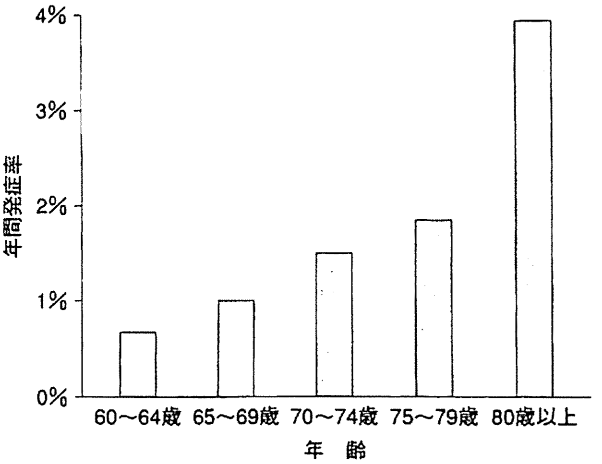

図２　認知症の年間発症率
「国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）」の８年間の縦断的観察から．

表１　認知症患者数および有病率推定値

年　度	推定患者数	65歳以上推定人口	有病率
2010	458万人	2,941万人	15.6%
2015	529万人	3,378万人	15.7%
2020	574万人	3,590万人	16.0%
2025	617万人	3,635万人	17.0%
2030	666万人	3,667万人	18.2%
2035	656万人	3,725万人	17.6%
2040	605万人	3,853万人	15.7%
2045	601万人	3,841万人	15.6%
2050	634万人	3,764万人	16.8%
2055	659万人	3,646万人	18.1%

率と，2008年度の65歳以上の全国人口2,822万人から，認知症患者数は406万人と推定された．しかし，施設入所者などを加えれば，これよりも患者数はさらに多い可能性がある．従来の方法での患者数推計は，認知症自立度Ⅱ以上を認知症として208万人との推計が出されていたが，患者数は少なくともその約２倍存在することになる．しかし，今回の調査は主として地方の市町村で実施されたので，今後は都市部における同様の調査を行い，検証を行う必要があろう．

認知症の発症率

発症率を推定するためには，同一対象集団について複数年にわたっての繰り返しの調査が必要であり，有病率の推定よりも難しく，わが国の疫学調査の結果では認知症の発症率の推定はほとんど行われていない．われわれは，無作為抽出された地域住民を長期にわたって追跡した「国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）」[4]のデータを用いて，８年間の縦断的な検討から認知症の発症率の推定を行った（図２）．その結果では，60歳以上の地域住民の1.5%が毎年認知症となっていた．年齢が高くなるほど発症率は上昇し，80歳以上では毎年4.0%が認知症となっていたという結果であった．

認知症患者数の将来推計

５歳ごとの性別・年齢別の認知症有病率が今後も大きく変わらないものとして，人口の高齢化に伴う認知症患者数の将来推計を行ってみた．性別・年齢別の認知症有病率は今回の全国調査の結果を用い，人口推計は国立社会保障・人口問題研究所の2006年度12月推計を用いた．2010年度の65歳以上の認知症推定患者数は全体として458万人で，有病率は約15.6%であると推定される．今後，高齢者人口，特に後期高齢者の人口が急増し，表１に示したように患者数は2020年度に574万人，2030年度には666万人と，これからの20年間に認知症の患者数はさらに大きく増加すると予測される．予防や治療法の開発など，早急な対策によって患者数削減を達成しないと，患者の介護や医療に関わる費用は大きく上昇し，それによって国民経済が破綻してしまうことにもなりかねない状況にある．

おわりに

世界有数の長寿の国であるわが国は急速に高齢化が進み，それとともに認知症患者の数も増大していく．今後15年間で認知症に関わる介護費用は大きく増加し，年間10兆円に達するとも予想される[5]．高齢化が進む一方で，少子化も進み，介護に関わることのできる労働人口は激減する．このままでは認知症によって日本の社会が崩壊するといっても過言ではない．しかし，認知症の発症を２年遅らせることができれば，それだけで年間１兆円もの介護費用，医療費が削減できる可能性がある[5]．最近は，認知症の進行を緩徐化する作用をもつ薬物が次々に開発され，またアルツハイマー病に対するワクチンの開発なども進められている．認知症は生活習慣病でもあり，生活習慣の改善である程度の予防が可能である．認知症の素因としての遺伝子多型の研究も進み始めている．このような研究の推進により認知症を克服して，高齢者の知的機能を守り，高

齢者の社会参画を可能にしていくことが，今後の日本の長寿社会を守っていくためにはぜひとも必要である．

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Epidemiological View of Dementia in Japan

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The methods of prevention and medical cure of dementia are still unclear. Disease situations chronically develop to severe stage over a long period of time. The burden for care and medical treatment of dementia is huge. The incidence of dementia increases with age. Therefore, number of dementia patients and cost for care and treatment will increase rapidly with aging in Japanese society. The epidemiological studies of dementia including prevalence and incidence statistics are very important for estimation of medical cost and policymaking of care and welfare in the elderly. The first national survey of dementia prevalence was tried in 7 areas in Japan. The prevalence rate of dementia was estimated to be 14.4 percent. Number of the elderly population 65 years and over is about 30 million in 2010 and number of dementia patients is estimated 4.5 million which was more than double of the previous estimation. Number of dementia patients will increase to 6.7 million in 2030. Researches on prevention and therapy for reduction of dementia are tasks of pressing urgency.

COLUMN コラム

高齢者のうつと栄養

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KEY WORD
うつ，高齢者，n-3 系多価不飽和脂肪酸，魚類脂肪，コレステロール，アミノ酸

うつとは

うつ病とは気分がひどく落ち込み，なにごとにも興味や喜びが感じられなくなり，そのことに著しい苦痛を感じ，日常生活に支障を生じるようになった状態で，正式には大うつ病（major depression disease）ともいい，気分障害（mood disorder）の一形態である[1,2]．

うつ病は先進諸国ではもっとも頻度の高い精神疾患の 1 つであり[2]，2004 年の WHO report によれば[3]，うつ病は下部呼吸器疾患，下痢性疾患についで「疾病による世界全体の負担」の第 3 位で，先進国を中心とした高収入国だけで推定すると，社会全体でもっとも負担となっている病気である．

うつ病は自殺とも関連し，自殺者の 30 ～ 70%がうつ病の診断に当てはまるとも，またうつ病患者の自殺率は一般人の 10 倍以上ともいわれている．わが国は先進諸国のなかでも自殺率が高いことが知られており，十数年来，自殺死亡者数は年間 3 万人前後で社会問題となっている．

昨今，「うつ（状態）」あるいは「抑うつ（状態）」という言葉は，大うつ病の診断基準を満たさない場合も含めて，より広い意味で用いられている．疫学調査では精神科医の診断を必要としない，自記式質問票を用いてうつの頻度や有病率の調査を行うことが多い．筆者らが 1997 年から行っている「国立長寿医療研究センター・老化に関する長期縦断疫学研究[4]」では CES-D（Center for epidemiology studies depression scale）というスクリーニング検査を用いて一般地域住民のうつを調査している．直近の第 6 次調査（2008 ～ 2010）では，40 歳から 80 歳代までのうつの頻度は 13.1%（男性 12.3%，女性 13.9%）で女性にやや多かった[5]（**表 1**）．国内の他の文献でもわが国の高齢者のうつの頻度はおおよそ 10 ～ 20%で，女性に多いことが知られている．

うつの関連要因（栄養要因以外）

うつ病には遺伝的要因が 40 ～ 50%，後天的要因が 50 ～ 60%関与すると考えられている．うつ病は単一遺伝子ではなく，多因子遺伝疾患である．後天的な関連要因としては，大脳成長期のストレスや精神的トラウマ，身体疾患や障害（副腎皮質ホルモンや甲状腺ホルモンの上昇・低下，膠原病，パーキンソン病，糖尿病，脳血管疾患，動脈硬化症，頭部外傷，あ

表 1　地域在住中高年者のうつの頻度（%）

	40 ～ 49 歳	50 ～ 59 歳	60 ～ 69 歳	70 ～ 79 歳	80 ～ 89 歳	全体
男性	12.1	10.2	8.7	17.4	15.1	12.3
女性	11.1	14.1	13.7	15.3	17.7	13.9
全体	11.6	12.0	11.2	16.4	16.4	13.1

国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）．第 6 次調査（2008 ～ 2010）での CES-D 検査結果による（16 点以上を「うつ」と定義）

る種のがん，気管支喘息など）の関与が報告されている．

ストレスも，うつやうつ病の大きな誘因である．慢性的なストレスや制御しがたいストレスに対して，人は不安や怒り，無気力感や抑うつ感，認知障害などの不適応的反応を示す[2]．高齢者ではとくに家族，知人との死別，役割・仕事からの離脱，健康・ADL の障害などがうつの契機となるといわれている．しかし同じようなストレス下にあっても，個人のストレスに対する対応パターン（ストレスコーピング）によってうつの発症は影響される．

このようにうつの発症にかかわる要因は多岐にわたり，相互にも関連していて非常に複雑である．

うつと栄養とのかかわり

食事をとることそのものが満足感，充足感につながることは誰もが実感している．うつや感情には脳内のセロトニンやノルエピネフリンが関連しているが，脳内伝達物質の前駆物質の多くは食物から供給される[6]．これまでにうつとの関連が検討された栄養学的要因は，セロトニンやノルエピネフリンの前駆物質であるトリプトファン，チロシン，フェニルアラニン等のアミノ酸，神経細胞膜の主成分である多価不飽和脂肪酸やコレステロール，動脈硬化との関連も報告されている葉酸・ビタミン B_{12}・ホモシステイン，さらにはグルタミン，タウリン，テアニン等のアミノ酸，ヨードや鉛，ビタミン D，炭水化物や糖，アルコール摂取や低栄養など，きわめて多岐にわたっている．ここでは多価不飽和脂肪酸，コレステロールと脳内伝達物質やアミノ酸についてまとめる．

多価不飽和脂肪酸とうつ

魚に多く含まれる n-3 系脂肪酸〔ドコサヘキサエン酸（DHA），エイコサペンタエン酸（EPA）等〕の摂取，あるいは魚摂取とうつとの関連を検討した報告は多い．Maes ら[7]は，うつ病患者で血漿リン脂質中の n-3 系多価脂肪酸の欠乏がみられた，と報告している．若年女性に関しては妊娠中の魚摂取が出産後うつ病を減らした[8]という報告や EPA，DHA 摂取が若年成人女性の 2 年後のうつを抑制した[9]という報告がある．また，うつの高齢者では血清 EPA が低く，うつ病の重症度と血清 EPA が逆相関していた[10]．さらに地域住民での大規模調査で EPA や EPA/AA 比が高い群では well-being の指標が高かった[11]．Hibbeln らは，各国の魚摂取量とうつの頻度の間に負の関連があることを示している[12]．しかし，n-3 系脂肪酸とうつとの関係を否定する報告も多数あり，一定の結論には達していない．肯定的研究，否定的研究ともに横断的な研究が多く，対象が限られているのも難点である．

筆者らは前述した NILS-LSA の詳細な栄養調査の結果を用いて，第 1 次調査で抑うつのなかった 65 歳以上の高齢者を対象として 2 年後の抑うつの有無と食品群・栄養素摂取との関係を報告している[13]．医学的・社会的交絡要因を調整したステップワイズ多重ロジスティック解析の結果，女性では有意な項目は認められなかったが，男性では，魚類脂肪，獣肉類，ビタミン D，アラキジン酸が有意となった（**表 2**）．魚介類脂肪に関しては摂取量が 1 標準偏差（2.5 g/ 日）増えるごとに抑うつの危険率が約 1/3 に減少することが示された．また魚介類脂肪を 1 日 4.8 g 以上摂取している群ではそれ未満の群よりも有意に 2 年後の CES-D 得点が低く，うつ傾向が小さいと考えられた．これはサバなら 30 g，アジなら 70 g から摂取される魚類由来脂肪量とほぼ同等であった（**図 1**）．n-3 系脂肪酸とうつとの関係は横断的検討では有意であったものの，縦断的検討で多くの交絡要因を調整すると有意ではなくなった．

n-3 系脂肪酸の抑うつとの関係の作用機序については，Hibbeln らは中枢神経系の細胞膜の n-3/n-6 比の低下が神経内分泌や受容体の性状に影響を与える可能性を指摘している[12]．また EPA や DHA は脳卒中や脳血管の動脈硬化を抑制することが知られているが，動脈硬化はうつと関連していることから，これらの n-3 系脂肪酸が抗動脈硬化作用を介してうつ発症に抑制的に作用している可能性もある．

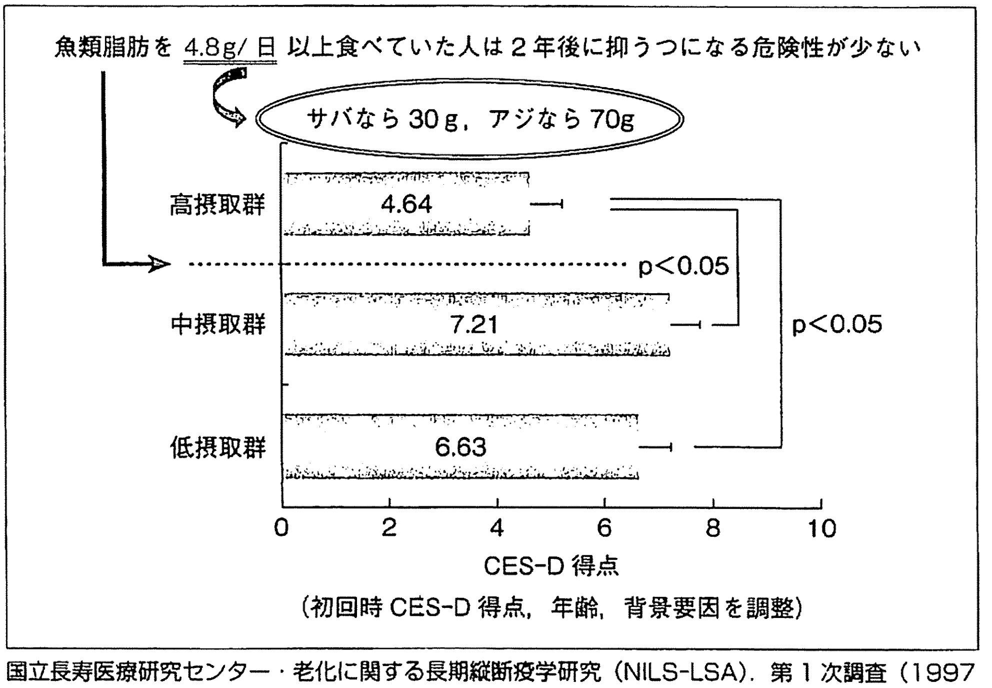
表2　抑うつと関連があった食品群・栄養素（縦断的検討，ステップワイズロジスティック回帰分析）

初回調査時に抑うつがなかった者を対象とし，年齢，初回時 CES-D 得点，老研式生活活動度指標，喫煙，自覚的健康度，就業，家庭内収入，学歴，HDL コレステロール，アルカリフォスファターゼ，遊離T3，甲状腺刺激ホルモン，血小板数，BMI を調整した．

	Odds 比（1 s.d. あたり）	95%信頼区間
男性		
魚類脂肪	0.308	0.105 ～ 0.908
ビタミンD	0.361	0.137 ～ 0.950
獣鳥肉類	2.261	1.154 ～ 4.431
アラキジン酸	1.660	1.016 ～ 2.712
女性		
（有意な項目なし）		

国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）．第1次調査（1997 ～ 2000），第2次調査（2000 ～ 2002）調査結果による

図1　魚類脂肪摂取量3分位別の2年後の抑うつ得点（男性）



国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）．第1次調査（1997 ～ 2000），第2次調査（2000 ～ 2002）調査結果による

コレステロールとうつ

コレステロールは生体の細胞膜の必須成分であり，血液中や胆汁中に多く含まれるが，これら以外に体内に蓄積されているコレステロールの約 30%は脳神経系に分布しているといわれている．コレステロールとうつとの関係の研究でいままでにもっとも注目を集めたのは，高脂血症治療薬による血清コレステロール低下と自殺や事故・暴力死との関係を報告した研究であろう[14]．24,187 人の男性を対象とした無作為割付臨床試験の結果として報告されたこの研究の後しばらく，この結果に肯定的な研究と否定的な研究がつぎつぎと発表された．一方，観察的な研究として 1993 年に Lancet に掲載された Morgan らの報告によると，地域在住高齢男性で低コレステロール血症者では高コレステロール血症者と比較して，10 年以上後での抑うつの危険性が約 3 倍で

あった[15]．カナダの国民栄養調査に基づいた研究では，血中コレステロール4分位でもっとも低い群ではいちばん高い群と比較して20年間の自殺率が6倍高かった[16]．その一方で，地域高齢者の抑うつと低コレステロール血症との見かけ上の関連は，関連要因を調整すると消失する，という報告もある[17]．

前述のMuldoonらはその後，高脂血症治療薬の大規模無作為試験のメタアナリシスを行い，高脂血症治療薬による血清コレステロールの低下と自殺死等の間には有意な関連が認められなかった，と報告している[18]．

チロシン，トリプトファン等のアミノ酸とうつ

うつに関連する脳内神経伝達物質であるセロトニンはトリプトファンから，ノルアドレナリンはチロシンやフェニルアラニンから生合成される．このようなアミノ酸の摂取がうつと関連する可能性は当然考えられるが，アミノ酸の食品成分に関するデータベース構築が不十分であるため，ヒトでの観察研究は限られている．

McTavishら[19]はラットにチロシン欠乏食を与えると脳内のカテコラミン放出やドーパミンの集積が低下した，と報告している．ヒトにおいてもトリプトファンの摂取や血中セロトニン濃度と抑うつとの関連が報告されている[20, 21]．ヒトにおける介入研究ではEllenbogenらが低トリプトファン食を用いた介入研究を行い，血清中トリプトファン濃度が80～90%低下した女性では対照群よりもうつ症状や疲労感などが強かったと報告している[22]．

最近筆者らはアミノ酸食品成分表を整備し，日常摂取されるたんぱく質の90%以上をアミノ酸に置き換えることに成功した[23]．この成分表を用いて，18種類のアミノ酸と抑うつとの関連を横断的・縦断的に検討したが，チロシンやトリプトファンとうつとの間に有意な関連は認められなかった[24]．

まとめ

食事は高齢者の心身の健康に影響を与える要因としてきわめて重要である．うつと栄養との関係についての研究もおびただしい数があるが，一定の結論は得られていない．このことは栄養がうつと無関係であることを意味するのではなく，栄養と健康事象との関連における疫学研究の難しさを示しているものである．

すなわち，食習慣とうつの双方に影響を与える個人のライフスタイルや社会経済的な要因を完全に調整することは困難であり，また食品とそれに含まれる栄養素との間には強い関連があることから，1つの栄養素と健康事象との間に関連が認められても，それが真にその栄養素による効果なのか，あるいはその栄養素を多く含有する食品に含まれている他の栄養素によるのか，あるいはそれらの栄養素の複合作用によるのか，明らかではない．ヒトでの介入研究で長期間にわたって食事を完全に制御することは困難であり，さらに栄養素の吸収，代謝，作用や脳内伝達物質の受容体などには遺伝的要因がかかわっており，因果関係をより複雑にしている．

今後は遺伝的要因や栄養素間の相互作用を考慮した，より詳細な研究が必要と考えられる．

しかしながら，従来の報告を俯瞰すると，高齢者において，n-3系脂肪酸やコレステロールを十分に含む，アミノ酸バランスのとれた良質な食生活を維持し，低栄養やビタミン類・微量元素の不足を防ぐことは，そのほかの心身の疾患にとって望ましいことであるだけでなく，うつの予防にも好ましいことであると考えられる．

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CONTENTS

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ORIGINAL ARTICLE

Relationship between number of metabolic syndrome components and dietary factors in middle-aged and elderly Japanese subjects

Rei Otsuka[1], Tomoko Imai[1,2], Yuki Kato[1], Fujiko Ando[1,3] and Hiroshi Shimokata[1]

Metabolic syndrome (MetS) represents a cluster of risk factors for atherosclerosis and is considered a risk factor for cardiovascular disease. The role of diet in the etiology of MetS is poorly understood, especially among Asian subjects. This cross-sectional study assessed the relationship between diet and the number of MetS components among Japanese men (*n*=609) and women (*n*=631). Mean (s.d.) age and body mass index were 57.1 (12.1) years and 22.8 (2.8) kg m^{-2} for men and 55.5 (12.0) years and 22.0 (3.0) kg m^{-2} for women, respectively. Diet was assessed by a 3-day dietary record that included photographs: 16 nutrients, 11 food groups, and energy % of protein and dietary fat were selected as a dietary index. The definition of MetS was based on modified National Cholesterol Education Program, Adult Treatment Panel III criteria, and the number of clustering MetS components was calculated by adding the presence of each five MetS components. A total of 61 men (10.0%) and 46 women (7.3%) were determined to have MetS. After adjusting for age, energy intake, alcohol intake, smoking status and physical activity, a lower intake of vitamin B6 and dietary fiber in men, and lower intake of calcium, milk and dairy products and higher intake of cereal in women were related to the number of MetS components. These results suggest that some dietary factors were related to the number of MetS components among community-dwelling Japanese men and women.
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Keywords: cross-sectional study; dietary record; Japanese; metabolic syndrome

INTRODUCTION

Metabolic syndrome (MetS) represents a cluster of risk factors for atherosclerosis, including visceral obesity, hypertension, dyslipidemia and hyperglycemia; MetS is considered a risk factor for cardiovascular disease.[1] The National Nutrition Survey in Japan, a population-based study among 40- to 74-year-olds, revealed that 24% of men and 12% of women were strongly suspected of having MetS, and 27% of men and 8% of women were suspected of having MetS.[2]

MetS has become a major public health challenge in Japan.[3] The pathophysiology of MetS appears to be largely attributable to insulin resistance with an excessive flux of fatty acids,[1] although this disorder presumably exists as a function of a complex interaction between environmental factors, including diet or physical activity and genetic factors.[4,5]

Although dietary aspects have been linked to individual features of MetS,[6–8] the role of diet in the etiology of this syndrome is poorly understood. Asians have different lifestyle and genetic factors compared with Caucasians,[9,10] but only a few epidemiologic studies examining diet and MetS among Asians have been conducted.[11–13] The aim of this study was to examine the relations between diet and the number of MetS factors among community-dwelling Japanese men and women.

METHODS

Study subjects

Data for this survey were collected as part of the National Institute for Longevity Sciences Longitudinal Study of Aging (NILS-LSA). In this project, the normal aging process has been assessed over time using detailed questionnaires and medical checkups, anthropometrical measurements, physical fitness tests and nutritional examinations. Participants in the NILS-LSA included randomly selected age- and sex-stratified individuals from the pool of residents in the NILS neighborhood areas, Obu City and Higashiura Town of Aichi Prefecture. Details of the NILS-LSA study are reported elsewhere.[14]

Subjects in this study included 1189 men and 1194 women aged 40–86 years who participated in the fourth wave of the NILS-LSA from June 2004 to July 2006. Subjects under non-pharmacological and/or pharmacological treatment for hypertension, hypertriglyceridemia or diabetes were excluded, as were subjects who indicated that they were aware of having these disorders but were not undergoing treatment. There were 334 men and 327 women with hypertension, 241 men and 174 women with hypertriglyceridemia and 104 men and 69 women with diabetes. As some subjects had multiple disorders, a total

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of 489 men and 492 women were excluded from the study. Additionally, subjects who did not fast overnight for venipuncture (11 men and 12 women), those who did not participate or complete the nutrition survey (54 men and 47 women) and those whose energy intake was <1200 kcal per day (2 men and 11 women) or more than 3000 kcal per day (24 men and 1 woman) were also excluded. After these exclusions, 609 men and 631 women remained in the study.

The study protocol was approved by the Committee of Ethics of Human Research of the National Center for Geriatrics and Gerontology. Written informed consent was obtained from all subjects.

Nutritional assessments

Nutritional intakes were assessed by a 3-day dietary record. The dietary record was completed over 3 continuous days (both weekend days and one weekday).[15] Food was weighed separately on a scale (1 kg kitchen scale, Sekisui Jushi, Tokyo, Japan) before being cooked or portion sizes were estimated. Subjects used a disposable camera (27 shots, Fuji Film, Tokyo, Japan) to take photos of meals before and after eating. Dietitians used the photos to complete missing data, and telephoned subjects to resolve any discrepancies or obtain further information when necessary. The averages of the 3-day food and nutrient intakes were calculated according to the fifth edition of the Standard Tables of Foods Composition in Japan and other sources.[15] Alcohol intake in the previous year was assessed by a food frequency questionnaire; trained dieticians interviewed subjects using this questionnaire. According to previous large epidemiological studies,[7,11] we selected 16 nutrients and 11 food groups as a dietary index, along with energy % of protein and dietary fat.

Other measurements

Anthropometric measurements included waist circumference, height and body weight. Waist circumference was measured at the umbilicus[16,17] and body mass index was calculated as weight/height^2 (kg m^{-2}). Blood pressure was measured by an automated sphygmomanometer (BP-203RVII, Omron Colin, Tokyo, Japan) after participants had been comfortably seated for at least 5 min. All venous blood samples were obtained after an overnight fast. The serum was separated promptly, and all lipid analyses were conducted at the clinical laboratory in the health examination center. Serum glucose and triglycerides were measured using enzymatic methods. HDL-cholesterol was measured after dextran sulfate-magnesium precipitation.

Medical history (past and current) and smoking status (yes/no) were collected using questionnaires. Physical activity was assessed by trained interviewers using the Met Score (a multiple of the resting metabolic rate). Participants were interviewed using a semi-quantitative assessment to determine their level of habitual physical activity during leisure time, on the job and sleeping hours,[18] and we calculated the total MetS*minutes score per day (MetS*1000 min per day). For example, walking for pleasure was assigned a 2.5 MetS intensity, and thus the leisure-time physical activity score was 50 MetS*min per day in the case of a 20 min walk every day.[18]

Definition of MetS and components

The definition of MetS was based on modified National Cholesterol Education Program, Adult Treatment Panel III (NCEP-ATP III) criteria.[19] Only the criteria of abdominal obesity was different from that of NCEP-ATP III criteria.[20] For abdominal obesity, we used the International Obesity task Force central obesity criteria for Asia, which defined abdominal obesity as a waist circumference of at least 90 cm for men and at least 80 cm for women.[21]

As stated earlier, study subjects under treatment for hypertension, hypertriglyceridemia and diabetes were excluded before the analyses. Thus, MetS was defined as the presence of three or more of the following five components: (1) abdominal obesity, defined as a waist circumference of at least 90 cm for men and at least 80 cm for women; (2) elevated blood pressure, defined as blood pressure $\geqslant$130/85 mm Hg; (3) hypertriglyceridemia, defined as triglycerides $\geqslant$150 mg per 100 ml ($\geqslant$1.70 mmol l^{-1}); (4) low HDL-cholesterol, defined as HDL-cholesterol <40 mg per 100 ml (<1.0 mmol l^{-1}) in men and <50 mg per 100 ml (<1.3 mmol l^{-1}) in women; and (5) elevated blood glucose levels, defined as fasting blood glucose $\geqslant$100 mg per 100 ml. The number of clustering MetS components was calculated by adding the number of MetS components.

Statistical analyses

All statistical analyses were conducted with Statistical Analysis System, release 9.1.3 (SAS Institute, Cary, NC, USA). Subjects were categorized into four groups according to the number of clustering MetS components (0, 1, 2, 3–5). Values of 3–5 were combined because only a few or no subjects had 4 or 5 MetS components (4 components: 12 men and 5 women; 5 components: 0 men and 2 women). Associations between categorical variables were tested by χ^2 test and 95% confidence interval (CI) was estimated using the PROC FREQ procedure. Comparisons between continuous variables were performed by analysis of variance and trend test. Linear regression models were constructed using the PROC GLM procedure to examine the association between the number of MetS components and dietary indexes, that is, the 11 food groups, 16 nutrients and energy % of protein and dietary fat. Mean nutritional intakes were calculated by the number of MetS components (0, 1, 2, 3–5) after multivariate adjustment for potential confounding factors, which included age, energy intake, alcohol intake, smoking status and physical activity. Additionally, demographic differences between subjects (609 men and 631 women) and those excluded from the study (580 men and 563 women) were analyzed by t-test.

All reported P-values were two-sided, and a P-value <0.05 was considered significant.

RESULTS

Subject characteristics are presented Table 1. Mean (s.d.) age and BMI were 57.1 (12.1) years and 22.8 (2.8) kg m^{-2} for men and 55.5 (12.0) years and 22.0 (3.0) kg m^{-2} for women, respectively. Age and BMI gradually increased with the number of MetS components in both men and in women, whereas mean age of subjects with 2 or 3–5 MetS components was similar in men (59.5 years and 59.5 years, respectively) and women (60.7 and 60.9 years, respectively).

Abdominal obesity, defined as waist circumference $\geqslant$90 cm, was noted in 20.0% of men (95% CI: 16.8–23.2), with a prevalence of 14.4, 41.9 and 70.5% among men with 1, 2 or 3–5 MetS components, respectively. Abdominal obesity, defined as waist circumference $\geqslant$80 cm, was noted in 44.1% of women (95% CI: 40.2–48.0), with a prevalence of 69.7, 84.5 and 97.8% among those with 1, 2 or 3–5 MetS components, respectively. Elevated blood glucose levels were seen in 38.1% of men and 17.9% of women according to the number of MetS components (1, 2 or 3–5) was 49.8, 61.5 and 91.8% in men and 17.1, 41.8 and 73.9% in women, respectively. Hypertriglyceridemia and hypertension were seen in 18.2 and 22.5% of men and 7.5 and 12.8% of women, respectively. Low HDL-C levels occurred in 5.9% of men and 7.0% of women. A total of 61 men (10.0%) and 46 women (7.3%) met the NCEP-ATP III modified criteria for MetS, that is, they had 3–5 MetS components.

In sub-analyses, demographic differences between subjects included in the study (609 men and 631 women) and those excluded from the study (580 men and 563 women) were analyzed. Age, BMI and the other anthropometric variables (for example, blood pressure, waist circumference or fasting glucose levels) were lower among subjects than those excluded (mean (s.d.) age: 56.9 (12.1) vs. 64.8 (11.7) years, mean BMI: 22.5 (2.9) vs. 23.6 (3.2) kg m^{-2}, respectively).

Table 2 shows multivariate adjusted mean food and nutrient intake according to the number of MetS components in men. Among the dietary indexes, daily intakes of vitamin B6 decreased from 1.36 to 1.21 mg, and dietary fiber decreased from 16.2 to 14.5 mg as the number of MetS components increased. Although analysis of covariance did not reach statistical significance, intake of vegetables was lower among men with higher number of MetS components, and decreased from 301.1 to 271.9 g as the number of MetS components increased (ANCOVA P=0.07, trend test P=0.03). In addition, although analysis of covariance or trend tests did not reach statistical

Table 1 Subject characteristics according to the number of metabolic syndrome (MetS) components

		Number of MetS components					
Variable	*All*	*0*	*1*	*2*	*3–5*	P[a]	*Trend P*
Men							
n, %	609 (100%)	222 (36.5%)	209 (34.3%)	117 (19.2%)	61 (10.0%)		
Age (year)	57.1±12.1	55.1±12.5	57.1±11.7	59.5±12.0	59.5±11.0	<0.01	<0.01
Body mass index (kg m^{-2})	22.8±2.8	21.7±2.4	22.5±2.5	24.0±2.7	25.6±2.6	<0.01	<0.01
Alcohol intake (g per day)	14.2±17.3	12.7±16.1	14.6±17.1	15.9±17.8	15.3±21.2	0.38	0.24
Physical activity (MetS*1000 min per day)	2116±302	2107±290	2109±266	2124±334	2159±389	0.65	0.21
Energy intake (kcal/)	2247±335	2247±308	2233±342	2283±337	2227±399	0.59	0.95
Current smoker (*n*, %)	186 (30.5%)	62 (27.9%)	67 (32.1%)	38 (32.5%)	19 (31.2%)	0.76	
Metabolic abnormalities (n, %)							
Waist circumference ⩾90 (cm)	122 (20.0%)	0 (–%)	30 (14.4%)	49 (41.9%)	43 (70.5%)		
Triglyceride ⩾150 (mg per 100 ml)	111 (18.2%)	0 (–%)	24 (11.5%)	44 (37.6%)	43 (70.5%)		
HDL-cholesterol <40 (mg per 100 ml)	36 (5.9%)	0 (–%)	7 (3.4%)	17 (14.5%)	12 (19.7%)		
Blood pressure ⩾130/85 mm Hg	137 (22.5%)	0 (–%)	44 (21.1%)	52 (44.4%)	41 (67.2%)		
Fasting glucose ⩾100 mg per 100 ml	232 (38.1%)	0 (–%)	104 (49.8%)	72 (61.5%)	56 (91.8%)		
Women							
n, %	631 (100%)	272 (43.1%)	210 (33.3%)	103 (16.3%)	46 (7.3%)		
Age (year)	55.5±12.0	51.5±10.9	56.8±12.1	60.7±11.8	60.9±10.9	<0.01	<0.01
Body mass index (kg m^{-2})	22.0±3.0	20.2±1.9	22.7±2.7	23.6±3.0	25.4±3.2	<0.01	<0.01
Alcohol intake (g per day)	3.4±7.6	3.7±7.3	3.2±7.7	2.3±5.3	4.6±12.1	0.27	0.60
Physical activity (MetS*1000 min per day)	2161±160	2187±152	2144±169	2132±131	2143±201	<0.01	0.07
Energy intake (kcal/	1884±288	1884±299	1878±293	1893±275	1895 ±229	0.97	0.72
Current smoker (*n*, %)	39 (6.2%)	21 (7.7%)	9 (4.3%)	4 (3.9%)	5 (10.9%)	0.17	
Metabolic abnormalities (n, %)							
Waist circumference ⩾80 (cm)	278 (44.1%)	0 (–%)	146 (69.7%)	87 (84.5%)	45 (97.8%)		
Triglyceride ⩾150 (mg per 100 ml)	47 (7.5%)	0 (–%)	6 (2.9%)	21 (20.4%)	20 (43.5%)		
HDL-cholesterol <50 (mg per 100 ml)	44 (7.0%)	0 (–%)	8 (3.8%)	19 (18.5%)	17 (37.0%)		
Blood pressure ⩾130/85 mm Hg	81 (12.8%)	0 (–%)	14 (6.7%)	36 (35.0%)	31 (67.4%)		
Fasting glucose ⩾100 mg per 100 ml	113 (17.9%)	0 (–%)	36 (17.1%)	43 (41.8%)	34 (73.9%)		

Values shown are mean ±s.d.
[a]Statistical significance was determined by analysis of variance or χ^2 test.

significance, higher daily intakes of cholesterol (379.2–404.6 mg) and eggs (52.5–58.2 g) were related to an increased number of MetS components (trend test $P<0.1$).

In women (Table 3), intake of calcium decreased from 609.2 to 549.9 mg daily, and intake of milk and dairy food decreased from 181.2 to 134.9 mg daily as the number of MetS components increased. Cereal intake increased from 382.3 to 418.4 g daily as the number of MetS components increased. Although analysis of covariance and trend test did not reach statistical significance, lower intake of saturated fat was related to an increased number of MetS components, and decreased from 15.7 to 14.8 g daily as MetS components increased (trend test $P<0.1$).

DISCUSSION

Our findings suggest that lower intakes of vitamin B6 and dietary fiber in men, and lower intakes of calcium, milk and dairy products and higher intake of cereal in women are related to the number of MetS components. To our knowledge, this is the first observational study to examine relations between dietary factors and the number of clustering MetS components among Japanese men and women.

In previous epidemiologic studies, dietary fiber, fruits, vegetables and moderate alcohol intake were negatively associated[22–24] and fat and red meat were positively associated[25–27] with MetS in Caucasian or Japanese-Brazilian subjects. Consistent with previous studies,[22,24,28] intake of dietary fiber in men was negatively related to clustering MetS components. Diets rich in dietary fiber are associated with a reduced risk of diabetes and cardiovascular disease. Dietary fiber has a higher satiety value compared with digestible complex carbohydrates and simple sugars because of its bulk and relatively low energy. Fiber may also affect secretion of gut hormones or peptides, such as cholecystokinin or glucagon-like peptid-1, which may act as satiety factors or alter glucose homeostasis.[28,29] Thus, an increased fiber intake may prevent MetS.

Although carbohydrate intake in women did not correlate with the number of MetS components, cereals that mainly consisted of carbohydrates showed a negative effect on the number of MetS components in this study. Carbohydrates are also implicated in changes in blood glucose and insulin concentrations and are known to affect satiety.[30] The beneficial effect of a high carbohydrate diet on glucose tolerance has been reported;[31] however, contradicting reports have also been published.[32–36] Dietary carbohydrate through cereal intake is thought to modulate lipolysis, and a low-carbohydrate diet reduces cardiovascular risk through improvement in hepatic, intravascular and peripheral processing of lipoproteins.[32] Although no positive relation was

Table 2 Energy and multivariate adjusted[a,b] mean food and nutrient intake according to the number of metabolic syndrome (MetS) components in men (n=609)

	Number of MetS components					
Variable	*0*	*1*	*2*	*3–5*	P[c]	*Trend P*
n (%)	222 (36.5%)	209 (34.3%)	117 (19.2%)	61 (10.0%)		
Energy (kcal)	2247±23	2233±23	2283±31	2227±43	0.59	0.95
Nutrients[a]						
Protein (energy %)	3.71±0.03	3.71±0.03	3.71±0.05	3.70±0.06	0.99	0.93
Fat (energy %)	2.71±0.03	2.67±0.04	2.66±0.05	2.79±0.07	0.35	0.36
Carbohydrate (energy %)	13.8±0.1	14.0±0.1	14.0±0.2	13.8±0.2	0.62	0.98
Nutrients[b]						
Protein (g)	82.9±0.7	82.8±0.8	83.5±1.0	82.5±1.4	0.93	0.92
Fat (g)	61.2±0.8	60.3±0.8	60.4±1.1	62.8±1.5	0.46	0.33
Carbohydrate (g)	310.3±2.4	312.7±2.5	312.1±3.3	309.8±4.6	0.89	0.88
Calcium (mg)	619.5±12.4	604.2±12.6	590.1±17.0	588.8±23.5	0.47	0.20
β-Carotene (μg)	3269±118	3274±121	2804±163	3003±225	0.08	0.11
Vitamin E (mg)	9.8±0.2	9.5±0.2	9.1±0.2	9.3±0.3	0.130	0.10
Vitamin B6 (mg)	1.36±0.02	1.35±0.02	1.29±0.03	1.21±0.04	0.006	0.001
Vitamin B12 (μg)	8.8±0.4	8.2±0.4	9.4±0.5	8.0±0.7	0.23	0.70
Folate (μg)	343.6±7.3	352.6±7.5	339.9±10.1	340.4±13.9	0.70	0.65
Vitamin C (mg)	126.4±7.1	127.2±7.2	135.1±9.7	125.1±13.4	0.89	0.93
Saturated fat (g)	16.5±0.3	15.9±0.3	16.0±0.4	16.1±0.5	0.58	0.57
Monounsaturated fat (g)	21.2±0.4	20.8±0.4	20.8±0.5	21.5±0.7	0.66	0.70
Polyunsaturated fat (g)	13.3±0.2	13.4±0.2	13.5±0.3	14.0±0.4	0.55	0.15
Cholesterol (mg)	379.2±8.8	369.0±9.0	396.7±12.2	404.6±16.8	0.15	0.08
Dietary fiber (g)	16.2±0.3	15.9±0.3	14.8±0.4	14.5±0.5	0.002	0.001
Salt (g)	11.8±0.1	12.1±0.1	11.9±0.2	11.6±0.3	0.29	0.28
Foods						
Cereals (g)	512.2±7.5	522.6±7.7	538.3±10.3	512.9±14.2	0.21	0.72
Beans (g)	76.5±4.7	86.9±4.8	86.6±6.4	82.8±8.9	0.41	0.55
Nuts and seeds (g)	6.0±0.6	4.0±0.6	3.9±0.8	5.4±1.2	0.07	0.61
Vegetables (g)	301.1±7.9	304.5±8.1	277.0±10.9	271.9±15.0	0.07	0.03
Fruits (g)	137.1±7.1	130.8±7.3	122.0±9.8	134.3±13.5	0.66	0.72
Fish and shellfish (g)	111.2±3.5	107.1±3.6	109.3±4.9	108.3±6.7	0.88	0.79
Meats (g)	86.2±3.1	89.4±3.2	93.9±4.2	95.0±5.9	0.38	0.13
Eggs (g)	52.5±1.9	53.5±1.9	59.5±2.6	58.2±3.6	0.11	0.07
Milk and dairy food (g)	163.6±8.0	144.3±8.1	140.7±10.9	129.8±15.1	0.12	0.049
Fats and oils (g)	11.3±0.4	11.6±0.4	11.6±0.6	11.6±0.8	0.97	0.77
Confectioneries (g)	45.1±3.3	46.6±3.4	43.2±4.5	46.7±6.3	0.94	0.95

Values shown are mean±s.e.
[a]Adjusted for age, alcohol intake, smoking and physical activity.
[b]Adjusted for age, energy intake, alcohol intake, smoking and physical activity.
[c]Statistical significance was determined by analysis of covariance.

shown between carbohydrate intake and the number of MetS components in this study, recent nutritional reviews indicate that the quantity and type of carbohydrate affect metabolic outcomes.[35] Among cereals, whole grain products that have a lower glycemic index and are richer in fiber and antioxidant vitamins than refined grain products were suggested to improve insulin sensitivity, probably by blunting postprandial glycemic and insulinemic responses.[36] Thus, control of these factors in future studies will be important to determine the most effective dietary approach to prevent metabolic disorders.

In Japan, there has been a significant reduction in the intake of cereals, and rice in particular, in recent decades,[2,37] On the other hand, dietary fat intake is increasing, and consumption of a more Westernized diet is thought to be associated with the evident increase in diabetes mellitus and obesity. In women in this study, saturated fat intake weakly decreased as the number of MetS components increased. Dietary intervention studies show that total fat is not associated with the risk of MetS, although saturated fats increase the risk of MetS, whereas monounsaturated and polyunsaturated fats reduce this risk.[38–40] Our results do not agree with studies that show that saturated fat-rich lipid infusion reduces the insulin sensitivity index more than polyunsaturated fat infusion.[41] Although the reason of this inverse relation was shown in this study is not clear, two possibilities can be considered. First, some intermediate event, such as dietary counseling, could have lead to changes in diet and might have confounded the association between saturated fat intake and metabolic

Table 3 Energy and multivariate adjusted[a,b] mean food and nutrient intake according to the number of metabolic syndrome (MetS) components in women (n=631)

Variable	Number of MetS components 0	1	2	3–5	P[c]	Trend P
n (%)	272 (43.1%)	210 (33.3%)	103 (16.3%)	46 (7.3%)		
Energy (kcal)	1884±18	1878±20	1893±29	1896±43	0.97	0.72
Nutrients[a]						
Protein (energy%)	3.75±0.03	3.84±0.03	3.79±0.05	3.70±0.07	0.15	0.45
Fat (energy%)	2.97±0.03	2.94±0.03	2.93±0.05	2.91±0.07	0.85	0.46
Carbohydrate (energy%)	14.2±0.1	14.2±0.1	14.1±0.2	14.2±0.2	0.97	0.99
Nutrients[b]						
Protein (g)	70.2±0.5	71.9±0.6	71.4±0.9	69.7±1.3	0.16	0.64
Fat (g)	56.4±0.6	55.7±0.7	55.5±0.9	54.7±1.4	0.67	0.28
Carbohydrate (g)	267.4±1.8	266.2±2.0	265.4±2.9	268.2±4.3	0.91	0.93
Calcium (mg)	609.2±11.0	604.8±12.3	556.3±17.9	549.9±26.4	0.024	0.01
β-Carotene (μg)	3358±112	3263±125	2931±181	3508±268	0.18	0.90
Vitamin E (mg)	9.1±0.1	9.0±0.2	9.0±0.2	9.4±0.3	0.70	0.35
Vitamin B6 (mg)	1.13±0.02	1.19±0.02	1.13±0.03	1.15±0.04	0.11	0.98
Vitamin B12 (μg)	6.9±0.3	7.0±0.4	7.4±0.5	6.9±0.8	0.87	0.95
Folate (μg)	333.9±6.8	342.7±7.6	334.2±11.0	360.0±16.3	0.45	0.21
Vitamin C (mg)	121.7±4.2	125.6±4.7	111.0±6.9	131.7±10.1	0.24	0.66
Saturated fat (g)	15.7±0.2	15.5±0.3	15.0±0.4	14.8±0.6	0.23	0.07
Monounsaturated fat (g)	19.1±0.3	19.0±0.3	19.1±0.4	18.8±0.6	0.96	0.74
Polyunsaturated fat (g)	12.1±0.2	12.0±0.2	12.2±0.3	12.2±0.4	0.91	0.67
Cholesterol (mg)	321.1±6.7	339.2±7.4	343.1±10.8	318.7±15.9	0.16	0.95
Dietary fiber (g)	15.2±0.2	15.7±0.3	15.2±0.4	15.5±0.5	0.49	0.82
Salt (g)	10.4±0.1	10.4±0.1	10.6±0.2	10.8±0.3	0.45	0.11
Foods[b]						
Cereals (g)	382.3±5.2	385.8±5.8	400.3±8.4	418.4±12.4	0.03	0.004
Beans (g)	75.4±4.1	80.7±4.6	76.0±6.6	83.1±9.8	0.77	0.58
Nuts and seeds (g)	6.3±0.7	6.9±0.7	6.2±1.1	5.3±1.6	0.81	0.48
Vegetables (g)	285.4±6.5	285.1±7.3	275.2±10.6	322.6±15.6	0.09	0.06
Fruits (g)	152.1±6.7	160.9±7.5	145.3±10.9	131.0±16.1	0.32	0.15
Fish and shellfish (g)	81.9±2.5	89.3±2.8	90.7±4.1	84.2±6.1	0.16	0.69
Meats (g)	65.5±2.0	70.8±2.3	71.1±3.3	66.1±4.9	0.27	0.90
Eggs (g)	48.2±1.6	52.1±1.8	53.1±2.6	50.6±3.9	0.33	0.54
Milk and dairy food (g)	181.2±6.7	177.0±7.4	153.7±10.8	134.9±16.0	0.018	0.003
Fats and oils (g)	11.2±0.3	10.7±0.4	10.6±0.6	10.2±0.8	0.64	0.28
Confectioneries (g)	65.5±2.7	61.6±3.0	60.1±4.4	56.9±6.5	0.52	0.21

Values shown are mean±s.e.
[a]Adjusted for age, alcohol intake, smoking and physical activity.
[b]Adjusted for age, energy intake, alcohol intake, smoking and physical activity.
[c]Statistical significance was determined by analysis of covariance.

risks. We tried to exclude subjects from the analysis who were aware of their potential risks and who may have made dietary changes based on perceived dangers. Second, Japanese subjects consume a relatively large amount of fish containing abundant polyunsaturated fatty acids. The ratio of saturated fat to polyunsaturated fat might be more important than the absolute intake considering the physiologic dietary effect on developing MetS. These factors might have affected our results. Further studies are needed to clarify the role of fat quality in the prevention of MetS.

Calcium, milk and dairy food intake in women decreased with the increase in the number of MetS components. Additionally, although findings were not statistically significant, a similar relation between milk and dairy products and MetS was shown in men (ANCOVA P=0.12, trend P=0.049). Diets rich in calcium, particularly calcium derived from dairy products, have been shown to be associated with a low prevalence of MetS.[42] The mechanism by which calcium intake can reduce MetS is unclear, but Scholz-Ahrens and Schrezenmeir[42] implied that dietary calcium intake has benefits on traits of MetS, specifically on weight reduction and fat loss. Meijl *et al.*[43] reviewed the physiological effects of three main dairy constituents (calcium, protein and fat) on MetS, and indicated that the effects of calcium might be related to intestinal binding to fatty acids or bile acids or to changes in intracellular calcium metabolism by suppressing calciotropic hormones. In an epidemiologic study, Otsuka *et al.*[44] reported that higher milk consumption was associated with a lower incidence of MetS after 5 years among middle-aged

Japanese male workers, suggesting that calcium derived from dairy products might help prevent MetS.

Vitamin B6 in men was also negatively related to the number of MetS components. Esmaillzadeh *et al.*[45] discussed the favorable effect of whole grain on MetS through the rich content of viscous fiber and showed that intake of whole grains was positively associated not only with dietary fiber (r=0.43) but also with vitamin B6 (r=0.48). Consistent with their study, the results of our study showed favorable effects of dietary fiber and vitamin B6 on the number of MetS components. Hayden and Tyagi[46] reported on the role of water soluble B vitamins, including vitamin B6, in lowering plasma total homocysteine, a risk marker of MetS, through remethylation. Although the precise mechanism of vitamin B6 on MetS is unclear, a favorable association of vitamin B6 to MetS in men may be attributed to a healthier diet that contained rich fiber, milk and dairy products or vegetables.

Although not statistically significant, lower intake of vegetables in men was related to an increased number of MetS components. Higher vegetable intake has been previously reported as a protective factor of MetS or inflammation in women.[7,22] Vegetables rich in dietary fiber are thought to reduce the risk of developing MetS by improving glucose control, and minerals, antioxidants or vitamins contained in vegetables are thought to have a favorable effect on glucose tolerance.[47,48] Our results regarding dietary fiber on MetS may represent the positive effect of vegetable intake.

In men, higher intakes of eggs and cholesterol were related to an increased number of MetS components, although this was not statistically significant (trend $P<0.1$). Excess consumption of eggs should be avoided from the standpoint of preventing hypercholesterolemia among Japanese subjects.[49] Increased dietary cholesterol intake is associated with atherosclerosis.[50] The result of this study may suggest that men with a lower number of MetS components tend to abstain from eating eggs or cholesterol-rich foods. As a result, a dose–response relationship between egg consumption and the number of MetS components was shown in our study.

The lack of other correlations between the number of MetS components and dietary factors, such as fruits, or meats in this study is thought to be due to differences in dietary intake[51] or metabolic responses[9,10] between Caucasian and Japanese subjects.

The relation of diet to the risk of MetS has been examined in many studies, but few have addressed the association with the number of MetS components.[52–54] We considered that the number of MetS components is more closely assessed through the effects of diet, that is, through a dose–response relationship, rather than the prevalence of MetS. In addition, to focus on the dose–response relationship, trend test by general linear model was used, and further *post hoc* analyses were not performed. MetS is a cluster of atherosclerotic cardiovascular disease risk factors[20] but there are some different criteria of MetS in Japan. The ideal threshold for waist circumference used to define abdominal obesity among Japanese men and women is still under discussion.[55] Recently, Kokubo *et al.*[19] reported that the number of MetS components (modified NCEP-ATP III criteria) might be more strongly associated with the incidence of cardiovascular disease than the presence of abdominal obesity (the Japanese criteria) in a general urban Japanese population. We used a modified NCEP-ATP III criteria, that is, a cutoff point of waist circumference that was different from NCEP ATP III (102 cm in men and 88 cm in women, modified: 90 cm in men and 80 cm in women), in this study.[20,21]

Several limitations of this study warrant consideration. First, the cross-sectional nature of the study did not permit the assessment of causality. Subjects under treatment for hypertension, hypertriglyceridemia or diabetes or those aware of morbidities might have modified their food intake, and these subjects were excluded from analysis. However, some plausible relationships between foods or nutrients and MetS have been identified in this study. NILS-LSA, which is a population-based prospective cohort study, followed participants for more than 10 years. Future analyses should examine the associations between the dietary index and MetS.

Second, we used foods and nutrients as an indicator of diet, although these items are consumed in combination, and their complex effects are likely to be interactive or synergistic.[56] Consumption of several foods or food groups might be a more comprehensive variable to assess the impact of diet on disease risk than any single nutrient or food. Third, nutritional intakes were assessed by a 3-day dietary records. The 3-day dietary record is one of the most reliable methods for nutritional assessment; however, it is limited because individual food intake varies greatly from day to day,[15] and it is not clear whether short-term records adequately reflect long-term dietary intake.[57] On the basis of this limitation, we preliminarily decided on 3 continuous days (both weekend days and one weekday) to avoid events or special days such as trips, long vacations or out-of-the-ordinary events and thus minimize food variations. Although the 3-day dietary record is not the best way to assess long-term dietary intake, it can be considered to have a certain level of accuracy that reflects the usual nutrient intakes in this cohort.

Fourth, food consumption and nutrient intake among Japanese have dramatically changed during the past five decades. For example, Westernization of the Japanese diet has lead to decreased consumption of carbohydrates, especially rice, and increased consumption of fat and meat.[2,37] In particular, younger Japanese subjects tend to eat a more Westernized diet.[37] As a result, not only food intake but also the number MetS components might differ among different generations of Japanese subjects. Thus, it may be difficult to detect statistically significant relationships between diet and the number of MetS components in the age group we studied.

In summary, this study showed that some foods and nutritional components are related to the number of MetS components. These results suggest the potential effect of diet on the prevention of MetS among community-dwelling Japanese men and women.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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一般住民における動脈硬化と骨粗鬆症の関連

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一般住民における動脈硬化と骨粗鬆症の関連

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はじめに

骨粗鬆症と動脈硬化の進行は，高齢者の自立を障害してquality of life(QOL)を低下させ，健康寿命に大きく影響する。これら両疾病はともに，加齢に伴い発症・増加する病態である。

骨密度(bone mineral density：BMD)と循環器疾患の関連については，これまでにも多方面からの研究報告が数多くあるが，日本人地域住民男女を対象としての疫学研究はまだ少ない。本研究では，地域在住中高年者を対象に，骨粗鬆症と動脈硬化の関連について横断的に検討を行った。

1　対象と方法

国立長寿医療センター研究所疫学研究所では，老化に関する包括的な疫学調査である「国立長寿医療センター研究所・老化に関する長期縦断疫学研究(NILS-LSA：National Institute for Longevity Sciences-Longitudinal Study of Aging)」を，1997年11月から縦断的(2年ごと)に実施している[1)]。調査対象は，センター周辺(愛知県大府市，知多郡東浦町)の地域住民から，年齢，性別で層化した無作為抽出法で選出された，ベースライン調査時年齢が40～79歳の2,267名である。

本研究では，第1次調査(1997年11月～2000年4月)の参加者のうち，BMD測定および頸動脈超音波検査を受けた女性1,050名(平均年齢±SD：59.0±10.9)，男性1,063名(59.2±10.9)を対象として横断研究を行った。表1に対象者特性を示す。

骨粗鬆症の評価は，dual energy X-ray absorptiometry(DXA：Hologic, QDR-4500)で第2～4腰椎と右大腿骨頸部のBMD測定を行い，日本骨代謝学会の「原発性骨粗鬆症の診断基準」[2)]に準じ，BMDが若年成人平均値(young adult mean：YAM)の70～80％を骨量減少，

表1　対象者特性

	男性	女性
対象者数(名)	1,063	1,050
40歳代	274	266
50歳代	267	266
60歳代	255	263
70歳代	267	255
年齢(歳)	59.2±10.9	59.0±10.9
BMI(kg/m^2)	22.9±2.8	22.9±3.3
腰椎BMD(g/cm^2)	1.0±0.2	0.9±0.2
大腿骨頸部BMD(g/cm^2)	0.8±0.1	0.7±0.1
IMT(mm)	0.9±0.5	0.8±0.3

平均値±標準偏差
BMI：body mass index, BMD：bone mineral density, IMT：intima-media thickness

Association between Arteriosclerosis and Osteoporosis in Community Dwelling Population
Marie Takemura：Department of Orthopedics National Center for Geriatrics and Gerontology, *et al.*
Key words：Osteoporosis, Arteriosclerosis, Epidemiology

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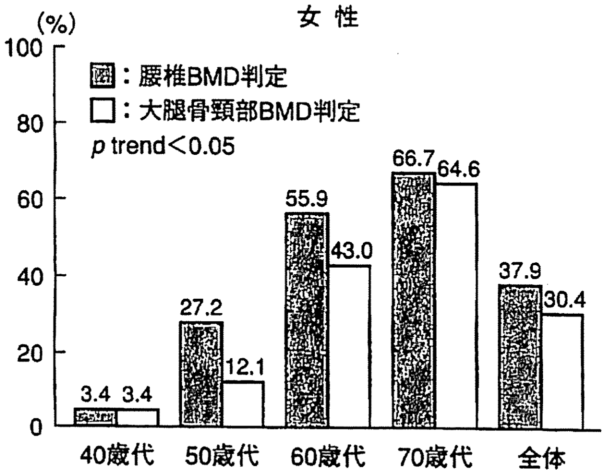

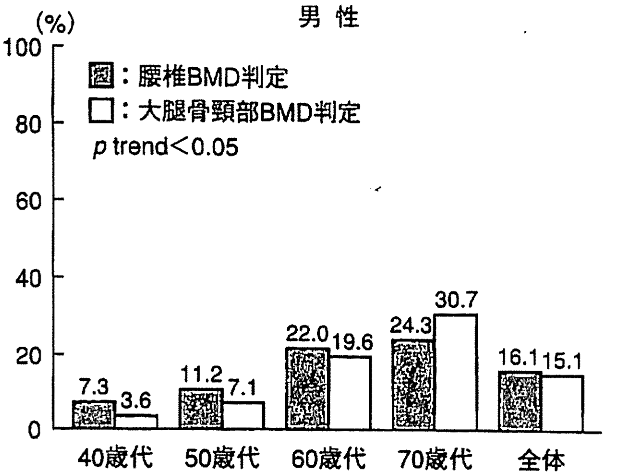

図1　骨粗鬆症／骨量減少の有病率

70％未満を骨粗鬆症と判定した。

また，動脈硬化の評価手段として頸動脈超音波検査(日立メディコ電子走査形超音波断層装置EUB−655，電子リニア形探触子EUP−L3 10MHz)を行った。頸動脈内膜中膜複合体厚(intima−media thickness：IMT)を左右総頸動脈および左右頸動脈分岐部で計測し，その最肥厚部をIMTの代表値とした。IMTが1.1mm以上を異常肥厚とし，動脈硬化ありと判定した。

統計学的検討として，骨粗鬆症および動脈硬化の地域在住中高年者の有病率を性別，年代別に求め，Cochran−Mantel−Haenszel法によるトレンド検定を行った。次に動脈硬化と骨粗鬆症の関連について検討するために，動脈硬化の有無を説明変数とし，年齢およびbody mass index(BMI)を調整した骨粗鬆症有病についての多重ロジスティック回帰分析を性別に行った。解析には，統計プログラムSAS release 9.1.3を使用した。

2　結　　果

1）骨粗鬆症／骨量減少の有病率(性別，年代別)

腰椎BMD判定での40歳以上の骨粗鬆症／骨量減少の有病率は，女性37.9％，男性16.1％であった。女性の有病率は加齢で有意に高くなり，特に60歳代以降は急速に高くなった。男性でも，有病率は加齢で有意に高くなった。大腿骨頸部BMD判定でも，女性30.4％，男性15.1％で，男女とも加齢で有意に高くなった(**図1**)。

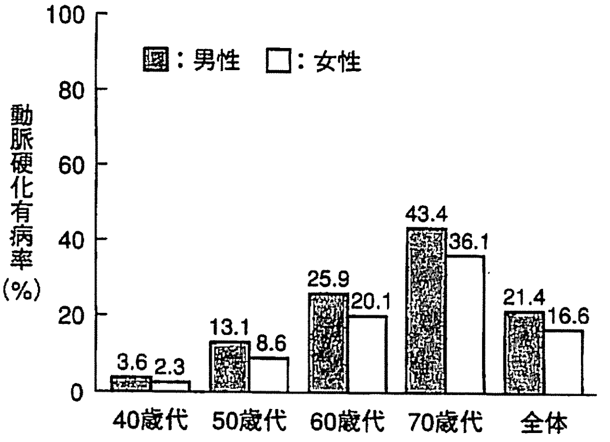

図2　動脈硬化有病率

2）動脈硬化有病率(性別，年代別)

40歳以上の女性の動脈硬化有病率は16.6％，男性は21.4％であった。動脈硬化の有病率は，男女とも加齢で有意に高くなった(**図2**)。

3）動脈硬化と骨粗鬆症との関連

女性で骨粗鬆症診断を腰椎BMDで判定した場合，動脈硬化のある者は，ない者に比べて骨粗鬆症／骨量減少の有病の割合が高かった(オッズ比1.97，95％信頼区間1.03～2.99，$p=0.0014$)。また，女性を未閉経群と閉経群に分けて検討したところ，閉経群のみで同様の結果が得られた(1.78，1.19～2.67，$p=0.00052$)。一方，大腿骨頸部BMD判定の場合には，いずれも有意な関連は認められなかった。男性での解析では，両部位BMDと動脈硬化のあいだに有意な

表2　多重ロジスティック回帰分析による動脈硬化と骨粗鬆症有病の関連

		オッズ比(95%信頼区間)	p値
腰椎BMD判定の場合	女性全体	1.97(1.03～2.99)	$p=0.0014$
	閉経女性	1.78(1.19～2.67)	$p=0.0052$
	男性全体	0.98(0.63～1.55)	NS
大腿骨頸部BMDの場合	女性全体	0.96(0.63～1.46)	NS
	閉経女性	0.94(0.60～1.43)	NS
	男性全体	0.74(0.27～1.17)	NS

NS：not significant

関連は認められなかった(**表2**)。

3 考　　察

BMDと心血管系疾患については，低BMDや骨密度減少が，心血管疾患による死亡リスク上昇と関連するという報告や[3,4]，骨粗鬆症の閉経後女性は，年齢や心血管疾患の危険因子を考慮しても，心・血管系イベントの発生リスクが有意に高い[5]など，これまでに多方面からの研究が行われている。日本人を対象とした疫学研究においても，骨粗鬆症や動脈硬化の評価手法はそれぞれの研究で異なるが，BMDと動脈硬化の程度とのあいだに関連を認めたと報告されている[6～9]。本研究では，脳・心血管疾患の予知因子として有用とされるIMT[10]とBMDのデータを用いて，地域住民男女における両疾病間の関連について解析を行った。その結果，骨粗鬆症評価を腰椎BMDで行った場合，女性で動脈硬化のある者は，ない者に比べて骨粗鬆症有病の割合が高くなった。この結果は，これまでの先行研究と矛盾するものではなかった。

女性の骨粗鬆症と心血管疾患は，どちらも閉経後より罹患率が高くなることが臨床的に広く知られている。またエストロゲン受容体は，骨芽細胞や破骨細胞，血管内皮細胞，血管平滑筋細胞に存在することが確認されており，両疾患の進行に共通して関与する因子としてエストロゲンがあげられる。本研究において，女性で両疾病間に有意な関連が認められた要因の一つに，エストロゲンの関与が示唆される。

またエストロゲン以外にも，酸化脂質やビタミンD，副甲状腺ホルモン，オステオカルシン，オステオポンチン，ホモシステイン，アンジオテンシン，マトリックスグラプロテイン，オステオプロテジェリン，一酸化窒素，インターロイキン(IL−6)などは，骨と血管の相互に関与する共通因子として近年検証が進み，いわゆる「骨・血管相関」の機序が解明されつつある。

腰椎は大腿骨頸部に比べ，構成組織として海綿骨の占める割合が高い。エストロゲン減少による骨代謝への影響は，皮質骨よりも海綿骨のほうがより反映されやすいと考えられている。今回の結果において，腰椎と大腿骨に相違を認めた要因の一つとしてエストロゲンの関与が示唆される。

一方，変形性脊椎症では椎体に骨棘形成を認めるが，その割合は，特に男性において加齢に伴い高くなるため，BMDが高く判定されてしまう。また腹部の大動脈石灰化が存在する場合にも，腰椎BMDが過大評価される可能性があり，結果への影響は否定できない。

両疾患の進行には性ホルモン以外にも喫煙，糖尿病，高脂血症など共通の危険因子が存在する。今後，これらの交絡因子を考慮しての検討を要すると考える。

患者のQOL低下を招くおそれのある骨粗鬆症性骨折予防の観点から，動脈硬化の基盤となる高血圧や高脂血症など生活習慣病の日常診療において，骨粗鬆症についても評価や治療の必要性がある。また逆に閉経後女性の骨粗鬆症有病者の日常診療において，脳・心血管疾患発症の基盤となる動脈硬化の存在にも留意すること