

# Dynapenic Abdominal Obesity as a Risk Factor for Metabolic Syndrome in Individual 50 Years of Age or Older: English Longitudinal Study of Ageing

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## Abstract

**OBJECTIVES:** To analyse whether dynapenic abdominal obesity is a risk factor for Metabolic syndrome (MetS) and its components in individuals 50 years of age or older.

**DESIGN:** A longitudinal study was conducted with an eight-year follow-up.

**SETTING:** Representative sample of community-dwelling participants of the English Longitudinal Study of Ageing (ELSA).

**PARTICIPANTS:** 3,952 individuals free of MetS at baseline.

**MEASUREMENTS:** Dynapenic abdominal obesity was defined based on waist circumference (> 102 cm for men and > 88 cm for women) and grip strength (< 26 kg for men and < 16 kg for women). The participants were classified as non-abdominally obese/non-dynapenic (NAO/ND - reference group), abdominally obese/non-dynapenic (AO/ND), non-abdominally obese/dynapenic (NAO/D) and abdominally obese/dynapenic (AO/D). The outcome was the incidence of MetS based on the presence of three or more of the following criteria: hypertriglyceridemia, hyperglycaemia, low HDL cholesterol, arterial hypertension or body mass index  $\geq 30$  kg/m<sup>2</sup> throughout eight-year follow-up. Additionally, the incidence of each component of MetS was also analyzed. Poisson regression models were run and controlled for sociodemographic, behavioural and clinical variables.

**RESULTS:** The mean age of the participants was 65 years and 55% were women. The prevalence of AO/ND, NAO/D and AO/D were 35.3, 4.3 and 2.2%, respectively. At the end of follow-up 558 incident cases of MetS were recorded. The adjusted model demonstrated that although abdominal obesity was a risk factor for MetS (IRR: 2.26; 95% CI: 1.87 – 2.73), the IRR was greater in AO/D individuals (IRR: 3.34; 95% CI: 2.03 – 5.50) compared with ND/NAO group. Furthermore, ND/AO was a risk factor for incidence of hypertriglyceridemia (IRR: 1.27; 95% CI: 1.06 – 1.52), hyperglycaemia (IRR: 1.41; 95% CI: 1.18 – 1.69), low HDL cholesterol (IRR: 1.70; 95% CI: 1.32 – 2.19) and BMI  $\geq 30$  kg/m<sup>2</sup> (IRR: 2.58; 95% CI: 2.04 – 3.26) while D/AO was a risk factor for hyperglycaemia (IRR: 1.78; 95% CI: 1.02 – 3.10), low HDL cholesterol (IRR: 2.36; 95% CI: 1.10 – 5.08), and BMI  $\geq 30$  kg/m<sup>2</sup> (IRR: 2.79; 95% CI: 1.38 – 5.62).

**CONCLUSIONS:** Dynapenic abdominal obesity increases the risk of MetS, with a higher IRR compared to obesity alone. The understanding of this synergic action could guide specific clinical strategies, enabling the prevention of metabolic changes that can lead to cardiovascular disease, disability and death.

**Key words:** Dynapenia, abdominal obesity, metabolic syndrome, grip strength, ELSA study.

**Abbreviations:** AO/D: abdominally obese/dynapenic; AO/ND: abdominally obese/non-dynapenic; MetS: metabolic syndrome; NAO/D: non-abdominally obese/dynapenic; NAO/ND: non-abdominally obese/non-dynapenic.

## Introduction

Metabolic syndrome (MetS) is defined as a set of interconnected factors that increase the risk of cardiovascular disease and diabetes (1), such as elevated blood glucose, high blood pressure, high triglyceride level, low levels of high-density lipoprotein (HDL) and obesity (2). An estimated 25% of the world population has MetS (3), with the prevalence ranging from 22 to 44%, depending on the criteria used to define the condition (4, 5). The different definitions of MetS are those proposed by the World Health Organization (WHO), American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI), National Cholesterol Education Program Adult Treatment Panel III (NCEP: ATP III), International Diabetes Federation (IDF) as well as others. The difference among definitions resides in the essential factor of establishing MetS, as insulin resistance in the WHO definition or abdominal obesity in the NCEP: ATP III and IDF definitions, as well as the use of different cut-off points for waist circumference and blood pressure. Among the several attempts to establish a consensus on the definition, the most widely accepted is the 2009 Consensus, which incorporates the IDF and AHA/NHLBI definitions (2, 6) and has abdominal obesity as a key (but not necessary) component as well as hypertriglyceridemia, hyperglycemia, high blood pressure and low HDL cholesterol. The clinical diagnosis is performed in the presence of three or more of these components.

The metabolic changes that characterize MetS have always been largely attributed to obesity (7). However, there is increasingly consistent evidence that adipocyte hypertrophy leads to an increase in muscle fat infiltration that impairs musculoskeletal structure, altering contractility, limiting muscle fiber activation, and disrupting the excitation-contraction coupling. This, in turn, results in neuromuscular strength loss known as dynapenia, which can occur even without a reduction

in muscle mass (8–11).

Although not yet fully understood, this deposition of adipose tissue within the muscle, which impairs muscle strength, is believed to result from changes such as inflammation, with macrophage infiltration into the muscle, mitochondrial dysfunction, leptin signaling deficiency, increased levels of glucocorticoids, alterations in estrogen and testosterone hormone levels, which could also trigger systemic metabolic changes that increase cardiovascular risk (12, 13).

The combination of abdominal obesity and dynapenia, known as dynapenic abdominal obesity, has been shown to be an important risk factor for morbidity and mortality, including cardiovascular mortality (14, 15). The associated increases in proinflammatory cytokines (adipokines and myokines), oxidative stress, insulin resistance and a reduction in physical activity are factors that contribute to the synergic relationship between dynapenia and abdominal obesity (16, 17). These events can exert a negative influence on the metabolism of lipids and carbohydrates, the renin-angiotensin system and sympathetic activity (6, 18) increasing the risk of developing MetS.

Cross-sectional studies have analysed the relationship between dynapenic abdominal obesity and metabolic health in older people. Sénechal and colleagues (19) found that abdominally obese/non-dynapenic (AO/ND) and abdominally obese/dynapenic (AO/D) individuals were more likely to have MetS compared to non-abdominally obese/non-dynapenic (NAO/ND) individuals. Alexandre and colleagues (20) also found that AO/D individuals were more likely to have MetS than their NAO/ND counterparts. Aubertin-Leheudre and colleagues (21) did not come to the same conclusion, but the analyses did not take the simultaneous occurrence of abdominal obesity and dynapenia into account to test the combined effect on the likelihood of MetS.

To the best of our knowledge, no longitudinal studies have evaluated dynapenic abdominal obesity as a risk factor for MetS in the population 50 years of age or older. Therefore, the aim of the present investigation was to analyse dynapenic abdominal obesity as a risk factor for MetS and its components in individuals 50 years of age or older considering an eight-year follow-up of participants of the English Longitudinal Study of Ageing.

## Methods

### *Study population*

ELSA began in 2002 using multistage, stratified probability sampling with postcode sectors selected in the first stage and household addresses selected in the second stage. ELSA interviews occur every two years with the administration of questionnaires. Health examinations, blood collection for the determination of biochemical measures and performance tests occur every four years with the visit of a nurse to the participants' homes. All participants of ELSA signed a statement of informed consent and all waves of the study received approval from the London Multicentre Research

Ethics Committee [MREC/01/2/91]). Detailed descriptions of the study, sampling procedures and data collection have been published previously and are described in greater detail in the supplementary material (Study Population Section) (22).

The present study involved the analysis of 3,952 participants of ELSA who were free of MetS at baseline (Supplemental Figure 1). The development of MetS was investigated in an eight-year follow-up period (2004/2005- 2012/13).

### *Dynapenic abdominal obesity*

Abdominal obesity was determined based on waist circumference (WC), which was measured using a flexible, non-elastic, metric tape positioned at the midpoint between the last rib and iliac crest with the participant standing, arms alongside the body, at the end of the expiratory phase with the abdomen relaxed. Abdominal obesity was defined as WC > 102 cm for men and > 88 cm for women (23).

Dynapenia was determined based on grip strength, which was measured using a Smedley handgrip dynamometer (range: 0 to 100 kg) adjusted to the hand size of each participant. The test was performed with the participant standing, arm alongside the trunk and elbow flexed at 90 degrees. Three trials were performed using each hand, with a one-minute rest period between repetitions (24). The largest strength value for the dominant hand was considered. Dynapenia was defined as grip strength < 26 kg for men and < 16 kg for women, which is the cut-off point recommended by the Foundation for the National Institute of Health Sarcopenia Project (FNIH) as the best indicator of muscle weakness in older people (25).

The determinations of abdominal obesity and dynapenia were used to classify the individuals into four groups: non-abdominally obese/non-dynapenic (NAO/ND), abdominally obese/non-dynapenic (AO/ND), non-abdominally obese/dynapenic (NAO/D) and abdominally obese/dynapenic (AO/D) (20).

### *Outcome Measure*

MetS was defined based on the recommendations of the 2009 Consensus (IDF and NHLBI) and self-reports of the use of medications (20). Individuals with at least three of the following criteria were considered as having MetS: hypertriglyceridemia (fasting triglycerides  $\geq$  150 mg/dl or use of omega-3 and/or fibrates and/or nicotinic acid); hyperglycemia (fasting glucose  $\geq$  100 mg/dl or use of oral hypoglycemic agent and/or insulin); low HDL cholesterol (< 50 mg/dl for women and < 40 mg/dl for men or use of nicotinic acid to increase HDL cholesterol and/or fibrates); arterial hypertension (resting systolic pressure  $\geq$  130 mmHg and/or resting diastolic pressure  $\geq$  85 mmHg or use of antihypertensive agent). The obesity measure was modified from the original definition to avoid collinearity, once obesity would constitute both, the exposure and the outcome of the study. Therefore, body mass index (BMI) was estimated using weight in kilograms divided by the square of height in meters ( $\text{kg}/\text{m}^2$ ), and use as cutoff point  $\geq$  30  $\text{kg}/\text{m}^2$ , which is part of

World Health Organization (WHO) (26) and International Diabetes Federation (IDF) (1, 27) definitions. This decision was made since BMI provides estimates of adiposity and makes independent contributions to cardiovascular risk assessment along with waist circumference (4). It is a simple, non-invasive approach widely used in clinical practice to identify individuals at risk of cardiovascular disease and mortality (28, 29) and it has demonstrated consistency in assessing this risk across different populations (30). The collinearity between BMI and WC was tested, and the Variance Inflation Factor (VIF) was 1.78, indicating that there was no collinearity between these two variables, allowing us to use BMI in the analyses.

Individuals with MetS at baseline were excluded. Incident cases were those that developed three or more of the components throughout the eight-year follow-up period. At the end of this period, the individuals were classified as “remained without MetS during follow-up” or “developed MetS during follow-up”. Furthermore, the incidence of each component of MetS was also analysed.

### Control variables

The control variables were selected based on previous studies that analysed factors associated with dynapenic abdominal obesity and MetS (6, 7, 31, 32). All control variables were measured at baseline. The sociodemographic variables were age (continuous), marital status (with or without conjugal life), family wealth (classified in quintiles) and schooling (0 to 11 years; 12 to 13 years; > 13 years).

The behavioural characteristics were smoking (non-smoker, ex-smoker or smoker) and weekly frequency of alcohol intake: “never or rarely” ( $\leq 1$  once per week); “frequently” (two to six times per week); “daily” (seven times per week) or “not declared” (24). Physical activity level was assessed using three questions about the frequency and intensity of physical activity that were extracted from the Physical Activity and Sedentary Behaviour Assessment Questionnaire (PASBAQ). The participants reported the frequency (once per week, more than once per week, one to three times per month and hardly ever or never) of vigorous exercises (e.g., running, swimming, cycling, tennis, aerobics, weightlifting or digging), moderate exercises (e.g., gardening, washing the car, walking at a moderate pace, dancing, or stretching) and light exercises (vacuuming, washing clothes or home repairs). Physical activity was classified as inactive (no weekly activity); low (only light activity at least once per week); moderate or vigorous (moderate or vigorous activity at least once per week) (27). The questions from the PASBAQ were validated by the Health Survey for England (33) and have been widely used in previous publications (15, 34–36).

Appendicular skeletal muscle mass (ASMM) was determined using the Lee equation (37). This equation was validated by Al-Gindan et al. (38) using whole-body magnetic resonance as a reference, finding a coefficient of determination  $R^2$  of 0.85 for both sexes. The equation has been previously employed in the ELSA Study to assess the effect of multimorbidity on the risk of sarcopenia onset (39) and the effect of sarcopenia

on mortality risk (40). After the estimation of ASMM, the appendicular skeletal muscle mass index (ASMMI) ( $\text{kg}/\text{m}^2$ ) was calculated. Low muscle mass (LMM) was considered when the ASMMI was  $< 9.36 \text{ kg}/\text{m}^2$  for men and  $< 6.73 \text{ kg}/\text{m}^2$  for women. ASMMI values were defined based on the 20th percentile of the sample distribution (41, 42).

Clinical conditions were recorded based on self-reports of stroke and heart disease. Depression was investigated using the Center for Epidemiological Studies-Depression Scale, for which a score of  $\geq 4$  was considered indicative of the presence of depressive symptoms (43).

### Statistical analyses

The characteristics of the sample were expressed as means and proportions. Differences among the four groups formed according to abdominal obesity and dynapenia status were evaluated using the chi-square test, ANOVA and the Bonferroni post hoc test. A p-value  $< 0.05$  was considered indicative of statistical significance.

Poisson regression models were used for the analysis of the association between dynapenic abdominal obesity and development of MetS with the NAO/ND group as reference. Occurrence of MetS was the development of three or more components of MetS during the eight-year follow-up period. Additionally, five Poisson models were conducted to analyze the association between dynapenic abdominal obesity and each component of MetS incidence.

Control variables with a p-value  $< 0.20$  in the bivariate analyses were incorporated into the multiple models using the stepwise forward method and those with a p-value  $< 0.05$  were maintained in the final model. All analyses were conducted with the aid of the STATA 15.0 SE statistical package (StataCorp, College Station, TX, USA).

The paper is reported following the STROBE Statement (44), (Appendix 1).

### Results

The 3,952 participants at baseline had a mean age of 65 years. Most were married, had a conjugal life, had a low level of schooling, had a low physical activity level, frequently consumed alcohol and were ex-smokers (Table 1). The AO/ND prevalence was 35.3% (95% CI: 34.0 – 36.8%), the NAO/D was 4.3% (95% CI: 3.7 – 5.0%) and AO/D 2.2% (95% CI: 1.8 – 2.7%). Heart disease (19.3%) was the most prevalent clinical condition, followed by depressive symptoms (11.9%). Mean grip strength and waist circumference were 32.1 kg ( $\pm 11.3$ ) and 91.6 cm ( $\pm 11.3$ ), respectively. Most participants had a high BMI, with rates of 44.3% and 27.4% for overweight and obesity. Hypertriglyceridemia was found in 39.1% of the individuals, 6.2% had high blood glucose and 4.9% had low serum HDL levels. Regarding blood pressure, 50.7% had systolic pressure equal to or greater than 130 mmHg and 15.6% had diastolic pressure equal to or greater than 85 mmHg.

AO/D individuals were older, were less likely to have a conjugal life, had less income and schooling, were more

**Table 1.** Baseline sociodemographic and behavioural characteristics according to dynapenic obesity status in 3,952 older adults from the English Longitudinal Study of Ageing (2004-05)

	Total n = 3,952	NAO/ND n = 2,297	AO/ND n = 1,396	NAO/D n = 171	AO/D n = 88
<b>Sociodemographic</b>					
Age, years (SD)	65.4 ± 9.3	64.5 ± 8.8	64.9 ± 8.9	76.5 ± 9.8 <sup>ab</sup>	74.7 ± 10.8 <sup>ab</sup>
Sex, female (%)	55.0	49.9	61.7 <sup>a</sup>	59.6 <sup>a</sup>	72.7 <sup>a</sup>
Marital status (with conjugal life), (%)	72.3	74.4	73.6	45.6 <sup>ab</sup>	47.7 <sup>ab</sup>
Family wealth, (%)					
Lowest quintile	12.1	10.1	12.7	27.5 <sup>ab</sup>	27.3 <sup>ab</sup>
2nd quintile	16.9	15.4	17.7	23.4 <sup>a</sup>	30.7 <sup>ab</sup>
3rd quintile	20.8	19.8	22.8	17.0	18.2
4th quintile	22.4	24.2	20.8	15.8 <sup>a</sup>	14.8
Highest quintile	26.3	29.3	23.7 <sup>a</sup>	15.7 <sup>a</sup>	7.9 <sup>ab</sup>
Not applicable	1.5	1.2	2.3	0.6	1.1
Schooling, (%)					
0-11 years	45.9	41.4	49.1 <sup>a</sup>	70.8 <sup>ab</sup>	64.8 <sup>ab</sup>
12-13 years	26.1	27.0	26.3	15.2 <sup>ab</sup>	20.4
> 13 years	28.0	31.6	24.6 <sup>a</sup>	14.0 <sup>ab</sup>	14.8 <sup>ab</sup>
<b>Behavioural</b>					
Physical activity, (%)					
Inactive	3.2	2.2	3.0	10.2 <sup>ab</sup>	14.8 <sup>ab</sup>
Low	94.4	96.0	94.5	82.7 <sup>ab</sup>	80.4 <sup>ab</sup>
Moderate/vigorous	2.4	1.8	2.5	7.1 <sup>ab</sup>	4.8 <sup>a</sup>
Alcohol intake, (%)					
Never/rarely	13.8	12.2	14.4 <sup>a</sup>	22.2 <sup>a</sup>	29.5 <sup>ab</sup>
Frequently	41.2	40.5	43.5	37.4	28.4 <sup>b</sup>
Daily	37.2	40.6	34.5	20.5 <sup>ab</sup>	23.9 <sup>ab</sup>
Not declared	7.8	6.7	7.6	19.9 <sup>ab</sup>	18.2 <sup>ab</sup>
Smoking, (%)					
Non-smoker	38.3	39.8	37.1	32.7	30.7
Ex-smoker	47.4	45.8	48.8 <sup>a</sup>	49.7	60.2 <sup>a</sup>
Smoker	14.3	14.4	14.1	17.6	9.1

Note: Data expressed as proportion, mean and standard deviation. Abbreviations: SD = standard deviation. a. Significantly different from non-abdominally obese/non-dynapenic; b. Significantly different from abdominally obese/non-dynapenic; c. Significantly different from non-abdominally obese/dynapenic ( $p < 0.05$ ).

inactive, had lower alcohol intake, were more likely to be ex-smokers, had a greater frequency of heart disease and depressive symptoms, had a higher waist circumference and BMI, had lower grip strength, had higher triglyceride levels, had lower HDL levels and mean diastolic pressure and had a greater frequency of overweight and obesity compared to the NAO/ND group. In the comparison to the AO/ND group, AO/D individuals were older, were less likely to have a conjugal life, had less income and schooling, were more inactive, had lower alcohol intake, had a greater frequency of heart disease and depressive symptoms and had lower grip strength and lower diastolic pressure. Lastly, AO/D individuals had a higher mean waist circumference and BMI, higher frequency of overweight and higher serum triglyceride levels compared to the NAO/D group.

NAO/D individuals were older, were less likely to have a conjugal life, had less income and schooling, were more inactive, had lower alcohol intake, had greater frequencies of heart disease, stroke and depressive symptoms, lower mean grip strength and waist circumference, lower mean BMI and diastolic blood pressure and a higher frequency of overweight than the NAO/ND group. Compared to the AO/ND group, NAO/D individuals were older, were less likely to have a conjugal life, had less income and schooling, were more inactive, had lower daily alcohol intake, had greater frequencies of heart disease and depressive symptoms, lower mean waist circumference, BMI, grip strength, serum triglyceride levels and diastolic blood pressure, higher serum HDL levels, a greater frequency of normal weight and a lower frequency of overweight.

**Table 2.** Baseline clinical characteristics according to dynapenic obesity status in 3,952 older adults from the English Longitudinal Study of Ageing (2004-05)

	Total n = 3,952	NAO/ND n = 2,297	AO/ND n = 1,396	NAO/D n = 171	AO/D n = 88
<b>Clinical conditions</b>					
Heart disease (yes), (%)	19.3	16.5	16.6	24.0 <sup>a,b</sup>	28.4 <sup>a,b</sup>
Stroke (yes), (%)	2.8	2.7	2.3	6.4 <sup>a</sup>	5.7
Depressive symptoms (yes), (%)	11.9	10.2	12.1 <sup>a</sup>	24.6 <sup>a,b</sup>	28.4 <sup>a,b</sup>
<b>Anthropometry</b>					
Grip strength, kg (SD)	32.1 ± 11.3	33.8 ± 10.6	32.5 ± 10.5 <sup>a</sup>	15.6 ± 5.8 <sup>a,b</sup>	14.3 ± 5.5 <sup>a,b</sup>
Waist circumference, cm (SD)	91.6 ± 11.3	86.4 ± 9.0	100.6 ± 8.7 <sup>a</sup>	84.6 ± 8.6 <sup>a,b</sup>	99.6 ± 8.3 <sup>a,c</sup>
Body mass index, kg/m <sup>2</sup> (SD)	26.2 ± 3.7	24.5 ± 2.6	29.3 ± 3.3 <sup>a</sup>	23.7 ± 2.8 <sup>a,b</sup>	28.6 ± 3.1 <sup>a,c</sup>
Obesity (BMI ≥ 30 kg/m <sup>2</sup> ), (%)	27.4	0.7	30.8 <sup>a</sup>	0.1	29.5 <sup>a</sup>
Low muscle mass (yes), (%)	24.7	34.7	3.6 <sup>a</sup>	67.8 <sup>a,b</sup>	17.0 <sup>a,b,c</sup>
<b>Metabolic profile and blood pressure</b>					
Triglycerides, mg/dl (SD)	140.0 ± 79.4	132.1 ± 76.7	152.7 ± 83.4 <sup>a</sup>	128.7 ± 64.4 <sup>b</sup>	164.2 ± 80.7 <sup>a,c</sup>
Triglycerides ≥ 150, (%)	39.1	36.9	42.9 <sup>a</sup>	33.3	48.9
HDL, mg/dl (SD)	62.2 ± 14.6	63.6 ± 15.5	60.0 ± 12.8 <sup>a</sup>	63.4 ± 14.8 <sup>b</sup>	59.1 ± 12.8 <sup>a</sup>
HDL < 40 men <50 women (%)	4.9	4.6	4.9	5.3	9.1
Glucose, mg/dl (SD)	87.3 ± 11.5	86.9 ± 11.2	88.2 ± 11.9	87.4 ± 10.2	86.0 ± 11.7
Glucose ≥ 100, (%)	6.2	5.7	7.2	4.1	7.9
Systolic pressure, mmHg (SD)	132.5 ± 18.4	131.7 ± 18.5	133.3 ± 17.7	135.8 ± 21.3	132.7 ± 20.0
Systolic pressure ≥ 130 (%)	50.7	50.2	50.5	56.2	56.8
Diastolic pressure, mmHg (SD)	74.3 ± 10.5	74.0 ± 10.5	75.8 ± 10.1 <sup>a</sup>	69.9 ± 10.9 <sup>a,b</sup>	70.2 ± 11.4 <sup>a,b</sup>
Diastolic pressure ≥ 85 (%)	15.6	15.1	17.2 <sup>a</sup>	9.6 <sup>b</sup>	16.2

Note: Data expressed as proportion, mean and standard deviation. Abbreviations: SD = standard deviation. a. Significantly different from non-abdominally obese/non-dynapenic; b. Significantly different from abdominally obese/non-dynapenic; c. Significantly different from non-abdominally obese/dynapenic (p < 0.05).

**Table 3.** Final adjusted Poisson regression model for incidence of metabolic syndrome during eight-year follow-up according to dynapenic abdominal obesity status, ELSA (2004/2005 - 2012/13)

	IRR <sup>1</sup>	95% confidence interval
Non-abdominally obese/non-dynapenic (NAO/ND)	1.00	
Abdominally obese/non-dynapenic (AO/ND)	2.26	1.87 – 2.73
Non-abdominally obese/dynapenic (NAO/D)	1.03	0.50 – 2.12
Abdominally obese/dynapenic (AO/D)	3.34	2.03 – 5.50

Note: 1 Adjusted for age, sex, physical activity, smoking, alcohol intake, schooling and heart disease, appendicular skeletal muscle mass index and depression.

**Table 4.** Final adjusted Poisson regression model for incidence of each component of metabolic syndrome during eight-year follow-up according to dynapenic abdominal obesity status, ELSA (2004/2005 - 2012/13)

	Hypertriglyceridemia	Hyperglycemia	Low HDL cholesterol	Arterial hypertension	Obesity (BMI)
	IRR <sup>1</sup> (95% confidence interval)	IRR <sup>1</sup> (95% confidence interval)	IRR <sup>1</sup> (95% confidence interval)	IRR <sup>1</sup> (95% confidence interval)	IRR <sup>1</sup> (95% confidence interval)
ND/NAO	1.00	1.00	1.00	1.00	1.00
ND/AO	1.27 (1.06, 1.52)	1.41 (1.18, 1.69)	1.70 (1.32, 2.19)	1.05 (0.89, 1.25)	2.58 (2.04, 3.26)
D/NAO	0.81 (0.44, 1.47)	1.07 (0.59, 1.92)	1.01 (0.40, 2.51)	1.01 (0.65, 1.57)	1.21 (0.52, 2.79)
D/AO	1.42 (0.78, 2.59)	1.78 (1.02, 3.10)	2.36 (1.10, 5.08)	1.17 (0.62, 2.23)	2.79 (1.38, 5.62)

Note: 1 Adjusted for age, sex, physical activity, smoking, alcohol intake, schooling and heart disease, appendicular skeletal muscle mass index and depression.

At the end of follow-up 558 incident cases of MetS were recorded. The adjusted Poisson regression model revealed that, compared to the NAO/ND group, the risk of the incidence of MetS was higher in the AO/ND (IRR: 2.26; 95% CI: 1.87 – 2.73) and AO/D (IRR: 3.34; 95% CI: 2.03 – 5.50) groups, with a larger IRR for the AO/D group (Table 3).

In the analysis of each MetS component, abdominal obesity (ND/AO) was a risk factor for incidence of hypertriglyceridemia (IRR: 1.27; 95% CI: 1.06 – 1.52), hyperglycemia (IRR: 1.41; 95% CI: 1.18 – 1.69), low HDL levels (IRR: 1.70; 95% CI: 1.32 – 2.19), and BMI  $\geq$  30 kg/m<sup>2</sup> (IRR: 2.58; 95% CI: 2.04 – 3.26) over the eight years of follow up. On the other hand, dynapenic abdominal obesity (D/AO) was risk factor for the incidence of hyperglycemia (IRR: 1.78; 95% CI: 1.02 – 3.10), low HDL levels (IRR: 2.36; 95% CI: 1.10 – 5.08), and BMI  $\geq$  30 kg/m<sup>2</sup> (IRR: 2.79; 95% CI: 1.38 – 5.62) with IRR of the associations being greater for D/AO than for ND/AO (Table 4).

## Discussion

The present findings demonstrated that AO/D individuals had a 234% higher risk of developing MetS in an eight-year follow-up period compared to NAO/ND individuals. The IRR was larger than that found in the AO/ND group, who had a 126% higher risk of developing MetS compared to the NAO/ND group.

These results are in agreement with findings described in cross-sectional studies. Sénechal and colleagues (19) analysed a sample of 3,007 Americans of the National Health and Nutrition Examination Survey (NHANES) and Alexandre and colleagues (20) analysed a sample of 833 Brazilian older people from the Estudo Saúde, Bem-Estar e Envelhecimento (SABE [Health, Wellbeing and Ageing] Study). The authors of these studies found a greater likelihood of MetS in AO/D and AO/ND individuals compared to NAO/ND individuals, with a larger effect size for the AO/D group (both conditions concomitantly), which lends support to our hypothesis of a synergic effect of the two conditions together.

In contrast, Aubertin-Leheudre and colleagues (21) conducted a cross-sectional study involving 1,453 individuals from the Lifestyle Interventions and Independence for Elders (LIFE) Study and found no association between obesity and MetS. The divergent findings may be explained by the fact that Aubertin-Leheudre and colleagues defined obesity based on BMI, which is less sensitive for metabolic outcomes than waist circumference (45, 46). Moreover, the FNII group (25) recommends grip strength cut-off points of < 16 kg for women and < 26 kg for men as the best indicators of weakness, whereas Aubertin-Leheudre and colleagues used < 19.9 kg for women and < 31.9 kg for men. Lastly, as the analyses did not take the simultaneous occurrence of abdominal obesity and dynapenia into account to test the combined effect on the likelihood of MetS, the results are not completely comparable to ours.

Our results support the hypothesis that abdominal obesity and dynapenia act synergistically, leading to a more detrimental effect on metabolism. The underlying mechanism

of this metabolic synergy is not fully understood but is likely to be related to insulin resistance, chronic inflammation, and increased oxidative stress.

With aging, there has been described an increase in adipose tissue and redistribution of fat deposits, which become more concentrated in the visceral region, triggering chronic mild inflammation known as “inflammaging” (47–49). This process leads to the production of proinflammatory cytokines, such as tumor necrosis factors alpha (TNF- $\alpha$ ) and interleukin 6 (IL-6), which negatively affect energy balance, compromise immune responses, blood pressure control, vascular homeostasis, angiogenesis and glucose and lipid metabolism, and increase insulin resistance (47, 48).

Similarly, in the skeletal muscle, there is an infiltration of muscle fat that impairs musculoskeletal structure, altering contractility, limiting muscle fiber activation, and disrupting the excitation-contraction coupling. This results in neuromuscular strength loss known as dynapenia, which can occur even without a reduction in muscle mass (8–11). Therefore, this infiltration of muscle fat, in addition to being responsible for muscle strength loss, induces metabolic dysfunctions in skeletal muscle, leading to lipotoxicity with an increase in local free fatty acids, oxidative stress, and mitochondrial dysfunction. This generates an elevated production of reactive oxygen species (ROS), causing muscle inflammation with macrophage infiltration, lipolysis, changes in myokine secretion, and alterations in blood flow. These factors collectively reduce insulin signaling, leading to greater insulin resistance, dysglycemia, and dyslipidemia (13, 50–52).

Therefore, there is a synergistic effect of the pro-inflammatory endocrine activity of myocytes and adipocytes, leading to a great metabolic dysregulation, exacerbating insulin resistance and chronic inflammation. The combined action of abdominal obesity and dynapenia intensifies each other, which can increase the risk of developing MetS (48, 53).

The strong points of the present study are the large representative sample of community-dwelling English people 50 years of age or older, the long follow-up period and the use of a set of objective measures in the analyses. Moreover, the Poisson model was adjusted by covariables widely reported in the literature as relevant to the development of MetS. To the best of our knowledge, this is the first longitudinal study to analyse dynapenic abdominal obesity as a risk factor for occurrence of MetS in the population older than 50 years of age.

This study also has limitations that should be recognised. First, the fact that serum insulin levels were not measured. Future studies are needed to confirm whether dynapenic abdominal obesity is associated with MetS through a change in the insulin signalling pathway. Second, lack of information on diet quality or changes in eating patterns to make adjustment of our models. Third, we do not have information on physical activity measured continuously in metabolic equivalent of task (METs), which would allow us to adjust our models for energy expenditure in each type of physical activity. However, the questions from the PASBAQ have been used and validated in previous publications. Fourth, the lack of objective methods to assess muscle mass such as dual-energy X-ray absorptiometry (DEXA) and computed tomography, which provide a much

more accurate measurement. Nevertheless, a determination of ASMM using Lee equation has been validated using such methods as reference with satisfactory results.

## Conclusions

Dynapenic abdominal obesity increases the risk of metabolic syndrome, with a larger IRR compared to obesity alone. The understanding of this synergic action could guide specific clinical strategies, enabling the prevention of metabolic changes that can lead to cardiovascular disease, disability and death.

## Data availability

Data from the English Longitudinal Study of Aging (ELSA) are available from the UK Data Service for researchers who meet the criteria for access to confidential data, under conditions of the End User License <http://ukdataservice.ac.uk/media/455131/cd137-enduserlicence.pdf>. The data can be accessed from: <http://discover.ukdataservice.ac.uk/series/?sn=200011>. Contact with the UK data service regarding access to the English Longitudinal Study of Ageing can be made through the website <http://ukdataservice.ac.uk/help/get-in-touch.aspx>, by phone +44 (0)1206872143 or by email at [help@ukdataservices.ac.uk](mailto:help@ukdataservices.ac.uk).

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**Data analysis and interpretation:** PCR, DCO, ROM, AFS, MML, MLBD, AS, CO, TSA.

**Writing, critical revision of content:** PCR, DCO, ROM, AFS, MML, MLBD, AS, CO, TSA.

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