詳細な生活調査，栄養調査，運動機能調査，心理検査など広汎で学際的な，しかも精度の高い調査・検査を実施している．

調査開始当初より調査参加者のほぼ全員からの血液サンプルを用いて，DNA を自動抽出装置で抽出し蓄積している．これほど背景因子が詳細に検討されている一般住民の DNA 検体の蓄積は，国内外でも他にはないと思われる．現在，老化・老年病に関連する 172 の遺伝子多型について検討を行っており，様々な老化関連疾患への罹患，疾患や老化のマーカーなどとの関連について数多くの背景因子を考慮した検討を行っており[13, 14]，その成果が期待される．

おわりに

高齢化が急速に進む日本の社会において，高齢になってもできる限り元気に過ごしたいという国民の共通の願いを実現することは急務である．高齢者の健康を増進させ，疾病を予防し，医療費を低減させることが求められている．さらに今後は医学だけでなく，心理学や社会システムまでをも含む学際的な研究の展開も必要であろう．特に最近のゲノム科学の進歩を取り入れた分子疫学の分野は，老化の進行や疾患罹患のリスク予測と効果的な予防法の開発には欠かせない．分子生物学の手法を老化の疫学的研究の中に取り入れていくことで，今後の老化および老年病に関わる遺伝子多型の探索，環境因子，生活習慣との相互作用など，今後の老年医学における新たな展開が期待できよう．

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地域在住中高者年の骨代謝マーカーによる骨量減少/骨粗鬆症予測

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地域在住中高者年の骨代謝マーカーによる骨量減少/骨粗鬆症予測

竹村真里枝[1)]・松井康素[1)]・原田　敦[1)]・安藤富士子[2)]
下方浩史[2)]

はじめに

急速に高齢化が進む現在，骨粗鬆症による脆弱性骨折は，高齢者のQOL(quality of life)を著しく低下させるため，大きな社会問題の一つである[1)]。

骨密度(BMD)は加齢で減少し，低骨密度は骨折危険因子の一つであることはよく知られている[2,3)]。また，骨代謝マーカーは，骨粗鬆症や脆弱性骨折リスクの予測因子として期待される[4)]一方，日常臨床応用意義についてはまだ議論が多く，またわが国における長期縦断研究もまだ少ない。今回，我々は地域在住中高年者を対象にして，骨代謝マーカーが将来の骨粗鬆症の発症を予測できうるかについて検討した。

1　対象と方法

国立長寿医療センター研究所疫学研究部では，1997年11月からセンター周辺(愛知県大府市，知多郡東浦町)の地域住民から年齢，性別で層化して無作為抽出法で選出した，ベースライン調査時の年齢が40～79歳の男女計約2,400人を対象に，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)』を縦断的(2年ごと)に実施している[5)]。

本研究では第1次調査(1997年11月～2000年4月)と，6年後の第4次調査(2004年6月～2006年7月，本研究では2006年3月までに調査完了した者について解析した)に参加した者のうち，骨代謝に影響する疾患治療歴，薬剤使用のある者は除外して，第1次調査と第4次調査ともに骨密度測定を受け，第1次調査時に骨代謝マーカーを測定した，男女計1,182名を対象とした。

調査項目として，dual energy X-ray absorptiometry(DXA：Hologic QDR 4500)にて，第2～4腰椎および右大腿骨頸部の骨密度測定を行った。日本骨代謝学会の原発性骨粗鬆症の診断基準[6)]に従い，骨密度が若年成人平均値80%未満である場合を骨量減少/骨粗鬆症と判定した。さらにベースライン調査時の血清，尿にて，骨形成マーカーとしてオステオカルシン(OC：EIA法)，骨型アルカリフォスファターゼ(BAP：EIA法)，骨吸収マーカーとして尿中I型コラーゲン架橋N-テロペプチド(NTX：ELISA法)，デオキシピリジノリン(DPD：EIA法)を測定した。

統計学的検討として，まず地域在住中高年者の骨代謝マーカー値の性別，年代別分布を求

Biochemical Markers of Bone Turnover Predict Osteoporosis in Middle Aged and Elderly Japanese Dwelling at community

Marie Takemura：National Center for Geriatrics and Gerontology, et al.

Key words：Biochemical markers of bone turnover, Osteoporosis, Epidemiology

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表1　対象者特性

	女性	男性
対象者数(人)	546	626
年齢(歳)	55.8 ± 9.8	57.4 ± 9.8
身長(cm)	152.5 ± 5.6	165.5 ± 5.9
体重(kg)	53.2 ± 7.9	63.2 ± 8.4
BMI(kg/m^2)	22.9 ± 3.2	23.0 ± 2.6
OC(ng/mL)	8.9 ± 3.6	7.5 ± 2.6
BAP(U/L)	26.9 ± 10.2	25.3 ± 8.0
NTX(nmolBCE/nmol・Cr)	50.0 ± 27.9	36.1 ± 14.3
DPD(nmol/nmol・Cr)	6.3 ± 2.1	3.9 ± 1.1

(平均値±標準偏差)

めた。次にベースライン時に骨量減少/骨粗鬆症のなかった者を対象にして，骨代謝マーカー値が将来(6年後)の新規骨量減少/骨粗鬆症発生を予測できうるかについて検討した。骨代謝マーカー値を説明変数とし，ベースライン調査時の年齢，BMIを補正して，新規の骨量減少/骨粗鬆症発生についてロジスティック回帰分析を性別に行った。さらに女性では，ベースライン調査時の月経情報から未閉経群と閉経群に群分けして同分析を行った。解析には，統計プログラムSAS release 8.2を使用した。

2　結　　果

1)性別，年代別骨代謝マーカー平均値

今回，研究対象となったのは女性546人(平均年齢±SD:55.8±9.8歳)，男性626人(57.4±9.8歳)であった。表1にベースライン調査時の各骨代謝マーカーの平均値を性別に示す。また，図1に性別，年代別骨代謝マーカー平均値を示した。女性では，骨代謝マーカー値はいずれも加齢で上昇する傾向があったが，男性では年代間に有意な差は認められなかった。

2)骨代謝マーカーによる新規骨粗鬆症/骨量減少の発生予測

骨代謝マーカー値で骨粗鬆症あるいは骨量減少の新規発生を予測できるかを検討するために，ベースライン調査時に骨量減少/骨粗鬆症のなかった女性437人(平均年齢±SD;53.3±8.6歳)，男性561人(56.7±9.7歳)を対象にして，ロジスティック回帰分析を性別ごとに行った。

新規骨量減少/骨粗鬆症判定を腰椎骨密度で行った場合，表2に示すように，女性ではベースライン時のOC，BAP，NTX値が高い者ほど6年後の骨量減少/骨粗鬆症の新規発生リスクが有意に高かったが，男性では有意な結果は得られなかった。

また，新規骨量減少/骨粗鬆症を大腿骨頸部骨密度で判定した場合，女性ではベースライン調査時のBAP，NTX，DPDが高い者ほど発生リスクが有意に高かった。男性においては，BAPのみが有意であった。

次に女性を未閉経(187人)，閉経後(243人)の二群に分けて同解析を行った。骨量減少/骨粗鬆症を腰椎骨密度で判定する場合，未閉経群ではBAP，NTXが，閉経女性ではOC，NTXが有意であった。大腿骨頸部判定の場合には，未閉経群には有意な結果は認められなかったが，閉経群では測定したすべての骨代謝マーカーで，有意な結果が得られた(表3)。

3　考　　察

骨代謝マーカーは測定時の骨代謝状況を示すので，これを用いての骨量変化予測や，fast bone loserを予測することが期待されている。

骨代謝マーカーと骨密度の相関についての検討は，Christiansen[7]らの尿中カルシウム(Ca)，ヒドロキシプロリン(Hyp)，総アルカリホスファターゼ(ALP)と前腕骨骨密度変化と

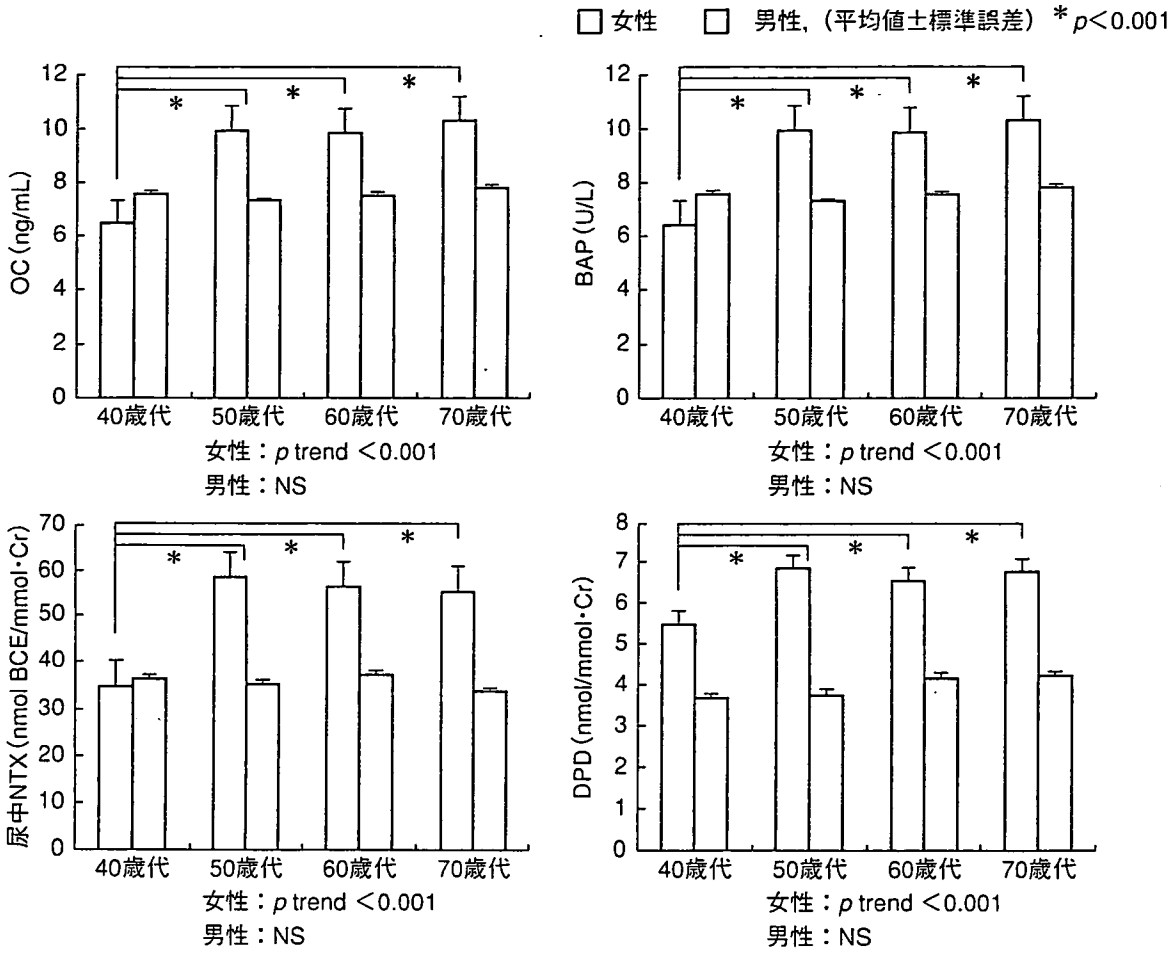

図1 骨代謝マーカー値分布(性別，年代別：一般線形モデルによる多重比較およびトレンド検定)

表2 骨代謝マーカー1SD上昇による骨粗鬆症/骨量減少有病発生のオッズ比

腰椎	女性	男性
	オッズ比(95%信頼区間)	オッズ比(95%信頼区間)
OC	1.32 (1.01～1.72) *	1.28 (0.88～1.86)
BAP	1.35 (1.03～1.76) *	1.37 (0.97～1.94)
NTX	1.56 (1.21～2.02) *	1.09 (0.74～1.62)
DPD	1.27 (0.99～1.63)	1.26 (0.88～1.78)

大腿骨頸部	女性	男性
	オッズ比(95%信頼区間)	オッズ比(95%信頼区間)
OC	1.18 (0.93～1.43)	1.22 (0.99～1.50)
BAP	1.413 (1.11～1.81) *	1.36 (1.10～1.66) *
NTX	1.387 (1.10～1.74) *	1.07 (0.87～1.32)
DPD	1.281 (1.03～1.60) *	1.12 (0.95～1.42)

*$p < 0.05$

表3　骨代謝マーカー1SD上昇による骨粗鬆症/骨量減少有病発生のオッズ比(女性閉経別)

腰　椎	未閉経	閉経後
	オッズ比(95%信頼区間)	オッズ比(95%信頼区間)
OC	1.05 (0.75～1.48)	1.63 (1.14～2.33)*
BAP	1.57 (1.07～2.30)*	1.34 (0.96～1.88)
NTX	1.62 (1.17～2.34)*	1.48 (1.05～2.07)*
DPD	1.17 (0.80～1.72)	1.31 (0.94～1.83)

大腿骨頸部	未閉経	閉経後
	オッズ比(95%信頼区間)	オッズ比(95%信頼区間)
OC	0.77 (0.48～1.24)	1.54 (1.15～2.10)*
BAP	0.88 (0.58～1.34)	1.73 (1.25～2.39)*
NTX	1.04 (0.71～1.52)	1.60 (1.18～2.16)*
DPD	1.07 (0.72～1.58)	1.43 (1.07～1.90)*

*$p < 0.05$

の関連についての研究で，重相関係数が0.52であったと報告したのに始まる。閉経後白人女性を対象としたGarneroら[8]は，4年間の前腕骨骨密度変化率とOC，BAP，Ⅰ型プロコラーゲン-C-プロペプチド(PICP)，Ⅰ型プロコラーゲン-N-プロペプチド(PINP)，尿中NTX，尿中Ⅰ型コラーゲン架橋Cテロペプチド(CTX)との四分位解析を行った研究で，BAPおよびPICP以外の各マーカーの各群間に有意差を認めたと報告した。Rogersら[9]は，49歳から62歳の閉経後女性60人を対象にNTX，総DPD，BAP，PICP，PINPと2～4年間の腰椎骨密度変化率との関連についての研究で，−0.35から−0.53の有意な相関を報告した。

またわが国では，茶木ら[10]は46歳から75歳の健常日本人女性を対象に，各種骨代謝マーカーと腰椎骨密度の検討を行った研究で，未閉経女性では有意な相関はなく，閉経女性においては尿中NTXと骨密度変化率に有意な負の相関を追跡開始時から3年間までは認めたが，4年以降はなかったと報告している。35歳以上の日本人女性を対象にした伊木ら[11]の研究では，骨代謝マーカーと2年間の腰椎骨密度変化との間に，未閉経女性では有意な相関はなかったが，閉経女性ではBAPと有意な負の相関があったと述べている。これまでの報告では，骨代謝マーカーによる骨密度変化予測は，比較的短期に限れば期待できる可能性があると考えられている。

今回我々は，骨代謝マーカーと6年間という比較的長期の将来の骨量減少/骨粗鬆症発生について両者の相関を求めた。骨量減少/骨粗鬆症判定を腰椎骨密度で行った場合，男性では有意な結果は得られなかったが，未閉経女性ではBAP，NTXが，閉経女性ではOC，NTXで有意な負の相関を認めた。大腿骨頸部判定の場合には，男性ではBAPが有意であった。閉経女性では測定したすべての骨代謝マーカーで有意な結果が得られたが，未閉経女性に有意な結果はえられなかった。骨代謝マーカーによる，10年後の新規骨粗鬆症発生の予知について検討した吉村ら[12]の報告では，骨粗鬆症を腰椎で診断した場合，男性は有意な結果は得られなかったが，女性ではPINP，β-CTXで有意な関連を示した。大腿骨頸部診断の場合，男性はOC，PICPが，女性ではDPDで有意な関連を示した。

骨粗鬆症の治療目標は「骨折の予防」である。低骨密度は骨折危険因子の一つであることはよ

く知られており，骨粗鬆症発生のハイリスク群を早期に選別して予防・治療介入していくことが，臨床上極めて重要と考える。今回の研究結果より，中～長期後の骨量減少/骨粗鬆症発症を骨代謝マーカーが予測する可能性が示唆された。

また，骨代謝マーカーは，値が高値であると骨密度の減少が大きく，骨折のリスクが上昇すると報告され，骨折予測因子としても期待されている[13,14]。今後，骨折発生をエンドポイントとした検討を進めていく必要がある。

まとめ

本研究では地域在住一般住民を対象に，骨代謝マーカーの分布について検討した。女性の骨代謝マーカーは，加齢に伴い高値になる傾向であった。また，骨代謝マーカー値が将来の骨量減少/骨粗鬆症を予測できうるか検討した。その結果，予測に反映される骨代謝マーカーは性別，部位別で異なっており，臨床応用には骨代謝マーカーの用途に沿った選択が必要と考えられた。

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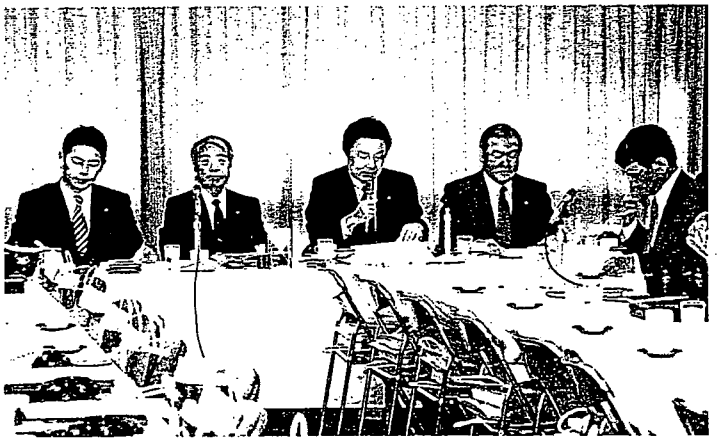


自民党厚生労働部会（記事6頁）

特報（社会保険庁改革）

「日本年金機構」で事業運営

特集（後期高齢者診療報酬）

「家庭医」への登録制導入等を検討

論壇

日本の福祉国家化と韓国の福祉国家化

田多 英範

時事評論

医療安全の新局面

大道 久

株式会社 法研

シリーズ

最前線 厚生労働科学研究㊲

国立長寿医療センター研究所疫学研究部部長　下方　浩史

<長寿科学総合研究の代表的な研究の紹介②>

“老化とその要因に関する長期縦断的疫学研究”の概要について

老化とその要因に関する長期縦断的疫学研究は、日本人の老化および老年病に関する詳細な縦断的基礎データを収集蓄積し日本人の老化像を明らかにするとともに、老化および老年病に関する危険因子を解明して、高齢者の心身の健康を守り、老年病を予防する方法を見いだすことを目的としている。

調査の対象者は長寿医療センター周辺の住民であり、地方自治体の協力を得て地域住民から年齢・性別に層化した無作為抽出を行っている。平成12年4月に2267名の基礎集団（観察開始時年齢が40歳～79歳）が完成し、以後は2年ごとに検査を繰り返し実施しており、現在は第5次調査を実施中である。追跡中のドロップアウトは同じ人数の新たな補充を行い、定常状態として約2400人のダイナミックコホートとしている。

調査は長寿医療センター内に設けられた検査センターで年間を通して1日7名ずつに実施している。朝9時から夕方4時までの間、分刻みでスケジュールを組み、頭部ＭＲＩ検査や心臓および頚動脈超音波断層検査等の医学検査のみならず、詳細な生活調査、写真撮影を併用した栄養調査、運動機能調査、心理検査などを含む数千項目以上にも及ぶ調査・検査を行っている。

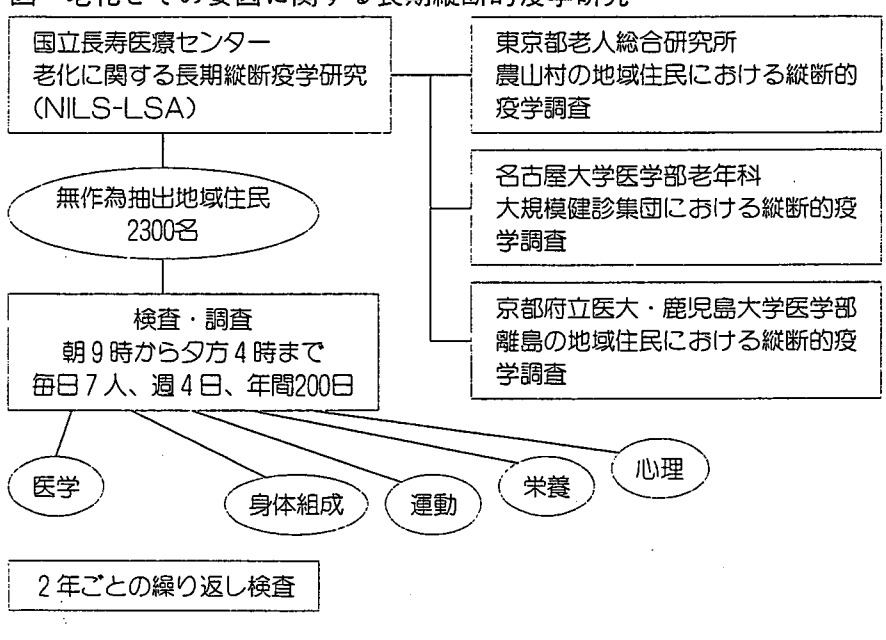
第1次調査から第4次調査までの結果をまとめインターネットにて英文で公開した（http://www.nils.go.jp/department/ep/index-j.html）。このように包括的かつ詳細な老化基礎データの公開は世界的にも他にほとんど例のないものである。

これらの蓄積されたデータを利用して、医学、栄養、心理、身体組成、運動の各分野での解析を行い、老化による変化、老年病に関連する因子等を検討している。研究成果として、歩行が特に高年期の抑うつ症状の低減に効果を持つこと、加齢による聴覚へ喫煙と騒音の相互作用があること、加齢により眼圧が下がること、コントラストを見分ける能力の加齢変化、中高年者のサプリメントの摂取率が50%以上あること等を明らかにしている。

これらを含め、NILS-LSAでは研究開始以来、500以上の論文、学会発表による成果発表を行っている。

本研究では、さらに分担研究者の協力を得て、都市と農村や離島、地域・文化による老化の進行の比較研究、集団の質による差の縦断的検討、重要ではあるが特殊な診断技術や方法論を必要とする神経学的検査所見の縦断的研究などNILS-LSAだけでは実施が困難な研究も行い、日本人の老化について総合的な研究を目指している。

図　老化とその要因に関する長期縦断的疫学研究



Association Between Change in Bone Mineral Density and Decline in Usual Walking Speed in Elderly Community-Dwelling Japanese Women During 2 Years of Follow-Up

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OBJECTIVES: To investigate the association between change in bone mineral density (BMD) and change in usual walking speed in elderly community-living Japanese women during 2 years of follow-up.

DESIGN: Longitudinal cohort study.

SETTING: Community-based.

PARTCIPANTS: A total of 182 women aged 70 to 84 who completed a baseline survey and a follow-up survey 2 years later.

MEASUREMENTS: An interview, anthropometric measurements, blood analysis, and physical performance tests were performed at baseline and at follow-up 2 years later. BMD was evaluated using dual-energy X-ray absorptiometry measured at the forearm. Annual percentage changes in BMD and usual walking speed during the 2-year follow-up period were calculated; annual percentage changes in BMD were summarized in quartiles. The association between annual bone loss rate and decline in usual walking speed was analyzed using multiple linear regression adjusted for changes in muscle strength, balance capability, and other potential confounders.

RESULTS: Change in BMD was significantly related to change in usual walking speed during the 2-year follow-up. After multivariate adjustment, usual walking speed declined significantly more in elderly women whose BMD decreased (−3.5% change in walking speed in the first quartile of percentage change in BMD and −3.1% in the second quartile) than in women whose BMD increased (+1.5% in fourth quartile).

CONCLUSION: Elderly women whose BMD decreased had a significantly greater decline in usual walking speed than women whose BMD increased, even after multivariate adjustment of potential confounders. J Am Geriatr Soc 55:240–244, 2007.

Key words: bone mineral density; decline in usual walking speed; Japanese community elderly women

The maintenance of physical performance in later life may improve quality of life for older adults.[1,2] To assess the physical performance of elderly community-dwelling people, muscle strength, balance capability, and walking speed are routinely measured.[3,4] Of these physical performance measures, walking speed has been reported to be an indicator of general morbidity and a good indicator of functional capacity.[3–5]

Alternatively, walking ability decreases with aging, and ambulatory difficulties are common in older people. Moreover, decrease in walking speed predisposes elderly people to deterioration in quality of life, aggravation of disability, and need for care.[6] The reasons for the decline in walking speed are multifactorial. In particular, muscle strength and balance capability have been found to be positively associated with walking speed.[6–8]

Several studies have shown that women with lower bone mineral density (BMD) have significantly lower muscle strength[9–11] and slower walking speed.[9,12] Improvement in grip strength during 10-year follow-up wass significantly associated with lower bone loss,[11] although the association between changes in BMD and walking speed with aging remains undefined, because most past reports were cross-sectional studies.

The aim of the present study was to investigate the association between change in BMD and change in usual walking speed adjusted for changes in muscle strength and balance capability in Japanese community-dwelling elderly women during a 2-year follow-up.

SUBJECTS AND METHODS

Data Source and Study Subjects

The data for this study were obtained from the mass health examinations for community-dwelling people ("Otasha-

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kenshin" in Japanese) aged 70 and older living in Itabashi-ku, Tokyo. "Otasha-kenshin," literally meaning "health examinations for successful aging," are comprehensive health examinations for community-dwelling older adults aimed at preventing geriatric syndromes including falls and fractures, incontinence, oral health and function, mild cognitive impairment, depression, and undernutrition. Details of the survey, such as the investigation methods and contents, have been described previously.[13,14]

The baseline survey for the present study was conducted in December 2002. Of 2,000 persons aged 70 to 84 randomly sampled from the resident registration records of Itabashi-ku in metropolitan Tokyo, 847 (456 men and 391 women) participated in the baseline survey. Of the 391 women, 205 (52.4%) also participated in the follow-up survey conducted in November 2004 and completed the interview, anthropometric measurements, blood analysis, and physical performance tests. Twenty-three people who participated in other intervention programs conducted at the Tokyo Metropolitan Institute of Gerontology for promoting independence were excluded. Thus the research subjects analyzed in this study consisted of 182 elderly women who participated in the baseline and follow-up surveys and had not participated in other intervention programs during the 2-year period. The ethics committee of the Tokyo Metropolitan Institute of Gerontology approved the study, and informed consent was obtained from all subjects.

Assessment of BMD

BMD was evaluated using dual-energy X-ray absorptiometry (DTX-200, Osteometer Medi-Tech, Hawthorne, CA) measured at the forearm. Specially trained personnel performed the measurements. The Osteometer DTX-200 can set region of interest automatically 24 mm proximal to the position where the radius and ulna are 8 mm apart. Baseline and follow-up examinations were conducted using densitometers of the same make and model. Annual percentage changes in BMD during the 2-year follow-up period were calculated using the following formula

$$100 \times (\text{BMD in 2004} - \text{BMD in 2002}) / (\text{BMD in 2002} \times \text{length of follow-up in years})$$

and summarized in quartiles of percentage change as follow: first (-12.57 to -4.18), second (-4.17 to -1.78), third (-1.77–0.72), and fourth (0.73–18.81).

Assessment of Physical Performance

Physical performance was assessed according to handgrip strength, functional reach, and walking speeds (usual and maximal). These assessments are routinely conducted as part of the Otasha-kenshin program, as described previously.[3,4]

Handgrip strength was measured using Smedley's Hand Dynamometer (Yagami, Tokyo, Japan). For functional reach, the subject stood sideways against a wall in a natural position and stretched both arms forward to the height of the shoulders. The positions of the fingertips were taken as the zero point. Then one arm was lowered. With the body tilted forward as far as possible, the subjects continued to stretch the arm parallel to the ground. The greatest distance of forward reach was measured. Three measurements were made, and the mean value was recorded.[15] To test walking speed, participants walked along a straight 11-m walkway on a flat floor. A stopwatch measured the time taken to walk 5 m, from the time when the foot touched the ground after the 3-m line to when the foot touched the ground after the 8-m mark. The participant first took the test by walking at usual speed and then by walking as fast as possible. Walking tests at usual and maximum speeds were repeated, and the faster speed was recorded in each walking test.

The change in physical performance was expressed as the change in value from 2002 to 2004 for each parameter. Annual percentage change in usual walking speed during the 2-year follow-up period was calculated by the formula

$$100 \times (\text{usual walking speed in 2004} - \text{usual walking speed in 2002}) / (\text{usual walking speed in 2002} \times \text{length of follow-up in years})$$

Assessment of Other Variables

An interview was conducted to assess the age, education level, subjective health status, regular exercise habits, chronic disease history, and higher-level functional capacity. Regular exercise per week was based on the following activities: walking outdoors, running, exercise, and sports. Chronic disease conditions were self-reported and included hypertension, stroke, heart attack, and diabetes mellitus. The higher-level functional capacity was measured using the Tokyo Metropolitan Institute of Gerontology Index of Competence.[16] This multidimensional 13-item index of competence comprises three subscales: instrumental activities of daily living, intellectual activity, and social roles. Blood samples were collected under a nonfasting state, in a sitting position. The analyses were performed centrally in one laboratory (Special Reference Laboratories, Inc., Tokyo, Japan). Serum albumin level was measured using a standard kit using the BCG method. Body mass index (BMI, kg/m^2) was calculated as weight (in kg) divided by the square of height (in m).

Statistical Analysis

All data were analyzed using SPSS software for Windows version 13.0 (SPSS Inc., Chicago, IL), and the level of significance was set at 5%. Population characteristics at baseline and at 2-year follow-up are expressed as frequency or mean ± standard deviation). Paired t tests were used to evaluate the changes in physical performance during the 2-year follow-up period. Simple correlation was used to test the association between changes in BMD and physical performance. Comparison of annual change in usual walking speed according to annual BMD change in quartile was conducted using analysis of covariance (ANCOVA). Trend analysis was conducted using linear regression and entering the quartiles of performance as ordinal variables.[9] The model was adjusted for age; subjective health status; regular exercise; BMI; serum albumin concentration; handgrip strength; functional reach; usual walking speed in 2002; and changes in BMI, serum albumin concentration, handgrip strength, and functional reach from 2002 to 2004.

Table 1. Characteristics of the Study Subjects (n = 182) in Baseline and Follow-Up Surveys

Characteristic	Value	*P*-value*
Age, mean ± SD	75.9 ± 3.6	
Education level ≥ high school, %	62.6	
Good subjective health status, %	80.2	
Regular exercise every day, %	42.3	
Chronic disease history, %		
Hypertension	50.5	
Stroke	5.5	
Heart attack	8.8	
Diabetes mellitus	4.9	
Higher-level functional capacity score, mean ± SD		
2002	12.2 ± 1.2	
2004	11.8 ± 1.4	<.001
Change 2004–2002	−0.48 ± 1.32	
Body mass index, kg/m², mean ± SD		
2002	22.8 ± 3.2	
2004	22.6 ± 3.2	.005
Change 2004–2002	−0.26 ± 1.23	
Bone mineral density, g/cm², mean ± SD		
2002	0.296 ± 0.068	
2004	0.286 ± 0.067	<.001
Change 2004–2002	−0.010 ± 0.023	
Serum albumin, g/dL, mean ± SD		
2002	4.25 ± 0.20	
2004	4.34 ± 0.20	<.001
Change 2004–2002	0.09 ± 0.16	
Handgrip strength, kg, mean ± SD		
2002	18.1 ± 4.4	
2004	17.4 ± 4.3	.001
Change 2004–2002	−0.74 ± 2.94	
Functional reach, cm, mean ± SD		
2002	32.0 ± 5.3	
2004	32.3 ± 5.3	.65
Change 2004–2002	0.16 ± 4.73	
Usual walking speed, m/sec, mean ± SD		
2002	1.15 ± 0.25	
2004	1.10 ± 0.26	.001
Change 2004–2002	−0.04 ± 0.18	
Maximal walking speed, m/sec, mean ± SD		
2002	1.61 ± 0.34	
2004	1.62 ± 0.39	.495
Change 2004–2002	0.01 ± 0.25	

* According to paired *t*-test.
SD = standard deviation.

Table 2. Correlations Between Changes in Bone Mineral Density (BMD) and Physical Performance During the 2-Year Follow-Up

	Change in BMD (g/cm2)	
Change in Physical Performance	Correlation Coefficient	*P*-value*
Handgrip strength, kg	−0.036	.63
Functional reach, cm	0.062	.41
Usual walking speed, m/sec	0.212	.004
Maximal walking speed, m/sec	0.129	.08

* According to Pearson correlation analysis.

RESULTS

Participants in the follow-up study were younger and had significantly better subjective health, higher scores in higher-level functional capacity, and higher scores in physical performance (functional reach, usual walking speed, and maximal walking speed) (data not shown) than nonparticipants.

The baseline characteristics and changes in BMD and physical performance during the 2-year follow-up period of the 182 study participants are shown in Table 1. The mean age in 2002 was 75.9 ± 3.6 (range 70–84). The frequency of good self-rated health was 80.2%, and the mean higher-level functional capacity score was 12.2 ± 1.2 out of a full score of 13. During the follow-up period, higher-level functional capacity ($P < .001$), BMI ($P = .005$), BMD ($P < .001$), handgrip strength ($P = .001$), and usual walking speed ($P = .001$) decreased significantly. Alternatively, serum albumin concentration increased significantly ($P < .001$). There were no significant changes in functional reach and maximal walking speed during the 2-year follow-up period.

Table 2 shows the correlation between the change in BMD and change in physical performance during the 2-year follow-up period. Change in BMD was significantly related only to change in usual walking speed (correlation coefficient = 0.212, $P = .004$). There was no significant relationship between changes in BMD, handgrip strength, functional reach, and maximal walking speed.

Figure 1 compares the change in usual walking speed according to the change in BMD presented in quartiles. Mean annual BMD change rate was −1.57 ± 4.12% (range −12.57–18.81), and mean annual usual walking speed change rate was −1.54 ± 8.58% (range −23.84–47.78). A significant association was observed between mean annual change in usual walking speed and annual BMD change presented in quartiles ($P = .03$, according to ANCOVA). Elderly women whose BMD decreased (−3.5% in the first quartile and −3.1% in the second quartile) over the 2-year follow-up showed significantly ($P = .01$) greater decline in usual walking speed than women whose BMD increased (1.5% in the fourth quartile). More-rapid annual bone loss was associated with greater decline in usual walking speed ($P = .005$, according to trend test). This result was adjusted for age; subjective health status; regular exercise; BMI; serum albumin concentration; handgrip strength; functional reach; usual walking speed in 2002; and changes in BMI, serum albumin concentration, handgrip strength, and functional reach from 2002 to 2004.

DISCUSSION

The present 2-year longitudinal follow-up study evaluated the association between changes in BMD and physical per-

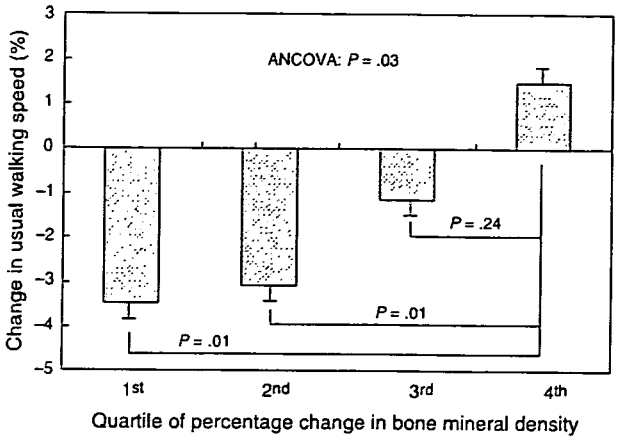

Figure 1. Associations between change in bone mineral density (expressed in quartiles) and change in usual walking speed during the 2-year follow-up. First quartile: −12.57 to −4.18; second quartile: −4.17 to −1.78; third quartile: −1.77–0.72; fourth quartile: 0.73–18.81. Annual percentage change = 100 × (data from 2004–data from 2002)/(data of 2002 × 2 (length of follow-up in years)). ANCOVA = analysis of covariance.

formance in a population-based random sample of 182 Japanese women aged 70 and older. It found that elderly women with more-rapid bone loss had a greater decline in usual walking speed.

To promote independence and to maintain quality of life in older people, the maintenance of physical performance, including muscle strength, balance capacity, and walking speed, is important.[1–4] Of these measures of physical performance, walking speed, especially usual walking speed, is the most sensitive predictor of functional dependence in older people.[3] Walking speed decreases with aging, is influenced by multiple factors, and should be modified through a lifestyle that strengthens muscles of the lower extremities.[4,17,18] For example, exercise and nutritional interventional interventions in relatively healthy community-dwelling elderly people have been shown to improve walking speed.[17,18]

BMD decreases with age, decreasing 1% per year after menopause in women,[19] although adequate dietary protein,[20] calcium and dairy,[21,22] and vitamin C intake;[23] weight maintenance;[21,23] higher BMI;[21] maintenance of daily physical activity;[21,22] supplementation;[24] and hormone replacement therapy[25] may contribute to healthy bones and prevent decline in bone mass.

Cross-sectional studies have reported that BMD in elderly people is significantly associated with physical performance.[9,10,12] Elderly women with lower BMD had significantly lower grip strength and knee extension power and poorer balance. These results suggest a strong role of maintaining muscular strength in the prevention of bone loss in healthy and functionally independent women. In the absence of neurological and degenerative disorders, poor physical performance in elderly people is likely to result from reduced physical activity, and a consequence of the reduced mechanical loading would be reduced bone mass and density.[9]

In the present study, elderly women with more-rapid bone loss during 2 years of follow-up had a greater risk of decline in usual walking speed than those with greater BMD. Because the directionality of the association between the change in mineral density and usual walking speed cannot be ascertained from this study design, the result does not imply that modification or improvement of BMD would have any effect upon walking speed. Intervention trials are needed to assess the effect of treatment of osteoporosis on walking speed and the effect of interventions targeting gait speed on bone density.

This study has some limitations. First, the characteristics of the subjects must be considered. Although the subjects analyzed were selected randomly from the population of an urban district, they were relatively healthy elderly persons who were able to travel from their homes to the health examination center at baseline and 2 years later. As a result, the present results may not be applicable to frail older people or those with multiple comorbidities who have low physical functional capacity. Second, BMD has been measured at virtually all available measurement sites (spine, proximal femur, forearm, whole body, calcaneus, and tibia) in other reports.[26] In the present study, only forearm BMD was used as indicator of bone loss. Therefore, the findings may not be directly comparable with those in other groups. To generalize this result, a more-comprehensive approach, including measuring bone mass at various sites in a large sample of elderly people and evaluating the associations between bone loss at different sites and changes in physical performance, is necessary. Forearm BMD measurement was chosen, because it is a quick, easy, and accurate method to evaluate the bone health of older people.[27] In addition, forearm BMD may be useful to assess osteoporosis in postmenopausal women because forearm BMD is significantly associated with BMD of the lumbar spine and hip.[28] Third, this study did not control for the type and dose of drugs that affect bone turnover, such as calcium, estrogens, vitamin D, and calcitonin, all of which may affect BMD. Finally, this study focused on the association between change in BMD and change in walking speed during the 2-year follow-up period and did not provide information on the cause-and-effect relationship. However, the relationship between the two parameters that were used in this study is expected to form a basis for further study. The number of elderly people with low bone mass and walking ability is going to increase in the future. Therefore, there will be an increasing need for strategies to strengthen these two parameters.

In conclusion, elderly women with more-rapid bone loss had greater decline in usual walking speed, even after multivariate adjustment including changes in muscle strength, balance capability, and other potential confounders. Further studies are needed to investigate the cause-and-effect relationship between BMD and walking speed.

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Author Contributions: All authors contributed to the design and conduct of the "Otasha-kenshin." Jinhee Kwon was involved in study conceptualization, analysis and collection of data, interpretation of data, and writing manuscript. Takao Suzuki was involved in study conceptualization, interpretation of data, manuscript preparation, critical revision of the manuscript for import intellectual content, and supervision. Hideyo Yoshida, Hunkyung Kim, Yuko Yoshida, Hajime Iwasa, Miho Sugiura, and Taketo Furuna were involved in collection of data, interpretation of data, and critical revision of the manuscript for import intellectual content.

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Age-specific change of prevalence of metabolic syndrome: Longitudinal observation of large Japanese cohort

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Abstract

To examine real age-related changes in the prevalence of metabolic syndrome, we studied longitudinal changes in the prevalence of metabolic syndrome in a single cohort of individuals. The participants included 112,960 Japanese (70,996 men, 14–94 years and 41,946 women, 17–85 years), who had received annual examinations between 1989 and 2004. Metabolic syndrome was defined according to the Japan Metabolic Syndrome Criteria Study Group and the US National Cholesterol Education Program (NCEP) guidelines. Overweight was defined as BMI $\geqq 25\,kg/m^2$. Longitudinal changes indicated a birth cohort effect in the prevalence rate of metabolic syndrome with a lower or higher prevalence in the younger birth cohort than in the older for females or males, respectively. The estimation of the age-specific prevalence of metabolic syndrome demonstrated that in males, the prevalence of metabolic syndrome increased up to 50 decades of life for the Japanese and 60 decades of life for the NCEP criteria. In females, the prevalence increased with age up to 80 years old for both criteria. The estimated secular trends suggested that the prevalence rate of metabolic syndrome decreased in females and increased in males during study periods.

Keywords: Metabolic syndrome; Aging; Secular trends; Longitudinal study

Metabolic syndrome has become one of the major public-health challenges worldwide [1,2]. The most important dimension of metabolic syndrome is its association with the risk of developing type 2 diabetes mellitus and atherosclerotic cardiovascular disease [3–9]. A number of metabolic syndrome definitions have been proposed, including the World Health Organization (WHO) Consultation for diabetes and its complications [10], the European Group for the Study of Insulin Resistance [11], the National Cholesterol Education Program (NCEP) Expert Panel [12], and, more recently, the International Diabetes Federation (IDF) [13] have formulated definitions for metabolic syndrome. In addition, the American Heart Association in conjunction with the National Heart, Lung, and Blood Institute have proposed a revised version of the NCEP-ATPIII definition [14]. In Japan, the National Metabolic Syndrome Criteria Study Group has proposed new criteria for metabolic syndrome in the Japanese [15].

Since several definitions of the syndrome are in use, it is difficult to compare the prevalence and impact between countries. However, a very consistent finding is that the prevalence of metabolic syndrome is highly age-dependent [16–18]. These previous findings were based on the cross-sectional observations, which may represent cohort, period, and/or survivorship effects rather than a true aging effect. Although longitudinal studies are required to examine real age-related changes in the prevalence of metabolic syndrome, to our knowledge, no studies have examined the longitudinal changes in the prevalence of metabolic syndrome in individuals over time.

We therefore studied longitudinal changes in the prevalence of metabolic syndrome in a single cohort of individuals to observe the effect of the natural aging process on the prevalence of metabolic syndrome as well as on obesity,

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hypertension, impaired glucose tolerance, and dyslipidemia as components of metabolic syndrome.

1. Methods

1.1. Study population

The study population consisted of office workers and their families residing in Aichi Prefecture in central Japan. The subjects included 112,960 Japanese (70,996 men and 41,946 women) with an average age of 44.6 years in men and 43.4 years in women, who had received annual examinations at a health examination center in Japan between 1989 and 2004 (Table 1). About 57% of the cohort (41,709 men and 23,001 women) had attended at least one follow-up examination. The average visits for the follow-up examinations were 3.4 times for men and 3.0 times for women.

1.2. Procedures and laboratory methods

The examinations included a questionnaire, physical examination, blood pressure measurement, an anthropometric measurement, and laboratory analysis of blood samples, all taken on the same day as described previously [19–21]. The anthropometric measurements included height and body weight. The body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Blood pressure was measured after the participants had been comfortably seated for at least 5 min.

All serum samples were obtained following a 12–14 h 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. No differences were seen in the sample collection, laboratory apparatus, or techniques used between 1989 and 2004.

1.3. Definition of metabolic syndrome

We applied both the Japanese criteria of metabolic syndrome [15] and the NCEP Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III; ATPIII) criteria [12]. According to the Japanese definition, someone has metabolic

Table 1
Characteristics of participants

	Males	Females
Number of subjects	70996	41946
Total number of measurements for 16 years	239879	122624
Number of subjects for whom measurements were taken at least twice	41709	23001
Number of measurements per subject for 16 years, mean (S.D.)	3.4 (3.4)	3.0 (2.9)
Average follow-up periods (years), mean (S.D.)	3.4 (4.3)	3.1 (4.1)
Initial measurements		
Age (years), mean (S.D.), age range (years)	44.6 (9.3), 14–94	43.4 (9.5), 17–85
Number of subjects in each age group, *n* (%)		
10–29 years	1914 (2.7)	2183 (5.2)
30–39 years	21173 (29.8)	1398 (31.5)
40–49 years	26583 (37.4)	15287 (36.4)
50–59 years	16783 (23.6)	9199 (21.9)
60–69 years	4152 (5.8)	1830 (4.4)
70–79 years	361 (0.5)	230 (0.6)
≥80 years	30 (0.04)	19 (0.05)
Hight (cm), mean (S.D.)	168.6 (6.0)	156.0 (5.5)
Body weight (kg), mean (S.D.)	65.7 (9.4)	52.4 (7.4)
BMI (kg/m^2), mean (S.D.)	23.1 (2.9)	21.6 (2.9)
Total cholesterol (mg/dl), mean (S.D.)	199.4 (35.0)	199.0 (36.5)
Triglyceride (mg/dl), mean (S.D.)	142.0 (103.5)	87.0 (49.7)
HDL-cholesterol (mg/dl), mean (S.D.)	55.2 (13.3)	67.8 (14.6)
Fasting plasma glucose levels (mg/dl), mean (S.D.)	98.5 (18.6)	91.4 (11.1)
Systolic blood pressure (mmHg), mean (S.D.)	121.2 (16.2)	113.7 (7.4)
Dyastolic blood pressure (mmHg), mean (S.D.)	73.0 (11.7)	66.5 (5.5)
Prevalence of obesity (%, BMI ≧ 25 kg/m^2)	24.1	11.5
Prevalence of hypertension (%, BP ≧ 130/85 mmHg or treated)	30.6	17.0
Prevalence of glucose intolerance (%, FSG ≧ 110 mg/dl or treated)	11.4	4.0
Prevalence of high triglyceride (%, ≧150 mg/dl)	32.2	8.0
Prevalence of low HDL (%, HDL male < 40, female < 50 mg/dl)	9.1	9.1
Prevalence of dyslipidaemia (%, TG ≧ 150 or HDL < 40 mg/dl)	35.1	8.5
Prevalence of metabolic syndrome		
Modified Japanese criteria, % (95% CI)	7.8 (7.6–8.0)	2.2 (2.0–2.3)
ATPIII-BMI25, % (95% CI)	11.6 (11.4–11.9)	4.0 (3.8–4.1)

BMI: body mass index, BP: blood pressure, FSG: fasting serum glucose, TG: triglyceride.

syndrome if he or she has central adiposity plus two or more of the following three factors [15]: (1) raised concentration of triglycerides, ≥150 mg/dl or reduced concentration of HDL-cholesterol, <40 mg/dl; (2) raised blood pressure: systolic blood pressure, ≥130 mmHg or diastolic blood pressure, ≥85 mmHg or treatment of previously diagnosed hypertension; and (3) raised fasting plasma glucose concentration, ≥110 mg/dl. The thresholds for waist circumference to define central adiposity: ≥85 cm for men and ≥90 cm for women. The ATPIII proposed the following five abnormalities to define metabolic syndrome [12]: (1) abdominal obesity (abdominal circumference >102 cm for men and >88 cm for women); (2) elevated serum triglyceride level (≥150 mg/dl); (3) decreased HDL-cholesterol level (<40 mg/dl for men and <50 mg/dl for women); (4) elevated blood pressure (systolic and diastolic blood pressure 130/85 mmHg); and (5) an elevated fasting glucose level (≥110 mg/dl). Individuals with three or more of the five abnormalities were considered to have metabolic syndrome. Because waist measurements were not available for the entire study sample, we substituted a BMI of 25 kg/m^2 or greater for all participants as an index of obesity for both criteria (the modified Japanese criteria and ATPIII-BMI25). A BMI of 25 kg/m^2 or greater has been proposed as a cutoff for the diagnosis of obesity in Asian people [22]. Individuals who were using antihypertensive or antidiabetic medications met the criteria for high blood pressure or high fasting glucose.

1.4. Data analysis

The data were analyzed with the Statistical Analysis System (SAS), release 8.2. We demonstrated that there is a birth cohort effect on the prevalence rate of metabolic syndrome based on a 16-year longitudinal analysis of the same cohort. Therefore, the pooled cross-sectional data at the initial examination of each subject from 1989 through 2004 were adjusted for the year of the examination using the logistic regression model, and estimated for the examination in 1997. The prevalence rate of metabolic syndrome for the modified Japanese and ATPIII-BMI25 definitions was estimated from an age younger than 40 years through age 70 years and older at 10-year intervals, and compared between these two definitions in each age group by paired *t*-test.

Longitudinal changes in the prevalence of metabolic syndrome were analyzed by a generalized-estimating-equation (GEE), which adjusts for repeated measurements in the same persons. For the longitudinal analyses, the subjects who did not receive follow-up examination were excluded. Age-related changes in the prevalence rate of metabolic syndrome, obesity, hypertension, impaired glucose tolerance and dyslipidemia were estimated by quadratic curve of age controlling for the observation year during which the subjects attended at least one follow-up examination. The GEE was also used to test for trends in the prevalence of metabolic syndrome during 1989–2004. The year of examination was used to test for temporal trends in prevalence. Age adjustment was performed by a least-squares regression approach. The model included age, square of age and year of examination as independent variables. A result was considered statistically significant if the *P* value was less than 0.05.

2. Results

Based on the pooled cross-sectional data of each subject at initial examination from 1989 through 2004, the mean prevalence rate of metabolic syndrome defined by the modified Japanese or ATPIII-BMI25 criteria was 7.8% in males and 2.2% in females, or 11.6% in males and 4.0% in females, respectively (Table 1). The prevalence of metabolic syndrome defined by two criteria was shown by age group and gender after adjusting for the examination year (Table 2). The prevalence rate of metabolic syndrome increased with age, with the highest rate in the 60–69 years group followed by a decline in the 70 years and older group in females with both criteria. In males, the highest prevalence rate was observed in the 50–59 years group or the 60–69 years group in the modified Japanese or ATPIII-BMI25 criteria, respectively. There was a significant difference between the two definitions in both genders and any age group with a higher prevalence rate in the ATPIII-BMI25 definition.

Longitudinal changes for 16 years in the prevalence rate of metabolic syndrome by birth cohort using the both criteria indicate the birth cohort effect in the prevalence rate of metabolic syndrome for females from the fifth decade of life, since at those ages, the prevalence rate of the younger

Table 2
The cross-sectional data of prevalence of metabolic syndrome at initial examination of each subject from 1989 through 2004

Age (years)	Females					Males				
	N	Modified Japanese		ATPIII-BMI25		*N*	Modified Japanese		ATPIII-BMI25	
		Mean (%)	95% CI	Mean (%)	95% CI		Mean (%)	95% CI	Mean (%)	95% CI
≤39	15381	0.5	(0.4, 0.6%)	1.1	(0.9, 1.3%)	23087	5.7	(5.4, 6.0%)	8.3	(7.9, 8.6%)
40–49	15287	1.9	(1.7, 2.1%)	3.5	(3.2, 3.7%)	26583	8.1	(7.7, 8.4%)	11.9	(11.5, 12.3%)
50–59	9199	4.0	(3.6, 4.5%)	7.4	(6.9, 8.0%)	16783	9.9	(9.4, ,10.3%)	15.0	(14.4, 15.5%)
60–69	1830	7.8	(6.6, 9.1%)	13.7	(12.1, 15.2%)	4152	9.6	(8.7, 10.5%)	15.2	(14.1, 16.3%)
≥70	249	7.2	(4.0, 10.5%)	12.1	(8.0, 16.1%)	391	7.4	(4.8, 10.0%)	13.6	(10.2, 17.0%)

Data were adjusted for year of initial examination, and estimated for the examination in 1997. Significant difference between two definitions in both genders and any age group with higher prevalence rate in ATPIII-BMI25 definition $P<0.0001$.

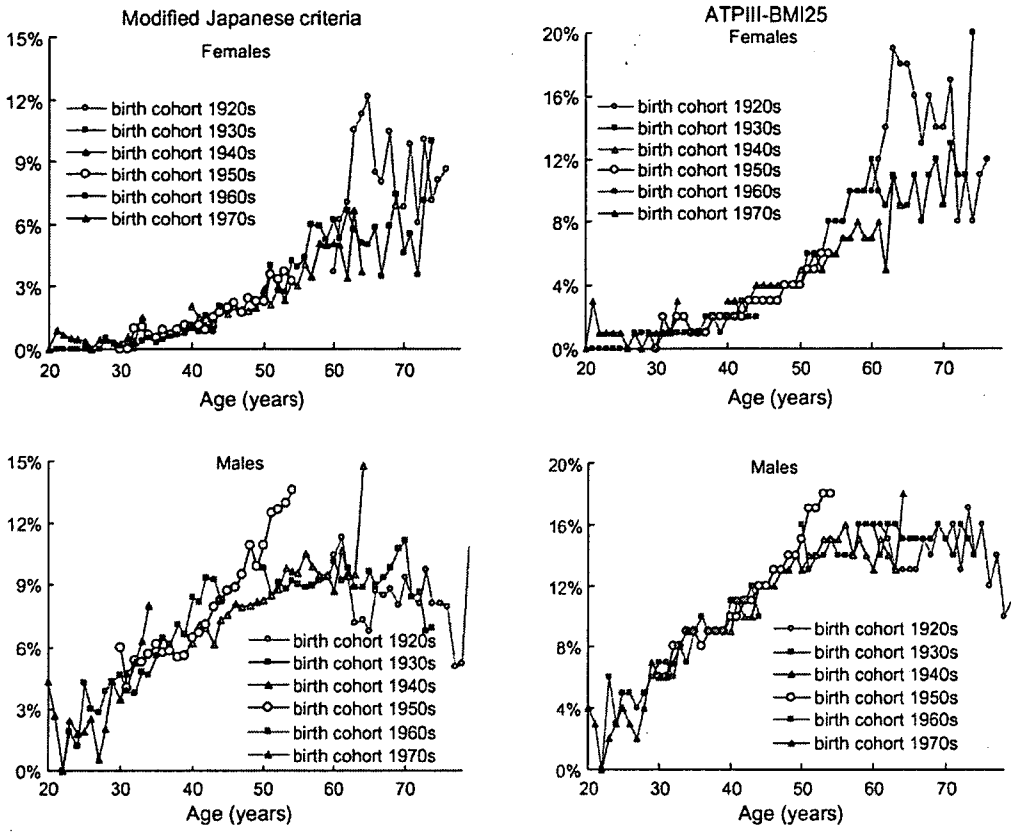

Fig. 1. Longitudinal changes for 16 years in the prevalence rate of metabolic syndrome by birth cohort in females and males using the modified Japanese and ATPIII-BMI25 criteria.

birth cohorts were lower than those of the older birth cohorts in both definitions (Fig. 1). There was a birth cohort effect in males at least between 40 and 55 years, indicating that the younger birth cohorts scored higher than the older birth cohorts in both criteria (Fig. 1).

Fig. 2 shows the prevalence rates of the individual components of metabolic syndrome in the modified Japanese criteria. There was no birth cohort effect on the prevalence rate of obesity in females, except for the cohort of the 1930s, which demonstrated a higher prevalence rate than that of the 1940s between age 50 and 64 years. However, the apparent birth cohort effect on the prevalence rate of obesity was detected in males with a higher prevalence in the younger cohort than the older one. Regarding the prevalence rate of hypertension, no apparent birth cohort effect was detected in either gender. There was no apparent birth cohort effect of the prevalence rate of impaired glucose tolerance in females, but there was an apparent effect in males with a higher prevalence rate in the younger cohort than that the older one. There seemed to be a birth cohort effect of the prevalence rate of dyslipidemia in both genders, with a lower prevalence rate in the younger cohort than the older one, at least for the birth cohort of the 1950s and older cohorts.

Fig. 3A shows the estimated prevalence rate of metabolic syndrome at individual ages according to the two different criteria after adjusting for the examination year (estimation at 1997). In male, the highest prevalence rate of metabolic syndrome was observed around 60 years for the ATPIII-BMI25 criteria and around 55 years for the modified Japanese criteria. In females, the highest rate was detected at the 70 years and older age group for both criteria.

Fig. 3B showed the estimated prevalence rate of each component of metabolic syndrome defined in the modified Japanese criteria at individual ages after adjusting for the examination year (estimation at 1997). The prevalence rates of obesity and dyslipidemia increased between 20 and 50 years, or 70 years in males, or females, respectively. The prevalence rate of hypertension increased in both genders from 20 years through the 80 years. Regarding impaired glucose tolerance, the prevalence rate increased up to the 60th or 70th decade and then declined in males or females, respectively.

Fig. 4A shows the secular change in the prevalence rate of metabolic syndrome defined by two different criteria from 1989 to 2004 from age younger than 40 years through age 70 years and older at 10-year intervals. In ATPIII-BMI25 criteria in females except for younger than 40 and 70 years and older age groups the prevalence rate of metabolic syndrome decreased (trends: 40–49 years, $P < 0.01$; 50–59 and 60–69 years, $P < 0.0001$). In males aged 40–49 and 50–59 years the

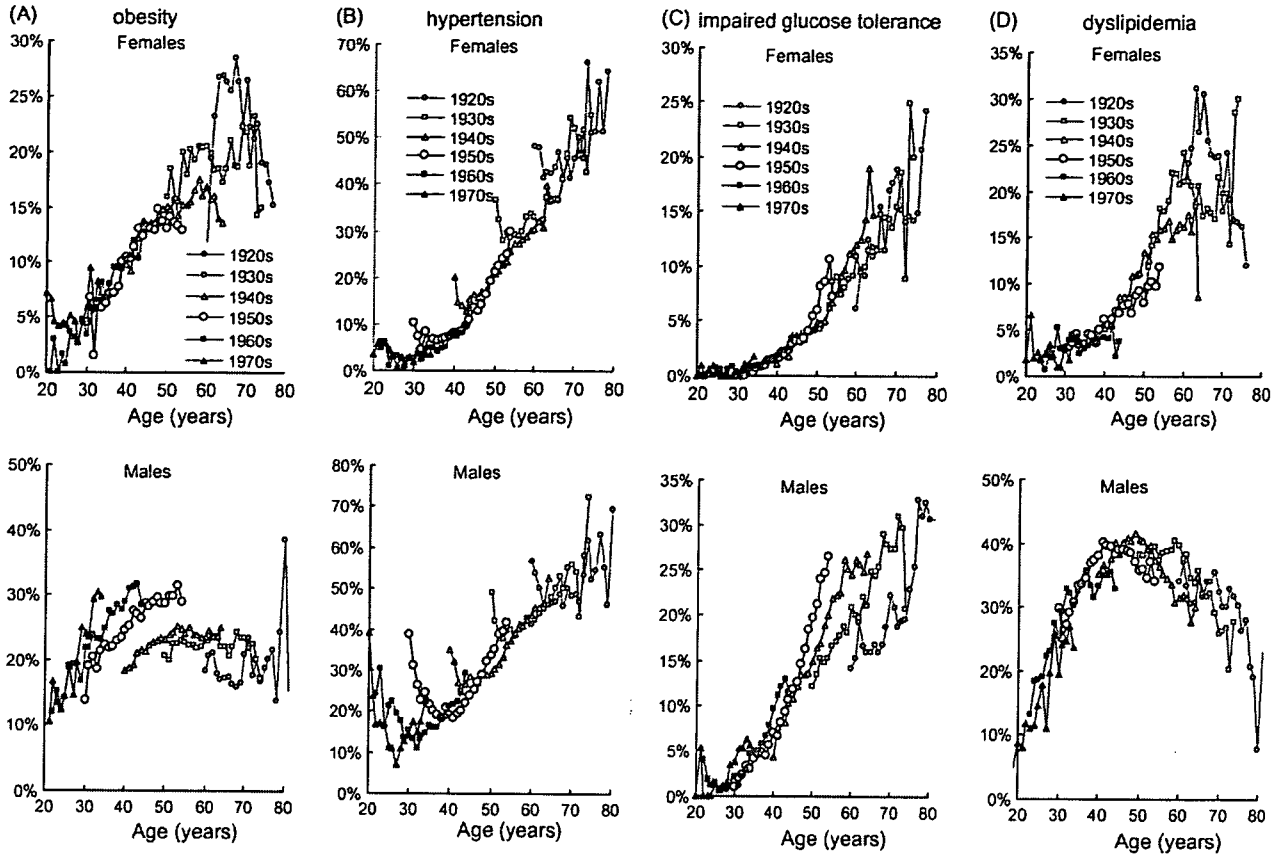

Fig. 2. Prevalence rates of individual component of metabolic syndrome in the modified Japanese criteria.

prevalence increased during study periods (trends, $P < 0.001$). According to the modified Japanese definition, the prevalence of metabolic syndrome decreased in females aged 50–59 and 60–69 years during study periods (trends, $P < 0.01$ and 0.001, respectively), and increased in males of youngest group, aged 40–49 and 50–59 years. Fig. 4B shows the trends in age-adjusted prevalence rate of metabolic syndrome defined by two criteria. The data were estimated age at 50 years. In both criteria the prevalence rate of metabolic syndrome decreased in females and increased in males, respectively.

3. Discussion

The cross-sectional observations suggested similar age-specific changes of the prevalence of metabolic syndrome with two different metabolic syndrome definitions. In addition, our results agree with the previous cross-sectional observations of age-specific prevalence of metabolic syndrome from other countries and ethnicities. The Third National Health and Nutrition Survey indicated that the prevalence of metabolic syndrome increased from 20–29 to 60–69 years [16]. A survey in Iran suggested that the prevalence increased with age, with the lowest prevalence at 20–29 years and the highest at 60–69 years in both genders [18]. A cross-sectional survey in China demonstrated that the prevalence of metabolic syndrome increased among men and women until age 65 years, when the prevalence decreased slightly among men and remained constant among women [17]. Although there are some differences in the peak age of the prevalence in males, it was surprising to find that there is a similarity of age-specific changes in the prevalence rate of metabolic syndrome among different ethnic groups and in different countries, which have different cultures, lifestyles, food habits, and longevity. This consistency may suggest that the aging effect highly regulates the prevalence of metabolic syndrome even if genetic and environmental influences may exist.

We clearly showed that the prevalence rate of metabolic syndrome was much higher in both genders as well as in all age groups with the ATPIII-BMI25 definition than with the modified Japanese definition. This is not surprising, since there are several noteworthy differences. The Japanese definition requires the presence of obesity [15]. In contrast, the NCEP definition makes obesity one of the five equally weighted criteria [12]. Furthermore, the thresholds for HDL-cholesterol levels under the modified Japanese definition are <40 mg/dl in both genders, but those under the NCEP definition are different between genders: men, <40 mg/dl; women, <50 mg/dl.

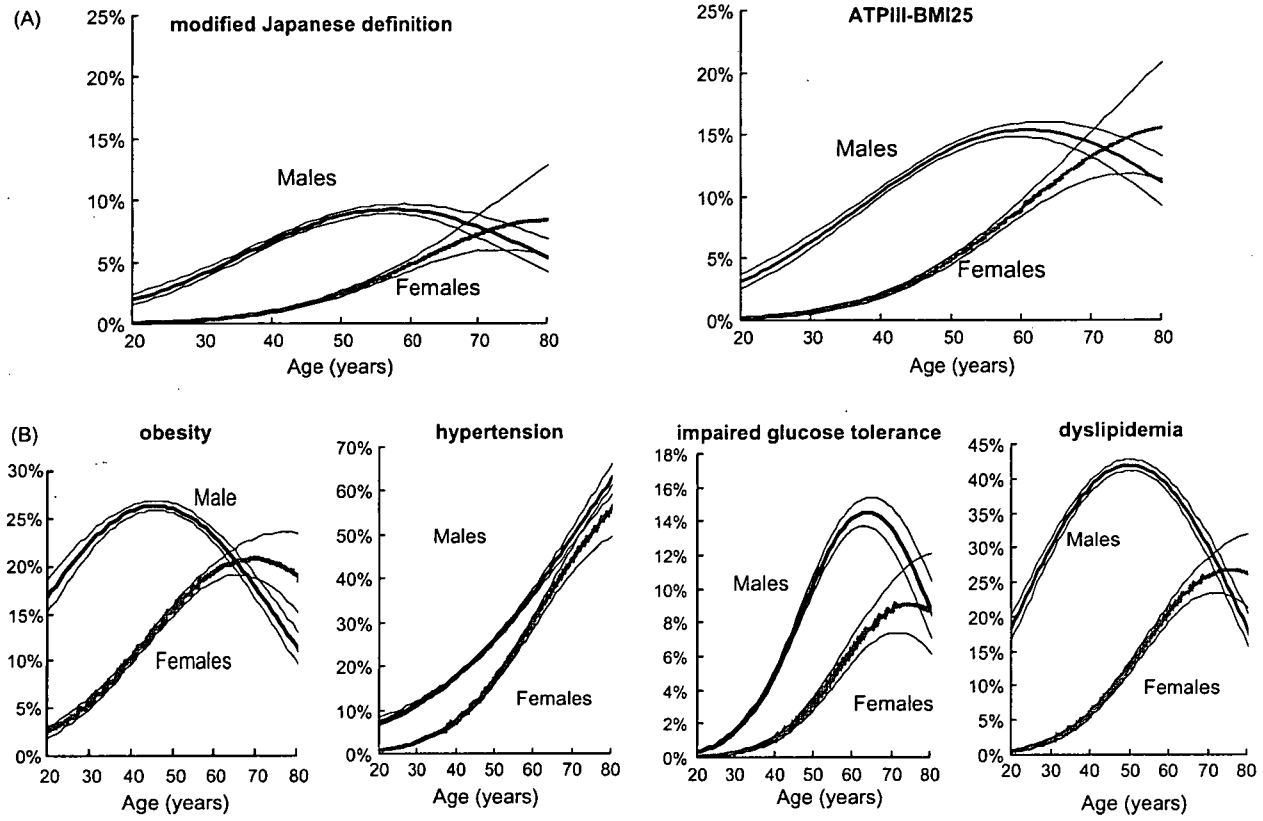

Fig. 3. (A) Estimated prevalence rate of metabolic syndrome at individual age according to the two different criteria after adjusting for examination year (estimation at 1997). (B) Estimated prevalence rate of each component of metabolic syndrome defined by the modified Japanese criteria at individual age after adjusting for examination year (estimation at 1997). Dotted curves indicate 95% CI.

Longitudinal observations demonstrated that there is a birth cohort effect on the prevalence rate of metabolic syndrome as well as the each of the components of metabolic syndrome in a large Japanese cohort. The estimated prevalence of metabolic syndrome increased from 20 up to 80 years in females both with the modified Japanese and ATPIII-BMI25 definitions. In males, the prevalence of metabolic syndrome gradually increased from 20 up to 50–59 years or up to 60–69 years followed by a decline at 70 years and older with the modified Japanese or ATPIII-BMI25 definition, respectively. It is obvious that the increasing trend of metabolic syndrome with age can be attributed to a similar age-related trend in each of the components of metabolic syndrome. The similar age-specific change of the prevalence rate was observed in obesity, impaired glucose tolerance, and dyslipidemia in males. The difference of the peak ages of the prevalence rate of metabolic syndrome in the ATPIII-BMI25 and modified Japanese criteria in males may be due to the requirement of obesity in the modified Japanese criteria, since the prevalence of obesity decreased after 50 years of age in males. In contrast to males, consistent age-specific changes of each component of the metabolic syndrome in females showed a consistent increase in the prevalence rate with age.

We showed the age-specific secular trends of the prevalence of metabolic syndrome in both genders from 1989 through 2004. In both definitions a similar trends of the prevalence of metabolic syndrome were demonstrated in both genders during study periods. The prevalence of metabolic syndrome decreased in females aged 50–69 years, and increased in males aged 40–59 years. Consistently the age-adjusted trends estimated at 50 years based on the longitudinal analysis decreased in females and increased in males in both criteria during study periods. Only a few reports regarding secular trends in the prevalence of metabolic syndrome are available. From two national surveys: the National Health and Nutrition Examination Survey (NHANES) III and NHANES 1999–2000, it has been demonstrated that the prevalence of metabolic syndrome increased significantly in females from 1988–1994 through 1999–2000 in US but increased much smaller without statistical significance in males [23]. The recent the Mexico City Diabetes Study, a population-based study, revealed that the prevalence of the metabolic syndrome has not increased in both genders between 1990–1992 and 1997–1999 [24]. These taken together with our findings suggest the secular trends of metabolic syndrome are dependent on each country or ethnicity which has differences in genetic background, social status, and diet. Two important determinants of the metabolic syndrome are obesity and physical activity. In our cohort the secular trends of the prevalence of obe-