific interventions may be developed to maintain or improve functional independence and to prevent adverse health outcomes.[4,5] Functional independence is usually measured with an instrument assessing basic activities of daily living (BADL) and/or instrumental activities of daily living (IADL).[6–8] The studies investigating levels of functioning in relation to survival or life expectancy have focused on the end of the continuum (IADL/BADL impairment) or in its earliest stages (prefrailty and frailty), but very few, if any, have done a comprehensive analysis of the full pathway from robustness to severe disability.[9–12] It has been argued that looking at a wider range of the functional continuum is important,[10,13] in particular, because those who are at risk of adverse outcomes and who are still independent in BADL may be a good target for intervention in terms of prevention.

The use of the frailty concept should be considered when distinguishing groups on the functional continuum. Recently, the European Joint Action ADVANTAGE has considered that frailty is a progressive age-related decline in physiological systems that results in decreased reserves of intrinsic capacity, which confers extreme vulnerability to stressors and increases the risk of adverse health outcomes.[14] There are various ways to establish this geriatric condition in daily clinical practice.[15] One of the most commonly used and well-validated operational definitions is the frailty phenotype developed by Fried et al,[16] which consists of 5 criteria such as unintentional weight loss, weakness, low walking speed, exhaustion, and low physical activity. Because frailty is seen as a predisability state,[14,17,18] it may be useful for identifying individuals at risk of mortality within the functionally independent group. So far, frailty has not been incorporated in studies on the functional continuum.[10,19]

In this study, we propose a new classification and measurement of the functional continuum, combining BADL, IADL, and frailty, to better capture the full range of this continuum. This new classification will be studied in relation to survival, to see whether it is effective in stratifying the risk for mortality. The main objective was to investigate whether the functional continuum, using a new classification system combining BADL, IADL, and frailty, is associated with mortality in older adults during 10 years of follow-up, using data from the Frailty and Dependence in Albacete (FRADEA) study, a population-based cohort study of Spanish older adults aged 70 and older.

Methods

Study Population

In this longitudinal study, data from the first wave of the FRADEA study (2007-2009) and follow-up data on mortality over a period of 10 years (2007-2017) were used. FRADEA is a population-based cohort study among older adults aged 70 and older from the urban area of Albacete in Spain. Details on the methods and sampling have been published before.[20] In summary, to obtain a representative sample of a Spanish urban older population, 1172 people aged 70 and older were randomly selected from registered health care holders in the city of Albacete in 2007 (n = 18,137), of which 993 people (84.7%) agreed to participate. Baseline data were collected by face-to-face interviews. Follow-up data collection was done in 2009-2011 (by telephone), in 2011-2013 (on site), and in 2017 (on site). Trained nurses collected the data at baseline and follow-up. Of the 993 people who agreed to participate in the FRADEA study, 924 had valid baseline data on the functional continuum variable and were included in the current analysis. The FRADEA study was approved by the local Independent Ethics Review Board. Signed informed consent was obtained from all participants. Figure A1 in the online appendix presents the general flow chart of the FRADEA study.

Defining the Functional Continuum

Participants were categorized into 8 groups representing the functional continuum, based on a new combined measure of BADL, IADL, and frailty. BADL was measured with the Barthel Index. This is a score from 0 to 100, where lower scores indicate reduced ability to perform basic activities of daily living, including bathing, grooming, dressing, eating, toileting, urinary and fecal continence, ambulation, transferring, and stair use.[21] The Lawton index was used to indicate IADL limitations. This index consists of 8 items: shopping, cooking, cleaning, laundry, use of telephone, medication control, finances, and transport.[22] Each item was scored as being able to perform the task, yes (1) or no (0), resulting in a total score between 0 and 8. Frailty was measured with the criteria of the frailty phenotype,[16] consisting of low physical activity, weight loss, weakness, exhaustion, and slow walking speed. All criteria were measured identically to the original ones proposed by Fried et al[16] except for physical activity, which was based on a different questionnaire to calculate kilocalories expended per week. For this item, the Calcumed instrument was used instead of the Minnesota Leisure Time Physical Activity Questionnaire.[6] The original sex-specific cut-offs were used to indicate low physical activity.[16] Weight loss was present if a person lost more than 4.6 kg or 5% of body weight in the past year.[16] Weakness was identified by low grip strength, based on the original BMI- and sex-specific cut-offs. The Jamar digital hand dynamometer was used to measure maximal grip strength in the dominant hand. Exhaustion was measured using 2 items of the Center for Epidemiologic Studies Depression Scale (CES-D), identical to the original criteria of Fried et al.[16,23] Walking speed was assessed by recording the time taken (in seconds) to walk 4 meters. Slow walking speed was defined by the lowest quintile, stratified by sex and height, using the same values as Fried et al.[16] Three frailty groups were distinguished: not frail (0 criteria present), prefrail (1-2 criteria present), and frail ($\geq$3 criteria present).

To create a new functional classification based on BADL, IADL, and frailty, we first distinguished 4 functional groups according to BADL status, using established cut-offs: BADL independent, mild impairment, moderate impairment, and severe impairment.[24] Then, we further divided the BADL independent group into 5 categories according to IADL and frailty status. See Figure 1 for an overview of all categories and cut-points. There were some respondents with missing data on frailty (n = 92), but they were all in the severe BADL impairment group (category 8), so this did not have any influence on the construction of the new functional classification.

Mortality

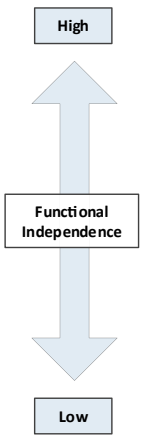
All deaths that occurred between the baseline measurement and the fourth follow-up of FRADEA (2017) were recorded. When participants were approached by telephone for a follow-up interview, occurrence of death was noted and subsequently checked with the death registry (100% ascertainment for the current study sample).

Covariates

Covariates included age, sex, Charlson Comorbidity Index, and institutionalization. The presence of chronic diseases was derived from medical records, where diseases are registered according to ICD-10 codes. Subsequently, comorbidity was summarized with the Charlson Comorbidity Index.[25] Institutionalization indicated whether a person lives in a nursing home (no/yes).

Statistical Analysis

Descriptive analyses were performed to show baseline characteristics for the total sample and according to mortality during follow-up.



Category	BADL	IADL	Frailty	Measure	N	5-year mortality N (%)	10-year mortality N (%)
1	Independent	Independent	Not frail	Barthel Index ≥90, IADL index = 8 Frailty phenotype = 0	76	1 (1.3)	12 (15.8)
2	Independent	Impairment	Not frail	Barthel Index ≥90, IADL index <8 Frailty phenotype = 0	124	13 (10.5)	33 (26.6)
3	Independent	Independent	Pre-frail	Barthel Index ≥90, IADL index = 8 Frailty phenotype = 1 or 2	174	12 (6.9)	39 (22.4)
4	Independent	Impairment	Pre-frail	Barthel Index ≥90, IADL index <8 Frailty phenotype = 1 or 2	181	42 (23.2)	90 (49.7)
5	BADL independent		Frail	Barthel Index ≥90 Frailty phenotype ≥3	49	19 (38.8)	31 (62.0)
6	Mild BADL impairment			Barthel Index 85-60	168	86 (51.2)	126 (75.0)
7	Moderate BADL impairment			Barthel Index 55-40	48	36 (75.0)	43 (89.6)
8	Severe BADL impairment			Barthel Index <40	104	82 (78.8)	101 (97.1)

Fig. 1. The new functional classification based on a combined measure of BADL, IADL, and frailty, including 5-year and 10-year mortality rates for each category.

Differences between groups were determined using chi-square tests and *t* tests. To evaluate the association of the new functional classification with 10-year all-cause mortality, Cox proportional hazard models were fitted. The first model was adjusted for age and sex. The second model additionally adjusted for comorbidity and institutionalization. Those who died during follow-up were censored at their date of death. Survivors were censored at the date of the last interview (approximately 10 years since baseline). To illustrate the differences in 10-year survival between the categories of the functional classification, Kaplan-Meier curves were fitted. Factor analysis was used to determine the percentage of mortality variability explained by the different variables of the study. All analyses were done in IBM SPSS Statistics 22 (IBM Corp, Armonk, NY).

Results

Table 1 shows the characteristics of the total study sample and by 10-year all-cause mortality status. The mean age of the 924 included older adults was 79.5 years, the majority were female (60.7%), and almost a quarter of the sample was living in a nursing home (22.3%). Participants who died during 10 years of follow-up were older (82.5 years vs 76.3 years), more often institutionalized (38.5% vs 5.1%), had higher comorbidity (1.8 diseases vs 0.8 diseases), lower functional scores (Barthel and Lawton), and were more often frail (31.8% vs 9.4%).

Of the study sample of 924 participants, 475 (51.4%) died during 10 years of follow-up. The median survival time was 3162 days (8.7 years). Mortality rates were higher toward the less functionally independent end of the functional continuum (Figure 1). Only 15.8% of the people in the first category died during the 10-year follow-up, compared to 97.1% of the people with severe BADL impairment (category 8). Similar patterns were seen when looking at 5-year mortality (Figure 1). The Kaplan-Meier analysis with data over a period of 10 years showed that the mean survival times for the different groups were as follows: category 1: 3518 days [standard deviation (SD) 66 days], category 2: 3280 days (SD 84 days), category 3: 3288 days (SD 54 days), category 4: 2773 days (SD 79 days), category 5: 2375 days (SD 157 days), category 6: 1954 days (SD 94 days), category 7: 1268 days (SD 146 days), and category 8: 1029 days (SD 95 days). Log rank (Mantel-Cox) was 534.7 ($P < .001$). Factor analysis showed that 3 variables explained 82.7% of mortality variability. The new functional classification was the first and most important factor explaining 44.4% of the variability, comorbidity was the second explaining 22.6% of the variability, and sex was the third explaining 15.6% of the variability (Bartlett's sphericity test, $P < .001$).

Cox regression analyses, adjusted for age and sex, showed that people with mild BADL impairment [hazard ratio (HR) = 5.47, 95% confidence interval (CI) = 2.99-10.02], moderate BADL impairment (HR = 8.47, 95% CI = 4.37-16.43), and severe BADL impairment (HR = 11.92, 95% CI = 6.38-22.2) had an increased risk of mortality compared to the reference group. Additionally adjusting for comorbidity and institutionalization slightly decreased the magnitude of the effects but gave similar results (Model 2 in Table 2). Statistically

Table 1
Baseline Characteristics for the Total Sample and by 10-Year All-Cause Mortality

Characteristics	Total	Deceased		*P**
	(n = 924)	No (n = 449)	Yes (n = 475)	
Age, mean (SD)	79.5 (6.5)	76.3 (4.5)	82.5 (6.6)	<.001
Sex, n (%)				
Male	363 (39.3)	176 (39.2)	187 (39.4)	.96
Female	561 (60.7)	273 (60.8)	288 (60.6)	
Institutionalization, n (%) yes	206 (22.3)	23 (5.1)	183 (38.5)	<.001
Charlson comorbidity index, mean (SD)	1.3 (1.5)	0.8 (1.1)	1.8 (1.7)	<.001
Barthel index, 0-100, mean (SD)	81.4 (28.5)	94.7 (10.8)	68.8 (33.8)	<.001
Lawton IADL index, 0-8, mean (SD)	5.0 (2.9)	6.7 (1.8)	3.5 (2.9)	<.001
Frailty, n (%)				
Not frail	203 (24.4)	156 (35.1)	47 (12.1)	<.001
Prefrail	464 (55.8)	247 (55.5)	217 (56.1)	
Frail	165 (19.8)	42 (9.4)	123 (31.8)	

*t test or chi-square test.

Table 2
Cox Regression Analyses: Hazard Ratios for 10-Year All-Cause Mortality

Functional Classification Categories	Model 1*		Model 2†	
	HR (95% CI)	*P*	HR (95% CI)	*P*
1. BADL independent, IADL independent, Not frail	1.0 (reference)		1.0 (reference)	
2. BADL independent, IADL impairment, Not Frail	1.25 (0.64-2.46)	.51	1.13 (0.58-2.23)	.71
3. BADL independent, IADL independent, Prefrail	1.53 (0.80-2.93)	.20	1.35 (0.70-2.59)	.36
4. BADL independent, IADL impairment, Prefrail	2.54 (1.38-4.70)	<.01	2.27 (1.22-4.20)	<.01
5. BADL independent, Frail	5.26 (2.69-10.30)	<.001	3.74 (1.88-7.42)	<.001
6. Mild BADL impairment	5.47 (2.99-10.02)	<.001	4.20 (2.27-7.78)	<.001
7. Moderate BADL impairment	8.47 (4.37-16.43)	<.001	5.59 (2.81-1.11)	<.001
8. Severe BADL impairment	11.92 (6.38-22.27)	<.001	7.25 (3.73-14.12)	<.001

*Model 1: adjusted for age and sex.
†Model 2: adjusted for age, sex, Charlson Comorbidity Index, and institutionalization.

significant differences were also observed between the groups that were BADL independent. The analyses revealed that those who were BADL independent, IADL dependent, and prefrail (HR = 2.27, 95% CI = 1.22-4.20), and those who were BADL independent and frail (HR = 3.74, 95% CI = 1.88-7.42) had a higher risk of mortality compared to people that were BADL independent, IADL independent, and not frail, which was the reference group. The cumulative survival curves shown in Figure 2 are derived from Cox regression analyses adjusted for age, sex, comorbidity, and institutionalization (Model 2 in Table 2). The Figure clearly shows that the risk of mortality gradually

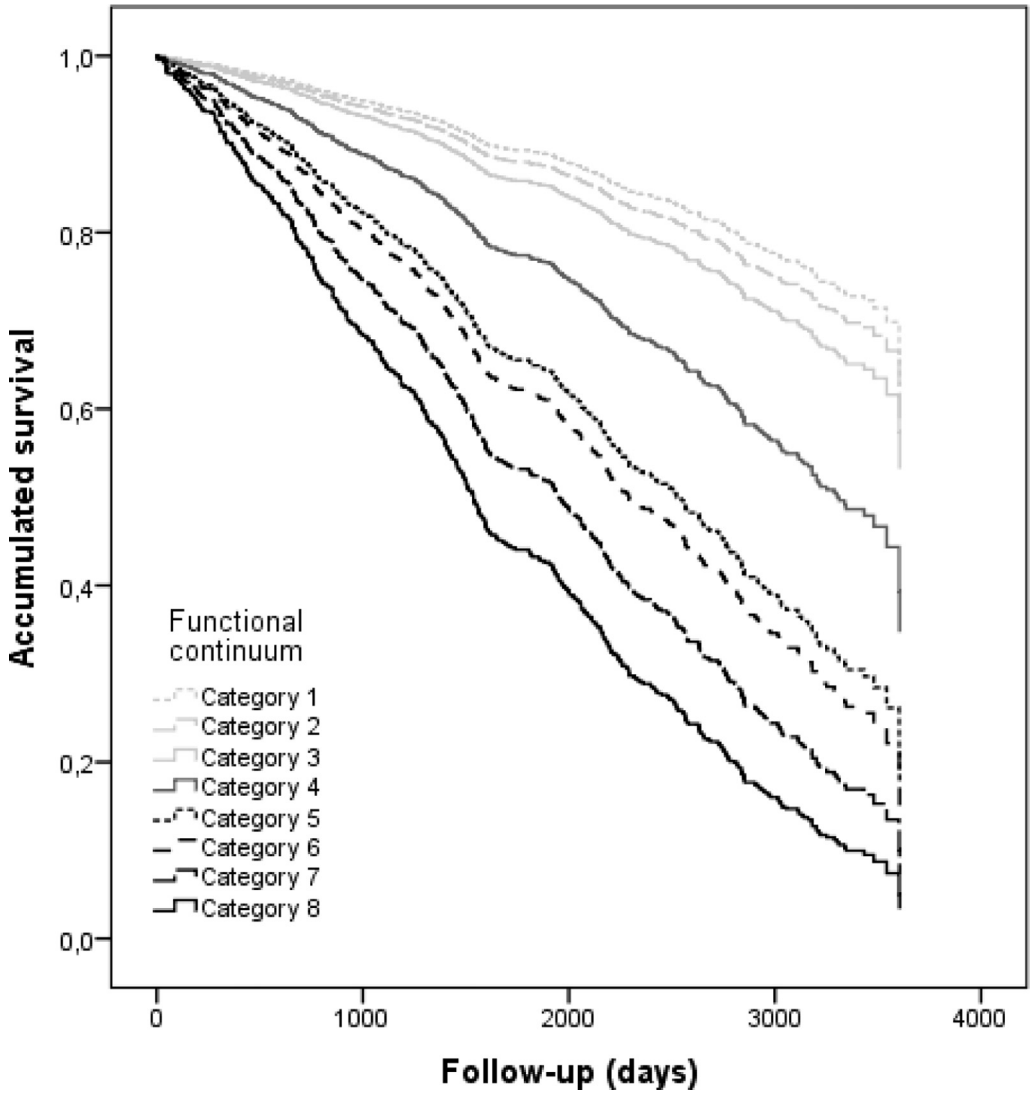


Fig. 2. Survival curves according to the new functional classification (Cox proportional hazard model adjusted for age, sex, comorbidity, and institutionalization): category 1: BADL independent + IADL independent + nonfrail; category 2: BADL independent + IADL dependent + non-frail; category 3: BADL independent + IADL independent + prefrail; category 4: BADL independent + IADL dependent + prefrail; category 5: BADL independent + frail; category 6: mild BADL impairment; category 7: moderate BADL impairment; category 8: Severe BADL impairment.

increased toward the less functionally independent end of the functional continuum.

Discussion

The main conclusion of our study is that a new functional classification composed of BADL, IADL, and frailty as 8 exclusive categories representing the functional continuum is effective in stratifying the risk for mortality in older adults, independently of age, sex, comorbidity, and institutionalization.

It is well known that disability in BADL and IADL[9–12] and frailty[26] are health conditions independently associated with mortality. Also it is known that frailty, as a predisability state, is an important independent factor for identifying older adults' risk for other health-related adverse outcomes like incident disability,[27] institutionalization,[28] hospitalization,[29] mobility loss,[6] falls,[30] dementia,[31] quality of life,[32] and health care costs.[33] Furthermore, in agreement with WHO framework for healthy aging, we have described in previous work that function is the better predictor of adverse events in older adults, more predictive than multimorbidity or polypharmacy,[34,35] and that it should be considered the cornerstone of geriatric medicine.[36]

The concept of frailty has not yet been included as part of the WHO framework for healthy aging. WHO considers healthy aging to be "the process of developing and maintaining the functional ability that enables well-being in older age." In this framework, the concept of intrinsic capacity, "the composite of all the physical and mental capacities of an individual," is considered the physiological basis of healthy aging, which should be seen in a holistic life course approach.[1] Until recently, information on intrinsic capacity was only indirectly achieved through the measurement of BADL and IADL, which had demonstrated to be useful in identifying dependency and the need for social care. The measurement of ADL and IADL fits well with how systems are currently designed; nevertheless, their utility is limited to identifying people with serious losses of functioning.[1] For this reason, the inclusion of frailty, a predisability state in the functional continuum construct, fills in the gap of small losses of functioning and completes the spectrum. Integration of intrinsic capacity, disability, frailty, and robustness can be achieved, only resting ambient factors that need parallel tools to be measured, to complete the WHO framework of healthy aging.

Our categories, coming from a population-based study, are not just an epidemiologic construct but may also help clinicians to implement diagnostic and therapeutic procedures, advanced care planning, and assign resources to older adult populations across the functional continuum, from absolute robustness (category 1) to maximum functional loss (category 8). The new functional classification could help in the always difficult decision process around when to stop health screening such as mammography and colonoscopy, which now is largely age-determined but would be better off if determined based on 5- and 10-year prognosis. Other procedures that could benefit from the use of the new classification in the decision-making process could be transcatheter aortic valve implantation, hemodialysis, high-risk surgeries, or chemotherapy. Our classification also has relevant policy implications, because health care and social service decisions may be adopted on the basis of validated stratification. Our work could be considered as a proof of concept; however, much work has to be done in order to better identify subpopulations of interest like prefrail older adults. Future research should also consider how the functional categories work across different settings, countries, and diseases.

Another interesting conclusion from our study is the high risk conferred by frailty itself. Since Fried et al published their frailty phenotype in 2001,[16] most frailty studies have included patients with different levels of disabilities in activities of daily living,[37] making it difficult to know the exact risk of frailty in a population without disability. Our study shows that frail nondisabled older adults have almost the same mortality risk as those with mild disability in BADL (HR 3.74 and HR 4.20, respectively). For this reason, strategies to revert or maintain functioning in frail older adults may need an intensive approach with a tight collaboration between primary care and geriatric medicine. In addition, prefrail older adults appear as a very interesting population. In this category, those with any impairment in IADL have an intermediate mortality risk and probably should be offered primary care interventions in order to delay or avoid the development toward frailty. However, those prefrail without impairments in IADL have a similar mortality risk as those that are nonfrail or robust and should be managed by primary care with usual preventive measures.

Although intrinsic capacity is a "positive" concept as stated by WHO that criticizes frailty for being a "negative" concept, clinicians are used to work with deficits like heart failure, chronic kidney disease, and respiratory insufficiency, among others. We think that both concepts are part of the same bottle that can be seen half full or half empty, and that intrinsic capacity may be better considered under a biological basis, and the functional continuum including frailty in the more clinical, systems approach and personal management basis. In recent years, different disease approaches to older adult populations have shared our point of view that function should be looked at first when assessing older adults with diseases, before chronologic age, sex, multimorbidity, or setting, in order to decide the best treatment options. This has been described in chronic kidney disease,[38] heart disease,[39] and diabetes.[40] Other specialties such as surgery or oncology[41,42] are beginning to incorporate frailty in their decision-making process.

Our study has 3 main limitations. The most important one is that it needs external validation in other countries and settings, although we think that it can be considered a solid and well-based proof of concept. The second is the construct in itself due to the categories' selection. Categories were created not based on statistical analysis, but on clinical experience, geriatric medicine knowledge and publications, and on a solid theoretical framework. Our results indicate that BADL dependency means the highest mortality risk for older adults and should be considered as independent category (category 6-8 in our construct). Thereafter, frailty and dependency in IADL are mixed conditions that can coexist. The high mortality and other adverse outcomes risk in frail participants made us include this category as a unique one. We then constructed 4 categories (category 1-4) mixing robustness or prefrailty with dependency or independency in IADL. The classification of these 4 categories, with IADL impairment based on the loss of only 1 IADL, is debatable. However, our intention was to create at least 1 category with the maximum intrinsic capacity, for those that were independent in each concept. The third limitation is that the prefrail category, a wide and mixed one, probably will need a better characterization in future research.

Conclusions and Implications

A new functional classification composed of BADL, IADL, and frailty, representing the functional continuum, is effective in stratifying the risk for mortality in older adults. Frailty is a higher-mortality-risk state close to subjects with mild disability in BADL, needing an intensive specialized approach. Prefrailty with any impairment in IADL has an intermediate mortality risk and should be offered primary care interventions. Our work emphasizes the need to base health care to older adults on function, and not on multimorbidity, chronic disease, setting, or chronological age, issues that—although of great interest—need to be evaluated at a second stage. More work is needed to better understand how the functional continuum works across different countries and settings.

Supplementary Data

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.jamda.2019.01.129.

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