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Physical frailty, activity limitation and mortality in older Brazilians: longitudinal findings from FIBRA-BH study (2009-2019)

Fragilidade física, limitação de atividades e mortalidade em idosos brasileiros: achados longitudinais do Estudo FIBRA-BH (2009-2019)

Claudia Venturini (https://orcid.org/0000-0003-4757-7440) [1]
Bruno de Souza Moreira (https://orcid.org/0000-0001-8840-4496) [2]
Silvia Lanziotti Azevedo da Silva (https://orcid.org/0000-0002-2323-2029) [3]
Rosana Ferreira Sampaio (https://orcid.org/0000-0002-4775-9650) [1]

Abstract *The aim was to investigate the longitudinal association between physical frailty and change in the profile of limitation to perform basic and instrumental activities of daily living (BADL and IADL) and mortality in a 10-year period in Brazilian community-dwelling older people. A longitudinal study was conducted with data from the Frailty in Brazilian Older People (FIBRA) study, 2009-2019. Physical frailty was categorized into vulnerability (pre-frail and frail) and robustness (non-frail). The generalized estimating equation and the Cox proportional hazards models were used in the data analysis. Out of 200 older people evaluated in 2009 (moment 1), 139 were located in 2019 (moment 2). Of these, 102 were interviewed and 37 deaths were recorded. The chance of vulnerable older people at moment 1 being dependent on performing BADL at moment 2 was 4.19-fold the chance of robust older people. For IADL, the chance of vulnerable older people at moment 1 being dependent at moment 2 was 3.12-fold the chance of robust older people. Cox's analysis showed that the risk of death among vulnerable older people was 2.50-fold that among robust older people. The results reinforce the importance of monitoring and early intervention to prevent frailty, and the limitation to performing activities of daily living and death among Brazilian older people.*

Key words *Older people, Mortality, Frailty, Activities of daily living*

Resumo *O objetivo foi investigar a associação longitudinal entre fragilidade física e mudança no perfil de limitação para realizar as atividades básicas e instrumentais de vida diária (ABVD e AIVD) e mortalidade em 10 anos em idosos comunitários brasileiros. Um estudo longitudinal foi conduzido com dados do Estudo da Fragilidade em Idosos Brasileiros (FIBRA), 2009-2019. A fragilidade física foi categorizada em vulnerabilidade (pré-frágil e frágil) e robustez (não frágil). Modelos de equação de estimação generalizada e de riscos proporcionais de Cox foram usados na análise dos dados. Dos 200 idosos avaliados em 2009 (momento 1), 139 foram localizados em 2019 (momento 2). Destes, 102 foram entrevistados e 37 óbitos foram registrados. A chance dos idosos vulneráveis no momento 1 serem dependentes nas ABVD no momento 2 foi de 4,19 vezes a chance dos idosos robustos. Para as AIVD, a chance dos idosos vulneráveis no momento 1 serem dependentes no momento 2 foi de 3,12 vezes a chance dos idosos robustos. A análise de Cox mostrou que o risco de morte entre os idosos vulneráveis foi 2,50 vezes o risco dos idosos robustos. Os resultados reforçam a importância do acompanhamento e intervenção precoce para prevenir a fragilidade, e a limitação para realização das atividades de vida diária e morte em idosos brasileiros.*

Palavras-chave *Idosos, Mortalidade, Fragilidade, Atividades de vida diária*

[1] Programa de Pós-Graduação em Ciências da Reabilitação, Departamento de Fisioterapia, Universidade Federal de Minas Gerais. Av. Antônio Carlos 6627, Pampulha. 31270-901 Belo Horizonte MG Brasil. venturinifisio@gmail.com
[2] Núcleo de Estudos em Saúde Pública e Envelhecimento, Instituto René Rachou (Fiocruz Minas). Belo Horizonte MG Brasil.
[3] Departamento de Saúde Coletiva, Faculdade de Medicina, Universidade Federal de Juiz de Fora. Juiz de Fora MG Brasil.

Introduction

Frailty is a public health problem, especially in countries undergoing an accelerated aging process, such as Brazil[1]. This geriatric condition is defined as a clinical syndrome of multifactorial character, characterized by reduced physiological reserve and reduced resistance to stressors resulting from the age-related cumulative decline in several organ systems, mainly the immune, endocrine, musculoskeletal, and nervous systems[2,3]. The physiological system decline leads to loss of homeostatic capacity and greater vulnerability to adverse outcomes, including falls, hospitalization, activity limitation, institutionalization, and death[2,3].

Despite the growing number of studies on frailty in recent decades, there is still no consensus on the concepts and measures used to investigate frailty. However, the most used instruments to measure it are the physical frailty phenotype proposed by Fried *et al.*[3] and the frailty index based on the Rockwood and Mitnitski model of accumulated deficits[4]. A previous systematic review of 21 international studies involving 61,500 community-dwelling older people (≥65 years) showed that the prevalence of frailty varies substantially between the included studies, with values between 4.0% and 59.1%[5]. Studies assessing frailty from a physical perspective consistently reported a lower prevalence of frailty (4.0% to 17.0%) than those using a multidimensional approach (4.2% to 59.1%)[5]. In Brazil, data from epidemiological studies show that the prevalence of frailty in people aged 65 years or older assessed by the physical phenotype ranges from 11.7%[6] to 16.2%[7].

Although they can occur simultaneously, frailty and activity limitation are different conditions[8]. The latter is often defined in studies in the field of gerontology as the difficulty, inability, or need for help to perform activities of daily living, which can be divided into basic activities of daily living (BADL) and instrumental activities of daily living (IADL)[9-11]. BADL refer to self-care or survival activities, while IADL involve more adaptive activities necessary for an independent life in the community[12].

According to the United Nations, 15% of the world's population have activity limitations, with a prevalence of 46% when considering only older people[13]. Older people's activity limitation is more frequent in the last years of life, which worsens quality of life and increases the need for specialized care and the risk of institutionalization and death[14]. Studies investigating activity limitation show that 30% of frail older people present limitations in at least one BADL[11], while 60% of frail older people present limitations in IADL[9].

The longitudinal association between frailty and adverse health outcomes varies according to the operational definition of frailty used, follow-up time, investigated adverse outcomes, and the population assessed[15,16]. Some systematic reviews demonstrate that the physical frailty phenotype is associated with activity limitation and mortality in the older population[10,17,18]. For example, systematic review by Kojima[17] showed that frail older people are more likely to develop or worsen limitation in BADL (12 studies, pooled odds ratio OR=2.76, 95% confidence interval 95%CI 2.23-3.44; 5 studies, pooled hazard ratio HR=2.23, 95%CI 1.42-3.49) and IADL (6 studies, pooled OR=3.62, 95%CI 2.32-5.64; 2 studies, pooled HR=4.24, 95%CI 0.85-21.28). As for mortality, a systematic review and meta-analysis showed that the risk of death was higher in the frail group than in the pre-frail group (relative risk RR=1.478, 95%CI 1.339-1.632) and the non-frail group (RR=2.00, 95%CI 1.727-2.316)[17].

However, few studies have investigated this issue in developing countries. A cohort study conducted on older people in Latin American countries, China, and India showed that the physical frailty phenotype is associated with functional dependence (RR=1.43, 95%CI 1.24-1.64) and mortality (RR=1.51, 95%CI 1.36-1.68)[19]. In Brazil, two longitudinal studies investigated the association of frailty with mortality using data from the Frailty in Brazilian Older People (FIBRA) study conducted in Campinas, São Paulo, Brazil[20,21]. Pereira *et al.*[20] investigated the association between frailty assessed by the frailty index and death in 674 older people (≥65 years; 68.7% women) and found that the frailty index was not associated with mortality over a five-year period in the studied sample. Pereira *et al.*[21] compared the accuracy of the frailty index and that of the physical frailty phenotype in predicting mortality and demonstrated that the phenotype was more accurate in predicting mortality in the older people evaluated. As far as we know, no longitudinal study has investigated the impact of frailty on changing the profile of activity limitation in older Brazilians. In this context, the objective of the present study was to investigate the longitudinal association between physical frailty and change in the profile of limitation to perform BADL and IADL and mortality in community-dwelling old-

er people using data from the FIBRA study conducted in Belo Horizonte, Minas Gerais, Brazil, over a 10-year period.

Methods

Study design

This is a longitudinal observational study derived from the FIBRA study. The FIBRA was a cross-sectional, multicenter, multidisciplinary, population-based study conducted in 17 cities between 2008 and 2009. The objective of the FIBRA was to investigate the prevalence of frailty using the phenotype proposed by Fried *et al.*[3] and the factors associated with this condition. The participants were selected through probabilistic sampling by census tracts to obtain a more complete overview of all older people in each sample city. Details of the methodological procedures used in the study are available in a previous study[22].

The inclusion criteria in the FIBRA study were older people aged 65 years or older, living in the community, of both sexes, and able to walk with or without a walking aid device. The exclusion criteria were cognitive deficit defined by a score below 17 points on the Mini-Mental State Examination (MMSE)[23], severe stroke sequelae with localized loss of muscle strength and/or aphasia, advanced or unstable Parkinson's disease, terminal illness, cancer treatment, and being temporarily or permanently restricted to a wheelchair or bedridden.

Participants and data collection procedure

Baseline data from a longitudinal study[24] derived from the FIBRA-Belo Horizonte survey were used in the present study. This previous study was designed to assess transitional patterns of frailty syndrome and determine which frailty phenotype variables were more involved in this process[24].

Our sample was composed of 200 older people who were assessed at home in 2009. Therefore, in the current study, the baseline is the year 2009 (moment 1). In 2019 (moment 2), the 200 older people were contacted for a new evaluation. The ones who accepted to participate in the study responded to a questionnaire through a telephone interview. Older people whose telephone numbers did not exist or who did not respond after four attempted calls made on different days and times received a household visit by one of the researchers, who invited them to participate in the study. Household interviews were conducted after the older person or family member agreed to receive the researcher.

The following situations were not eligible: non-existent or out-of-service telephones, numbers that did not answer four call attempts made on different days and times, including Saturdays and night periods, and also those that were not located at home because the older person or family members did not live at the same address registered in the FIBRA file. The FIBRA-Belo Horizonte study was approved by the Research Ethics Committee of the Federal University of Minas Gerais, Brazil (ETIC number 187/07). The present study was submitted and approved as an addendum to the original project.

Variables and measurements

Physical frailty

The variable physical frailty considered the five frailty phenotype criteria proposed by Fried *et al.*[3]. These data were collected only in 2009. The physical phenotype criteria were (1) unintentional weight loss greater than 4.5 kg in the previous year or loss of 5% of total body weight; (2) self-reported exhaustion evaluated by the response "always" or "most of the time" to at least one of the statements of the Center for Epidemiological Studies-Depression Scale (CES-D), "In the last week, I felt that everything I did was an effort" and "In the last week, I felt that I could not get going"; (3) low level of physical activity measured as the level of caloric expenditure assessed by the Minnesota Leisure Time Activity Questionnaire, translated and adapted to Brazilian Portuguese[25]; (4) muscle weakness assessed using the handgrip strength test measured by the JAMAR dynamometer®; and (5) gait slowness assessed by the time taken to cover a distance of 4.6 meters at the usual speed. Older people with three or more criteria were classified as frail, those with one or two criteria were classified as pre-frail, and those with no criteria were considered non-frail.[3] In the present study, the variable physical frailty was recoded into two categories, that is, vulnerable (pre-frail or frail) and robust (non-frail), according to previous studies[26,27].

Activity limitation

The limitations in BADL and IADL were considered in two moments (2009 and 2019). Dependence/independence in performing BADL and IADL was assessed using the Brazilian version of

the Katz Index[28] and the Lawton & Brody Scale[29], respectively. The Katz Index assesses six self-care activities: bathing, dressing, toileting, transferring, continence, and feeding. The Lawton & Brody Scale assesses the following activities: ability to use the phone, using transportation, shopping, preparing meals, doing household chores, handling medication, and managing money. For both BADL and IADL, activity limitation was defined as a self-report of having any difficulty in performing (little or great) or being unable to perform at least one of the activities included in the scales.

Mortality

The mortality outcome considered information and confirmation of the older person's year of death by family members and/or guardians. The variable was categorized as "yes" or "no," and the year of death was computed to calculate survival.

Covariates

The variables age, sex, and self-report of a medical diagnosis of depression evaluated at moment 1 were considered for adjustment purposes. The models were not adjusted for the number of chronic diseases because the sample in our study was homogeneous in relation to this variable.

Statistical analysis

Descriptive analysis characterized the sample with frequency distribution for categorical variables and central tendency and variability measurement for the numerical variable.

The association between frailty and change in the profile of limitation in BADL and IADL was analyzed using generalized estimating equations (GEEs), whose results are presented as OR and 95%CI[30]. The GEE method is considered an extension of the generalized linear model and is more robust for evaluating longitudinal data[31]. It is an iterative procedure that uses quasi-likelihood to estimate the regression coefficients[32]. This analysis considered the 102 older people evaluated in 2019 regarding the activities of daily living.

Survival analysis was performed to verify the time until death due to physical frailty. Kaplan-Meier survival curves of older people classified as vulnerable or robust were compared using the log-rank test. The Cox proportional hazards model was used to analyze physical frailty as a risk factor for death over 10 years, which provided an HR and 95%CI. The Schoenfeld residual analysis was used to verify risk proportionality. This analysis considered the 139 older people located in 2019.

All models were adjusted for age, sex, and self-reported medical diagnosis of depression. A significance level of 5% was considered, and the R statistical software (https://www.r-project.org/) was used for all analyses.

Results

Of the 200 older people evaluated at moment 1 in 2009, 61 were not located in 2019, and, therefore, 139 were part of the sample at moment 2. Of these, 102 were interviewed by telephone or at their home and 37 deaths were registered in the period between 2009 and 2019.

At moment 1, the sample was predominantly composed of women (68.0%), with a mean age of 75.0±6.0 years. Most participants were in the range of 70 to 80 years. As for the level of physical frailty, 71 older people (35.5%) were classified as non-frail, 101 (50.5%) as pre-frail, and 28 (14.0%) as frail. The recoding of frailty into two categories showed that 35.5% were robust and 64.5% were vulnerable older people. As for the activities of daily living, 142 (71.0%) and 109 (54.5%) participants were considered independent in performing BADL and IADL, respectively. As for the self-report of medical diagnosis of depression, 160 (80.0%) participants reported not having this diagnosis (Table 1).

At moment 2, of the 102 participants evaluated, 59 (57.8%) were independent and 43 (42.2%) were dependent on performing BADL. For the IADL, 39 (38.2%) and 63 (61.8%) were independent and dependent, respectively.

Analysis of the association between frailty at moment 1 and BADL at moment 2 adjusted for age, sex, and self-report of a medical diagnosis of depression showed that the chance of older people classified as vulnerable at moment 1 being dependent at moment 2 was 4.19-fold the chance of those classified as robust (95%CI 2.36-7.44). The analysis of the impact of time (10 years) showed that the older people evaluated at moment 2 had 2.19-fold the chance of being dependent in this second evaluation compared to the evaluation at moment 1 (95%CI 1.33-3.63) (Table 2).

As for IADL, the adjusted association between frailty at moment 1 and IADL at moment 2 showed that the chance of older people classified as vulnerable at moment 1 being dependent

at moment 2 was 3.12-fold the chance of those classified as robust (95%CI 1.18-5.55). In addition, older people assessed at moment 2 had, in this second assessment, 2.77-fold the chance of being dependent compared to the assessment at moment 1 (95%CI 1.69-4.76) (Table 2).

The log-rank test was initially used in survival analysis to compare the survival curves of vulnerable and robust older people, and a statistically significant difference was found between the curves (p=0.003). The Cox multiple regression analysis adjusted for age, sex, and self-report of medical diagnosis of depression showed that the death rate for vulnerable older people was 2.50-fold the death rate for robust older people (95%CI 1.02-6.11). The assumption of the constant death rate of the Cox model was confirmed by a global p-value of 0.74 and by graphical analysis of the Schoenfeld residuals (results not shown).

The estimated Kaplan-Meier graphical representation of physical frailty and survival is shown in Figure 1. Over the years, physically vulnerable older people lived less than robust older people.

Table 1. Characteristics of the participants at moment 1. Frailty in Brazilian Older People (FIBRA) study, Belo Horizonte, Brazil, 2009.

Variables	n=200
Age (years), mean (SD)	75.0 (6.0)
Sex, n (%)	
Women	136 (68.0)
Men	64 (32.0)
Self-reported medical diagnosis of depression, n (%)	
Yes	40 (20.0)
No	160 (80.0)
Classification of physical frailty, n (%)	
Non-frail	71 (35.5)
Pre-frail	101 (50.5)
Frail	28 (14.0)
Basic activities of daily living, n (%)	
Independent	142 (71.0)
Dependent	58 (29.0)
Instrumental activities of daily living, n (%)	
Independent	109 (54.5)
Dependent	91 (45.5)

SD: Standard deviation.

Source: Authors.

Table 2. Generalized estimating equation regression models for the association between physical frailty and activities of daily living. Frailty in Brazilian Older People (FIBRA) study, Belo Horizonte, Brazil, 2009-2019.

Variables	OR*	95%CI	p-value
Basic activities of daily living			
Vulnerable	4.19	2.36;7.44	<0.001
Moment 2	2.19	1.33;3.63	0.002
Instrumental activities of daily living			
Vulnerable	3.12	1.18;5.55	<0.001
Moment 2	2.77	1.69;4.76	<0.001

OR: odds ratio; 95%CI: 95% confidence interval. *Models adjusted for age, sex, and self-reported medical diagnosis of depression.

Source: Authors.

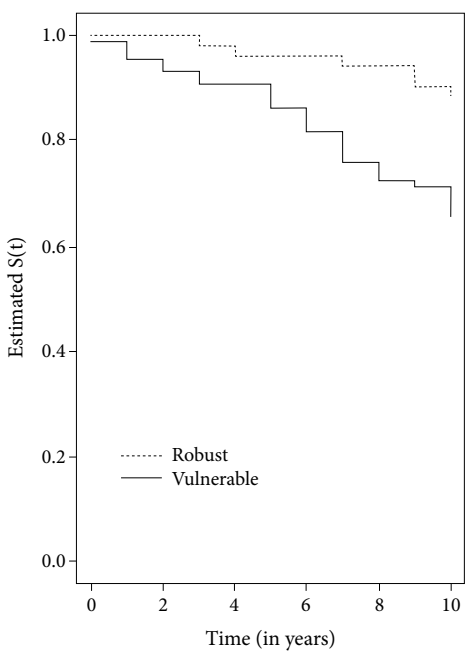

Figure 1. Survival function estimated by the Kaplan-Meier comparing vulnerable and robust older people over time. Frailty in Brazilian Older People (FIBRA) study, Belo Horizonte, Brazil, 2009-2019.

Note: Estimated S(t): Kaplan-Meier survival estimate.

Source: Authors.

Discussion

The present study analyzed the association between physical frailty and change in the profile of limitation to perform the activities of daily living and mortality after 10 years in the FIBRA-Belo Horizonte survey. The sample had a low frequency of older people classified as frail (14.0%), while pre-frail older people represented 50.5% of the sample in the baseline study. Pre-frail and frail older people were grouped into a single category for analysis. The frailty classification was not reassessed after 10 years, and due to its dynamic nature, it can be expected that these older people underwent transition or progression of frailty levels over time[24,33]. Regardless of the final stage of frailty, it is important to highlight the fact that the presence of one or more physical frailty phenotype criteria is associated with the limitation to perform BADL and IADL and death, corroborating the findings of other studies[10,17,34]. These results reinforce the importance of identifying and monitoring vulnerable older people to prevent health problems.

The longitudinal analysis of the profile of activity limitation showed that the chance of vulnerable older people at the beginning of the study to present limitations in BADL after 10 years is fourfold the chance of robust older people. The analysis of time showed that the chance of limitations in BADL at time 2 is twofold the chance of limitation in these activities at time 1. As for IADL, the results showed that the chance of vulnerable older people at moment 1 being dependent at moment 2 is similar to the effect of time on the development of limitations for these activities. These findings suggest that physical frailty has a greater impact on the limitation to perform BADL than time, but its effect is similar to that of time on the limitation to perform IADL.

Despite the differences in population, the definition of frailty, and methodological aspects, the results of the present study corroborate the findings of previous studies, which also demonstrated a longitudinal association between the physical frailty phenotype and activity limitation in community-dwelling older people[13,16,35]. For example, a recent meta-analysis of nine longitudinal studies with a mean follow-up period of approximately 31 months and totaling 32,998 older people (≥60 years) showed that frailty increased fivefold the risk of limitation in performing BADL, while pre-frailty increased threefold the risk of limitation in these activities. As for limitations in performing IADL, the HR was 3.87 for frail and 2.03 for pre-frail older people compared with robust older people[13].

The greater chance of activity limitation after 10 years observed in vulnerable older people compared to robust older people can be explained by the pathophysiological cycle of frailty. This cycle is related to the declining function of multiple organ systems, with decreased muscle mass, lower physical activity level, lower capacity to generate muscle strength and power, and, consequently, functional limitation[3,9,36]. Frailty, therefore, reduces the physiological reserve necessary for performing BADL, which involve the physical aspects necessary to maintain self-care, mobility, and autonomy to live without the help of other people[36]. On the other hand, IADL involve both physical and cognitive aspects in their performance[34]. In this case, the greater chance of limitation in performing BADL among vulnerable older people may be related to difficulties in the physical aspects of the tasks assessed.

As for the association between frailty and mortality, the results of this study show that vulnerable older people have a higher risk of death than robust older people. This finding corroborates the results found by Harmand *et al.*[15] in a study on 1,278 French older people aged 65 or older followed up for 12 years. The authors showed that the group of non-robust older people (pre-frail and frail) had a higher risk of death compared to the robust group (HR=1.29, 95%CI 1.05-1.59). A study on 4,984 American older people (71.1±0.19 years, 56% women) followed for a median period of 95.8 months (interquartile range: 78-124 months) showed a 64% higher mortality rate (HR=1.64, 95%CI 1.45-1.85) in pre-frail older people than in robust ones and an almost threefold higher rate in frail ones (HR=2.79, 95%CI 2.35-3.30)[33]. As for the Brazilian older population, a study conducted on 674 participants of the FIBRA-Campinas study showed that frail participants assessed by the physical frailty phenotype had a tenfold higher risk of death than non-frail participants (RR=10.03, 95%CI 4.43-22.74)[21]. On the other hand, our study found a lower risk of death over a 10-year period (HR=2.50, 95%CI 1.02-6.11), which could be partly explained by the fact that pre-frail and frail older people were grouped in a single analytical category.

The results of this study show the importance of proposing screening, monitoring, and multidisciplinary treatment of vulnerable older people (pre-frail and frail), including home care and regular practices of individual and group phys-

ical activities in order to prevent the onset and progression of activity limitation and death[37,38]. A systematic review has recently shown evidence A for group exercise practice to prevent the progression of frailty stages and evidence B for exercise practice associated with nutritional supplementation[39]. Furthermore, frailty can be prevented by implementing interventions that can delay gait slowness and muscle weakness, which are considered the most common criteria associated with an increased risk of mortality[33]. It is worth emphasizing the importance of including pre-frail and frail older people in interdisciplinary intervention studies with long-term follow-up to define more effective strategies since time is a factor associated with activity limitation in the results presented here. Additionally, a French population-based study compared the predictive values of frailty assessed by two multidimensional instruments and by the physical phenotype for adverse outcomes such as activity limitation, falls, institutionalization, and death, reporting greater predictive capacity of multidimensional instruments compared to the physical phenotype[15]. In this context, future studies should be conducted on the Brazilian older population to identify the best frailty assessment tool for predicting adverse outcomes such as activity limitation and mortality.

This is the first longitudinal study that evaluated the association between frailty and adverse health outcomes in the FIBRA-Belo Horizonte study and one of the few studies conducted in this field in Brazil. The results show the importance of the association between the positive items of the frailty phenotype and change in the profile of activity limitation and mortality in community-dwelling older people in Brazil. The frailty phenotype is a valid and reliable measure to assess frailty, is widely used in national and international scientific research, and allows for the comparability of findings between different studies.

This study has some limitations that need to be stated. First, due to the eligibility criteria of the FIBRA study, older people with cognitive disorders and those who are bedridden and institutionalized were excluded, which introduced a sample selection bias and reduced the possibility of including the most vulnerable older people. Second, the participants were categorized for analysis purposes as vulnerable and robust rather than considering the three stages of the frailty phenotype. Thus, the risk of pre-frailty and frailty in the occurrence of the adverse health outcomes investigated in this study was not separately examined. Third, the analyses were also adjusted for a limited number of covariates, and therefore, residual confounding may bias our results. Finally, approximately 30% of the older people were not found for reassessment at moment 2, which may have produced some bias, especially in the analysis of mortality. However, the literature considers such loss acceptable in studies with a long period of participants' reassessment[40].

Conclusion

This study confirmed the longitudinal association between frailty and change in the profile of limitation to perform the activities of daily living and mortality after 10 years in the older population of a large Brazilian municipality. The vulnerable group (pre-frail and frail) in the baseline had a greater chance of limitation in performing BADL and IADL and of death compared to the group of robust older people. These results show the need not only for preventive and long-term follow-up strategies that involve patient-centered approaches but also for public policies of healthy aging to avoid and/or minimize the adverse outcomes of frailty, which negatively impact the patient's life and their family members and create an enormous burden on health systems.

Collaborations

All authors have worked in the completion of the present study, have read the manuscript, agree with the publication of the paper and accept responsibility for its contents.

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