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ORIGINAL ARTICLE

Association of a 7-year percent change in fat mass and muscle mass with subsequent cognitive dysfunction: the EPIDOS-Toulouse cohort

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Abstract
Background Cognitive dysfunction and changes in body composition share common pathophysiological pathways. The aim of the present paper was to evaluate whether changes in appendicular muscle mass (AMM) and fat mass (FM) are associated factors with an increased risk of cognitive dysfunction in community-dwelling older women.
Methods A nested case–control study was performed in 181 women aged 75 years and older from a subsample of the *Epidemiologie de l'Osteoporose* participants from Toulouse. Body composition parameters at inclusion and 7 years later (assessed by dual energy X-ray absorptiometry), and the presence of cognitive dysfunction (dementia and mild cognitive impairment) at 7 years of follow-up, assured by two memory experts based on best clinical practice and validated criteria, were obtained. Multivariate logistic regression models assessed the association of percent change in AMM and FM with risk of cognitive dysfunction.
Results At 7 years of follow-up, 15 participants suffered from dementia, 6 suffered from mild cognitive impairment, and 160 were cognitively normal. Neither body composition changes nor gait speed was found to be statistically associated with cognitive dysfunction after controlling for potential confounders. Only age, over 85 years, was associated with an increased risk of subsequent cognitive impairment (odds ratio 3.10; 95 % confidence interval 1.07–8.87).
Conclusions No significant association could be evidenced between changes in body composition and cognitive dysfunction. Due to the small sample size, statistical power could be an issue. The study could also suggest the possibility that the risk of cognitive dysfunction is not mediated by changes in body composition.

Keywords Body composition · Fat mass · Muscle mass · Cognitive decline · Old age

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1 Introduction

Although recent surveys evidenced a relationship between changes over time in age-related body composition parameters (i.e., fat mass or muscle mass), cognitive decline, and brain atrophy, suggesting common underlying pathophysiological mechanisms, supporting data to confirm this hypothesis are still scarce and controversial [1–5].

Up to date, all surveys have presented data based on a single body composition assessment, so that the dynamic nature of muscle mass (MM) or fat mass (FM) has not been taken into account. This single-assessment approach could dampen the association between body composition and cognitive dysfunction [6]. Indeed, changes in MM over time, rather than a single-point assessment, could be associated with cognitive decline as shown for other adverse clinical events like onset of mobility disability [7]. In the line with this hypothesis, changes in body mass index (BMI) over time

are associated with cognitive decline, and the presence of cognitive decline or dementia has reciprocally been associated with involuntary weight loss [8].

The hypothesis, of the present paper, is that the dynamic nature of body composition (assessed by percentage change in MM and FM over time) rather than a single assessment might be related to subsequent risk of cognitive dysfunction in community-dwelling older women. To this end, a nested case–control study was performed in the *Epidemiologie de l'Osteoporose* (EPIDOS) study.

2 Methods

2.1 EPIDOS cohort

Data are from the EPIDOS cohort, a French observational prospective multicenter cohort study designed to evaluate risk factors for hip fractures in community-dwelling women aged 75 years and older. Details about the study have previously been published [9]. Briefly, between January 1992 and January 1994, 7,598 women from five French cities volunteered to participate in EPIDOS. Women unable to walk independently (aids were allowed), with history of femoral neck fracture or hip replacement, or were institutionalized were excluded. Local ethics committee of the participating centers approved the study, and each participant provided informed consent. An additional study on dementia risk factors in 1999–2000 was proposed to all the volunteers from Toulouse. In this new investigation, data on cognitive performances were collected during a standardized interview by trained memory experts, and some of the participants also volunteered for a new body composition assessment by dual energy X-ray absorptiometry (DXA) [10, 11].

2.2 Study sample

From the participants of the EPIDOS Toulouse center (n=1,492), a subsample with full cognitive assessment at 7 years of follow-up (n=714), also with a new DXA assessment (n=181) were considered for the present analyses (Fig. 1).

2.3 Assessment of baseline covariates

Participants underwent standardized visits, including administration of structured questionnaires, clinical examination, and assessment of physical performance. Visits were conducted by trained nurses. Education was defined by a dichotomous variable (i.e., graduate versus not). Self-reported recreational activities (such as walking, gymnastics, cycling, swimming, or gardening), their type, frequency, and duration were also recorded. The variable "physically active" was defined to approximately identify the fittest 20 % of the study sample, which is equivalent at having practiced at least a 1-h activity or more per week over the past month [4, 6]. A standardized assessment of gait speed was performed at baseline. Participants were asked to perform a 6-m walk at their usual pace. Walking aids were allowed. Testing began when the command "start" was given by the assessor, and time (in seconds) required to complete the task was recorded. The faster of two walks was retained for the present analysis.

2.4 Assessment of body composition parameters (baseline and at 7 years)

Body composition parameters were assessed at baseline (1992–1994) using a DXA scanner (Lunar DPX-Plus, GE Lunar Corp., Madison, WI) and a different scan at 7 years (1999–2000) of follow-up (QDR 4500 W Hologic, Waltham, MA). DXA measurements were performed by a trained technician, and the DXA machines were regularly calibrated. The muscle mass index (MMI; appendicular lean mass, in kilograms, relative to height squared) and the fat mass index (FMI; total fat mass, relative to height squared) were obtained for each participant during the two assessments [12]. As height changes over time, square height was derived from the height (in meters) measured at each assessments. The change in the MMI and the FMI was obtained by a simple subtraction, expressing the difference of each of the indexes as a percent change of the baseline value. Although different DXA machines were used, no adjustment of body composition values was performed as all participants underwent the same study procedure and due to the fact that the magnitude of linear calibration would identically affect the delta of body composition of all participants. Cross-calibration of the two DXA machines was performed in the year 2000 using the body composition assessment (bone, muscle, and fat mass) of seven healthy female volunteers. There were no statistical differences in between the measurements when comparing fat mass and lean mass, so that the data obtained of the two DXA machines could be comparable [13].

2.5 Assessment of cognitive performances at 7 years of follow-up

At the seventh year of follow-up, all cases of dementia were recorded during a single structured and standardized home-based interview. During this visit, cognitive performances were assessed with the Mini-Mental State Examination [14], the Grober and Buschke test [15], and the IADL test [16]. In a double-blind manner, two memory specialists established the diagnosis of dementia or mild cognitive impairment. Clinical suspicion of dementia was diagnosed using the *Diagnostic and Statistical Manual of Mental Disorders, 4th ed.* criteria [17]. Mild cognitive impairment (MCI) was based on the Peterson criteria [18].

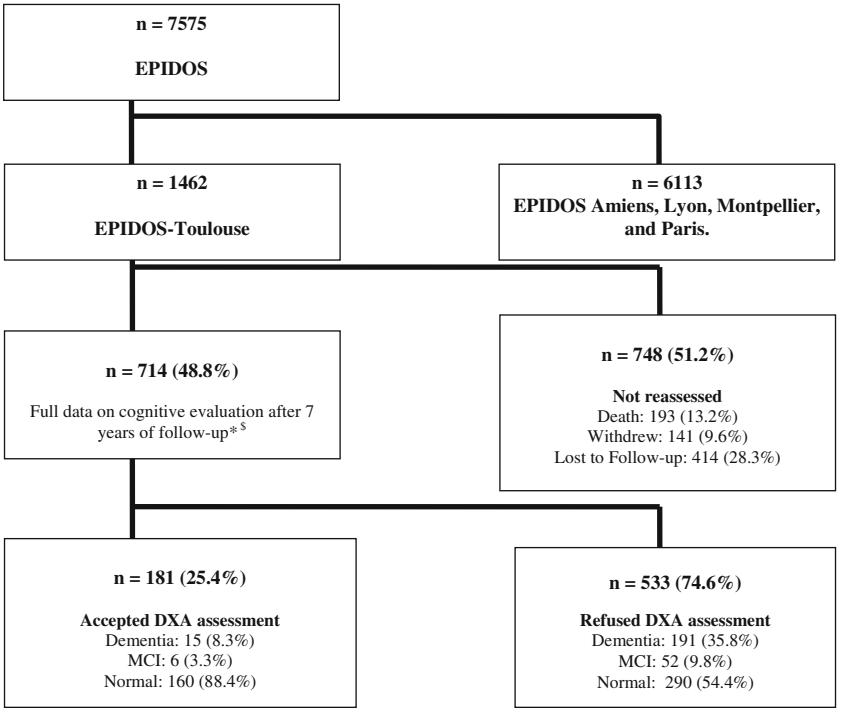

Fig. 1 Flow chart of study population. MCI stands for mild cognitive impairment; dementia stands for all subtypes of dementia (Alzheimer's disease, vascular or mixed dementia, Lewy corps dementia, fronto-temporal dementia, Parkinson dementia). The *asterisk* indicates that the diagnosis of dementia at 7 years was established after a standardized home-based assessment with cognitive performances evaluated by the Mini-Mental State Examination, Grober and Buschke test, and instrumental activities of daily living tests. The *dollar sign* indicates that the baseline cognitive impairment was assessed using the Short Portable Mental Status Questionnaire with a score of 8 or above as the validated cutoff value for normal cognitive functioning

2.6 Statistical analyses

Data were analyzed with STATA v11.0 (Stata Corp., College Station, TX). Variables were compared according to the presence/absence of dementia using Student's *t* test or chi-square statistics as appropriate. Multivariate logistic regression analyses assessed the association of change in the MMI and the FMI with subsequent dementia risk. The models were adjusted for age and gait speed, known risk factors for dementia onset [4].

3 Results

The main baseline and follow-up characteristics of the study participants according to their dementia status are presented in Table 1. Of 181 women, 21 (11.6 %) suffered from cognitive dysfunction (6 presented MCI and 15, dementia). A nonsignificant difference was found for most of the studied variables (i.e., education, physical activity, percent change in MMI and FM) across cognitive dysfunction groups. Only age, gait speed, and difference in BMI over time were found statistically significant. Participants with cognitive dysfunction at 7 years presented a significant lower MMSE score. All participants had a score over 15, so that all cases of dementia were at the mild and moderate stages of the disease.

Results of the adjusted regression models are presented in Table 2. No statistical association could be evidenced between cognitive dysfunction and percent change in body composition (expressed in tertiles, *p* for trend 0.18). Neither gait speed nor change in BMI was associated with an increased risk of cognitive dysfunction, suggesting that the results for percent changes in body composition in the present study may be underpowered. Only age, over 85 years, was associated with an increased risk of cognitive dysfunction (odds ratio (OR) 3.10; 95 % confidence interval (CI) 1.07–8.87).

4 Discussion

In the present analyses, no association could be found between 7-year changes in body composition and cognitive dysfunction. These results are consistent with previous cross-sectional analysis based on sarcopenia definitions related to cognitive dysfunction [6]. And although common underlying pathophysiological mechanisms have been hypothesized, current data do not support the existence of a link between changes in body composition and increased risk of dementia. Another hypothesis suggested by the results of a recent survey (and needing further inquiry) is that body composition could be a prognostic factor for cognitive decline at the dementia stage, with the possibility that changes in body composition occur at later and more severe stages of cognitive decline [5]. It is also possible, like for other critical health outcomes, that performance but not changes in MM or FM are associated with dementia [19, 20].

Finally, the main limit is that the study could be underpowered as evidenced by a nonstatistical association between gait speed and cognitive dysfunction (contradictory with the results performed in a larger EPIDOS population)

Table 1 Characteristics according to the presence of cognitive dysfunction (n=181)

Variables[a]		No cognitive dysfunction[b] (n=160)	Cognitive dysfunction[b] (n=21)	p value[c]
Age		77.8±2.2	79.1±2.2	*0.01*
Age (year)	<80	126 (78.7)	11 (52.4)	*<0.01*
	≥80	34 (21.3)	10 (47.6)	
Body mass index		24.2±3.3	24.2±2.9	0.99
Body mass index at 7 years		24.3±3.6	22.8±3.6	0.07
MMSE scores at 7 years		28.4±1.4	22.5±3.3	*<0.01*
Certificate of graduation	Graduate	146 (91.2)	18 (85.7)	0.41
	Less than graduate	14 (8.8)	3 (14.3)	
Physically active	Yes	57 (35.8)	6 (28.6)	0.51
	No	102 (64.2)	15 (71.4)	
Gait speed (m s^{-1})	>0.8	121 (75.6)	11 (52.4)	*0.02*
	≤0.8	39 (24.4)	10 (47.6)	
Tertiles of percent change in the MMI (%)	−37.3 to −9.1	51 (83.6)	10 (16.4)	0.34
	−9.2 to −3.9	54 (90.0)	6 (10.0)	
	−3.8 to 19.4	55 (91.7)	5 (8.3)	
Tertiles of percent change in the FMI (%)	−71.5 to −9.8	51 (83.6)	10 (16.4)	0.34
	−9.5 to 3.6	54 (90.0)	6 (10.0)	
	3.8 to 144.5	55 (91.7)	5 (8.3)	
Difference in body mass index		0.2±1.7	−1.0±2.2	*<0.01*

MMI muscle mass index (in kilograms/squared height), *FMI* fat mass index (in kilograms/squared height), *MMSE* Mini-Mental State Examination (score over 30). Italics represent a statistical significant difference

[a] Age, body mass index (in kilograms/squared height), certificate of graduation, physically active, and gait speed are baseline characteristics

[b] Results are presented as number (percentage) or mean ± standard deviation

[c] Based on Student's or chi-square statistics or nonparametric tests as appropriate

and by the large CI found for the variables [4]. Due to the small study sample, dementia and MCI both were categorized in cognitive dysfunction. This could dampen the association as a minority of MCI participants will eventually not evolve to a dementia stage. The generalizability of the results is also challenged by the restriction of the EPIDOS study to only relatively healthy older women; therefore, our findings might not be applicable to men, different settings, and other health profiles. Even more, as shown in the flow chart, participants suffering from dementia at 7 years of follow-up were more likely to refuse a new DXA assessment than cognitively intact participants. This issue could affect the possible association in the EPIDOS study. Although the DXA assessments were comparable during the cross-calibration performed during the follow-up study at 7 years, the results need to be interpreted with caution. The main limit is that no cross-calibration could be performed at baseline. Software upgrades, calibrations, and tube changes over the 7-year period could render the baseline assessment not comparable. Although not true for fat mass, and lean mass, the significant bone measurement differences found in the cross-calibration could be explained by these factors.

Table 2 Association of percent change in muscle mass and fat mass with cognitive dysfunction

Variables		Adjusted model OR (95 % CI)	p value	
			For OR	For trend
Age (year)	<80	Ref	–	–
	≥80	3.10 (1.07–8.87)	*0.04*	
Gait speed (m s^{-1})	>0.8	Ref	–	–
	≤0.8	2.21 (0.79–6.18)	0.13	
7-year difference in BMI		0.80 (0.59–1.08)	0.14	–
Tertiles of percentage change in MMI (%)	−37.3 to −9.1	2.08 (0.56–7.71)	0.27	0.18
	−9.2 to −3.9	1.07 (0.27–4.20)	0.93	
	−3.8 to 19.4	Ref	–	
Tertiles of percentage change in FMI (%)	−71.5 to −9.8	1.66 (0.34–8.23)	0.54	0.18
	−9.5 to 3.6	2.72 (0.64–11.67)	0.18	
	3.8 to 144.5	Ref	–	

OR odds ratio, *CI* confidence interval, *MMI* muscle mass index (in kilograms/squared height), *FMI* fat mass index (in kilograms/squared height), *BMI* body mass index (in kilograms/squared height)

5 Conclusions

In this cohort of community-dwelling independent older women, percent change in body composition parameters was not found to be associated with cognitive dysfunction. Differently, age was confirmed to be associated with cognitive decline. The analyses suggest that the study might be underpowered, or that no association exists between changes in body composition and cognitive dysfunction. Further studies on the topic are needed to confirm these findings, including larger samples including more DXA assessments over time or participants with cognitive dysfunction at a later dementia stage.

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Conflict of interest Gabor Abellan van Kan, Matteo Cesari, Sophie Gillette-Guyonnet, and Bruno Vellas declare that they have no conflict of interest. Charlotte Dupuy is supported by CIFRE PhD studentship (no. 2010/1072) which was jointly funded by the Nutrition Clinique and the French National Association of Technical Research (ANRT). Yves Rolland is board member from Nutritia.

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