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# Metabolic syndrome and functional ability in older age: The InCHIANTI study

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## summary

**Background & aims:** Metabolic syndrome (MetS) is associated with incident disability in middle-aged subjects. We evaluated the association of MetS with functional ability in an older population.

**Methods:** We enrolled 1155 participants aged 65þ, derived from the InCHIANTI study, and followed for 3 years. MetS was diagnosed according to the National Cholesterol Education Program's ATP-III criteria. Functional ability was estimated using the Katz's activities of daily living (ADLs), and the Lawton and Brody for the instrumental activities of daily living (IADLs) scales. The association between disability and MetS at baseline and after follow-up was assessed by logistic regression.

**Results:** At baseline, MetS was associated with reduced probability of ADLs disability among participants aged $74_{+}$ (OR = .33, 95% CI = .14–.77; $p = .010$), but not in younger (5.08, 95% CI = .88–29.24; $p = .069$). Also, MetS was associated with reduced probability of incident ADLs disability (OR = .61, 95% CI .41–.91; $p = .016$), but neither with prevalent, nor incident IADLs disability.

**Conclusions:** In older persons, MetS is associated with reduced probability of prevalent and incident ADLs disability. Whether older persons with MetS should receive treatment and whether the current diagnostic criteria for MetS apply to older individuals need further investigation.

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Conflict of interest

The authors declare that they have no conflict of interest in this study.

Statement of authorship

AL, SB carried out the study and data analyses, and drafted the manuscript. AL, AG carried out the samples analyses. AL, LF,RAI participated in the design of the study and performed the statistical analysis. SB LF conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

**Keywords**

Metabolic syndrome; Disability; Elderly; Epidemiology

## 1. Introduction

Paralleling the aging of populations, the prevalence of functional disability is constantly increasing in Western countries.[1] Increasing knowledge of the determinants of disability is becoming a public health priority for evidence-based health decision-making.[2] Disability in older subjects accounts for almost half of total healthcare expenditure in the United States.[3]

The metabolic syndrome (MetS) is increasingly being reported in geriatric populations.[4] MetS is an intriguing entity, because it includes potentially reversible risk factors, and is associated with several adverse outcomes, including cardiovascular and cerebrovascular morbidity and mortality.[5] Also, insulin resistance has been considered as a contributing factor to age-related muscle mass loss, which is causally related to decline in functional ability. In addition, MetS is associated with central obesity which in turn is considered a determinant of sarcopenia in the setting of so-called sarcopenic obesity. Noticeably, MetS has been associated with increased risk of disability in middle aged subjects, but data in elderly and oldest populations are still scanty and controversial.[6]

The aim of the present study was to evaluate the association of MetS with prevalent and incident (three-year) disability in community-dwelling elderly.

## 2. Materials and methods

### 2.1. Study design and participants

The present study is based upon data from the “Invecchiare in Chianti” study, a prospective population-based study of older persons in Tuscany, Italy that aims to identify risk factors for late-life disability.[7]

The Italian National Research Council on Aging Ethical Committee ratified the study protocol and participants provided written consent to participate.

At baseline, analyses for the present study included all 1155 participants aged 65+. Analyses were also conducted after stratifying participants according to the median age (74+ yrs). After three years of follow-up, data on functional ability were available for 867 participants who were not dependent in at least two activities of daily living (ADLs) at baseline.

### 2.2. Functional ability

Functional ability was estimated by self-report using the Katz’ questionnaire investigating ADLs,[8] and the Lawton and Brody scale for instrumental activities of daily living (IADLs).[9] These assessment tools are most commonly adopted for assessing functional independency for clinical and epidemiological purposes. The ADLs questionnaire explores independency in bathing, dressing, toileting, transferring, continence, and feeding.[8] The IADLs rate independency in more physically and cognitively complex tasks such as using the telephone,

shopping, food preparation, housekeeping, laundering, traveling, taking medications, and handling finances.[9] Disability in the ADLs was defined as need of assistance for performing two or more ADLs. The reason for not choosing a singlepoint decline is that impairment in two ADLs is less likely to capture physiological fluctuations in functional performance.[10] Impairment in IADL function was identified by a score <7; this higher cutoff level is generally adopted to avoid a "floor effect".[11]

### 2.3. Metabolic syndrome

MetS was defined according to the National Cholesterol Education Program's ATP-III criteria, adding use of hypolipemic, hypoglycaemic, and antihypertensive medications, as already done in several epidemiological studies; the diagnosis of the metabolic syndrome was defined by the presence of three or more of the following features: waist circumference >88 cm in women and >102 cm in men; fasting serum triglycerides ≥150 mg/dL; serum HDL <50 mg/dL in women and <40 mg/dL in men, or use of hypolipemic drugs; blood pressure ≥130/85 mmHg, or use of antihypertensive drugs; fasting blood glucose levels ≥110 mg/dL, or use of hypoglycaemic drugs.[12]

### 2.4. Covariates

Education was expressed as years of school attendance. Smoking was self-reported, and expressed as total lifetime pack-years. Current alcohol consumption was evaluated as glasses of wine per week. Diagnostic algorithms for diseases were modified versions of those created for the Women's Health and Aging Study.[13]

Comorbidity was quantified using the Charlson comorbidity index score.[14] All drugs assumed by participants were coded according to the Anatomical, Therapeutic, and Chemical codes.[15] Data on dietary intake were collected by the food-frequency questionnaire created for the European Prospective Investigation into Cancer and nutrition (EPIC) study.[16]

Hand grip strength was measured by a hand-held dynamometer (hydraulic hand BASELINE; Smith&Nephew, Agrate Brianza, Milan, Italy). The participants were asked to perform the task twice with each hand. The average of the best results obtained for each side was used for the analyses. Depressive symptoms were assessed using the original 20-item version of the Center for Epidemiological Studies-Depression Scale (CES-D).[17]

Cognitive performance was evaluated using the 30-item Mini Mental State Examination.[18] Blood samples were obtained from participants after 12-h fasting and after resting for at least 15 min. Aliquots of serum were stored at −80 °C and were not thawed until analyzed.

### 2.5. Statistical analyses

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS for Windows version 17.0, 2008, SPSS Inc., Chicago, IL); differences were considered significant at the $p < .050$ level. Data of continuous variables are presented as mean values ± standard deviation (SD). Analysis of variance for normally distributed variables according to MetS were performed by ANOVA comparisons; otherwise, the nonparametric Kruskal

−Wallis H test was adopted. Chi-square analysis was used for dichotomous variables. Serum interleukin 6 (IL-6) and C-reactive protein (CRP) levels were analyzed after log transformation.

Logistic regression analysis was used to estimate the association of variables of interest, including MetS, with baseline prevalent ADLs and IADLs disability.

To assess independent correlates of functional disability which might confound the association of ADLs and IADLs disability with MetS, groups of variables (demographics, comorbid conditions, medications, and objective tests, as depicted in Table 1) were first examined using separate age-and sex-adjusted logistic regression models. Those variables, significant at the $p < .050$ level in these initial models, were simultaneously entered into a summary model. In addition, the same models were analyzed in participants above or below the median age (Table 3). Indeed, most previous studies found that the association of Mets with different outcomes (such as survival and physical performance) changed beyond the age of 75.[19,20]

Logistic regression analysis was also adopted to assess the association of MetS with incident disability, i.e. dependence in at least two ADLs, after three years among participants without disability at baseline, after adjusting for potential confounders as depicted in Table 1, adjusting for baseline ADLs or IADL scores and the variations in body mass index (Table 4). To ensure that the adoption of an impairment in at least two ADLs for defining disability did not affect the results, we repeated cross-sectional, as well as prospective analyses, considering disability as an impairment in even a single activity of daily living.

Eventually, the cross-sectional and the prospective models were reanalyzed by entering the single components of MetS.

## 3. Results

The main characteristics of participants according to the presence of MetS are depicted in Table 1. The main characteristics of participants above or below the median age according to the presence of MetS are showed in Table 2. MetS was found in 268/1155 (23.2%) subjects, in 121/545 (22.2%) participants above the median age, and in 147/610 (24.1%) younger subjects. MetS was more prevalent in women than in men (Fisher exact $p = .001$). At baseline, disability in the ADLs was found in 76/1155 (6.6%) participants, while disability in the IADLs was found in 217/1155 (18.8%) subjects, with no significant differences in the whole population according to the presence of MetS.

Also, in participants above the median age at baseline, disability in two or more the ADLs was found in 9/121 (7.4%) participants with MetS and in 58/424 (13.7%) subjects without MetS ($p = .083$), while disability in two or more IADLs was found in 35/121 (28.9%) participants with MetS and in 160/424 (37.7%) persons without MetS ($p = .085$).

In addition, in participants below the median age, disability in two or more the ADLs was found at baseline in 6/147 (4.1%) participants with MetS and in 3/463 (0.6%) subjects

without MetS ($p$ = .008), while disability in two or more IADLs was found in 11/147 (7.5%) participants with MetS and in 11/463 (2.4%) persons without MetS ($p$ = .009).

After the 3-years follow-up, incident ADLs disability was present in 57/867 (6.6%) participants and IADLs disability was present in 167/867 (19.3%).

### 3.1. Characteristics of participants according to diagnosis of MetS

Participants with MetS, as compared with other participants, were more likely to be female, and to report less alcohol, carbohydrates, proteins, and lipids consumption and energy intake. Participants with MetS also were more likely to have a diagnosis of heart failure, peripheral arterial disease or coronary disease, and had higher Charlson index. They reported more frequent use of ACE-inhibitors, antiplatelets, and loop diuretics. In addition, subjects with MetS presented with higher CRP levels, as compared with other participants. Also, participants with MetS had a higher CES-D score, body mass index and lower hand grip strength (Table 1).

The main characteristics of participants above or below the median age according to diagnosis of MetS are showed in Table 2.

### 3.2. Multivariable analyses

At baseline, MetS was not associated with prevalent ADLs disability (OR = .55; 95% CI = .28–1.12; $p$ = .099) in the whole population. However, in the model limited to participants above the median age (74+ yrs) participants with MetS compared to controls were less likely to report ADL disability, and these findings were confirmed after adjusting for multiple confounders (OR =.33, 95% CI =.14−.77; p = .010) (Table 3). In the subgroup of participants below the median age, MetS was not associated with baseline disability in the initial model (OR = 5.08, 95% CI = .88−29.25; $p$ = .069). To assess any age-related differences in the adjusted association of MetS with disability, the summary model (as described in Table 3) was reanalyzed in participants below the median age. In these younger subjects, MetS was again not associated with disability (OR = 4.06, 95% CI = .83–19.82; p =.083).

When the summary regression model was analyzed considering a single-point impairment in the ADLs, MetS was again associated with disability in participants above the median age (OR =.29, 95% CI =.14–.60; $p$ =.001). In participants below the median age, MetS was not associated with disability (OR = 1.32, 95% CI =.40–4.29; $p$ = 649).

After the three-years follow-up, in the initial regression models age, diagnosis of heart failure, peripheral arterial disease, and use of loop diuretics were all associated with increased probability of incident disability in the ADLs, while baseline ADLs score, and the MetS were associated with reduced probability of incident ADLs disability (Table 4). After simultaneously adjusting for all these potential confounders in the summary model (Table 4), MetS was associated with reduced probability of incident ADLs disability (OR = .61, 95% CI = .41–.91; $p$ = .016).

When the summary regression model (not including baseline ADLs, that were all preserved) was analyzed considering a singlepoint loss in the ADLs, MetS was again associated with incident disability (OR = .56, 95% CI = .38–.84; $p = .005$).

Using the same logistic regression models, MetS was not associated with prevalent IADLs disability at baseline, neither in the whole population (OR = .70, 95% CI = .36−1.35; $p = .288$) nor in participants above the median age (OR = .61, 95% CI = .28−1.31; p = .206). Also, MetS was not associated with incident IADLs disability according to the prospective regression model (OR = 1.31, 95% CI = .84−2.04; p = .232). Eventually, when the single compo-nents of MetS were entered into the baseline final regression-model, abdominal obesity, hypertriglyceridemia, and high blood pressure were all associated with reduced probability of prevalent disability, while low HDL cholesterol levels were associated with increased probability of prevalent disability (Table 5). According to the prospective regression modeling, high blood pressure was associated with reduced probability of incident disability after three years, while no significant associations were found for the other components of the MetS.

## 4. Discussion

Results of the present study indicate that MetS is independently associated with reduced probability of prevalent disability in the ADLs among subjects aged 74þ, and of three years incident ADLs disability beyond the age of 65. This finding was not affected by the degree of impairment (≥1 or ≥2) in the ADLs adopted to define disability. Instead, no association was found between MetS and IADLs. This finding might be due to a “floor” effect or -a prevailing role of depression in conditioning IADLs abilities. Indeed, in our regression models the associations between disability in the IADLs and MetS lost statistical significance after adjusting for the CES-D score. Noticeably, it has been found that depressive symptoms in late life (measured by the CES-D score) are associated with increased incident disability in the IADLs.[21]

Disability in elderly populations is associated with huge medical, social and economic impact; therefore, knowledge of determinants of disability is a critical issue also in the social and health perspective.[2] MetS is an interesting potential cause of loss of functional ability, because of its prevalence and potential reversibility with adequate pharmacological and health education interventions. MetS has been proven a relevant determinant of loss of functional ability in middle aged populations; however, data regarding older populations are few, and conflicting.[22,23] Indeed, our finding of an apparently protective effect of acknowledged risk factors in older individuals is not new; for instance, obesity has been associated with lower mortality rates, as compared with normal body weight, among older hospitalized patients, as well as in older nursing home residents, and higher blood pressure levels have been associated with better cognitive functioning in hospitalized elderly with heart failure.[24,25] This epidemiological oddity is not unique of older subjects; in fact, higher serum cholesterol levels, waist circumference and body mass index have been associated with increased survival in patients with heart failure.[26] Also, higher body mass index, serum cholesterol and blood pressure levels have been associated with lower mortality rates in patients with end-stage renal disease.[27] Thus, the phenomenon of an established

cardiovascular risk factor in the general population having a markedly different, or even opposite, predictive pattern seems to be common to “frail” populations.

Specifically, the association between MetS and disability has been explored in an appreciable number of epidemiological studies; however, all these studies included participants whose median age was sensibly lower than that of our study sample. Indeed, in our study the presence of MetS among participants whose age was below 75 years was associated with a five-fold increase in the probability of disability, even though confidence intervals were too large to yield statistical significance. Noticeably, a study has recently documented that the adverse effect of MetS on muscle strength is age-dependent, so that no significant association was found beyond the age of 75.[19] Also, MetS has not been found to be associated with increased mortality in populations whose mean age was beyond 75.[20] Thus, this age cutoff for the adverse effects of MetS might have relevant implications for practicing physicians and decision makers. In a more general sense, advanced age per se might represent a condition of frailty, that is associated with the epidemiological phenomenon of “reverse epidemiology”.[28] In this perspective, it has been suggested that in older and frailer subjects any factor that may improve short-term survival, such as high blood pressure, obesity, and hypercholesterolemia, might exert a desirable effect on longevity.[27,28]

In the present study participants with MetS had lower protein, carbohydrates, lipidis and energy intake; nonetheless, the laboratory indicators of nutritional status were not worse, but even better, than those of other participants. Indeed, obese persons have been found to underreport their caloric intake, even when assessed by the EPIC questionnaire.[29] This might explain the aforementioned incongruity of reported nutrient intake and objective nutritional parameters. Alternatively, MetS subjects might need a lower nutrient intake to meet their metabolic needs.[30]

Another possible explanation for our results is represented by selective survival, according to which our older participants might be “survivors” who were less susceptible to the effects of cardiovascular risk factors included in the MetS.

The lack of association in the present study between disability and the single components of MetS might reflect insufficient statistical power of the single items. Nevertheless, this result might also support the current view that the clinical significance of MetS exceeds the mere arithmetic sum of its individual components.

### 4.1. Strengths and limitations

This study includes a representative community-dwelling population, with high participation rate and with extensive information regarding risk factors, comorbid conditions, and objective parameters. However, this study only indicated a significant trend towards preserved functional ability in subjects with MetS; further studies are needed to assess any cause−effect relationship, as well as the clinical significance of such an association.

Also, we were unable to exclude that subjects with MetS received better health counseling because of their condition. We could only hypothesize that larger use of selected drugs that

yield protective cardiovascular effects, e.g., ACE-inhibitors or antiplatelets, might contribute to prevent loss of functional ability.

We normalyzed the nutrient intake by body weight (Tables 1 and 2); this might lead to underestimation of real intake in obese subjects, whose fat mass is metabolically less active. However, this made our analyses more conservative.

## 5. Conclusion

In older subjects, MetS is associated with reduced probability of prevalent and incident disability in the ADLs. Results of the present study might indicate that different targets should be considered in the treatment of MetS in older and frailer subjects or, at least, a specific alimentary counseling might be advisable.

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## Non-standardized abbreviations:

| | |
|---|---|
| **MetS** | metabolic syndrome |
| **ADLs** | Katz’s activities of daily living |
| **IADLs** | Lawton and Brody scale for instrumental activities of daily living |
| **CES-D** | 20-item version of the Center for Epidemiological Studies-Depression Scale |
| **IL-6** | interleukin 6 |
| **CRP** | C-reactive protein |

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## Table 1

Characteristics of the 1155 participants aged 65 plus according to diagnosis of the metabolic syndrome.

| | **Participants with metabolic syndrome (*n* = 268) *n* (%) or mean ± SD** | **Participants without metabolic syndrome (*n* = 887) *n* (%) or mean ± SD** | **p** |
|---|---|---|---|
| *Demographics & lifestyle habits* | | | |
| Age (years) | 75 ± 7 | 76 ± 8 | .072 |
| Sex (female) | 182 (68.3%) | 472 (53.2%) | <.0001 |
| Education (years) | 5 ± 3 | 5.4 ± 3.4 | .132 |
| Current alcohol consumption[a] | 8.8 ± 7.7 | 10.4 ± 9.6 | .021 |
| Smoking[b] | 11.6 ± 21.6 | 12.7 ± 21.3 | .058 |
| Protein consumption (g/Kg/day) | 1.01 ± 0.30 | 1.16 ± 0.32 | <.0001 |
| Total lipids consumption (g/Kg/day) | 0.9 ± 0.27 | 1.0 ± 0.31 | <.0001 |
| Carbohydrates consumption (g/Kg/day) | 3.27 ± 1.14 | 3.88 ± 1.21 | <.0001 |
| Total energy (kcal/Kg/day) | 25.10 ± 7.28 | 29.90 ± 8.36 | <.0001 |
| Comorbid conditions | | | |
| Chronic pulmonary disease | 21 (7.8%) | 68 (7.7%) | .897 |
| Heart failure | 28 (10.4%) | 31 (3.5%) | <.0001 |
| Stroke | 25 (9.3%) | 60 (6.8%) | .182 |
| Arthritis | 27 (10.1%) | 89 (10.1%) | .999 |
| Parkinson's disease | 2 (0.7%) | 14(1.6%) | .387 |
| Peripheral arterial disease | 45 (16.8%) | 79 (8.9%) | <.0001 |
| Coronary disease | 33 (12.3%) | 48 (5.4%) | <.0001 |
| Charlson comorbidity score index | 1.3 ± 1.4 | 0.7 ± 1.1 | <.0001 |
| Medications | | | |
| Beta-blockers | 7 (2.6%) | 20 (2.3%) | .817 |
| Corticosteroids | 4 (1.5%) | 19(2.1%) | .624 |
| ACE-I[c] | 51 (19%) | 109 (12.3%) | .006 |
| Loop diuretics | 38 (14.2%) | 67 (7.6%) | .002 |
| NSAIDs | 7 (2.6%) | 13 (1.5%) | .282 |
| Antiplatelets | 41 (15.3%) | 86 (9.7%) | .014 |
| Objective tests | | | |
| Total proteins (g/dl) | 7.2 ± 0.4 | 7.1 ± 0.4 | .065 |
| Serum creatinine (mg/dl) | 0.9 ± 0.3 | 0.9 ± 0.2 | .306 |
| Interleukin 6 (pg/ml) | 2.6 ± 5.8 | 2.2 ± 3.6 | .141 |
| CRP-HS (mgml)[d] | 6.7 ± 12.5 | 5.0 ± 8.3 | .012 |
| Mini Mental State Examination | 24 ± 4 | 24 ± 6 | .170 |
| CES-D[e] | 14 ± 9 | 13 ± 8 | .037 |
| Body mass index at baseline | 30 ± 4.3 | 26.5 ± 3.6 | <.0001 |
| Body mass index at follo-up[f] | 28.7 ± 4 | 25.7 ± 3.6 | <.0001 |
| Hemoglobin at baseline (g/dL) | 13.8 ± 1.4 | 13.9 ± 1.4 | .433 |

| | **Participants with metabolic syndrome (*n* = 268) *n* (%) or mean ± SD** | **Participants without metabolic syndrome (*n* = 887) *n* (%) or mean ± SD** | **p** |
|---|---|---|---|
| Hand grip (Kg) | 25.9 ± 11.2 | 29.5 ± 12.1 | <.0001 |
| Baseline ADLs disability[g] | 15 (5.6%) | 61 (6.9%) | .574 |
| Incident ADLs disability[f,g] | 64 (24%) | 278 (31%) | .022 |
| Baseline IADLs disability[h] | 46(17.2%) | 171 (19.3%) | .476 |
| Incident IADLs disability[f,h] | 52 (23%) | 145 (21.6%) | .710 |

[a]Number of weekly wine glasses.

[b]Total lifetime pack years.

[c]Angiotensin-Converting Enzyme inhibitors.

[d]High-sensitivity C-Reactive Protein.

[e]20-item version of the Center for Epidemiological Studies-Depression Scale.

[f]Number of participants after three-year of follow-up: 897.

[g]Defined by impairment in 2+ activities of Daily Living.

[h]Defined by impairment in 2+ Instrumental Activities of Daily Living.

## Table 2

Baseline characteristics of participants above or below the median age (75 yrs) according to diagnosis of the metabolic syndrome (MetS).

| | Subjects below the median age (*n* = 610) | | | Subjects above the median age (*n* = 545) | | |
|---|---|---|---|---|---|---|
| | **Participants with MetS (*n* = 147) *n* (%) or mean ± SD** | **Participants without MetS (*n* = 463) *n* (%) or mean ± SD** | **p** | **Participants with MetS (*n* = 121) *n* (%) or mean ± SD** | **Participants with MetS (*n* = 424) *n* (%) or mean ± SD** | **p** |
| *Demographics & lifestyle habits* | | | | | | |
| Age (years) | 69.5 ± 2.8 | 69.5 ± 2.9 | .989 | 81.0 ± 5.1 | 82.3 ± 5.70 | .18 |
| Sex (female) | 94 (63.9%) | 228 (49.2%) | .002 | 89 (73.6%) | 244 (57.5%) | .001 |
| Education (years) | 5.7 ± 3.0 | 6.1 ± 3.3 | .222 | 4.1 ± 2.8 | 4.5 ± 3.3 | .222 |
| Current alcohol consumption[a] | 8.6 ± 6.8 | 11.4 ± 10.0 | .006 | 8.9 ± 8.7 | 9.4 ± 9.1 | .649 |
| Smoking[b] | 13.1 ± 22.1 | 13.8 ± 20.5 | .248 | 9.7 ± 21.0 | 11.5 ± 22.0 | .071 |
| Protein consumption (g/Kg/day) | 1.02 ± 0.32 | 1.16 ± 0.32 | <.0001 | 0.99 ± 0.26 | 1.16 ± 0.32 | <.0001 |
| Total lipids consumption (g/Kg/day) | 0.87 ± 0.26 | 1.01 ± 0.32 | <.0001 | 0.86 ± 0.28 | 0.98 ± 0.30 | <.0001 |
| Carbohydrates consumption (g/Kg/day) | 3.24 ± 1.21 | 3.86 ± 1.20 | <.0001 | 3.31 ± 1.04 | 3.92 ± 1.22 | <.0001 |
| Total energy (kcal/Kg/day) | 25.18 ± 7.72 | 30.01 ± 8.46 | <.0001 | 25.0 ± 6.70 | 29.73 ± 8.23 | <.0001 |
| *Comorbid conditions* | | | | | | |
| Chronic pulmonary disease | 12 (8.2%) | 36 (7.8%) | .861 | 9 (7.4%) | 32 (7.5%) | 1.000 |
| Heart failure | 10 (6.8%) | 6 (1.3%) | <.0001 | 18 (14.9%) | 25 (5.9%) | .003 |
| Stroke | 11 (7.5%) | 22 (4.8%) | .211 | 14 (11.6%) | 38 (9.0%) | .384 |
| Arthritis | 12 (8.2%) | 39 (8.4%) | 1.000 | 15 (12.4%) | 50 (11.8%) | .874 |
| Parkinson's disease | 1 (0.7%) | 5 (1.1%) | 1.000 | 1 (0.8%) | 9 (2.1%) | .700 |
| Peripheral arterial disease | 12 (8.2%) | 26 (5.6%) | .326 | 33 (27.3%) | 54 (12.7%) | <.0001 |
| Coronary disease | 15 (10.2%) | 13 (2.8%) | .001 | 18 (14.9%) | 35 (8.3%) | .037 |
| Charlson comorbidity score index | 1.0 ± 1.3 | 0.6 ± 09 | <.0001 | 1.6 ± 1.4 | 0.9 ± 1.2 | <.0001 |
| *Medications* | | | | | | |
| Beta-blockers | 3 (2%) | 13 (2.8%) | .773 | 4 (3.3%) | 7 (1.7%) | .273 |
| Corticosteroids | 1 (0.7%) | 9(1.9%) | .465 | 3 (2.5%) | 10 (2.4%) | 1.000 |
| ACE-I[c] | 24 (16.3%) | 44 (9.5%) | .034 | 27 (22.3%) | 65 (15.3%) | .075 |
| Loop diuretics | 16(10.9%) | 16 (3.5%) | .001 | 22 (18.2%) | 51 (12.0%) | .095 |
| NSAIDs | 3 (2.0%) | 8 (1.7%) | .731 | 4 (3.3%) | 5 (1.2%) | .116 |
| Antiplatelets | 14 (9.5%) | 22 (4.8%) | .043 | 27 (22.3%) | 64 (15.1%) | .072 |
| *Objective tests* | | | | | | |
| Total proteins (g/dl) | 7.2 ± 0.4 | 7.1 ± 0.4 | .861 | 7.2 ± 0.4 | 7.1 ± 0.5 | .019 |
| Serum creatinine (mg/dl) | 0.9 ± 0.2 | 0.9 ± 0.1 | .235 | 1.0 ± 0.4 | 0.9 ± 0.2 | .042 |
| Interleukin 6 (pg/ml) | 1.9 ± 2.1 | 1.6 ± 1.6 | .046 | 3.5 ± 8.2 | 2.8 ± 5.0 | .060 |
| CRP-HS (mgml)[d] | 5.8 ± 10.5 | 4.1 ± 5.5 | <.0001 | 7.8 ± 14.5 | 6.1 ± 10.5 | .009 |
| Mini Mental State Examination | 26 ± 3 | 26 ± 2 | .133 | 22 ± 5 | 21 ± 7 | .035 |
| CES-D[e] | 12 ± 8 | 11 ± 8 | .123 | 16 ± 10 | 15 ± 9 | .107 |
| Body mass index | 30.4 ± 4.3 | 26.9 ± 3.5 | <.0001 | 29.3 ± 4.2 | 26.0 ± 3.7 | <.0001 |

| | Subjects below the median age (*n* = 610) | | | Subjects above the median age (*n* = 545) | | |
|---|---|---|---|---|---|---|
| | **Participants with MetS (*n* = 147) *n* (%) or mean ± SD** | **Participants without MetS (*n* = 463) *n* (%) or mean ± SD** | **p** | **Participants with MetS (*n* = 121) *n* (%) or mean ± SD** | **Participants with MetS (*n* = 424) *n* (%) or mean ± SD** | **p** |
| Hemoglobin (g/dL) | 14.1 ± 1.2 | 14.0 ± 1.3 | .367 | 13.4 ± 1.5 | 13.3 ± 1.5 | .746 |
| Hand grip (Kg) | 29.1 ± 12.2 | 33.0 ± 12.0 | .002 | 22.2 ± 8.5 | 24.5 ± 10.4 | .024 |
| Baseline ADLs disability[f] | 6 (4.1%) | 3 (0.6%) | .008 | 9 (7.4%) | 58 (13.7%) | .083 |
| Baseline IADLs disability[g] | 11 (7.5%) | 11 (2.4%) | .009 | 35 (28.9%) | 160 (37.7%) | .085 |

[a]Number of weekly wine glasses.

[b]Total lifetime pack years.

[c]Angiotensin-Converting Enzyme inhibitors.

[d]High-sensitivity C-Reactive Protein.

[e]20-item version of the Center for Epidemiological Studies-Depression Scale.

[f]Defined by impairment in 2+ activities of Daily Living.

[g]Defined by impairment in 2+ Instrumental Activities of Daily Living.

## Table 3

Association (Odds Ratio, OR and 95% confidence intervals, CI) of disability in the activities of daily living at baseline according to the initial (age-and sex-adjusted), and "summary" (fully adjusted) logistic regression models in 545 participants aged above the median value (74 yrs). All the covariates were entered simultaneously into the regression models.

| | Age- and sex-adjusted models | | | Summary model | | |
|---|---|---|---|---|---|---|
| | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** |
| *Demographics & lifestyle habits* | | | | | | |
| Age (years) | 1.14 | 1.03–1.27 | .015 | 1.13 | 1.08–1.19 | <.0001 |
| Sex (female) | 1.63 | .40–6.67 | .498 | 1.60 | .87–2.95 | .132 |
| Education (years) | .92 | .71–1.17 | .491 | | | |
| Current alcohol consumption[a] | 1.01 | .94–1.08 | .832 | | | |
| Smoking[b] | 1.01 | .98–1.04 | .498 | | | |
| Protein consumption (g/Kg/day) | 2.33 | .03–16.88 | .698 | | | |
| Total lipids consumption (g/Kg/day) | 2.72 | .01–18.06 | .718 | | | |
| Carbohydrates consumption (g/Kg/day) | 2.62 | .43–16.12 | .299 | | | |
| Total energy (kcal/Kg/day) | .83 | .53–1.30 | .409 | | | |
| *Comorbid conditions* | | | | | | |
| Chronic pulmonary disease | .72 | .25–2.06 | .541 | | | |
| Heart failure | .83 | .29–2.37 | .727 | | | |
| Stroke | 1.20 | .48–3.01 | .690 | | | |
| Arthritis | .42 | .14–1.27 | .125 | | | |
| Parkinson's disease | 5.11 | 1.29–20.21 | .020 | 5.24 | 1.35–20.34 | .017 |
| Peripheral arterial disease | .50 | .21–1.20 | .122 | | | |
| Coronary disease | .28 | .07–1.10 | .069 | | | |
| Charlson comorbidity score index | 1.97 | 1.51–2.56 | <.0001 | 1.80 | 1.48–2.19 | <.0001 |
| Metabolic syndrome | .37 | .15–.90 | .027 | .33 | .14–.77 | .010 |
| *Medications* | | | | | | |
| Beta-blockers | .86 | .11–6.80 | .885 | | | |
| Corticosteroids | .52 | .06–4.13 | .534 | | | |
| ACE-I[c] | .93 | .47–1.86 | .841 | | | |
| Loop diuretics | 1.53 | .74–3.13 | .249 | | | |
| NSAIDs | 1.20 | .15–9.61 | .865 | | | |
| Antiplatelets | 1.24 | .64–2.42 | .527 | | | |
| *Objective tests* | | | | | | |
| Total proteins (g/dl) | 1.44 | .11–18.16 | .780 | | | |
| Serum creatinine (mg/dl) | 3.81 | .02–67.89 | .613 | | | |
| Interleukin 6 (pg/ml) | .99 | .24–4.05 | .994 | | | |
| CRP-HS (mgml)[d] | .50 | .13–1.98 | .325 | | | |
| Mini Mental State Examination | .73 | .52–1.03 | .072 | | | |
| CES-D[e] | 1.11 | .99–1.23 | .066 | | | |

| | Age- and sex-adjusted models | | | Summary model | | |
|---|---|---|---|---|---|---|
| | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** |
| Body mass index | 1.07 | .83–1.40 | .592 | | | |
| Hemoglobin (g/dL) | 3.31 | .85–12.96 | .086 | | | |
| Handgrip (Kgs) | .85 | .72–1.01 | .065 | | | |

[a] Number of weekly wine glasses.

[b] Total lifetime pack years.

[c] Angiotensin-Converting Enzyme inhibitors.

[d] Log–transformed.

[e] 20-item version of the Center for Epidemiological Studies-Depression Scale.

## Table 4

Association (Odds Ratio, OR and 95% confidence intervals, CI) of incident disability in the activities of daily living after three-years follow-up according to the initial (age-and sex-adjusted), and "summary" (fully adjusted) logistic regression models in 867 participants. All the covariates were entered simultaneously into the regression models.

| | Age- and sex-adjusted models | | | Summary model | | |
|---|---|---|---|---|---|---|
| | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** |
| *Demographics & lifestyle habits* | | | | | | |
| Age (years) | 1.13 | 1.10–1.16 | <.0001 | 1.12 | 1.09–1.14 | <.0001 |
| Sex (female) | 1.02 | .64–1.63 | .931 | 1.16 | .84–1.60 | .359 |
| Education (years) | .94 | .88–1.01 | .092 | | | |
| Current alcohol consumption[a] | .99 | .96–1.01 | .299 | | | |
| Smoking[b] | 1.01 | .99–1.01 | .420 | | | |
| Protein consumption (g/Kg/day) | .92 | .23–3.77 | .914 | | | |
| Total lipids consumption (g/Kg/day) | 1.41 | .30–6.48 | .662 | | | |
| Carbohydrates consumption (g/Kg/day) | 1.24 | .77–1.98 | .378 | | | |
| Total energy (kcal/Kg/day) | .96 | .86–1.07 | .477 | | | |
| *Comorbid conditions* | | | | | | |
| Chronic pulmonary disease | 1.45 | .77–2.73 | .252 | | | |
| Heart failure | 3.20 | 1.55 –6.60 | .002 | 2.16 | 1.02–4.55 | .044 |
| Stroke | 1.77 | .93–3.37 | .083 | | | |
| Arthritis | 1.25 | .78–2.02 | .351 | | | |
| Parkinson's disease | 1.27 | .33–4.91 | .727 | | | |
| Peripheral arterial disease | 1.71 | 1.04–2.82 | .035 | 1.74 | 1.10–2.77 | .019 |
| Coronary disease | .69 | .37–1.29 | .246 | | | |
| Charlson comorbidity score index | 1.01 | .84–1.22 | .913 | | | |
| Metabolic syndrome | .60 | .40-.89 | .012 | .61 | .41-.91 | .016 |
| *Medications* | | | | | | |
| Beta-blockers | .72 | .25–2.08 | .545 | | | |
| Corticosteroids | .75 | .26–2.14 | .594 | | | |
| ACE-I[c] | 1.12 | .73–1.74 | .599 | | | |
| Loop diuretics | 2.07 | 1.24–3.47 | .006 | 1.68 | .99–2.87 | .057 |
| NSAIDs | 1.75 | .62–4.93 | .289 | | | |
| Antiplatelets | .76 | .47–1.21 | .247 | | | |
| *Objective tests* | | | | | | |
| Total proteins (g/dl) | 2.58 | .94–7.02 | .064 | | | |
| Serum creatinine (mg/dl) | .72 | .05–10.58 | .810 | | | |
| Interleukin 6 (pg/ml)[d] | 1.37 | .79–2.38 | .262 | | | |
| CRP-HS (mgml)[d] | .97 | .56–1.68 | .912 | | | |
| Mini Mental State Examination | .94 | .80–1.09 | .398 | | | |
| Baseline activities of daily living | .06 | .01 -.29 | <.0001 | .25 | .11-.57 | .016 |

| | Age- and sex-adjusted models | | | Summary model | | |
|---|---|---|---|---|---|---|
| | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** |
| CES-D[e] | 1.04 | .99–1.10 | .084 | | | |
| Variations in body mass index[f] | 1.17 | .90–1.52 | .228 | | | |
| Hemoglobin (g/dL) | 1.03 | .70–1.51 | .895 | | | |
| Handgrip (Kg) | .96 | .89–1.03 | .272 | | | |

[a] Number of weekly wine glasses.

[b] Total lifetime pack years.

[c] Angiotensin-Converting Enzyme inhibitors.

[d] Log–transformed.

[e] 20-item version of the Center for Epidemiological Studies-Depression Scale.

[f] Body Mass Index at follow-up - Body Mass Index al baseline

## Table 5

Association (Odds Ratio,OR and 95% confidence intervals, CI) of disability in ADLs at baseline and after 3 years with the individual components of the metabolic syndrome according to the fully adjusted regression models. All the covariates were entered simultaneously into the regression model.

| | Baseline[a] | | | Three-year follow-up[b] | | |
|---|---|---|---|---|---|---|
| | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** |
| Abdominal obesity | .21 | .07–.58 | .003 | .99 | .69–1.44 | .995 |
| Hypertriglyceridemia | .34 | .13–.88 | .027 | .66 | .43–1.01 | .056 |
| Low HDL-cholesterol | 2.54 | 1.24–5.19 | .011 | .86 | .57–1.29 | .467 |
| High blood pressure | .33 | .17–.63 | .001 | .68 | .49–.94 | .020 |
| High fasting blood glucose | .91 | .39–2.11 | .827 | 1.09 | .71–1.66 | .690 |

[a]Adjusted for: age, sex, diagnosis of Parkinson's disease, and Charlson comorbidity score index, as depicted in Table 3.

[b]Adjusted for: age, sex, diagnosis of heart failure, and peripheral arterial disease, baseline ADLs score, and use of loop diuretics, as depicted in Table 4.