Frailty, depression and mortality in a cohort of community-dwelling older adults

Priscila Pascarelli Pedrico do Nascimento[1]
Ivan Aprahamian[1,2]
Mônica Sanches Yassuda[1,3]
Anita Liberalesso Neri[3,4]
Samila Sathler Tavares Batistoni[1,3]

Abstract

Objective: To estimate the risk represented by the combined conditions of frailty and depression in relation to mortality in a cohort of older adults in a prospective measure. *Method:* Prospective cohort study derived from baseline (2008/2009) and follow-up (2016/2017) measurements of the FIBRA Study - Polo Unicamp. Data from 739 older adults (67,2% female; 73,1+5.87 years) living in two urban centers in the state of São Paulo (Brazil) were analyzed to examine survival curves and to estimate mortality risk. The analyzes included four conditions resulting from the combination of depression (presence x absence of symptoms) and frailty (frail x robust) and the covariates sex, age, education, cognitive performance and comorbidities. *Results:* The percentage of deaths was 25.7%. There were significant differences between the survival curves regarding the combinations between frailty and depression. Male sex, age over 75 years, low education, low cognitive performance and the combinations "depression-robust", "depression-frail" and "no depression-frail" presented independent risks for mortality. In the multivariate model, the highest risks were given, respectively, by older ages, the combinations "depression-robust", "depression-frail", "no depression-frail", male sex and lower cognitive performance. *Conclusion:* Combinations between frailty and depression can result in differences in survival and mortality among older adults. In the nine-year period, depression proved to be the ordering variable of the groups in relation to risk estimates, even in the presence of important covariates. Investments in the prevention of both syndromes and their associations may result in a decrease in mortality in older people from general causes.

Keywords: Frailty. Depression. Mortality. Survival Analysis. Older adults.

[1] Universidade Estadual de Campinas, Faculdade de Ciências Médicas, Programa de Pós-graduação em Gerontologia. Campinas, SP, Brasil.

[2] Faculdade de Medicina de Jundiaí, Departamento de Clínica Médica. Jundiaí, SP, Brasil.

[3] Universidade de São Paulo, Escola de Artes, Ciências e Humanidades, Programa de Pós-graduação em Gerontologia. São Paulo, SP, Brasil.

[4] Universidade Estadual de Campinas, Departamento de Psicologia Médica e Psiquiatria da Faculdade de Ciências Médicas. Campinas, SP, Brasil.

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Correspondence
Samila Sathler Tavares Batistoni
samilabatistoni@usp.br

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INTRODUCTION

Since the proposition of a characteristic phenotype of frailty in older adults[1], it has been recognized that associations between this syndrome and the presence of depressive symptoms have important effects on clinical management and lead to different impacts on quality of life and on the risk of morbidity and mortality in older adults[2,3]. There is evidence that both conditions are associated with greater functional dependence, cognitive impairment, greater use of health services and risk of institutionalization[2,4-6]. However, a smaller number of investigations have been devoted to the effects resulting from the associations between different combinations of frailty and depression on the mortality of older adults in prospective surveys[7].

Meta-analysis strategies applied to recent studies have suggested that there is a prevalence of 38.6% of depression among frail older adults and a 40.4% prevalence of frailty in depressive older adults[8]. The possibility of shared pathophysiological factors, such as inflammatory markers, and antecedent conditions of a psychosocial nature, are considered in the production of common manifestations between the syndromes[9]. Older adults with depressive symptoms present complaints that, in addition to changes in mood, physical and cognitive disposition and social withdrawal, coincide with the criteria for identifying frailty associated with reports of fatigue, unintentional loss of body mass, and low physical activity levels, gait speed and handgrip strength[8-10].

Both frailty and depression represent risks for mortality, according to evidence generated by examining each of these conditions separately or by statistically controlling for the presence of the other[11]. A meta-analysis study showed an increase in all-cause mortality, attributed to frailty, a higher risk among frail older adults than among pre-frail and robust older adults, and greater risks for males[12]. These results were interpreted as indicators of the progression of the syndrome and its reflexes on the reduced availability of resources to maintain the integrity of the organism, culminating in death[13].

The increased risk of mortality attributed to depression in the general population reveals more heterogeneous evidence resulting from the variety of measurements and criteria used and from the peculiarities of the presentation of this condition at different stages of life[6]. Differences in age, sex, health behaviors, comorbidities, functional and cognitive impairments, and intensity and duration of depressive symptoms can act as potential moderators of the outcome of death[14]. However, in a review and meta-analysis of prospective cohort studies with older adult samples, Wei et al.[15] estimated that depression increases the risk of all-cause mortality by 34% and of specific mortality from cardiovascular diseases by 31%.

Chang et al[6] reported results from the combination of frailty (measured as accumulation of functional deficits) and depression over time (18 years). Frail and depressed older adults showed a lower chance for the remission of depressive symptoms. This profile also presented a higher probability of mortality when compared with frail, non-depressed older adults. Ruiz-Grao et al.[7] compared the proportional hazards represented by six different combinations of presence or absence of depression and frailty at baseline to mortality recorded over a subsequent 10-year period. After adjusting for sociodemographic variables, institutionalization, comorbidities and polypharmacy, only the combination of depression and pre-frailty represented a risk of death in the period under study.

In order to obtain and explore evidence from a sample of Brazilian older adults, this study sought to estimate the risk for mortality represented by different combinations of depression and frailty in a cohort of older adults. The covariation of these combinations with sociodemographic characteristics, cognitive performance, and number of diseases at baseline in relation to the outcome of death recorded at follow-up was considered.

METHODS

A prospective cohort study developed from data derived from baseline (2008/2009) and follow-up (2016/2017) surveys from the Frailty Profile of Elderly Brazilians (FIBRA UNICAMP) study. This is a multicenter study, with a baseline sample

composed of older adults living in seven Brazilian cities[17], which prospectively followed cohorts from two of these locations (Campinas and the subdistrict of Ermelino Matarazzo, São Paulo, Brazil) in a follow-up survey. At the time of the first data collection, Campinas (SP; human development index HDI= 0.852) had a general population of 1,083,113 inhabitants, 11.5% of which were people aged 65 years old and over. The sub-district of Ermelino Matarazzo (HDI= 0.730), located in the east of the city of São Paulo (SP), had 207,509 inhabitants, 10.8% of which were people aged 60 years old and over. Based on standardized protocols, the study aimed to investigate the frailty conditions of urban older adults residing in the community (not institutionalized). and the relationships between this condition and sociodemographic, psychosocial, health, and functionality variables. The study also obtained and recorded information concerning deaths that occurred between baseline and follow-up.

Baseline data were collected in 2008/2009, by recruiting older adult females and males, 65 years old or over, with different sociodemographic conditions, who resided in randomly selected census tracts. The older adults were invited to attend community service locations (primary health care units, community centers, parish halls and clubs) to be evaluated by trained interviewers. At the time, those who presented severe cognitive or physical deficits that made their participation unfeasible or difficult were not included in the study.

A total of 1,284 older adults living in the city of Campinas (n=900) and in the sub-district of Ermelino Matarazzo (n=384), in the city of São Paulo participated in the baseline study. The samples were selected by means of a simple drawing of urban census sectors in the two locations (90 in Campinas and 62 in Ermelino Matarazzo), for which quotas of men and women aged 65 to 69, 70 to 74, 75 to 79 and 80 years old or over, representative of the older adult population, in 2007, plus 25% to cover possible losses.

In the follow-up survey, conducted in 2016/2017, trained researchers returned to the households registered in the database at baseline. All the older adults who consented to participate responded to the Mini Mental State Examination (MMSE) cognitive screening test, adopting the criteria by Brucki et al.[18] to define the cut-off scores. Older adults who scored below the criterion for their level of education responded only to the cognitive assessment, physical assessment and frailty items. Questions concerning health, functionality and psychosocial variables were answered by a family member. In the case of death of the older adult, a family member was invited to answer a questionnaire about signs and symptoms, and chronic non-communicable diseases in the last year of life and about the circumstances of their death.

In the follow-up study, 549 older adults were located and interviewed at home, among which 130 were helped by a family member, given the fact that they scored below the MMSE cut-off score. Another 192 had died and 543 were not located, refused to participate, abandoned the interview, were excluded by research criteria or were not interviewed because their place of residence posed risks to the interviewers' safety (Figure 1).

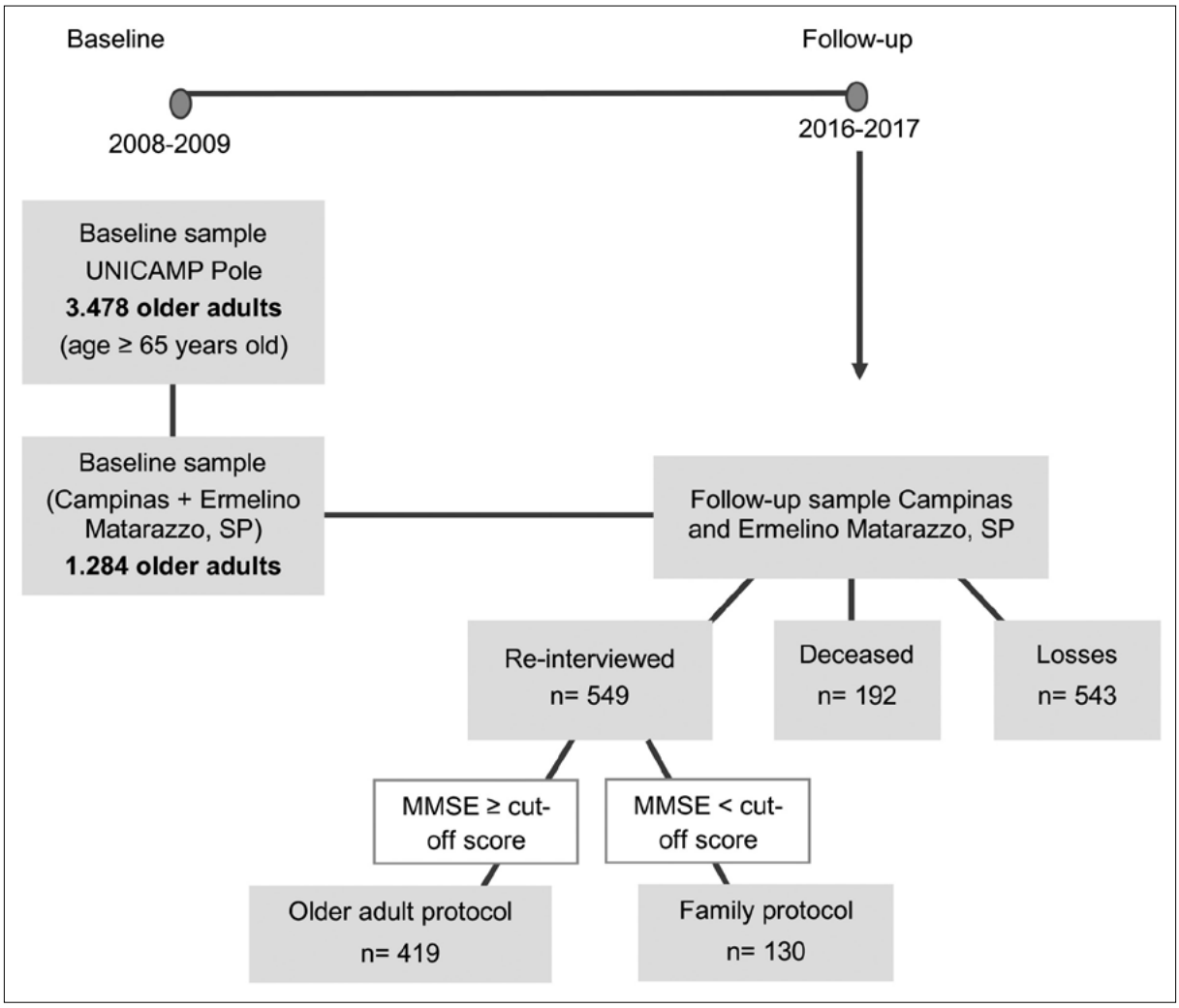

Figure 1. Flowchart of the composition of the FIBRA Study sample at baseline and follow-up survey. FIBRA Study, Older adults, Campinas and Ermelino Matarazzo, SP, Brazil, 2008/2009 and 2016/2017.

As shown in Figure 1, the 1,284 participants in the baseline measurements of the FIBRA Campinas and Ermelino Matarazzo Study, both located in the State of São Paulo, were considered eligible for this study. Of this total, data were collected and analyzed from 549 older adults located at their former addresses, and from 192 deceased older adults whose data concerning their last year of life and the circumstances of their death were informed by a family member. These data were verified and confirmed by the death certificate of each deceased older adult and by consulting the *Sistema de Informação sobre Mortalidade* (SIM) [Mortality Information System] of the municipality of Campinas. It was not possible to access SIM data for the subdistrict of Ermelino Matarazzo.

Variables and measurements

The outcome of interest in this study was the occurrence of death from all causes, for the period between the baseline and follow-up surveys. The date of death was recorded to calculate survival during the period.

The presence of depression in the cohort was identified by applying the Geriatric Depression Scale-15 (GDS-15)[19], determined as obtaining any score below 6 (>5 points) at baseline.

Frailty was identified by measurements of the five frailty phenotype criteria, as described by Fried et al.[1]. According to the authors, individuals who meet

one or two of the following criteria are considered pre-frail and those who meet three or more criteria are considered frail. Individuals that do not meet any of these criteria are considered robust:

1) Unintentional weight loss equal to or greater than 4.5 kg or 5% of body weight in the previous year, considering the sex of the older adult;

2) Fatigue, assessed by two items that correspond to this complaint on the CES-D (Center for Epidemiological Studies-Depression) screening scale. The criteria for frailty are the answers "always" or "most of the time" as the frequency of occurrence of fatigue to any of the two items[20];

3) Low hand grip strength, in kilogram-force, measured with a portable hydraulic dynamometer in the dominant hand[21] (Jamar® - Lafayette Instruments, Lafayette, Indiana, United States), over three attempts, with means adjusted for sex and body mass index (BMI). Older adults with a mean below the 1st quintile of the distribution score for frailty;

4) Physical activity level, assessed by self-reporting of physical exercise and housework performed in the preceding seven days, according to the items in the Minnesota Leisure Time Activities Questionnaire[22] with means adjusted for sex. Older adults with a mean below the 1st quintile of the distribution score for frailty;

5) Slow gait speed indicated by the average time taken to walk a distance of 4 m three times, on a level floor, at their normal pace, with means adjusted according to sex and height[23]. Older adults with a mean above the 80th percentile of the sample score for frailty.

As covariates of the relationships between frailty, depression and mortality, the following information derived from baseline measures were selected:

a) Sociodemographic variables: sex, male or female; age, <75 years old, 75-79 years old, ≥80 years old; and education, number of years of formal education: 0, 1 to 4, 5 to 8, 9 or more;

b) Chronic diseases: identified by the number of self-reported diseases based on an inventory of nine dichotomous items composed of the most prevalent chronic non-communicable diseases in the older adult population;

c) Cognitive performance: estimated by the total score on the MMSE[18,24] with scores ranging from 0 to 30 points and a specific cut-off point for number of years of education completed.

To describe the sample under study alone, certain indicators of functional capacity were included, in this case, the performance of instrumental activities of daily living (IADLs) in the baseline survey. The inventory and criteria described by Lawton & Brody[25] were used, which involve a list of seven activities of practical life used to identify independence or total or partial dependence in their performance.

The FIBRA study baseline and follow-up surveys were approved by the Research Ethics Committee of the State University of Campinas (UNICAMP) under report no. 208/2007, on May 22, 2007, and report no. 1,332,651, on November 23, 2015. A term of free, informed consent was signed by all participants in both surveys. The use of data to conduct this study was also approved by the aforementioned committee, under report no. 3,097,048, on December 20, 2018.

The variables of interest were described according to their percentage distribution and position measurements (mean and standard deviation). Data from living and deceased older adults were compared using the Mann-Whitney and Fisher's exact tests, due to the absence of normal data distribution. From the data on depression and frailty, four categories of association were generated, derived from the combinations between absence or presence of depression and frailty status (robust or frail): 1) no depression and robust; 2) no depression and frail; 3) with depression and robust; 4) with depression and frail. Kaplan-Maier survival curves were determined and nonparametric log-rank, Gehan-Breslow, and Tarone-Ware tests were performed to identify differences between the combined conditions of depression and frailty. To estimate the mortality risk for the groups of associations between depression and

frailty, crude and adjusted Cox proportional hazards models were used, considering their covariation with sociodemographic variables (sex, age and education), cognitive performance and comorbidities. The significance level for the tests was 95% or p<0.05.

RESULTS

The sample was characterized by a higher percentage of female participants (67.2%), aged between 65 and 74 years (64%) with four years of education or less. The average cognitive performance on the MMSE was 23.8+4.14 points. There was also a higher percentage of older adults reporting at least one chronic disease, but a high degree of the preservation of functional independence when performing IADLs in baseline measurements (70.5%).

Considering only the current sample, in the follow-up survey, 190 deaths (25.7%) were recorded. The subsample of deceased older adults differed from the subsample of living participants in terms of distribution in all the variables of interest, with the exception of the number of self-reported diseases. Male sex, aged 80 years old and over, lack of formal education, greater functional disability, depression and frailty were present to a greater extent in the subsample of deceased than in the subsample of living participants. Compared with participating older adults, deceased older adults also showed lower mean scores on cognitive performance and a higher percentage of older adults who exhibited more unfavorable combinations of depression and frailty (Table 1).

Figure 2 shows the survival curves (Kaplan-Maier) corresponding to the combinations of frailty and depression conditions. The log-rank test (X^2=17.79; gl=3; p<0.001) resulted in significant differences between them. Measured in months, the mean survival of the robust and non-depressed older adults was 116.7+1 months (95%CI =114.8–1118.5); those without depression and frail was 112.8+0.9 months (95%CI =111.1–114.5); those with depression and robust was 106.7+3.9 months (95%CI=98.5–113.8); and those with depression and frail was 110.7+1.3 months (95%CI =108.1–113.3). The Gehan-Breslow (X^2=13.83; gl=3; p=0.003) and Tarone-Wade (X^2=14.74; gl=3; p=0.002) tests also showed differences between the combined conditions of frailty and depression. Graphic signs along the curves refer to the occurrence of assessments.

Table 1. Characterization of the baseline sample and subsamples of participating and deceased older adults according to sociodemographic variables, number of diseases and functional disabilities, cognition and isolated and combined conditions of depression and frailty. FIBRA Study, Older adults, Campinas and Ermelino Matarazzo, SP, Brazil, 2008/2009 and 2016/2017.

Sample characteristics	Baseline	Follow-up		
	(N=739)	Participants (n=549)	Deceased (n=190)	p-valor
	n(%)	n(%)	n(%)	
Sex				
Female	497 (67.2)	384 (**70.0**)	113 (59.5)	p=0.008*
Male	242 (32.8)	165 (30.0)	77 (**40.5**)	
Age (M±DP)	73.1 (±5.9)	72.3 (±5.3)	75.6 (±6.8)	p<0.001**
65-74 years old	473 (64.0)	384 (**70.0**)	89 (46.8)	p<0.001*
75-79 years old	161 (21.8)	112 (20.4)	49 (25.8)	
≥ 80 years old	105 (14.2)	53 (9.7)	52 (**27.4**)	
Education (M±DP)	3.9 (±3.6)	4.3 (±3.8)	3.1 (±3.0)	p<0.001**
0 years	140 (19.0)	88 (16.1)	52 (**27.4**)	p<0.001*
1-4 years	428 (58.0)	325 (59.3)	103 (54.2)	
5-8 years	103 (14.0)	76 (13.9)	27 (14.2)	
≥ 9 years	67 (9.0)	59 (**10.8**)	8 (4.2)	

to be continued

Continuation of Table 1

Sample characteristics	Baseline	Follow-up		
	(N=739)	Participants (n=549)	Deceased (n=190)	p-valor
	n(%)	n(%)	n(%)	
MMSE (M±DP)	23.8 (±4.2)	24.5 (±3.6)	22.0 (±5.0)	p<0.001**
No. of diseases (M±DP)	2.1 (±1.3)	2.1 (±1.4)	2.1 (±1.3)	p=0.999**
0	57 (9.7)	45 (10.0)	12 (9.1)	p=0.846*
1-2	328 (56.2)	251 (55.5)	77 (58.3)	
≥ 3	199 (34.1)	156 (34.5)	43 (32.6)	
No. of incapacities (M±DP)	0.6 (±1.1)	0.5 (±1.0)	1.0 (±1.5)	p<0.001**
0	409 (70.5)	334 (**74.5**)	75 (56.8)	p<0.001*
1-2	121 (20.9)	86 (19.2)	35 (**26.5**)	
≥ 3	50 (8.6)	28 (6.3)	22 (**16.7**)	
Depression (M±DP)	3.5 (±2.8)	3.4 (±2.7)	4.2 (±3.1)	p=0.011**
Yes	121 (20.9)	85 (19.0)	36 (**27.7**)	p=0.032*
No	457 (79.1)	363 (**81.0**)	94 (72.3)	
Frailty status				
Pre-frail & Frail	516 (69.8)	365 (66.5)	151 (**79.5**)	p<0.001*
Robust	223 (30.2)	184 (**33.5**)	39 (20.5)	
Combined conditions				
No depression-Robust	175 (30.3)	150 (**33.5**)	25 (19.2)	p=0.007*
No depression-Frail	282 (48.8)	213 (47.5)	69 (**53.1**)	
With depression-Robust	18 (3.1)	11 (2.5)	7 (5.4)	
With depression-Frail	103 (17.8)	74 (16.5)	29 (22.3)	

* p-value for the Mann-Whitney test comparing values between two groups; ** p-value for comparing means. In bold, significant percentage differences between subsamples are specified.

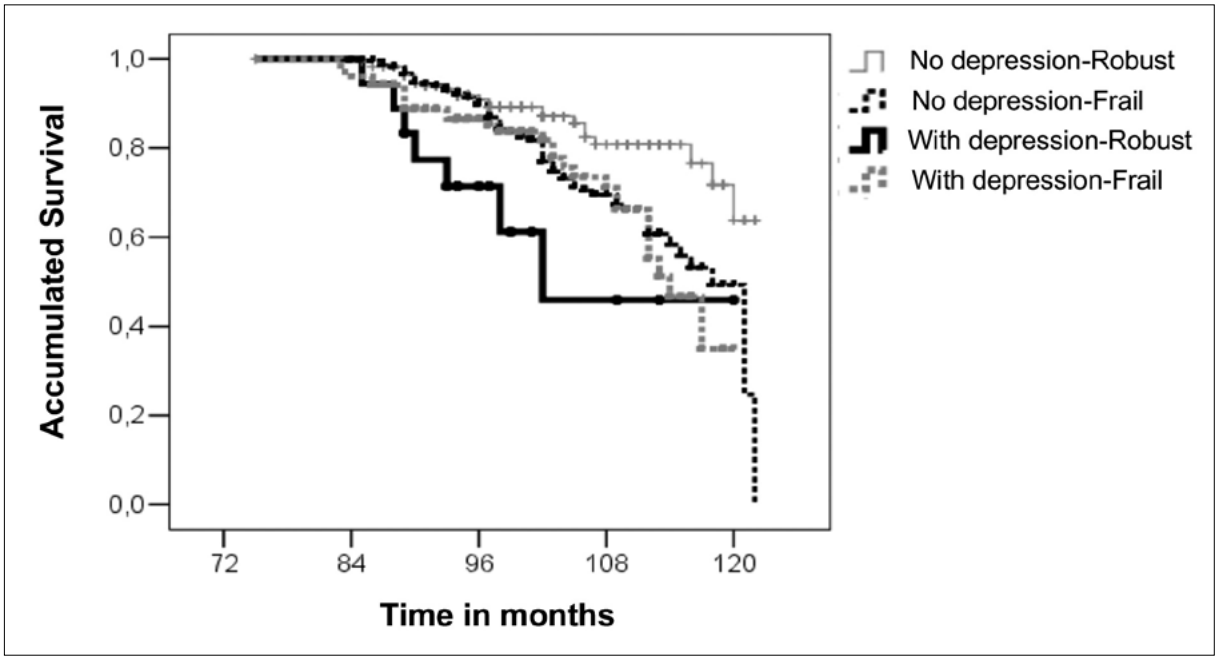

Figure 2. Survival curves according to combined conditions of depression and frailty. FIBRA Study, Older adults, Campinas and Ermelino Matarazzo, SP, Brazil, 2008/2009 and 2016/2017.

In Table 2, the crude and adjusted risk ratios (HR) are described for the variables sex, age, education, cognitive performance, number of diseases, and combined conditions of frailty and depression.

In the crude analysis, the highest risk ratio for mortality over time was determined for category age, with the oldest age group (>80 years) showing the highest rate compared with the age group 65 to 74 years old. The absence of formal education showed a risk ratio of 3.59 (95%CI = 1.70–7.56) compared with older adults with more years of education (>9 years); men showed a risk 33% higher than women. Compared with the condition "no depression and robust," all other combinations represented a significant risk, the highest was that obtained for the condition "with depression and robust," followed by "with depression and frail," and "no depression and frail." Regarding performance on the MMSE, the increase in total score by one point represented a reduction in the risk of death, or increase in survival, of 11.6%.

The results of the adjusted analysis revealed that education lost statistical significance. Higher indices were associated with the age groups >80 years old and 75 to 79 years old, for the condition "with depression and robust," followed by "with depression and frail," and "no depression and frail," and by total score on the MMSE, in which one point represented a reduction in the risk of death, or an increase in survival, of 8%.

Table 2. Crude and adjusted Cox regression for overall survival (N=733). FIBRA Study, Older adults, Campinas and Ermelino Matarazzo, SP, Brazil, 2008/2009 and 2016/2017.

Sample characteristics	Crude analysis		Adjusted analysis	
	HR	95%CI	HR	95%CI
Sex				
Female (ref.)	1.00	-	1.00	-
Male	1.33	1.01 – 1.78	1.62	1.13 – 2.32
Age				
65-74 years old (ref.)	1.00	-	1.00	-
75-79 years old	5.53	3.71 – 8.23	6.43	3.99 – 10.36
≥ 80 years old	9.96	6.69 – 14.81	8.18	4.82 – 13.88
Education				
≥ 9 years (ref.)	1.00	-	-	-
5-8 years	1.86	0.84 – 4.09	-	-
1-4 years	1.96	0.96 – 4.03	-	-
0 years	3.59	1.70 – 7.56	-	-
MMSE score	0.884	0.858 – 0.910	0.920	0.870 – 0.974
Number of diseases				
0 (ref.)	1.00	-	-	-
1-2	1.21	-0.66 – 2.23	-	-
≥ 3	1.04	0.55 – 1.98	-	-
Combined conditions				
No depression-Robust (ref.)	1.00	-	1.00	-
No depression-Frail	1.91	1.21 – 3.00	1.64	1.02 – 2.63
With depression-Robust	4.00	1.72 – 9.28	3.19	1.37 – 7.43
With depression-Frail	2.27	1.32 – 3.90	1.98	1.14 – 3.44

HR, risk ratio for death; Crude analysis: n=543 assessments and n=190 deaths; Adjusted analysis: n=442 assessments and n=128 deaths; 95%CI, 95% confidence interval for hazard ratio; (ref.), reference category.

DISCUSSION

The results support the hypothesis that different combinations of frailty and depression in older adults have different probabilities of mortality over time. Here, sociodemographic conditions and cognitive performance contributed to the differentiation in risk indices.

In Brazil, the prevalence of depression in older adults, estimated by the application of screening scales, is 21.0% (95%CI: 18.0–25.0)[26], a value similar to that found in the baseline survey of this study. The identification of frailty by the phenotype described by Fried et al.[1] requires the fulfilment of specific criteria. The presence of three or more criteria estimated for Brazil is 16%, and based on data from the FIBRA Study in the UNICAMP Pole, 9.1% of frail and 51.8% of pre-frail older adults were observed[27]. The combination of pre-frailty and frailty in this study showed a high percentage of older adults who meet some of the frailty criteria (69.8%). This percentage was similar to that reported by Ruiz-Grão et al.[15] in Spain (75.6%), though their sample also included institutionalized older adults.

Frailty and depression screening measurements in the older adult population are used to determine different aspects of health, but have the potential to generate specific association subgroups[7]. The results suggested the importance of verifying this potential based on three forms of analyzing mortality: percentage distribution based on dichotomous outcomes, survival curves, and calculating risk ratios.

Concerning the dichotomous outcome, the subsample of deceased older adults differed from that of participating older adults, in terms of the percentage of deaths that occurred for the condition "no depression and frail", that is, isolated frailty was present more often among older adults who died than among participating older adults.

However, when considering the time of occurrence of these deaths, the combinations of conditions revealed different survival trajectories. Regarding accumulated survival, the condition "with depression and robust" stood out from the first months of recorded deaths onwards, and was only surpassed by the condition "with depression and frail," and later by "no depression and frail," by the end of the last third of the period under study. Different non-parametric tests for comparing trajectories were used to capture possible biases in the distribution of deaths over time, given the long interval between the surveys. The log-rank test assigns the same weight to associations over time. In turn, the Gerhan-Breslow test is influenced by the initial portion and the Tarone-Ware test by the intermediate portion. All of them confirmed the differences in the curves of the groups.

To calculate the risk ratios, the condition "no depression and robust" was used as the reference for comparisons. The remaining conditions all presented significant risks independently or adjusted for covariates. The independent risks identified for the covariates were advanced age, male sex, and lack of formal education. An increase in the score for cognitive performance was associated with a reduced risk of death. Advanced age, male sex and cognitive performance significantly and jointly affected the risk-adjusted calculation represented by the different combinations.

As expected, advanced age is an independent indicator of mortality. However, age also acts as a source of variation for the relationship between depression and frailty. A study by Ji et al.[28] showed that the associations between frailty and depression and their effects on mortality became weaker with advancing age. The authors suggested that the performance of adaptive mechanisms of emotional regulation were more active in older adults, even in the presence of frailty criteria.

In studies on mortality in older adults with depression and studies on frailty, there is evidence of a higher risk for men[7,29], possibly mediated by cardiovascular causes, in the context of depression and frailty[30]. Although there is a higher percentage of frail women than frail men, in the presence of depression, this condition represents an increased risk of death for men[28,30]. In a prospective study, depressive symptoms at baseline represented a risk of mortality in men, with or without adjustment for frailty[29]. One of the explanatory hypotheses lies in shared vascular risk, which is associated both with

mortality from general and specific causes in men and with depression, which manifests itself later in life[14].

Cho et al.[31] observed associations between low socioeconomic status and frailty and risk of mortality, even after adjusting for covariates of health and functionality. In this study, the absence of formal education was associated with an independent risk of mortality. In the adjusted analyses, it is possible that it lost explanatory power when aligned with performance in the MMSE, a test that is highly sensitive to education level[8].

The greatest difficulties and sources of criticism of mortality studies come from controlling confounding variables[32]. In this study, we opted to control the number of self-reported diseases (those which did not show independent or joint effects), but not to control the presence of disabilities in performing instrumental activities of daily living (IADLs)[4]. This choice was motivated by criticism directed at the study by Ruiz-Grao et al.[7] for saturating the regression model with variables of great influence on mortality, such as IADLs, weighted comorbidities and health behaviors, and for including older adults institutionalized in the sample. Their critics[33] considered that the explanatory power of frailty was reduced, given that the only significant combination between depression and frailty in relation to the risk of mortality was "pre-frailty and depression."

In the short term, the presence of functional disabilities is perhaps one of the most common consequences of the combination of depression and frailty[4,7,8]. The purpose of this study was to draw attention to groups of association based on mortality estimates, with adjustments only for less specific sociodemographic and health variables.

The available data set and our analytical choices could be considered methodological limitations. Frail older adults may not have been sufficiently included in the baseline survey. Baseline frailty results of older adults lost to the follow-up survey or the incidence of other chronic diseases during the period were not analyzed. These data may have biases from several sources, and these possibilities were not considered.

Similarly, due to the size of the sample and its distribution in subgroups, separating the status of pre-frailty and frailty was not considered in the best interests of the study. Thus, more than combinations of depression and frailty, the study analyzed the relationship between the presence of depressive symptoms in a significant number and some of the frailty criteria. We believe this strategy is justified, since the distinctive feature of the frailty phenotype lies in its continuous nature, in which the criteria have been useful to explain the mortality and morbidity of older adults from different cultural contexts[2].

Whether the risks represented by the different combinations of frailty and their criteria are additive or synergistic falls outside the scope of this study, more so when considering that there is simply insufficient data for such a task. Park et al.[34] suggested that there is a synergistic effect between depression and handgrip strength, especially among older adult males. Ward and Bhat[33] affirmed that statements regarding interactions between risks is premature, given the lack of consensus on shared causal mechanisms.

In this study, it seems reasonable to affirm that depression was the ordering variable of the risks, since its presence in isolation, and again in combination with frailty, represented higher risks than the condition of frailty alone[35]. In future research on the subject, analyzes of all-cause mortality should aim to compare the effects represented by the associations of depression with the levels of frailty, with each of its criteria and with pre-frailty, with adjustments for specific diseases, for example, cardiovascular diseases[30].

CONCLUSION

Screening measurements for frailty and depressive symptoms taken in community-dwelling older adults can help to compose specific risk stratification criteria, since different combinations of conditions manifest in different aging trajectories and, in particular, different mortality risks. The greatest risks were identified in the presence of the combinations

"with depression and robust", "with depression and frail", and "no depression and frail", respectively.

The presence of depressive symptoms may be the ordering factor of the combinations on mortality within a period of approximately a decade of life, especially when the older adults are men, 75 years old and over, who present lower cognitive performance.

Depression in old age is an identifiable and treatable condition, and evidence and effective interventions in the management of the frailty syndrome are growing. Investment in the prevention of and interventions in these conditions can minimize indicators of excess mortality from general causes.

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