| 1 | DYNAPENIC ABDOMINAL OBESITY AS PREDICTOR OF MORTALITY AND DISABILITY |
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| 2 | WORSENING IN OLDER ADULTS: A 10-YEAR PROSPECTIVE STUDY |
| 3 | |
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| 24 | Key words: sarcopenic obesity, muscle strength, dynapenia, disability, mortality |
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1 SUMMARY

| 2 | There are relatively few prospective studies evaluating the combined effect of abdominal obesity |
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| 3 | and low muscle strength on worsening disability and on mortality. The study aimed at evaluating |
| 4 | prospectively the prognostic value of dynapenic abdominal obesity definition on disability |
| 5 | worsening in a 5.5-year follow-up and mortality in a 10-year follow-up. |
| 6 | Methods: in 93 men and 169 women aged between 66 and 78 years, leg isometric strength, waist |
| 7 | circumference (WC), BMI, glycaemia, HOMA, lipid profile, vitamin D3, albumin, fibrinogen, |
| 8 | physical activity level, income, smoking status and comorbidities were evaluated at the baseline. |
| 9 | Reported disabilities were measured at baseline, 1-y, 2-y, 3-y and 5.5-y follow-up and mortality rate |
| 10 | was evaluated during a 10-y follow-up. The study population was categorized in dynapenic |
| 11 | abdominal obese (D/AO), non dynapenic abdominal obese (ND/AO), dynapenic non abdominal |
| 12 | obese (D/NAO), non dynapenic non abdominal obese (ND/NAO) according to muscle strength/WC |
| 13 | tertiles. |
| 14 | Results: D/NAO subjects presented a disability worsening risk of 1.69 times (95%CI:1.11-2.57), |
| 15 | ND/AO subjects showed a 2-fold increase in risk (95%CI:1.34-2.98), while being D/AO more than |
| 16 | trebled the risk, even after considering confounding variables (HR:3.39,95%CI:1.91-6.02). |
| 17 | Mortality risk after adjustment for other confounding variables was 1.57 (95%CI:1.16-2.13) for |
| 18 | ND/AO and 2.46 (95%CI:1.34-4.52) for D/AO. |
| 19 | Conclusions: Dynapenic abdominal obese subjects are at higher risk of worsening disability and |
| 20 | mortality than subjects with dynapenia or central fat distribution only. |
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1 INTRODUCTION

2 Together with body composition changes associated with aging, an increase in prevalence of 3 obesity observed in the last decades even in older ages leads to a condition called sarcopenic obesity 4 (SO), where the relationship between fat and muscle mass (1-2) presents incongruities. There are 5 relatively few studies that have evaluated the effect of SO in older people as pertains to physical 6 functioning or disability, with conflicting results (3-5). Alternative definitions of SO have been 7 proposed considering muscle impairment, expressed by muscle strength, rather than muscle mass, 8 and waist circumference (WC) rather than total body fat indexes, and introduce the concept of 9 dynapenic abdominal obesity, but without receiving an unanimously accepted diagnostic definition 10 so far (5). Dynapenia has a better prognostic value compared to sarcopenia to predict worsening 11 disability (6). Even abdominal obesity, as assessed by WC, has shown association with disability in 12 older adults (7). Moreover dynapenic obesity has been shown to create adverse physical functioning 13 effects and on the risk of developing mobility disability (4,5,8). An association between dynapenia 14 and mortality has been shown (9), which takes into consideration adjustments for total body fat and 15 comorbidities (10). Numerous studies showed that WC is more strongly associated with higher 16 mortality, including fat mass adjustment, than obesity itself in the elderly (11). 17 However, prospective studies evaluating the combination of abdominal obesity and muscle strength 18 on worsening disability and mortality are still lacking. The scope of this study soughtto compare the 19 prognostic value of dynapenic/abdominal obesity on worsening disability and mortality in our 20 group of older adults. 21 22 23

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1 MATERIALS AND METHODS

2 Subjects

Subjects were randomly chosen from patient lists of 11 general practitioners family doctors in the
city of Verona. Those subjects who were able to walk at least 1/2 mile without difficulty and if they
had no cognitive impairment (Mini-mental Status Examination score >24) were accepted.
Anthropometric measurements and disability were evaluated at baseline in a cohort of community-

7 dwelling older adults.

8 None of the subjects were partecipated in regular physical exercise more than once weekly during 9 the study. Subjects with renal failure, disabling knee osteoarthritis, heart failure (NYHA≥2), cancer 10 and serious lung disease were excluded. Individuals with more than a 5% weight loss in the year 11 previous to the study were also excluded. At baseline, 177 women and 97 men, aged between 66 to 12 78 years, were considered eligible and consented to participate in the study. 4 men and 8 women 13 moved to another city and were excluded, due absence of data on disability and mortality. The study 14 was conducted on a final cohort of 262 subjects, 93 men and 169 women. 15 Mortality rate was obtained from death certificates of Verona's registry office. Initial, intermediate 16 and final death causes, identified through the Italian National Statistics Institute (ISTAT) death 17 certificates, were categorized in neoplastic, cardiac (ischemic, valvular, heart failure), infectious, respiratory cerebrovascular and other causes (malnutrition, fractures and neurodegeneratives). 18 19 All subjects gave their written informed consent to be part of the study, which was approved by the

- 20 University of Verona's Ethics Committee.
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22 Anthropometry

23 Subjects were weighed barefoot and wearing light indoor clothing to the nearest .1 kg (Salus scale,

24 Milan, Italy), and height was measured to the nearest .5 cm using a stadiometer (Salus stadiometer,

Milan, Italy). Body weight adjusted by stature (kg/h²) were used to give BMI. A measuring tape
 was used to measure WC at the narrowest part of the torso as viewed from the front.

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- 4 Strength

Maximal voluntary isometric strength of the dominant knee extensors was tested by a Spark
Handheld Dynamometer model 160 (Spark, Iowa City, IA, USA) as previously reported (12). A
familiarization testing session was conducted one week before knee extensor strength measurement.
Test retest reliability was evaluated in a sample of 30 older subjects, the interclass correlation
coefficient was .914 and the coefficient of variation (CV) was 9.69% for the dominant leg as
previously reported (12).

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- 12 Health status

Acute and chronic conditions were assessed by standardized questionnaires of the Italian Longitudinal Study on Aging (12). The study started with a thorough clinical investigation of the subjects and then it was repeated at the 1, 2, 3 and 5.5-y follow-up. Information about the appearance of new diseases was collected for each subject from their family doctors, hospital documentation, physical examination and laboratory tests. Chronic conditions assessed included: hypertension, diabetes, hypercholesterolemia, cardiovascular disease (myocardial infarction and heart failure), chronic obstructive pulmonary disease (COPD) and stroke.

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21 Classification of groups

22 Isometric leg muscle strength sex-specific tertiles were created. Subjects in the lowest tertile of leg

- 23 muscle strength (<15.33 kg and <8.33 kg respectively in men and women) were considered
- 24 dynapenic, while those in the second and third tertiles were considered non dynapenic. Sex-specific
- 25 cutoffs based on WC tertiles were used to categorize individuals as abdominal obese (above the

highest tertile of WC, 100 cm and 87 cm respectively in men and women) or non abdominal obese
(those in the first and in the second tertiles).

3 The study population was categorized into four groups based on sex-specific WC and strength

4 tertiles: dynapenic abdominal obese (D/AO), non dynapenic abdominal obese (ND/AO), dynapenic

5 non abdominal obese (D/NAO), non dynapenic non abdominal obese (ND/NAO).

6

7 Reported disability

8 The definition of reported disability as per Langlois et al., was used (13), regarding capacity to do

9 four of the six items from the Activity of Daily Living scale (ADLs) associated with three Rosowe-

10 Breslau physical function items and selected Instrumental Activity of Daily Living scale (IADLs) as

11 previously reported (12).

12

13 Four groups were identified:

14 1. Participants with disability – for subjects reporting that ≥ 1 of the ADL items were difficult,

15 very difficult or impossible.

16 2. Participants with moderate disability – for subjects reporting that ≥ 1 physical function items 17 was very difficult or impossible and/or could not walk 800 metres

18 3. Participants with mild disability – for subjects reporting that ≥ 1 higher level of physical

19 function items or IADL difficult but all other physical function tasks, except walking 800 m and

20 ADL, were easy.

Participants without disability – if subjects reported "easy" for all the ADLs, "no difficulty"
 in the physical functions items, and "no difficulty" or "don't do" for all IADLs.

23 Changes in any reported disability score between baseline and subsequent assessment (2,3,4 and

24 5.5-y follow-up) were assessed in 262 subjects divided into two classifications:

25 Unchanged: having an unchanged score over the follow-up period.

1 Worsened: when score decreased by one or more points in the scale over the follow-up period.

2

3 Biochemical measures

4 At baseline blood samples were taken from each participant after overnight fasting. A compact

5 chemistry analyzer method (Eastman Kodak, Inc., Rochester, NY) was used to measure plasma

6 glucose. This method had an interassay CV of 2% (14).

Plasma immune-reactive insulin underwent duplicate measurements by double antibody
radioimmunoassay with a commercial kit (Diagnostic Products Corp., Los Angeles, CA).
Sensitivity was 6 pmol/L and the intra-assay CV was 4.9%. Insulin resistance was estimated with
the HOMA (homeostasis model assessment of insulin resistance) method (14).

11 Cholesterol and triglycerides were determined using a compact chemistry analyzer (Eastman 12 Kodak) method resulting in an interassay CV of 2.2% for triglycerides, and 2% for cholesterol. 13 HDL separation (14) was determined through dextran-magnesium precipitation. Calculated LDL level was derived using the Friedewald formula. A calorimetric test (Vitros 950 ALB slides; J&J 14 15 Health, Cone Systems, Piscataway, NJ, USA) determined albumin; the color complex formed was measured by reflectance spectrophotometry. The sensitivity of the assay was10 gL⁻¹; intra-assay CV 16 17 was 1.3-1.5%. 25-hydroxyvitamin D (25[OH]D) was measured as previously described elsewhere (14). 18

19

20 Covariates

21 Level of physical activity was evaluated by SF-36 questionnaire (15), and it was considered low if

22 <70 points. Subjects were classified as low income if they earned < 516,52 euro. Smoking was

23 evaluated through self report, and according to answers participant were classified as never

smokers, ex-smokers and current smokers.

1 Participants Subjects declared the amount of alcohol consumed weekly. Study participants

2 consuming alcohol >30 g for men and >20 g for women on a daily basis (exceeding 21 and 14

3 Units/week respectively) were considered heavy alcohol drinkers (16).

4 Information on diseases were obtained from a geriatrician as per standard, pre-established criteria,

5 collating information from self-reported physician diagnoses, current pharmacological treatment,

6 medical records, clinical examination and blood tests. The following chronic conditions were used

7 in the analyses: diabetes, hypercolesterolemia, myocardial infarction, heart failure, COPD and
8 stroke.

9

10 Statistical analysis

Study results are presented as means±SD. All variables were considered as normally distributed
according as per the Kolmogorov–Smirnov test.

13 One-way ANOVA was carried out to investigate group differences at baseline dividing the study on

14 the basis of dynamometry combined with WC measurement. Categorical variables underwent Chi-

15 square testing.

16 Group differences at baseline between dead/survived subjects and subjects with stable/worsened

17 disability were tested with one way-ANOVA.

18 Cox regression was performed to assess mortality risk and worsening disability risk, among each

19 follow-up period, with population divided into groups on the basis of muscle strength and WC

20 tertiles. Adjusted and unadjusted for gender and age hazard ratio was calculated; it has been further

21 adjusted for physical activity level, presence of disability at baseline, income, alcohol use,

22 fibrinogen, vitamin D3 level, smoking status and comorbidity (diabetes, hypercolesterolemia,

23 cardiovascular disease, COPD and stroke).

24 Kaplan-Meier curves were constructed for different groups and differences in survival were tested

25 using log-rank tests. Deaths and person time at risk (person-time survived) were calculated.

1 Kaplan-Meier curves were constructed for different groups and differences in survival without

2 worsening disability were tested using log-rank tests. Number of deaths and person time at risk

3 (follow-up time minus months with worsening disability) were calculated.

A significance level of .05 was employed for the entire study. R 2.14.1 (17) was used to perform all
statistical analyses.

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8 **RESULTS**

9 93 men and 169 women ranging in ages between 66 and 78, with an average of 71.8 ±2.2 years
10 were included in this analysis.

11 The main baseline characteristics of the study population (mean±SD) are shown in Table 1 as per

12 muscle strength/WC tertiles groups. At baseline ND/AO and D/AO showed higher weight, BMI,

13 WC, basal glycemia, HOMA index, triglycerides, fibrinogen and lower HDL cholesterol compared

14 to other groups. Instead D/NAO and D/AO showed lower leg strength, albumin, vitamin D3,

15 physical activity level and higher presence of disability at baseline compared to other groups.

16 111 subjects (42.4%) declined in one or more levels of the reported disability scale (worsening

17 disability) over the 5.5-y follow-up. Subjects with worsening disability showed higher levels of

18 BMI and HOMA index at baseline (not included in Table).

19 With study population classified according to strength and WC in a Cox regression, with ND/NAO

20 as the referent category, the risk of disability worsening, after gender and age adjustment, was 1.84

21 (95%CI:1.25-2.72) for the D/NAO group, 1.96 (95%CI:1.35-2.86) for the ND/AO group and 3.61

22 (95%CI:2.12-6.15) for D/AO group. Furthermore, after adjusting for other confounding variables,

23 HR was 1.69 (95%CI:1.11-2.57) for the D/NAO group, 2.00 (95%CI:1.34-2.98) for the ND/AO

24 group and 3.39 (95%CI:1.91-6.02) for the D/AO group (Table 2).

Figure 1A shows Kaplan Meier curves adjusted for categorical variables contrasting the relative
 strength/WC groups, in which the D/AO group showed the highest rate of worsening disability
 compared to the other groups, and a shorter disability-free period.

Through an average follow-up of 9.8 years and 2566 person-years of observation, 72 (27.5%)

5 deaths occurred, corresponding to an overall crude mortality rate of 28.1% person-years. 6 Malignancies were the first cause of death in 52.9% of men and 41.9% of women, followed by 7 23.6% of men and 35.5% of women who died of cardiac death, while respiratory was the third 8 cause of death in 6% of men and 16.2% of women. The percentage of deceased subjects after a 10-9 year follow-up was significantly higher in men (36.5%) compared to women (22.4%). Deceased 10 subjects showed higher weight, WC, basal glycaemia, fibrinogen and lower physical activity level 11 compared with survived subjects. When considering NAO, mortality was not significantly different 12 between non dynapenic and dynapenic subjects (likelihood ratio test=0.34; p>0.5). On the other 13 hand, AO showed an hazard for mortality significantly higher with respect to NAO (likelihood ratio 14 test=7.79; p=0.005). Furthermore, when considering within AO subjects without or with 15 dynapenia separately, a significant trend in mortality was found (likelihood ratio test=9.94; 16 p=0.002). Therefore subjects were divided into three groups: NAO, D/AO and ND/AO. 17 As shown in Table 3 in a Cox regression analysis considering these groups, with NAO as the 18 referent category, the risk of death, considering gender and age, was 1.63 (95%CI:1.22-2.18) for 19 ND/AO and 2.66 (95%CI:1.50-4.74) for D/AO group. Moreover after adjustment for the other 20 categorical variables, death risk was 1.57 (95%CI:1.16-2.13) for ND/AO and 2.46 (95%CI:1.34-21 4.52) for D/AO group. 22 Figure 1B shows Kaplan Meier curves in contrast to the relative strength/WC groups, where the

23 D/AO group showed the highest mortality rate compared to the other groups.

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1 **DISCUSSION**

In this study involving older adults aged 66-78 years, participants with low muscle strength and
abdominal obesity showed higher disability worsening and mortality compared to subjects
presenting low muscle strength or abdominal fat distribution alone.

5 In our study population abdominal obese subjects with dynapenia showed a more than trebled 6 increase in risk of disability worsening. Our results are consistent with Baumgartner et al. (3) which 7 showed that older subjects with baseline sarcopenic obesity, defined as a simultaneous presence of 8 low appendicular muscle mass and high body fat percent as measured by DXA, more than doubled 9 their risk of developing IADL disability compared with non-sarcopenic obese. Similarly Bouchard 10 et al., in a observational study with a population of more than 2000 men and women, where lower 11 limb extension strength was evaluated with a dynamometer, showed that dynapenic obese subjects 12 had the a lower walking speed compared to non-dynapenic/non-obese individuals (8). Stenholm et 13 al. in the InChianti Study and on the Finnish population for the Health 2000 Survey observed that 14 elderly adults with elevated body fat percentage and low muscle strength had a greater decline in 15 walking speed (4,5).

16 Since our results were observed in a longer follow-up study by using a combination of 2 17 standardized methods (strength and WC), they confirm and expand those previous reports 18 identifying dynapenic abdominal obese subjects as the population with the highest risk of functional 19 decline compared to other groups. Our results, combined with those of previous studies (4.5,10) are 20 not surprising since it has been clearly shown that strength loss is much faster and more strictly 21 associated with incident disability than with associated muscle mass decline (6,18). Moreover, it 22 should be taken into account that a recent systematic review of the literature confirmed that muscle 23 strength in older adults is related to a decline in functions, while, after pooled meta-analysis, no 24 significant association was observed with low muscle mass (19). Even a high value of waist 25 circumference alone is related with higher risk of developing disability (7).

In our population, subjects presenting central adiposity and low muscle strength simultaneously
 presented the highest risk of all cause mortality compared with all other groups, even after
 adjustments for age, gender, lifestyle variables and comorbidities.

4 That the results show the highest mortality risk in D/AO group is in line with previous reports. In a 5 large population of adults, with a 5.8 year follow-up, Bigaard et al. observed that fat mass and lean 6 mass, measured by impedentiometry, represent independent predictors of all-cause mortality (20). 7 Similarly Wannamethee, with a study population of more than 4000 men, observed that subjects 8 with a WC higher than 102 cm and reduced lean mass, as assessed by measurement of the midarm 9 muscle circumference, are at higher risk of all-cause mortality (21). Atkins and colleagues noticed 10 that sarcopenia and central adiposity, assessed respectively with midarm muscle circumference and 11 WC measurements, were connected to greater cardiovascular mortality and all-cause mortality (22). 12 Stenholm et al., in a population of 3594 adults ranging in ages between 50 and 91 followed for 33 13 years, observed instead that both low handgrip strength and obesity independently predict the risk 14 of death (12). To our knowledge, no studies have shown that concurrence of high WC value and 15 low muscle strength increases the risk of all-cause mortality in the older adults. 16 Although the link between obesity and mortality is still under debate (23,24), the association of high 17 WC value with high death rate is known. In an analysis of the Cardiovascular Health Study 18 population, Janssen et al. observed a 13% increase of death rate for each increased SD of WC (23). 19 Moreover Visscher et al. comparing the predictive value of BMI and WC in a non-geriatric 20 population, discovered that WC is more predictive for a 5 year mortality risk than BMI (24). 21 Our results seem to show that dynapenia and central obesity may contribute to disability worsening 22 and mortality risks. 23 A physiopatological link between low muscle strength and visceral obesity can partially explain this

result. Changes in age-related body composition, which include an increase in both visceral

25 abdominal adipose tissue and intermuscular fat, are associated with an increase in secretion of pro-

inflammatory cytokines, reduced muscle strength, incidence of mobility disability and insulin
resistance (6, 25, 26). In our population D/AO subjects presented higher fibrinogen, lower physical
activity and vitamin D level at baseline compared to other groups. Reduced physical activity and
increased inflammation causes an unfavourable unbalance between anabolic and catabolic stimulus
to skeletal muscle and low vitamin D is associated per se with an increase in the risk of mobility
disability in older adults (27).

7 The synergistic effect of central adiposity and low muscle strength on mortality, instead, could be 8 partially due to unfavourable metabolic profile and cardiovascular mortality. Indeed, for our study, 9 D/AO subjects showed lower HDL and higher triglycerides and prevalence of heart failure 10 compared to other groups; it must also be noted that this subgroup showed the highest risk of 11 mortality, even considering potential confounders. Previously Stephen and Janssen observed 12 increased cardiovascular risk at 8 years in 3366 elderly subjects with high WC and low muscle 13 strength (28), associated with insulin resistance, higher levels of IGF-I, increased exposure to 14 systemic inflammation, reduced antioxidant defence and immune function (28,29). Moreover obese 15 subjects with low muscle strength are often physically inactive and disabled, which makes them 16 more vulnerable to falls, or other adverse events, and at higher risk of hospitalization (30). Muscle 17 is considered as the main reserve of protein in the body. Consequently, in elderly subjects with 18 depleted muscle, recovery from acute disease, injury or surgery may be compromised with 19 important health consequences. Muscle strength and fat distribution, as measured with handheld 20 dynamometers and WC respectively, is inexpensive and can be quickly used in different clinical 21 settings and allows to identify a population at higher risk of adverse events better. 22 Some potential limits in this study have to be acknowledged. 23 To begin with, our study population was restricted to healthy older well-functioning men and 24 women in good health condition at baseline, and therefore did not wholly reflect a normal aging

24 women in good health condition at baseline, and therefore did not whony reflect a normal agin25 population.

Second, as disability report was recorded at annual intervals, we used a discrete rather than a
 continuous time-scale for disability worsening.

Third, the small study sample limited the possibility of statistically investigating the association
between dynapenic abdominal obesity and different causes of mortality.

5 However, the high predictive power of dynapenic abdominal obesity on mortality and disability

6 worsening shown in our study should be particularly valuable because of its easy implementation in

7 clinical practice requiring two measurements that are relatively simple to obtain and interpret,

8 especially in outpatient settings.

9 In conclusion, our results showed that D/AO subjects are at higher risk of disability worsening and

10 mortality when compared to subjects with normal muscle strength and waist circumference.

11 Identifying older subjects with central fat distribution and concurrent low muscle strength could

12 help to select groups of subjects with particularly high health risks. Interventions aimed at

13 improving muscle strength and physical performance and capable of decreasing prevalence of

14 obesity in older adults could lead to not only decreasing future disability but might also be effective

15 in controlling the large economic burden associated with disability worsening.

16

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18 The authors' responsibilities were as follows—AR, FF, CC, RM and MZ: analysis and

19 interpretation of data and preparation of manuscript; EZ, FF and MZ: study concept and design and

20 preparation of manuscript; MZ, GM, EZ: consulted on study design, recruited subjects, and edited

21 the manuscript and EZ, GM edited the manuscript. EZ, GM, VZ, CC, MZ: acquisition of subjects,

22 collection of data, and review of the manuscript.

23

24 CONFLICT OF INTEREST

25 None

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TABLE 1 LEGEND Baseline Characteristics of the Study Population According to the Dynapenic/Abdominal Obese status TABLE 2 LEGEND Worsening Disability Risk According to Dynapenic Abdominal Obesity Groups, using non Dynapenic non Abdominal Obese as Reference Group. TABLE 3 LEGEND Mortality Risk According to Dynapenic Abdominal Obesity Groups, Using non Abdominal Obese Group as Reference Group. **FIGURE 1 LEGEND** Kaplan-Meier survival curves for worsening disability (A) and all-cause mortality (B) according to study groups, non dynapenic non abdominal obese (...), dynapenic $(- \cdot -)$, abdominal obese (....) and dynapenic abdominal obese (--).

1 Table 1 Baseline Characteristics of the Study Population According to Dynapenic/Abdominal Obese Status

| | Non dynapenic/Non abdominal obese (n=116) x ± SD (min-max) | Dynapenic/Non abdominal obese (n=56) x ± SD (min-max) | Non dynapenic /Abdominal obese (n=58) x ± SD (min-max) | Dynapenic/Abdominal obese (n=32) x ± SD (min-max) | р |
|--|--|---|--|---|-------|
| Age (years) | 71.65 ±2.31 (68-76) | 72.16 ±2.00 (69-78) | 70.95 ±2.32 (66-76) | 72.06 ±2.45 (67-78) | <.05 |
| Sex (female) n (%) | 72 (62.1%) | 38 (67.8%) | 39 (67.2%) | 20 (62.5%) | .844 |
| Weight (kg) | 65.52 ±9.37 (43.30-86.50) | 62.39 ±10.04 (45.40-89.30) ^b | 83.95 ±13.33 (63.50-118.90) ^d | 75.21 ±8.1 (56-95.20) ^d | <.001 |
| Height (m) | 1.61 ±0.09 (1.42-1.90) | 1.60 ±0.08 (1.40-1.85) ^b | 1.62 ±0.10 (1.41-1.86) ^b | 1.60 ±0.08 (1.41-1.78) ^b | .586 |
| BMI (kg/m²) | 25.20 ±2.72 (18.74-31.40) | 24.12 ±2.75 (18.19-30.19) ^b | 31.78 ±4.22 (25.47-50.58) ^d | 29.25 ±2.86 (23.17-35.61) ^d | <.001 |
| Waist circumference (cm) | 83.62 ±8.38 (64.50-100) | 80.55 ±8.58 (66-98) ^b | 99.90 ±9.43 (87-124) ^d | 97.33 ±6.35 (87-110) ^d | <.001 |
| Glycemia (mg/dl) | 98.07 ±25.52 (73-281) | 97.05 ±15.63 (80-187) | $105.55 \pm 24.22 (82-205)^{d}$ | $105.19 \pm 35.88 (70-254)^{d}$ | .134 |
| HOMA index | 1.92 ±0.90 (0.2-4.99) | 1.93 ±1.21 (0.2-7.1) | 3.35 ±1.84 (0.5-12.7) ^d | 2.88 ±1.39 (1.0-8.8) ^d | <.001 |
| Total Cholesterol (mg/dl) | 239.33 ±38.37 (147-375) | 238.07 ±37.72 (161-322) | 236.22 ±34.23 (164-307) | 245.16 ±45.59 (148-326) | .760 |
| HDL cholesterol (mg/dl) | 62.77 ±14.56 (22-111) | 66.27 ±16.95 (36-106) | 56.50 ±14.70 (34-95) ° | 55.97 ±15.56 (31-98) ^b | <.01 |
| LDL cholesterol (mg/dl) | 150.63 ±35.17 (66-244.4) | 148.00 ±34.65 (73.0-224.2) | 147.77 ±29.04 (90-223.2) | 153.52 ±32.93 (90.4-219.6) | .840 |
| Triglycerides (mg/dl) | 129.63 ±53.22 (39-292) | 119.03 ±47.44 (49-264) | 159.77 ±73.70 (55-331) ° | 178.34 ±88.41 (74-474) ^d | <.001 |
| Albumin (g/L) | 43.74 ±2.72 (36.6-52.3) | $41.72 \pm 3.42 (34-47.9)^{d}$ | 43.39 ±3.78 (35.5-55) | 42.06 ±4.61 (23-48.1) ^b | <.01 |
| Vitamin D (ng/dl) | 49.42 ±28.51 (11-169) | 40.43 ±21.06 (1-95) ^b | 43.52 ±22.65 (11-108) | 36.25 ±44.03 (1-265) ^b | .062 |
| Fibrinogen (mg/dl) | 290.64 ±63.32 (151-501) | 309.36 ±55.36 (208-480) | 315.98 ±66.83 (205-547) ^b | 317.81 ±49.58 (217-460) ^b | <.05 |
| ADL (1-4) | 3.77 ±0.44 (1-3) | 3.45 ± 0.74 (1-4) ^c | 3.43 ±0.73 (1-4) ^d | 3.19 ±0.78 (1-4) ^d | <.001 |
| Right leg strength at dynamometer (kg) | 15.47 ±5.21 (8.33-30) | 7.64 ±3.16 (2.33-15) ^d | 16.25 ±6.27 (8.33-32) | $8.13 \pm 3.76 (3.66-15)^{d}$ | <.001 |

| Presence of disability at baseline n (%) | 26 (22.4%) | 24 (42.8%) ° | 26 (44.8%) ^c | 20 (62.5%) ^d | <.001 |
|--|------------|-------------------------|-------------------------|-------------------------|-------|
| Low income n (%) | 12 (10.3%) | 10 (17.8%) | 15 (25.9%) ° | 7 (21.9%) | .057 |
| Low physical activity n (%) | 28 (24.1%) | 24 (42.8%) ^b | 19 (32.7%) | 15 (46.9%) ^b | <.05 |
| Actual or past smoking n (%) | 50 (43.1%) | 21 (37.5%) | 25 (43.1%) | 15 (46.8%) | .838 |
| High alcohol intake n (%) | 28 (24.1%) | 12 (21.4%) | 15 (25.9%) | 5 (15.6%) | .702 |
| Diseases | | | | | |
| Hypertension n (%) | 63 (54.3%) | 24 (42.8%) | 32 (55.2%) | 20 (62.5%) | .300 |
| Diabetes n (%) | 10 (8.6%) | 1 (1.8%) | 7 (12.1%) | 5 (15.6%) | .108 |
| Hypercholesterolemia n (%) | 55 (47.4%) | 21 (37.5%) | 28 (48.3%) | 15 (46.9%) | .594 |
| COPD n (%) | 3 (2.6%) | 2 (3.6%) | 4 (6.9%) | 1 (3.1%) | .567 |
| Chronic heart failure n (%) | 2 (1.7%) | 4 (7.1%) | 1 (1.7%) | 4 (12.5%) ^c | <.05 |
| Myocardial infarction n (%) | 5 (4.3%) | 2 (3.6%) | 3 (5.2%) | 1 (3.1%) | .962 |
| Stroke n (%) | 2 (1.7%) | 1 (1.8%) | 1 (1.7%) | 0 (3.1%) | .934 |

2 ADL: Activity Daily Living

3 BMI: Body Mass Index

4 HOMA index: homeostasis model assessment of insulin resistence index

5 a In comparison with reference category (Non dynapenic/ Non abdominal obese) $_{b}$ P < 0.05 $_{c}$ P < 0.01 $_{d}$ P < 0.001

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Table 2 Worsening Disability Risk According to Dynapenic Abdominal Obesity Groups, using non

Dynapenic non Abdominal Obese as Reference Group.

| | Model 1 (unadjusted) | | Model 2 (adjusted for age and gender) | | Model 3 (adjusted for age, gender and other variables _a) | |
|-----------------------------------|-------------------------|-----------|---|-----------|--|-----------|
| | Hazard ratio | CI (95%) | Hazard ratio | CI (95%) | Hazard ratio | CI (95%) |
| Dynapenic/ Non abdominal obese | 1.76 | 1.20-2.57 | 1.84 | 1.25-2.72 | 1.69 | 1.11-2.57 |
| Non dynapenic/ Abdominal obese | 2.02 | 1.39-2.93 | 1.96 | 1.35-2.86 | 2.00 | 1.34-2.98 |
| Dynapenic/ Abdominal obese | 3.54 | 2.08-6.01 | 3.61 | 2.12-6.15 | 3.39 | 1.91-6.02 |

a disability at baseline, low income, actual or past smoking, high alcohol intake, fibrinogen, vitamin D3 level, hypertension, diabetes, hypercholesterolemia, COPD, chronic heart failure, myocardial infarction and stroke.

Table 3 Mortality Risk According to Dynapenic Abdominal Obesity Groups, Using non Abdominal Obese Group as Reference Group.

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| 5 | | Model 1 (unadjusted) | | Model 2 (adjusted for age and gender) | | Model 3 (adjusted for age, gender and other variables _a) | | |
|------------------|---|-------------------------|-----------|---|-----------|--|-----------|--|
| | | Hazard ratio | CI (95%) | Hazard ratio | CI (95%) | Hazard ratio | CI (95%) | |
| | Non dynapenic/ Abdominal Obese Dynapenic/ Abdominal Obese | 1.61 | 1.20-2.15 | 1.63 | 1.22-2.18 | 1.57 | 1.16-2.13 | |
| | | 2.59 | 1.45-4.62 | 2.66 | 1.50-4.74 | 2.46 | 1.34-4.52 | |
| 4 5 6 7 | 4 ^a disability at baseline, low income, actual or past smoking, high alcohol intake, fibrinogen, vita hypertension, diabetes, hypercholesterolemia, COPD, chronic heart failure, myocardial infarction | | | | | | | |
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