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Patterns, predictors, and outcomes of frailty trajectories in community-dwelling older adults: Results from the FREEDOM Cohort Study

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HIGHLIGHTS

- The primary question addressed by this study?
- This cohort study allowed to determine frailty trajectories among community-dwelling older adults population.
- What is the main finding of this study?
- The more significant predictive factors for poor frailty trajectories were cognitive impairment and dementia. Hypertension was discriminate factor between (frail regressing to pre-frail) and (frail progressing to more severe frailty).
- Frailty trajectories were associated with clinical outcomes including falls, hospitalization, and cognition deficit.
- What is the meaning of the finding?
- This study determines four frailty trajectories among community-dwelling older adults. The modifiable predictive factors associated with poor frailty trajectory were hypertension, cognitive deficit and depressive symptoms.

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Keywords:
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ABSTRACT

Objectives: To identify subgroups of people with distinct frailty trajectories, identify baseline characteristics associated with these trajectories, and determine their coincident clinical outcomes.
Design: This study examined the longitudinal database from the FREEDOM Cohort Study.
Setting and Participants: All 497 participants of the FREEDOM *(French Acronym for "**FR**agilité **Et** Evaluation à **DOM**icile" / In English "Frailty and Evaluation at Home")* cohort requested a comprehensive geriatric assessment. Community-dwelling subjects over 75 years, or over 65 years with at least two comorbidities were included.
Methods: Frailty was assessed using Fried's criteria, depression using the Geriatric Depression Scale (GDS) and cognitive function using the Mini Mental State Examination (MMSE) questionnaire. Frailty trajectories were modelled using k-means algorithms. Predictive factors were determined by multivariate logistic regression. Clinical outcomes included incident cognitive deficit, falls and hospitalization.
Results: The trajectory models allowed determine four frailty trajectories: "**robust stable**" (Trajectory A, 26.8%), "**pre-frail worsening to frailty**" (Trajectory B, 35.8%), "**frail improving to less frailty**" (Trajectory C, 23.3%), and "**frail worsening to more frailty**" (Trajectory D, 14.1%). Trajectory B was associated with age (OR 1.2

Abbreviations: ADL, Activity of Daily Living; AGGIR, Instrument for evaluating dependency in elderly in France; CGA, Comprehensive Geriatric Assessment; EQ-5D, EuroQol-5 Dimension; FRIED'S CRITERIA, Physical frailty; FREEDOM-LNA cohort, French acronym for Frailty, Clinical Research and Evaluation at Home in Limousin – Nouvelle Aquitaine; GDS, Geriatric Depression Scale; IADL, Instrumental Activities for Daily Living; MMSE, Mini Mental State Examination; MNA, Mini Nutritional Assessment; SMAF, Functional Autonomy Measurement system; SPPB, Short Physical Performance Battery; UPSAV, Geriatric mobile team (*Unité de Prévention de Suivi et d'Analyse du Vieillissement*).

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(95CI, 1.05 - 1.17)), potential cognitive deficit/dementia (OR 2.01 (95CI, 1.01- 4.05)) and depressive symptoms (OR 2.36 (95CI, 1.36 - 4.12)). Hypertension was distinguishing factor between" trajectory B vs. C and D. Depressive symptoms were two time more associated with D (OR 10.51) vs. C (OR 4.55). The incidence of clinical outcomes was significantly increased in poor frailty trajectories.

Conclusions and Implications: This study allowed to determine frailty trajectories among older subjects requested a comprehensive geriatric assessment. The more significant predictive factors associated with poor frailty trajectory were advanced in age, potential cognitive deficit/dementia, depressive symptoms and hypertension. This emphasizes the need for adequate measures to controlled hypertension, depressive symptoms and to maintain or improve cognition in older adults.

1. Introduction

Life expectancy has increased significantly since several decades in industrialized countries. The needs of older people are thus increasing and must be addressed. One public health challenge is to keep older subjects in good health and autonomy with sustained sense of well-being, extended periods of social engagement and productivity, and minimal illness, disability, and dependency. According to the WHO guidelines, (Integrated Care for Older People, 2017) "there is a need to detect impairments in physical and mental capacities and deliver effective intervention to prevent or delay progression, since early detection can reverse or delay the loss of intrinsic capacity". Therefore, the importance of the comprehensive geriatric evaluation and the patient follow up especially in relation to early detection and prevention appear necessary. The implementation of such a policy should improve quality of care and promote healthy aging as well as diminish the pressure on the health care system.

Older adults are a highly heterogeneous group with variable health and functional life courses (Integrated Care for Older People, 2017; Lowsky et al., 2014). While some older subjects are living healthy even after 85 years old, others present a risk of functional decompensation, including confusion, depression, and malnutrition, when exposed to a minor environmental challenge, which can worsen their health status and dependence (Fried et al., 2001). This pre-disability condition or early-stage disability is the basis of the concept of frailty syndrome in older subjects (Morley et al., 2013). More precisely, frailty can be defined as a state of increased vulnerability to poor resolution of homeostasis following a stress, which increases the risk of adverse outcomes including falls, delirium and disability (Clegg et al., 2013). This is a state of high vulnerability for adverse health outcomes, such as disability, falls, hospitalization, institutionalization, and mortality.

Different phenotypes of frailty have been described considering various levels of weakness, slowness, physical activity, energy, and body weight loss (Fried et al., 2001). There is also evidence for the association with other contributors like cognitive impairment, depression, and poor well-being (Li et al., 2020; Wleklik et al., 2020). It is also established that frailty was a common, serious and costly clinical state, and there is a consensus that it is partly reversible with appropriate interventions including exercise, nutrition, and management of all reversible diseases (Cesari, 2012; Lim et al., 2019; Morley et al., 2013). Thus, efforts are called to reduce the burden of frailty. Various simple screening tools can be used by physicians and are considered reliable to detect frailty in older subjects (Morley et al., 2013). The detection of frailty and associated factors appears imperative to implement adapted clinical management and personalized actions to delay or reduce frailty, its physical, socio-environmental, and psychological consequences and therefore the onset of dependency and disability. In this way, we built and followed a regional longitudinal cohort of community-dwelling older subjects starting in 2010, with the aim to study the trajectories of frailty and associated predictive risk factors. We also analysed the clinical impact of frailty trajectory on clinical outcomes (incident cognitive decline, falls, and hospitalization) during the follow up.

2. Materials and methods

This prospective longitudinal cohort study (FREEDOM, French Acronym for "**FR**agilité **E**t **E**valuation à **DOM**icile" / In English "Frailty and Evaluation at Home") was performed by UPSAV unit (Unité de Prévention, de Suivi et d'Analyse du Vieillissement) at home. This unit is a preventive health service to help robust or frail subjects with the aim for maintenance at home. Community-dwelling subjects over 75 years, or over 65 years with at least two comorbidities were included. All participants requested a comprehensive geriatric assessment and they were enrolled from UPSAV. Subjects with a short-term (< 1 month) vital prognostic were excluded. All subjects (or the family physician, or caregivers) asked the services of the UPSAV for a comprehensive geriatric assessment at home. They were followed for at least 2 years (every 6 months the first year and then one visit each year) between 01/01/2010 and 31/08/2017 or until study discontinuation due to death, entry in institution, or lost to follow-up. At each visit, a comprehensive geriatric assessment was performed and a personalised action plan including additional medical and social assessments, reeducation/readaptation and/or psychosocial readaptation was proposed if necessary. Detailed characteristics of the FREEDOM cohort have been reported previously. (Boyer et al., 2022)

The study protocol was reviewed and approved by the local Institutional Review Board (CEREES " *Comité expertise pour les recherche, les études et les evaluations dans le domaine de la Santé*", Limoges; Approval number: TPS 429669) and by the French Data Protection Authority (CNIL) insuring protection of individualized data according to the French law. Informed consent for data processing was obtained from all subjects (or legal representatives). All procedures were carried out in accordance with the Helsinki Declaration and its later amendments.

2.1. Measurements

Measurements were recorded at home and included socioeconomic variables (age, gender, educational level, marital status), lifestyle factors (body mass index (BMI), smoking status, alcohol consumption), Health-related factors (diabetes, hypertension, dyslipidaemia, history of stroke, history of myocardial infarction, and polymedication (defined as more than 4 medications per day). The nutritional status was assessed using the Mini Nutritional Assessment (MNA) (Guigoz et al., 1996). The functional status was assessed using the Katz's index for basic daily living (ADL), and using the Lawton's scale for instrumental activities of daily living (IADL) (Katz, 1983; Lawton & Brody, 1969). Cognition was primarily assessed using the Mini Mental State Examination (MMSE) questionnaire (Folstein, Folstein, & McHugh, 1975). Subjects were considered to have a potential cognitive deficits/dementia if MMSE score was $\leq$ 20 in subjects with low education, $\leq$ 23 in subjects with medium education and $\leq$ 26 in subjects with a high education. Depression over the past week was monitored using the Geriatric Depression Scale (GDS) as described previously (Kojima et al., 2019; Yesavage et al., 1983). GDS scores ranging from 0 to 5 were indicative of normal mood; scores between 5 and 9 of a risk of depressive symptoms, and scores > 9 of severe depressive symptoms.

2.2. Measurement of frailty

Frailty was assessed using questionnaires administered by the health professional (geriatric physician or trained nurse) during scheduled visits at home. Fried criteria were assessed as described previously (Fried et al., 2001): weakness (grip strength of the dominant hand < 20%, we have used the cut-offs of 29 kg for men and 18 kg for women), slowness (walking speed < 20% of normal), low level of physical activity (< 20% of energy expenditure), low energy or self-reported exhaustion, and unintentional weight loss (4 to 5 kg since the previous year). Subjects were considered as frail when at least 3 criteria were present, pre-frail when there were one or two criteria and robust when there was no criterion.

2.3. Clinical outcomes

Falls and unscheduled hospitalizations which occurred between two successive visits and emergence or worsening of a pathologic cognitive function (MMSE) since the previous visit were assessed at each post-baseline visit.

2.4. Explanatory variables

The explanatory variables considered as potential predictors of frailty were age, sex, tobacco consumption (Yes/No), alcohol consumption (Yes/No), BMI, hypertension (Yes/No), dyslipidaemia (Yes/No), diabetes (Yes/No), polymedication (≤4 or > 4 medications per day) depression (GDS ≤ 9 or > 9), potential cognitive deficits/dementia ~~cognitivedeficit~~ (Pathologic MMSE or not), and the proposition of a geriatric plan at the end of the first visit (Yes/No).

2.5. Statistical analysis

Statistical analysis was performed using the SAS software, version 9.4 (SAS Institute, Cary, NC, USA). The trajectories were analysed using frailty as a binary variable (frail, versus pre-frail/not frail) using the k-means modelization (Genolini & Falissard, 2011). The k-means algorithm was implemented using the package KmlCov of the R software version 3.2.2 which allows taking into account covariates in the choice of clusters. The optimal number of trajectories was determined according to the Calinski-Harabasz criterion (Genolini & Falissard, 2011). Once the number of optimal clusters of subjects was determined, the variable was plotted with time; the number of subjects in each trajectory and the intra-group homogeneity was determined. Multinomial regression models were used to determine predictive factors adjusting on covariates. All factors with a p-value < 0.20 in univariates models were included in the model. Sex was kept in the model as confounding variables. Backward selection was used to select only the significant factors (at the 5% level). Odds ratios (ORs) were given with 95% confidence intervals (CI). The clinical outcomes (falls, hospitalisations, and pathologic cognition) were determined with their 95%CI and tested between trajectories using a chi-squared test. All tests were bilateral and considered as significant at the alpha level of 0.05.

3. Results

Analyses were performed in 497 subjects with available FRIED criteria in at least two visits. The mean duration of follow-up was 19.8 ± 16.0 months and the mean number of visits per subject was 3.4 ± 1.5. Main baseline characteristics in these patients are described in Table 1. At Visit 1, 124 (26.6%) subjects were frail, 291 (62.4%) were pre-frail, and 51 (10.9%) were robust. The most frequent frailty criteria in this cohort were weakness (79.6% of subjects), low physical activity (51.2%), and slowness (25.7%).

Table 1
Main characteristics of the study population ($N = 497$) at Visit 1 (inclusion).

Main characteristics		N (%)
Age at inclusion	N	486
	Mean ± SD	82.7 ± 5.5
	>75	399 (82.1%)
Sex (Female)	N	488
	Female	342 (70.1%)
Education*	N	487
	Low	276 (56.7%)
	Medium	84 (17.2%)
	High	127 (26.1%)
Lifestyle	N	487
	Living alone	276 (56.7%)
	Living with a partner	186 (38.2%)
	Living in family	25 (5.1%)
Cardiovascular risk factors	Hypertension	350/476 (73.5%)
	Dyslipidaemia	248/475 (52.2%)
	Obesity	131/472 (27.8%)
	Diabetes	94/475 (19.8%)
	Smoking	58/473 (12.3%)
	Alcohol	16/474 (3.4%)
Polymedication	N	476
	≥ 5 medications	379 (79.6%)
Nutritional status	N	484
MNA score	Mean ± SD	24.6 ± 3.5
Functional status	N	486
ADL score	Mean ± SD	5.4 ± 0.8
IADL score	Mean ± SD	6.1 ± 1.9
Geriatric depression score (GDS)	N	433
	GDS > 9	204 (47.1%)
Minimal Mental State (MMS)	N	472
	MMS <24	136 (28.8%)
FRIED criteria	Weight loss	47/487 (9.7%)
	Low energy/exhaustion	92/484 (19.0%)
	Low grip strength	382/480 (79.6%)
	Low walking speed	121/471 (25.7%)
	Low physical activity	248/484 (51.2%)
Frailty	N	466
	Frail	124 (26.6%)
	Pre-frail	291 (62.4%)
	Robust	51 (10.9%)
Personalized action plan	N	497
	Medical plan	383 (79.1%)
	Social plan	181 (36.4%)
	Psychomotricity	181 (36.4%)
	Occupational therapy	146 (29.4%)

* Low: primary certificate level; Medium: Middle school, High: Secondary or high school.

3.1. Frailty trajectories

The k-means methodology led to 4 trajectories of frailty (Fig. 1): A population of relatively robust participants with no Fried criteria (comprising 26.8% of the population) who remained robust throughout the follow up (Trajectory A), a population of pre-frail participants (1 or 2 Fried's criteria) who worsened to frailty (more than 2 criteria) at the end of the follow-up (35.8% of the population); a population of frail participants (just 3 criteria) who improved to pre-frail (1 or 2 criteria) at the end of the follow-up (Trajectory C, 23.3%) and a population of frail participants (3 criteria) who worsened to more severe frailty (4 to 5 criteria) at the end of the follow-up (Trajectory D, 14.1% of participants). In this FREEDOM analysis of frailty trajectories, we don't observe significant interaction (modified effect) on the age cut-off 75 (65 to 75 vs. >75) (p>0.05).

3.2. Predictive factors

In univariate analysis, the variables significantly (at the 20% level) associated with frailty trajectories were age (P<0.0001), polymedication (P = 0.043), hypertension (P = 0.018), a GDS > 9 (P<0.0001), a potential cognitive deficits/dementia (MMS<24)

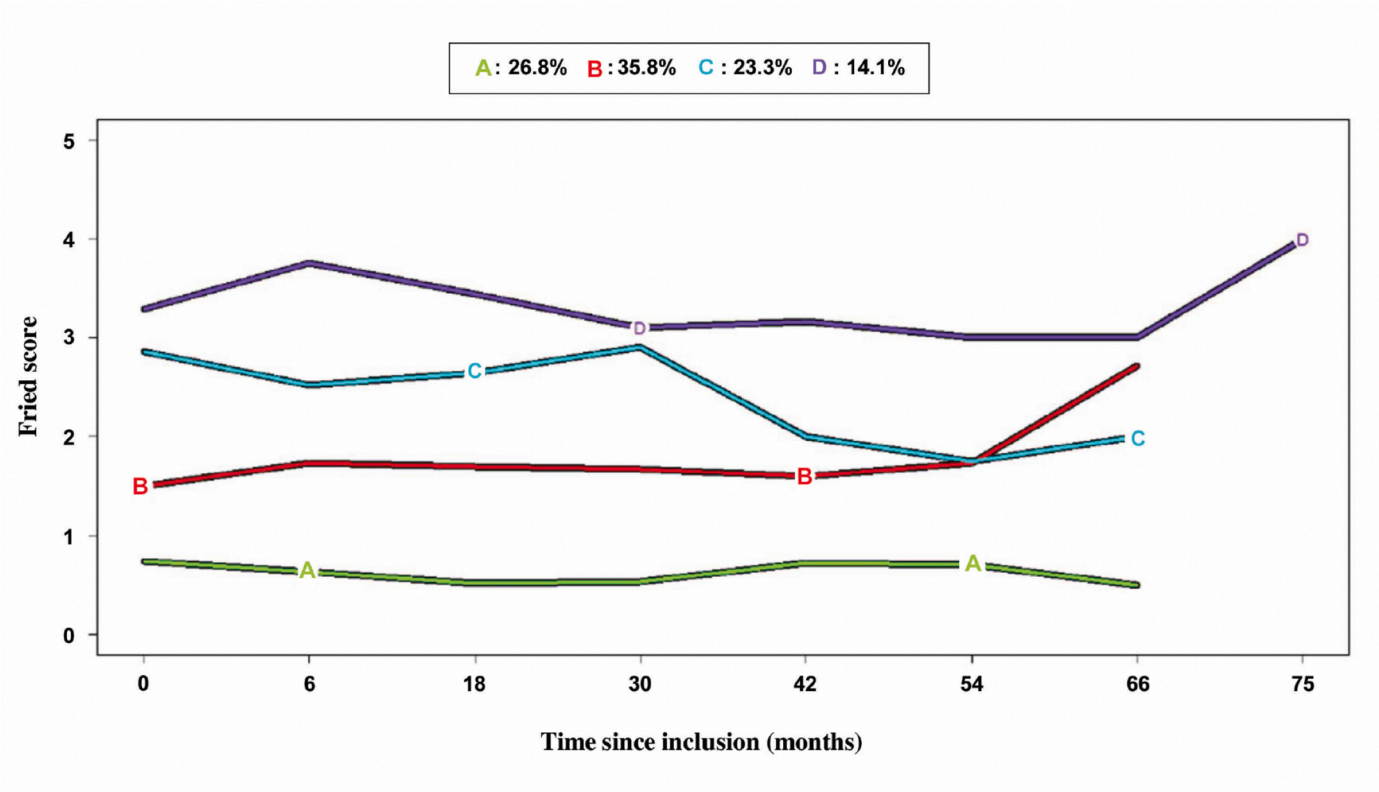

Fig. 1. Frailty trajectories (k-means methodology)
Four trajectories were modelled: Trajectory A, relatively robust participants remaining stable; Trajectory B, prefrail participants worsening to frailty; Trajectory C, frail participants improving toward prefrail; and Trajectory D, frail participants worsening to more severe frailty. The percentage of the population in each trajectory is indicated.

($P<0.0001$), and a proposition for a personalised action plan ($P = 0.087$). Other variables including sex, education level, type of life (alone), smoking, alcohol, and other cardiovascular risk factors such as BMI, diabetes, and dyslipidaemia were not significantly associated with the frailty trajectories at the 20% level.

The factors significantly associated with k-means trajectories in multivariate analyses were age, a MMS<24, a GDS score > 9 and presence of hypertension (Table 2). Three risk factors were significantly associated with Trajectory B (robust subjects progressing to pre-frailty) relatively to A (robust stable trajectory): Age (OR=1.12, $P<0.0001$), a MMS<24 (OR=2.01, $P = 0.049$) and a GDS > 9 (OR=2.36, $P = 0.0024$). Hypertension was an additional factor allowing to discriminate between Trajectory A and Trajectory C (frail regressing to pre-frail) with an odd ratio of 2.71 ($P = 0.0068$) or Trajectory D (frail progressing to more severe frailty) with an odd ratio of 2.53 ($P = 0.034$). GDS>9 was the only factor significantly associated with Trajectory C relative to Trajectory D (OR=0.43, $P = 0.040$). All Fried-s criteria items have changed during follow-up. The major changes were in the following order: low level of physical activity (< 20% of energy expenditure), followed by low energy or self-reported exhaustion, slowness (walking speed < 20% of normal), weakness (grip strength of the dominant hand < 20%), and unintentional weight loss (4 to 5 kg since the previous year).

3.3. Clinical outcomes according to trajectories

At last visit, 35.4% of subjects had a potential cognitive deficits/dementia as assessed using the MMSE score, 33.8% had occurring falls and 17.5% had occurring hospitalisations between the two last visits.

Table 2
Adjusted odds ratios for every unit increase or category change in the predictors of frail trajectory: results from multinomial logistic regressions at baseline (n = 466*), The FREEDOM Cohort Study.

Reference	Trajectory	Variable	OR	95%CI	P-value
A (Robust stable Trajectory)	**B** (Pre-frail worsening to frailty)	Age (in years)	1.12	1.06; 1.17	<0.0001
		Potential cognitive deficits/dementia (MMS < 24)	2.01	1.01; 4.05	0.0495
		Depressive symptoms (GDS > 9)	2.36	1.36; 4.12	0.0024
A (Robust stable Trajectory)	**C** (Frail improving to less frailty)	Age (in years)	1.16	1.09; 1.23	<0.0001
		Potential cognitive deficits/dementia (MMS < 24)	3.63	1.72; 7.66	0.0007
		Depressive symptoms (GDS > 9)	4.55	2.40; 8.62	<0.0001
		Hypertension	2.71	1.32; 5.57	0.0068
A (Robust stable Trajectory)	**D** (Frail worsening to more frailty)	Age (in years)	1.12	1.05; 1.20	0.0011
		Potential cognitive deficits/dementia (MMS < 24)	4.56	1.97; 10.58	0.0004
		Depressive symptoms (GDS > 9)	10.51	4.61; 23.95	<0.0001
		Hypertension	2.53	1.07; 5.99	0.0342

Adjusted variables: sociodemographic characteristics, medical condition and personalized care plan.
*Missing value ($n = 31$ on Fried's criteria).

The incidence of clinical outcome was clearly dependent on the trajectory (Fig. 2): the more pejorative frailty trajectory (e.g. Trajectory C or D), the higher was the incidence of these clinical outcomes. Of note, Trajectory A (prefrail subjects worsening to frailty) and Trajectory C (frail subjects improving to less frailty) had quite similar rate of incident falls (39.4% vs. 36.9%).

4. Discussion

The FREEDOM cohort was established to determine potential measures which could be implemented to maintain older people in good health and acceptable dependency. Frailty has been previously associated with adverse clinical outcomes including fall, hospitalization, loss of autonomy, institutionalization, and death (Fried et al., 2001; Rockwood et al., 2007), and is believed to be reversed by appropriate measures. Prevention of frailty requires a sound understanding of the risk factors. In this study, we found that frailty trajectories were predicted by some modifiable factors after adjusting for age and sex, including hypertension, impaired cognition, and depression. In addition, we found that the most pejorative trajectories were associated with poor clinical outcomes including falls, hospitalization and severe cognitive deficit.

In this cohort composed of relatively old patients (> 80 yrs on average) and women in majority, with various frailty phenotypes at first visit, the trajectories models showed that the baseline level of frailty could remain relatively stable, worsened or improved after 5 to 6 years. The most robust subjects remained generally robust (Trajectory A). Some pre-frail subjects tended to frailty (Trajectory B) which may be predicted by age, but also by depression and cognitive impairment. Among the frailest subjects, some evolved toward pre-frail (Trajectory C) and others to more severe frailty (Trajectory D). This was mainly predicted by depression, but also hypertension, and a pathologic cognitive deficit. It is important to understand why some subjects with the same level frailty, evolved to different trajectories. Here we found that among the frailest subjects at baseline, only depression can predict the evolution toward improvement (Trajectory C) or degradation (Trajectory D). By contrast a cognitive decline was not discriminant between trajectories C and D.

Previous study showed evidence for an association between frailty and cognitive impairment and this was supported by some potential mechanisms from brain neuropathology and hormonal dysregulation to cardiovascular risk and psychological factors (Robertson et al., 2013). In a prospective study in China, the incidence rate of dementia was higher in frail subjects (determined using a multidimentional frailty definition) compared with non-frail subjects (Li et al., 2020). In another prospective study, mental decline was shown to be independently predicted by frailty in the younger subjects (65–75 years old) but not in the older (> 75 years old) (Turusheva et al., 2016). Here we found that a pathologic cognitive deficit as assessed by the MMSE score could predict the trajectories of frailty.

Depression is also a common condition in older people, but may be under-diagnosed and inadequately treated. Previous study conducted suggested that frailty was an independent predictor of depressive symptoms in community-dwelling older people (Makizako et al., 2015).

There is evidence that depression and frailty are strongly related (Lakey et al., 2012; Lohman et al., 2017), and both lead to impaired functional status, increase mortality and greater use of health care services. Consistently, emotional and affective dimensions strongly influence the individual's vulnerability and should be taken into account when addressing the multidimensional syndrome of frailty. Pathological emotional responses (e.g. anxiety and depression) have been found to considerably affect the onset, course over time, and severity of various medical conditions including heart disease, hypertension, cancers, and infectious diseases as result of well-established interactions with nervous, endocrine, and immune systems.

It should be noted that other potential predictive factors of frailty were not significant in these models. In a population-based cohort of older adults, several social and behavioural factors (education, marital status, living arrangements, smoking status and alcohol use) were associated with a higher frailty trajectory over time, with stronger associations observed in younger ages (Chamberlain et al., 2016). In a cross-sectional survey of subjects aged ≥60 yrs, old age, low education and marital status were the common risk factors of cognitive, psychological and/or functionally frailty (Zhang et al., 2020). In the FREEDOM-LNA cohort, educational level and the marital status (being alone or in couple), smoking, and alcohol use were not significant risk factors in univariate or multivariate analyses. Regarding cardiovascular risk factors, only hypertension could predict frailty trajectories independently of age, sex, depression, or cognition in our cohort. Diabetes, dyslipidaemia or obesity were not significant risk factors in univariate and multivariate analyses. We found that hypertension could significantly predict the frailty trajectory (Trajectories C and D). Although hypertension is a significant cardiovascular risk factor, the association between hypertension and frailty syndrome in older people is unclear. Few longitudinal studies have assessed the impact of hypertension on incident frailty, providing conflicting results. Treating hypertension in frail older persons might have no benefits and could lead to negative outcomes (Anker et al., 2019; Vetrano et al., 2018). On the contrary, others advocate intensive control of hypertension to influence the trajectory of frailty (Aprahamian et al., 2018).

Taken together, our results indicate that cognition and emotional/affective status are major determinants of individual frailty and clinical outcomes. Thus, the dysfunctions of these domains should be therefore carefully investigated and managed. According to the literature. (Ding et al., 2017), depressive symptoms and cognitive impairment are potentially modifiable factors to prevent or reduce physical frailty in older people, including the very old. Cognitive impairment, depressive symptoms, poor social support, and poor social integration are potentially modifiable target conditions for population-level health and social

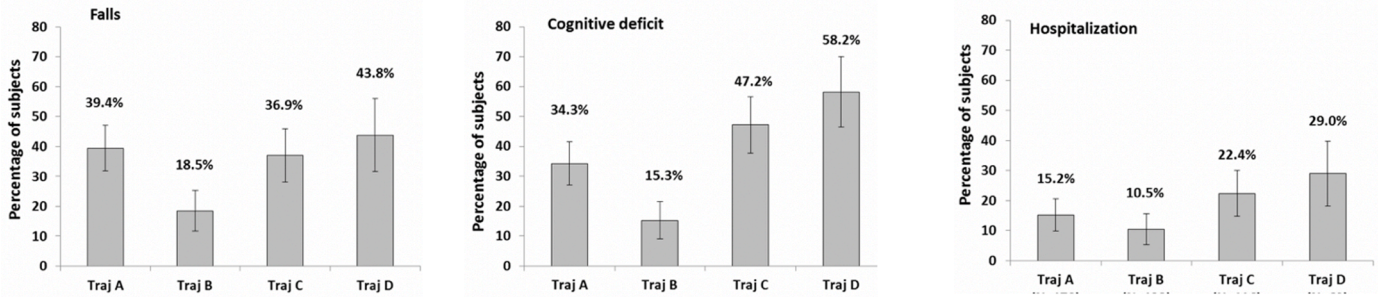

Fig. 2. Clinical outcomes according to frailty trajectories
The rate of clinical outcomes (cognitive deficit as assessed by a MMSE < 24, falls or hospitalization since the previous visit) with 95% confidence interval is indicated for each trajectory. The total number of participants in each trajectory is indicated in brackets along the x-axis. Dataset for clinical outcomes * $N = 472$ for cognitive deficit; $N = 459$ for falls and $N = 496$ for hospitalization.

interventions to reduce future physical frailty in older people (Ding et al., 2017). By contrast, a recent guideline did not recommend systematic cognitive therapy for the treatment of frailty (Lim et al., 2019), because of lack of evidence. Our study suggests to reinforce cognitive and psychosocial support to reduce the risk of severe cognitive decline and depression associated with pejorative frailty trajectories. This is consistent with a small study showing that cognitive therapy improves frailty, gait speed, knee strength, and exhaustion levels (Ng et al., 2015). Differently from cognitive disorders, emotional and affective disturbances may be more responsive to diverse non-pharmacological (e.g. psychotherapy) and pharmacological interventions. These strategies may positively influence the overall health status by improving the capacity to cope with stressors and dysfunctions. Both cognitive and emotional intervention in frail older subjects should be addressed in common with reinforcement of physical activity since physical activity is known to protect against early cognitive decline and poor cognition in late life, and improved mood and well-being (Landi et al., 2010). Exercising every day was found a protective factor against multi-frail, cognitive and functionally frail, and a lower level of physical activity was a risk factor for various frailty phenotypes (Zhang et al., 2020).

Regarding clinical adverse outcomes, a systematic review and meta-analysis in community-dwelling older subjects confirmed that frail older subjects were more likely to experience recurrent falls compared with robust older subjects (Cheng & Chang, 2017) and frail older people exhibited the highest risk for hospitalization, following by prefrail and robust older people (Chang et al., 2018). Some authors showed that frailty was a risk factor for incident geriatric cognitive disorders and thus could be a novel modifiable target in early cognitive impairment (Borges et al., 2019).

By contrast, another prospective cohort study of community-dwelling older subjects, did not confirm that frail and prefrail status were good predictors of mental decline as well as dependency, physical decline or mortality (Turusheva et al., 2016). Here, we showed that frailty trajectories were significantly associated with various clinical outcomes measured at last visit including pathologic cognitive deficit, falls or hospitalization, with higher incidences in poor frailty trajectories. Depression could explain a significant proportion of nursing home admission or a serious fall over time associated with frailty, which is consistent with our study (Lohman et al., 2017).

Our study has some limitations to be mentioned. This population is representative of the older subjects living in communities who asked for a comprehensive geriatric assessment plan. Thus, the population was relatively aged, and a high proportion presented with a high GDS score or high MMSE score at baseline which may be confounding factors. Since all patients received a comprehensive geriatric assessment, this might have impacted the clinical outcome (Puts et al., 2017). However, our analyses were adjusted for the implementation of a geriatric intervention plan which included individualized medical and psychosocial support, and we did not found any impact on frailty trajectories in univariate or multivariate analyses. There are still some debates about the most effective method to assess frailty (Bongue et al., 2017; Welstead et al., 2021), but Fried's criteria have been validated as a broad screening test of physical frailty, and was shown to predict vulnerability and mortality (Fried et al., 2001). Cognitive impairment and depression were assessed using questionnaire (GDS, and MMSE). These questionnaires are well known and commonly used in clinical research and clinical practice. Falls trajectories also were demonstrated to be good indicators of cognitive deficit and depression (Tchalla et al., 2014).

5. Conclusions and implications

This cohort study allowed to predict frailty trajectories among community-dwelling older subjects. The more significant predictive factors for poor frailty trajectories were cognitive impairment and dementia. Frailty trajectories were associated with clinical outcomes including falls, hospitalization, and potential cognitive deficits/dementia. This emphasizes the need for adequate measures to limit depression and to maintain or improve cognition in older subjects.

Funding

No funding was obtained for this study.

Impact statement

We certify that this work is novel. This research specifically adds to the literature that Hypertension was an additional factor allowing to discriminate between frailty trajectories (frail regressing to pre-frail) and (frail progressing to more severe frailty).

Key points

- This cohort study allowed to determine frailty trajectories among community-dwelling older subjects.
- The more significant predictive factors for poor frailty trajectories were cognitive impairment and dementia. Hypertension was discriminate factor between (frail regressing to pre-frail) and (frail progressing to more severe frailty).
- Frailty trajectories were associated with clinical outcomes including falls, hospitalization, and pathologic cognition.

Why does this paper matter?

This study determines four frailty trajectories among community-dwelling older adults. The modifiable predictive factors associated with poor frailty trajectory were hypertension, cognitive deficit and depressive symptoms.

Ethics approval and consent to participate

The study protocol was reviewed and approved by the local Institutional Review Board (CEREES, Limoges; Approval number: TPS 429669). The protocol was also approved by the French Data Protection Authority (CNIL) insuring protection of individualized data according to the French law. Informed consent for data processing was obtained from all subjects (or legal representatives). All procedures were carried out in accordance with the 1964 Helsinki Declaration and its later amendments.

Consent to publish

Not Applicable.

Availability of data and materials

Doctor Sophie Boyer, PhD (sophie.boyer@chu-limoges.fr) who should be contacted if someone wants to request the data.

Authors contributions

AT, NC, CG, CLM, SB.: Conceptualization, Methodology, Software, Formal analysis, Data curation, Writing – original draft – review & editing. KR, ND, MDC and MLL : Methodology, Writing – review & editing. All authors read, revised and approved the final manuscript.

Data statement

The data has not been previously presented orally or by poster at scientific meetings.

Declaration of Competing Interest

The authors declare no competing interests.

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